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Common Electrolyte Problems in Pediatric Patients Presenting to the ED

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Electrolyte disorders are an important sequelae of many diseases that result in pediatric visits to general and pediatric emergency departments (EDs). Accurate identification of such abnormalities has the potential to impact treatment, outcome, and disposition of these patients.

Electrolyte panels are a common tool used to evaluate children who present to EDs. Although this test is relatively inexpensive on an individual basis, studies have shown that ordering serum electrolyte tests regularly can be costly.[1] It has been estimated that in excess of $1 billion per year could be saved in U.S. health care costs with small modifications to clinicians' patterns of ordering electrolytes.[1]

While sets of high-yield criteria for obtaining electrolytes have been identified in the adult and elderly ED populations, few studies have identified criteria for obtaining this test in children. One study found that the presence of any of the following criteria identified all children with clinically significant electrolyte abnormalities: age younger than 6 months, vomiting, delayed capillary refill, dry mucous membranes, tachycardia, or the presence of diabetes mellitus.[1] The patient population in this study was primarily well children with acute illness. Further analysis will be required to determine whether these or other predictors might aid overall electrolyte panel decision making.

Changes in volume and composition of body fluids due to disorders of fluid and electrolyte balance cause or result from various common clinical illnesses. Following introductory comments about body fluid volume and composition, an overview of some of the etiologies of the disorders of volume, tonicity, and composition of body fluids and the therapy to correct these disorders is provided. The focus is on abnormalities of cation concentration: sodium, potassium, calcium, and magnesium.

— The Editor

Sodium, Osmolality, and the Volume of Body Fluids

Total body water, which is 55-72% of body mass, varies with sex, age, and fat content, and is distributed between the intracellular and extracellular spaces.[2] The extracellular fluid (ECF), which comprises about one-third of total body water, includes the intravascular plasma fluid and the extravascular

interstitial fluid. Plasma ions include primarily sodium (Na+), chloride (Cl-), and bicarbonate (HCO_3-), which are excluded from intracellular environments, and lesser amounts of potassium (K+), magnesium, calcium, phosphates, sulfates, organic acids, and protein. Interstitial fluid, which surrounds the cells, has the same composition as plasma, but with less protein. The principal components of intracellular fluid (ICF) are potassium, proteins, magnesium, sulfates, and phosphates.

In the ECF, Na+ and Cl- constitute 90% or more of the effective solutes. Serum Na+ concentration defines the relative amount of sodium and water in plasma; the maintenance of a normal Na+ concentration, thus, contributes to regulation of the volume of body fluids.[2] The size of the ECF and ICF compartments depends on the amount of water within each; the distribution of water depends on their osmolality. It is important to recognize that osmolality and tonicity are not identical. Osmolality is a measure of the number of solute particles per unit volume. Measured osmolality of a solution includes all particles whether they are osmotically active or inactive. Sodium chloride or other impermeable solutes such as mannitol or glucose do not readily cross cell membranes to enter cells. They remain restricted to the ECF space and are thus "effective osmols" by obligating water to remain extracellularly. Cell membranes are freely permeable to solutes such as urea, methanol, or ethanol. While contributing to measured osmolality, these "ineffective osmols" do not obligate water to remain in the ECF space. Tonicity takes into account only osmotically active impermeable solutes and is the important physiological parameter.

In a given patient, the osmolality may be calculated as follows, using the values of 2.8 and 18 to convert values of blood urea nitrogen (BUN) and glucose, respectively, to mOsm/L:

Osmolality = 2[Na+ in mEq/L] + [BUN in mg/dL]/2.8 + [glucose in mg/dL]/18.

Normal serum osmolality is maintained by kidney function, which dilutes or concentrates urine. This is accomplished by a variety of mechanisms involving glomerular filtration; arterial pressure; blood flow; physical factors in the kidneys; the sympathetic nervous system; and hormones such as aldosterone, atrial natriuretic factor, vasopressin, and dopamine.[2] These systems converge to control water and electrolyte balance through glomerular ultrafiltration of the plasma followed by changes in the electrolyte content of this ultrafiltrate by tubular reabsorption and secretion. These mechanisms, together with thirst, control both plasma osmolality and plasma volume.

Hyponatremia

Hyponatremia is generally defined as a plasma sodium concentration of less than 130 mEq/L (130 mmol/L). When assessing the child with hyponatremia, it is important to determine whether the low serum sodium is true or fictitious. It also is important to determine the patient's volume status (i.e., euvolemia, hypovolemia, or hypervolemia). This allows the basic distinction between hyponatremia caused by sodium loss or hyponatremia caused by an increase in total body water (TBW), resulting in a relative dilution of the ECF compartment. The serum sodium concentration generally cannot be used to estimate the patient's total body fluid status. Figures 1 and 2 summarize the causes of hyponatremia.

The severity of signs and symptoms of hyponatremia is dependent on the rapidity of its development and the degree of decline in plasma osmolality.[3-5] As the plasma osmolality decreases, an osmotic gradient across the blood-brain barrier develops, which results in water movement into the brain. This cerebral overhydration is responsible for the majority of symptoms seen in hyponatremia. In general, neurologic manifestations do not occur until the serum sodium concentration is less than 125 mEq/L. However, patients with preexisting neuropathology may exhibit symptoms at higher serum sodium levels. Signs and symptoms may include headache, agitation, disorientation, lethargy, nausea, vomiting, muscular cramps, decreased deep tendon reflexes, seizures, coma, pseudobulbar

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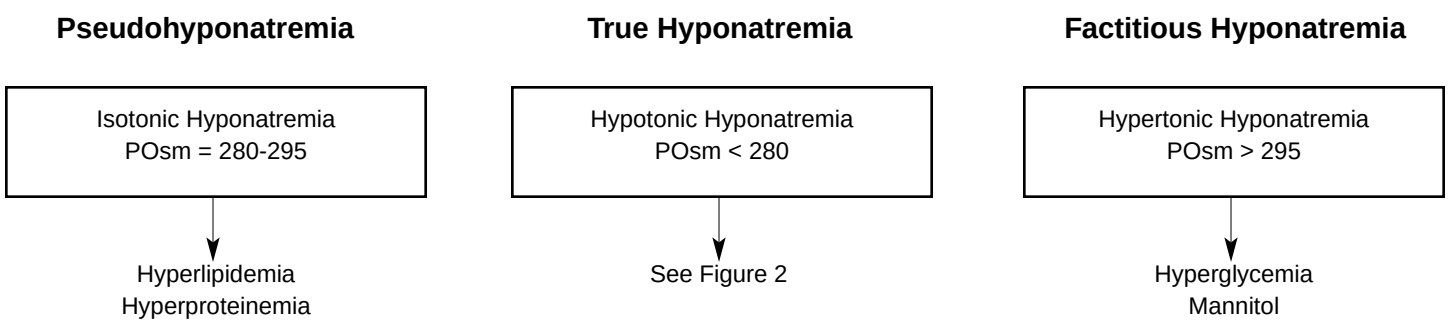
Figure 1. Classification of Hyponatremic States



palsies, and signs of cerebral herniation.[3,6] The rapid development of hyponatremia (< 24 hours) carries significant morbidity and mortality.[3,5-7]

Within 24 hours, the brain cells partially adapt to the overhydration or hypoosmolality by gradually losing intracellular osmotically active solutes. Along with these solutes, water leaves the brain cells and partially reverses the cerebral edema. Therefore, patients whose hyponatremia developed over several days or weeks are less symptomatic than patients whose hyponatremia developed acutely.[3] These concepts are important to remember when correcting hyponatremia.

Hyponatremia is a common cause of seizures in infants; it is the leading cause of afebrile seizures in this population.[8-13] It is frequently due to water intoxication.[10] Child abuse should be considered as part of the differential diagnosis of children who present with hyponatremic seizures.[9,13]

Hyponatremic seizures usually are generalized, with frequent progression to status epilepticus.[10] Respiratory failure requiring intubation is not uncommon, although most require mechanical ventilation for fewer than 24 hours. Decreased body temperature, another finding in acute symptomatic hyponatremia, occurs in 80-90% of hyponatremic patients.[10] Hyponatremic seizures are more difficult to treat than simple febrile seizures.[8] Correction of the underlying electrolyte disturbance is more effective than the use of anticonvulsants.[10] It is now well established that prompt and appropriate therapy with adequate amounts of sodium can lead to recovery in children with hyponatremic encephalopathy, even after respiratory arrest.[9,14]

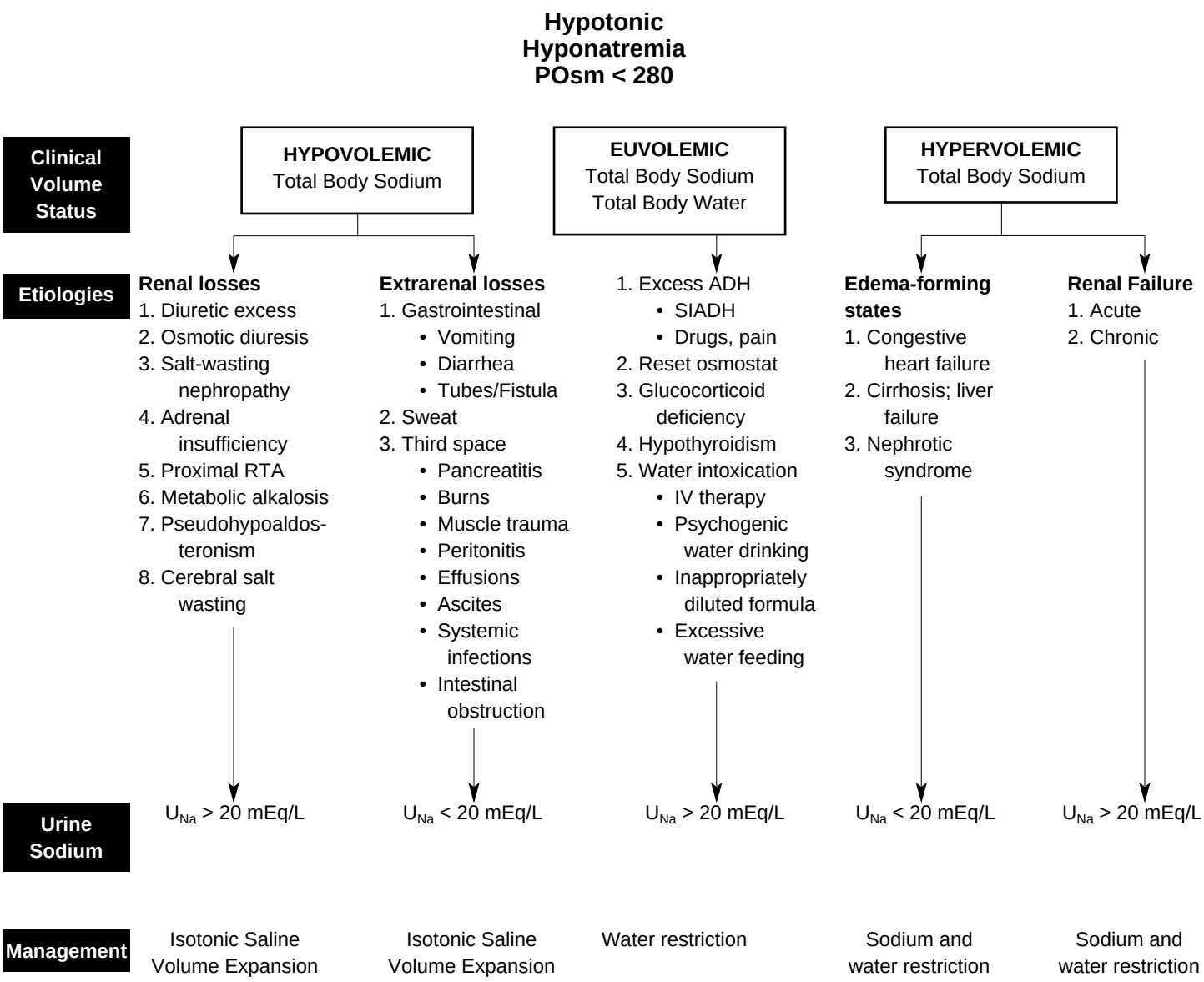
Hyponatremia occurs as a result of water retention, or sodium loss, or both; therefore, the ECF volume may be low, normal, or high. An analysis of the urine sodium concentration may be a diagnostic aid in determining the etiology of the hyponatremia.

Since serum sodium concentration is the main determinant of plasma osmolality, hyponatremia usually reflects hypoosmolality.[15,16] Initially, one must determine whether hyponatremia reflects true hypotonicity. There are two clinical circumstances in which hyponatremia may be present without hypotonicity. High levels of plasma lipids or proteins increase plasma volume, which decreases the percentage of plasma volume that is water. Because many clinical laboratories measure and report sodium concentrations in mEq/L of plasma (not in mEq/L of plasma water), the reported sodium concentration will be artificially low. Newer methods of sodium measurement that use ion selective electrodes measure serum sodium activity directly in plasma water and are not affected by the proportion of serum occupied by lipids and proteins. A clinical clue to such "pseudohyponatremia" is the presence of lipemic serum and a normal measured serum osmolality (because lipids or proteins have large molecular weights and, therefore, are minor components of overall plasma osmolality). In patients with nephrotic syndrome, a clinical rule of thumb is that an increase of triglycerides of 1 g/dL will decrease serum sodium concentrations by 2 mEq/L.[15]

The second situation in which a patient may be hyponatremic, but not hypotonic, occurs when an osmotically active solute (e.g., glucose or mannitol) has been added to the extracellular space. Water drawn out of cells by such an osmotically active particle will dilute the serum sodium concentration despite isotonicity or even hypertonicity. When hyperglycemia is present, a clinically useful method for bedside prediction of the serum sodium concentration once normoglycemia is achieved is that the serum sodium concentration is lowered by 1.6 mEq/L for each 100 mg/dL increase in glucose concentration.[16] The presence of an osmotically active nonglucose solute in the extracellular space is identified readily by comparing the calculated osmolality with measured osmolality. If they differ by more than 10 mOsm/L, it can be inferred that some other solute (mannitol or glycerol) may be present.[16] Such an osmolal gap might be the first clue to ingestion of a foreign substance such as methanol or ethanol.

Hyponatremia with Hypovolemia. Most instances of hyponatremia presenting in the ED are caused by volume depletion that is the result of an underlying disease; thus, appropriate fluid administration, as well as treatment of the underlying disease, usually is required to correct the hyponatremic state.[4] Extrarenal losses most commonly occur via the gastrointestinal tract (vomiting or diarrhea) but may be secondary to other disorders such as burns, pancreatitis, or peritonitis. The normal kidney responds to these hypovolemic states by conserving sodium and water; thus, a hypertonic urine with a sodium concentration of less than 20 mEq/L should be expected. In hyponatremic hypovolemic patients with urine sodium concentrations greater than 20 mEq/L, the possibility of adrenal insufficiency exists, particularly if the serum potassium concentration is elevated. The most common

Figure 2. Diagnosis and Treatment of True Hyponatremia



cause in the infant and young child is the salt-losing form of congenital adrenal hyperplasia. Other causes include congenital adrenal hypoplasia, acute infection, hemorrhage into the adrenal glands, inadequate replacement of adrenocorticosteroids, and inappropriate tapering of steroids.

Hyponatremia is a well-recognized complication of traumatic brain injury and subarachnoid hemorrhage and frequently is ascribed to the syndrome of inappropriate antidiuretic hormone secretion (SIADH) or to cerebral salt wasting (CSW). The latter, which first was described in 1950, is characterized by hyponatremia, diuresis, and natriuresis in the face of a contracted ECF, in contrast to SIADH, in which patients are euvolemic.[17-22] The distinction is important, as CSW is thought to be caused by excess secretion of natriuretic peptide and the treatment is saline replacement, whereas fluid restriction would be the treatment of SIADH.

The treatment of hyponatremia in the volume-depleted patient should be directed toward expansion of the ECF volume with salt-containing solutions. Replacement with salt-containing solutions will correct systemic and renal hemodynamics and allow the normal function of the osmoreceptor-antidiuretic hormone system to normalize plasma osmolality. Enough fluid should be given to provide maintenance requirements plus the volume of deficit. The adequacy of volume repletion must be evaluated from the findings on physical examination and laboratory data. Attention must be directed to the underlying disease and attempts made to control abnormal ongoing losses. When shock is present, isotonic saline can be given rapidly using 10-20 mL per kg intravenously over 10-20 minutes. This can be done repeatedly until systemic arterial blood pressure is restored and urine produced.

In addition to adequate water and salt, patients with adrenal insufficiency will require efforts to correct hypoglycemia and

hyperkalemia, and will need replacement of deficient adrenal corticosteroids.[23] If a patient presents with a salt-losing crisis, high doses of hydrocortisone (50-140 mg/m^2 per day in 3-4 divided doses) are required.[23]

Acute symptomatic hyponatremia is a medical emergency for which the use of hypertonic saline may be required.[24-27] Because of the dangers of congestive heart failure, osmotic demyelination syndrome, or cerebral hemorrhage, only enough hypertonic saline should be used to correct serum sodium to levels of 125 mEq/L. The amount of hypertonic saline needed can be calculated using the following formula:

mEq Na+ = (0.6) (body wt in kg) (125 – [Na+]),

where [Na+] = serum sodium concentration in mEq/L.

In the water intoxicated patient, spontaneous water diuresis occurs so rapidly that treatment with hypertonic saline is usually unneccessary.[14]

Neurologic complications as a result of overly rapid correction of hyponatremia have been reported in adults and older children.[3,5] The syndrome of osmotic demyelination, or central pontine myelinolysis, is the result of neuronal dehydration. Hyponatremia-induced losses of intracellular potassium and amino acids shift the cells to a hypotonic state, predisposing them to acute dehydration when exposed to a normotonic or hypertonic solution aimed at rapidly correcting hyponatremia. Caution is required when contemplating rapid correction of acute symptomatic hyponatremia.[3]

Euvolemic Hyponatremia. In patients with hyponatremia who have neither contraction of extracellular fluid volume nor expansion to the point of clinical edema, SIADH should be considered. Patients with SIADH have a concentrated urine in spite of the hyponatremia, and the urinary sodium concentration closely parallels the intake and is usually greater than 20 mEq/L.

There are several factors that affect antidiuretic hormone (ADH) secretion, the most important of which is plasma osmolality.[3] Hyponatremia from SIADH occurs due to water retention secondary to a persistently elevated ADH level inappropriate to any osmotic stimuli that normally affects ADH secretion.

SIADH is seen in a variety of clinical disorders that can be subdivided into four categories: increased hypothalamic production of antidiuretic hormone because of disease or the action of drugs; ectopic production of antidiuretic hormone; potentiation of antidiuretic hormone as an effect of drugs; and exogenous administration of antidiuretic hormone. The diagnosis ultimately rests on the demonstration of inappropriately high plasma concentration of arginine vasopressin when hyponatremia has appeared spontaneously or has been induced by an increase of water intake. In the absence of levels, the following criteria can be used: 1) hyponatremia with corresponding plasma hypo-osmolality; 2) inappropriately elevated urine osmolality relative to plasma osmolality; 3) normal renal function; 4) normal adrenal and thyroid functions (particularly ruling out glucocorticoid deficiency and hypothyroidism); 5) high urine sodium excretion in the presence of normovolemia; 6) absence of clinical signs of hypovolemia and dehydration; 7) absence of edema-forming states or evidence of volume depletion; and 8) correction of hyponatremia and natriuresis by fluid restriction.[15] SIADH commonly is seen with disorders that affect the central nervous system, in the presence of pulmonary diseases, and with use of certain drugs.

The management of SIADH can be considered under two headings: treatment of the hyponatremia and treatment of the disease process responsible for the syndrome. Since all the signs of uncomplicated SIADH result from excessive retention of water, they all respond to simple restriction of fluids.[3] Reduction of fluid intake to the point where urinary and insensible losses induce a negative water balance will lead to restoration of normal body fluid volume, a reduction in urinary sodium excretion, and an increase in serum sodium concentration. Ordinarily, a fluid intake of 50-75 percent of maintenance will accomplish this goal. Full restoration of serum sodium concentration requires that some sodium be made available. However, excessive amounts of sodium are promptly excreted in the urine. In some cases, the hyponatremia is so severe or has occurred so rapidly that signs of water intoxication (convulsions, coma) develop. In such instances, a rapid form of treatment is preferred. The recommended treatment is hypertonic saline and furosemide.[15, 27] This combination will cause a rise in serum sodium concentration and concurrent water diuresis. This treatment is reserved for emergency situations and should be followed by fluid restriction.

It must be stressed that in the presence of high vasopressin levels (appropriate or inappropriate) the imprudent administration of hypotonic fluids can culminate in severe cerebral edema.[7,17,27]

Hyponatremia with Hypervolemia (Dilutional Syndromes). Hypervolemic hyponatremia occurs when the net water retention exceeds that of sodium. Clinically, it may be seen with: 1) edema-forming states such as congestive heart failure, cirrhosis, and nephrosis; and 2) acute or chronic renal failure. Under normal conditions, an increase in sodium intake will result in sodium and water retention and an increase in intravascular volume. This increase in intravascular volume will in turn result in an increase in renal perfusion and in subsequent activation of the afferent and efferent mechanisms controlling renal sodium excretion. The net effect is an increase in renal sodium excretion in an attempt to return the intravascular volume to normal.[2] In the presence of disease states such as congestive heart failure, nephrotic syndrome, and cirrhosis, afferent and efferent mechanisms of sodium retention are activated.

These patients have an increase in total body sodium but even larger increases in total body water. Therapy should be directed at maximal improvement of the underlying disorder. Since total body sodium already is elevated, efforts to increase serum sodium through administration of saline will result only in further expansion of ECF volume and may worsen the clinical status of the patient. Attempting to decrease total body water by severe restriction of fluid is the most appropriate therapy. The excess sodium needs to be treated concomitantly by sodium restriction and judicious use of diuretics.

Hypernatremia

Hypernatremia, defined as a rise in the serum sodium concentration to a value exceeding 145 mmol/L, is a common electrolyte disorder.[28] Because sodium is a functionally impermeable solute, it contributes to tonicity and induces the movement of water across cell membranes.[28,29] Therefore, hypernatremia invariably denotes hypertonic hyperosmolality and always causes cellular dehydration, at least transiently. The resultant morbidity may be inconsequential, serious, or even life-threatening.

Hypernatremia represents a deficit of water in relation to the body's sodium stores, which can result from a net water loss or a hypertonic sodium gain. Net water loss accounts for the majority of cases of hypernatremia.[3,15,28] It can occur in the absence of a sodium deficit (pure water loss) or in its presence (hypotonic fluid loss). Hypertonic sodium gain usually results from clinical interventions or accidental sodium loading. Intentional salt poisoning also has been described as a form of child abuse.[30]

Because sustained hypernatremia can occur only when thirst or access to water is impaired, the groups at highest risk are patients with altered mental status, infants, and elderly patients. Hypernatremia in infants usually results from diarrhea.

Clinical signs and symptoms of hypernatremia with associated hypertonicity are directly related to cerebral cell dehydration resulting from water movement from the ICF to the ECF. Neurologic manifestations include varying degrees of depressed sensorium, ranging from lethargy to coma.[3,28] The majority of patients exhibit marked irritability, a high-pitched cry, and seizure activity. Muscle tone may be normal or increased, and may be accompanied by hyperreflexia or twitching. Examination of the cerebrospinal fluid may show an elevated protein without pleocytosis. Some patients may also have hyperglycemia, hypercalcemia or hypokalemia and/or metabolic acidosis.[3] With extreme hypertonicity and resultant water movement from brain cells into ECF, the entire brain can shrink away from the cranium and produce rupture of cerebral vessels. Consequently, focal intracerebral and subdural hemorrhages and venous thrombosis may occur.[15,28]

Since the central nervous system particularly is vulnerable to hypertonicity, the brain cells adapt within hours by increasing intracellular osmolality with resultant movement of water back into the brain cells. Myoinositol, taurine, glycerylphosphorylcholine, and betaine are the organic osmolytes (formerly called idiogenic osmoles) responsible for normalizing brain water content.[29] If hypertonicity develops rapidly, these intracellular osmoles or osmoprotective molecules may not be generated fast enough to prevent brain cell shrinkage. Therefore, the severity of clinical manifestations of hypernatremia and associated hypertonicity is relative to its degree and rate of development.

The mechanism of hypernatremia with normal volume status is excessive sodium intake. The majority of cases are iatrogenic, including the use of sodium bicarbonate or improperly diluted infant formula. Ultimately, even these disturbances will result in a deficit of water since water will be lost as the kidney attempts to excrete the salt load.

In clinical medicine, the most common cause of hypernatremia is primary water deficit in excess of sodium, resulting in hypernatremia with decreased volume status.[28,31] Water and sodium loss may occur via the extrarenal route or the renal route. Included in this category are patients with diabetes insipidus (DI). DI is characterized by complete or partial failure of ADH secretion (central DI) or renal response to ADH (nephrogenic DI), resulting in excretion of hypotonic urine.[31] Central DI may be idiopathic, but the majority of affected patients have a history of head trauma, central nervous system infections, or tumors. Nephrogenic DI may be congenital or acquired, and results in hypernatremia usually associated with decreased water intake.

Hypernatremic dehydration also is well described in breastfed newborns.[32] The serum sodium concentration in these cases may be elevated dramatically and frequently is associated with complications. These infants may present in the first week of life with fever, and the absence of overt signs of dehydration. Serum bilirubin concentrations also may be elevated. Within a few hours of rehydration, the fever subsides quickly, and the serum bilirubin concentrations fall rapidly. In general the infants make an uneventful recovery without permanent neurological sequelae. Such cases emphasize the importance of early and regular measurement of body weight in exclusively breastfed infants.

Hypervolemic hypernatremia results when sodium gain is greater than water intake. This may include administration of hypertonic saline or sodium bicarbonate. Hypernatremia with increased volume status also may be seen in patients with primary hyperaldosteronism or Cushing's syndrome because of sodium retention.

Whenever possible, therapy of hypernatremic patients should be directed at the underlying disease process (e.g., administration of vasopressin analogues in DI). In the presence of shock or severe ECF volume contraction, restoration of the intravascular volume takes precedence over normalization of plasma osmolality. In this setting, isotonic saline solutions are the recommended fluid replacement to restore circulating blood volume.

The speed of correction of hypernatremia depends on the rate of its development and the accompanying clinical presentation. Correction of hypernatremia should be accomplished slowly, except in the setting of acute massive salt poisoning. Rapid lowering of serum sodium may result in water movement from the ECF into the brain cells, resulting in cerebral edema and possible herniation. When serum sodium acutely exceeds 175 mEq/L (as in salt poisoning), dialysis may be performed to rapidly lower serum sodium. Once serum sodium concentration is at 170 mEq/L, further reduction should be carried out over 48 hours, with the aim to lower serum sodium at a rate no greater than 1 mEq/L/hour.[28]

A slower pace of correction is prudent in patients with hypernatremia of longer or unknown duration, because the full dissipation of accumulated brain solutes occurs over a period of several days. In such patients, reducing the serum sodium concentration at a maximal rate of 0.5 mEq/L/hr prevents cerebral edema and convulsions.[28]

Hyperkalemia

Table 1. Emergency Treatment of Hyperkalemia Onset/Duration

TECHNIQUE	AGENT	DOSE	ONSET/DURATION OF ACTION	COMMENT
Reversal of membrane effects	10% Calcium gluconate	0.5 mL/kg	Min/30-60 min	ECG monitor; discontinue if pulse rate < 100.
Movement of K into cells	Sodium bicarbonate, 7.5% (1 mEq = 1 mL)	2-3 mL/kg	30 min/1-4 hr	May use in the absence of acidosis.
	Glucose 50% plus insulin (regular)	1 unit for every 5-6 g glucose	Same	Monitor blood glucose.
	Albuterol 0.5% solution	0.01-0.05 mL/kg (max 1 mL) aerosolized with 1-2 ml saline	15-30 min	Monitor heart rate.
Enhanced excretion of K	Kayexalate	1 g/kg	Hours/variable	Can be given PO or by rectum. Give with sorbitol (70%).

Key:
IV = intravenous; ECG = electrocardiogram; K = potassium; PO = orally.

Potassium is the major intracellular cation; only a very small fraction of total body potassium is in the intravascular space.[33] Increased potassium concentration in serum is infrequent in pediatrics, but it can be life-threatening because of its effect on membrane potentials, particularly of heart muscle.

The serum potassium concentration is affected primarily by the kidney. Potassium is filtered by the glomerulus, then reabsorbed and secreted by the tubule. Processes that interfere with filtration or secretion (e.g., acute or chronic glomerulonephritis, interstitial nephritis) may cause hyperkalemia; processes that interfere with reabsorption may cause hypokalemia.[33,34]

The most common cause of an increased serum potassium is "pseudohyperkalemia" due to hemolysis or to tissue hypoxia distal to the placement of a tourniquet at the time the specimen was obtained. A repeat determination generally is sufficient to resolve whether hyperkalemia is present. True hyperkalemia in children most commonly is associated with acute or chronic renal failure. Certain drugs, used infrequently in pediatric practice, can produce hyperkalemia: spironolactone, amiloride, triamterene, cyclosporin, and angiotensin-converting enzyme inhibitors (e.g., captopril, enalopril).[33,34] Overuse of nonsteroidal anti-inflammatory agents may produce hyperkalemia, secondary to chronic renal injury.

Clinical signs of hyperkalemia generally are absent until the serum potassium is quite high, particularly when the accumulation of potassium has occurred gradually. At concentrations higher than 7 mEq/L (generally higher than 8.5 mEq/L), the patient may develop ascending muscle weakness to the point of flaccid paralysis. Cerebration and cranial nerve function are preserved. There generally are no clinical signs of altered cardiac function until concentrations are higher than 9 or 10 mEq/L, when the patient may develop ventricular fibrillation or asystole.

Changes in the wave form on electrocardiography provide clues to the degree of hyperkalemia.[35,36] The earliest changes are tall, peaked T waves, with a normal or shortened QT interval and shortened PR interval; these are present at serum potassium concentrations of 5.5 to 6.5 mEq/L. As the serum potassium concentration rises, cardiac conduction is impaired. The QRS complex begins to widen and the PR interval to lengthen at serum potassium concentrations of 6.5 to 7.5 mEq/L. With further increases in the serum potassium concentration, the P waves become broad and of low amplitude, the QT interval is prolonged, and the ST segment is either elevated or depressed (7.0 to 8.0 mEq/L). When the serum potassium concentration exceeds 8.0 mEq/L, P waves disappear; the QRS becomes markedly widened and may progress to a "sine wave" configuration, identifying the patient to be at risk of ventricular fibrillation or asystole.

Potential treatment (see Table 1) includes: 1) protecting the heart from the effects of hyperkalemia (e.g., calcium ion); 2) shifting potassium from the intravascular space to the intracellular space (e.g., sodium bicarbonate, insulin/glucose); and 3) eliminating potassium from the body (e.g., dialysis, ion exchange resins).

An intravenous infusion of calcium ion acts rapidly but its effects last only approximately 1 hour.[33,34] Sodium bicarbonate or insulin/glucose cause potassium to move intracellularly. Sodium bicarbonate has no significant action on plasma potassium in the first 60 minutes after administration.[37-39] Insulin binds to specific membrane receptors and via a second messenger, stimulates the sodium-potassium adenosine triphosphatase pump resulting in intracellular uptake of potassium.[37] This effect is independent of its hypoglycemic action. In children, a glucose load of 0.5g/kg/hr should be given. This is because many children will increase their endogenous insulin production with the administration of a glucose load. If blood glucose is elevated, insulin can be added starting at 0.05u/kg/hr.[37]

$ß_2$-agonists drive K+ into cells by increasing Na-K-ATPase activity. They are effective in reducing the serum potassium concentration rapidly and can be delivered by aerosol.[40] Studies have shown that albuterol in some patients can lower the K+ by up to 1.5 mEq/L within 30 minutes.[39,41]

Effects of calcium, insulin, bicarbonate, and $ß_2$-agonists are transient. Therefore, these measures usually are followed by a cation exchange resin, diuretics, or dialysis to remove

the excess K+ from the body. Sodium polystyrene sulfonate resin (Kayexalate) is given at a dose of 1 g/kg in 20% sorbitol orally or in a 70% sorbitol rectal installation. The latter must be retained for 20-30 minutes and can be repeated every 4-6 hours. In the gut, this resin takes up K+ and, to lesser degrees, Ca+2 and Mg+2, while it releases Na+. Each gram of resin may bind 1 mEq of K+ and release 1-2 mEq of Na+. The major side effects are nausea, constipation, hypokalemia, and retention of Na+ exchanged for K+. Loop and thiazide diuretics increase urinary K+ excretion by enhancing K+ secretion in the distal nephron but are not widely used because patients with impaired renal function are unlikely to respond. In acute or chronic renal failure, the above measures are used while preparations are made for dialysis. Hemodialysis is preferred to peritoneal dialysis because the rate of K+ removal is faster in stable patients with acute renal failure.

Hypokalemia

Hypokalemia is defined as a serum potassium level less than 3.5 mEq/L. As with hyperkalemia, nerves and muscles (including the heart) are most affected by hypokalemia, particularly if the patient has other, preexisting disease, such as cardiovascular disease.[33,41]

Both the total body stores of potassium and its distribution within the body are closely regulated by key hormones. The normal transcellular distribution of potassium (a high ratio of intracellular to extracellular potassium) is maintained by at least two hormonal signals that promote the entry of this cation into cells. Both insulin and β-adrenergic catecholamines increase cellular potassium uptake by stimulating cell-membrane Na+/K+ -ATPase.[42] For insulin, there is a feedback system in which hyperkalemia stimulates insulin secretion and hypokalemia inhibits it.[41] No feedback system has been identified for β-adrenergic stimulation, but β-blockade increases serum potassium and β-agonists decrease it, an effect that is independent of body stores of potassium. Synthesis of Na+/K+ ATPase is also stimulated by thyroid hormone, which may contribute to the hypokalemia that occurs in patients with hyperthyroidism.[41] Administration of alkali causes a shift of potassium into cells, but the response is quite variable. In general, serum K+ decreases by approximately 0.3 mEq/L for every 0.1 increase in pH above normal.[36] In patients with end-stage renal disease, administration of bicarbonate has only a slight effect on the transcellular distribution of potassium.[43]

It remains unclear whether aldosterone affects the transcellular distribution of potassium, but this hormone is clearly the major regulator of body stores of potassium through its effect on the excretion of potassium by the kidney.[44] As in the case of insulin, there is a feedback control; hyperkalemia stimulates the release of aldosterone (with synergy from angiotensin II), and hypokalemia inhibits it. Other hormonal and nonhormonal factors modulate renal potassium excretion, but they do not appear to have a role in normal potassium homeostasis.

The regulation of extracellular potassium concentration and body stores of potassium is asymmetric. Depletion of potassium and hypokalemia can occur simply through a reduction in potassium intake and can persist for long periods of time, despite normal hormone signaling and renal function.[41] Hyperkalemia, by contrast, elicits a brisk response and only is sustained when there is continued disruption or impairment of the normal regulatory systems.

Patients with hypokalemia often have no symptoms, particularly when the disorder is mild (serum potassium, 3.0-3.5 mEq/L). With more severe hypokalemia, nonspecific symptoms, such as generalized weakness, lassitude, and constipation, are more common. When serum potassium decreases to less than 2.5 mEq/L, muscle necrosis can occur, and at serum concentrations of less than 2.0 mEq/L, an ascending paralysis can develop, with eventual impairment of respiratory function.[41,45] The likelihood of symptoms appears to correlate with the rapidity of the decrease in serum potassium. In patients without underlying heart disease, abnormalities in cardiac conduction are extremely unusual, even when the serum potassium concentration is below 3.0 mEq/L. In patients with cardiac ischemia, heart failure, or left ventricular hypertrophy, however, even mild-to-moderate hypokalemia increases the likelihood of cardiac arrhythmias.[41] Hypokalemia increases the arrhythmogenic potential of digoxin. Thus, hypokalemia should be avoided or treated promptly in patients receiving digitalis derivatives.

Hypokalemia is rarely suspected on the basis of clinical presentation; the diagnosis is made by measurement of serum potassium. A low serum potassium concentration indicates disruption of normal homeostasis, with one very rare exception. In some patients with leukemia and markedly elevated white cell counts, potassium is taken up by the abnormal cells if the blood is left at room temperature for several hours.[46] More commonly, hypokalemia in patients with leukemia is the result of renal potassium wasting.

Hypokalemia is suggested by changes in the ECG, including:

- U waves;
- T wave flattening;
- ST segment changes;
- Arrhythmias (especially if the patient is taking digoxin); and
- Pulseless electrical activity (PEA) or asystole.

Hypokalemia almost always is the result of potassium depletion induced by abnormal losses of potassium. More rarely, hypokalemia occurs because of an abrupt shift of potassium from the extracellular compartment into cells. In either case, drugs prescribed by physicians are the most common causes of hypokalemia. Thus, the first step in the management of hypokalemia is to review the patient's drug record.

In the absence of an inciting drug, hypokalemia can result from an acute shift of potassium from the extracellular compartment to cells, from inadequate intake, or from abnormal losses. Most commonly, hypokalemia is the result of either abnormal loss through the kidney induced by metabolic alkalosis or loss in the stool induced by diarrhea. A brief description of the more common etiologies of hypokalemia follows.

β_2-Sympathomimetic Drugs. A wide range of drugs have β2-sympathomimetic activity, including decongestants and bronchodilators. A standard dose of nebulized albuterol reduces serum potassium by 0.2 to 0.4 mEq/L, and a second dose taken within one hour reduces it by almost 1 mEq/L.[41,47]

The hypokalemia caused by these drugs is sustained for up to four hours.

Diuretics. The most common cause of hypokalemia is diuretic therapy. Both the thiazide and loop diuretics block chloride-associated sodium reabsorption (with each inhibiting a different membrane-transport protein) and, as a result, increase delivery of sodium to the collecting tubules, where its reabsorption creates a favorable electrochemical gradient for potassium secretion.[41] The degree of hypokalemia is directly related to the dose of the thiazide diuretic. The combined use of furosemide or bumetanide with metolazone invariably causes moderate-to-severe hypokalemia, despite potassium supplementation. Diuretic-induced hypokalemia is usually but not always associated with a mild-to-moderate metabolic alkalosis (serum bicarbonate concentration, 28-36 mmol per liter). The diuretic drug acetazolamide, however, promotes potassium excretion by impeding hydrogen-linked sodium reabsorption and thus causes a metabolic acidosis along with hypokalemia.

Losses in Stool. The concentration of potassium in stool is 80-90 mEq/L, but because of the low volume of water in normal stool, only about 10 mmol usually is lost each day. In diarrheal states, the potassium concentration in stool decreases, but large quantities of potassium can nonetheless be lost as the volume of stool increases. Anything that increases stool volume, from infectious diarrhea to chemotherapy, can result in clinically significant potassium depletion and hypokalemia.[39,41]

Loss Through the Kidney. Large amounts of potassium are lost through the kidney in patients with a variety of disorders. For ease of diagnosis, these disorders are categorized according to acid-base status.

Metabolic Alkalosis. Hypokalemia is an almost invariable consequence of metabolic alkalosis. In the most common form of this disorder, induced by selective chloride depletion due to vomiting or nasogastric drainage, hypokalemia develops during the induction of alkalosis as a result of increased renal potassium loss. In the chloride-sensitive form of metabolic alkalosis, the administration of chloride corrects the alkalosis and allows the repletion of body stores of potassium if potassium intake is adequate.

More rarely, metabolic alkalosis occurs independently of chloride depletion as a result of systemic or intrarenal abnormalities that augment sodium reabsorption in the distal nephron. The most common of these abnormalities is primary hyperaldosteronism, a disorder often heralded by severe hypokalemia (serum potassium, < 3.0 mEq/L). Hypokalemia also may develop in patients with Cushing's syndrome, but it usually is milder than in patients with hyperaldosteronism.[41]

Genetic abnormalities that influence the activity of renal ion transporters are rare causes of metabolic alkalosis and hypokalemia.[41,48] Two of these disorders (Liddle's syndrome and 11β-hydroxysteroid dehydrogenase deficiency) stimulate reabsorption of sodium by collecting duct cells and cause the syndrome of apparent mineralocorticoid excess, so named because this transport abnormality results in hypertension and hypokalemia, but serum aldosterone concentrations are low rather than high. In two other disorders, genetic mutations inactivate or impede the activity of chloride-associated sodium transporters in the loop of Henle (Bartter's syndrome) and early distal tubule (Gitelman's syndrome), causing metabolic alkalosis and hypokalemia without hypertension.[48]

Metabolic Acidosis. Hypokalemia is a cardinal feature of type I or classic distal renal tubular acidosis. The degree of hypokalemia in this disorder is not directly correlated to the degree of acidosis but more likely reflects dietary sodium and potassium intake and serum aldosterone concentrations. Life-threatening hypokalemia (serum potassium, < 2.0 mEq/L) may occur in patients with untreated distal renal tubular acidosis.

Other Disorders

Magnesium depletion, induced either by dietary restriction or by abnormal loss, reduces the intracellular potassium concentration and causes renal potassium wasting.[49] Magnesium depletion often coexists with potassium depletion as a result of drugs (e.g., diuretics and amphotericin B) or disease processes (e.g., hyperaldosteronism and diarrhea) that cause loss of both ions, making it difficult to assess whether the hypokalemia is caused by the hypomagnesemia or is an independent effect. Regardless of the cause, the ability to correct potassium deficiency is impaired when magnesium deficiency is present.

Severe and often refractory hypokalemia due to renal potassium wasting occurs in patients with acute myelogenous, monomyeloblastic, or lymphoblastic leukemia.[41]

In uncontrolled diabetes mellitus, renal glucose loss causes osmotic diuresis, increasing sodium delivery to the distal nephron and promoting potassium excretion. With prolonged glycosuria, there is considerable depletion of body stores of potassium, but hypokalemia usually is mild or absent because both hypertonicity and insulin deficiency impede the entry of potassium into cells. The underlying potassium deficiency is rapidly unmasked when insulin is given, and severe hypokalemia can develop, particularly in patients with diabetic ketoacidosis, unless aggressive replacement of potassium stores is undertaken at the same time.

Severe hypokalemia (serum potassium, < 3.0 mEq/L) can occur, although rarely, in association with hyperthyroidism, which results in a clinical syndrome characterized by the sudden onset of severe muscle weakness and paralysis.[41] The symptoms respond rapidly to the administration of potassium.

Familial hypokalemic periodic paralysis is a rare autosomal dominant disease that has been associated with mutations of the gene encoding the dihydropyridine receptor, a voltage-gated calcium channel.[50] The disorder is characterized by sudden attacks of muscle paralysis associated with a decrease in serum potassium to low concentrations, often less than 2.5 mmol/L. Attacks can be provoked by high intake of carbohydrates or sodium or by exertion and usually subside spontaneously in fewer than 24 hours. Although the hypokalemia is caused by a shift of potassium into cells, the administration of potassium can be life-saving and should be given to treat acute attacks. Various approaches have been used to prevent recurrences with varying degrees of success, including the administration of spironolactone, triamterene, and acetazolamide.[51]

Principles of Potassium Replacement

Potassium replacement is the cornerstone of therapy for hypokalemia. Unfortunately, supplemental potassium administration is also the most common cause of severe hyperkalemia in patients who are hospitalized, and this risk must be kept in mind when one is initiating treatment. The risk is greatest with the administration of intravenous potassium, which should be avoided if possible.

The treatment of hypokalemia includes minimizing further potassium loss and giving potassium replacement. IV administration of potassium is indicated when arrhythmias are present or hypokalemia is severe (K+ < 2.5 mEq/L).

Acute potassium administration may be empirical in emergent conditions. When indicated, maximum IV K+ replacement should be 0.3–1.0 mEq/kg/hr (max 40 mEq/hr) with continuous ECG monitoring during infusion. Central or peripheral IV sites may be used. A more concentrated solution of potassium may be infused if a central line is used, but the catheter tip should not extend into the right atrium.

If cardiac arrest from hypokalemia is imminent (i.e., malignant ventricular arrhythmias), more rapid replacement of potassium is required.[36] In the patient's chart, document that rapid infusion is intentional in response to life-threatening hypokalemia. Once the patient is stabilized, reduce the infusion to continue potassium replacement more gradually.

Calcium

Calcium is an essential ion for function of all cells in the body. It is the primary regulator of motion and regulates excitation-contraction coupling, neurotransmission, hormonal secretion, mitosis, ciliary motion, phagocytosis, and many other processes. These are all vital cell functions which are essential for cellular health.[52]

In the serum, it consists of three fractions: 1) ionized or free calcium, accounting for 50% of total calcium; 2) protein-bound calcium which is not filterable by the kidney, accounting for approximately 40%; and 3) calcium complexed to anions such as bicarbonate, citrate, sulfate, phosphate, and lactate, accounting for the remaining 10%. Ionized calcium is the physiologically active portion. Aside from serum protein concentration (principally albumin), pH also influences protein binding of calcium and, thus, the ionized calcium level. When clinically available, the ionized calcium level should be followed.

Abnormalities in serum calcium concentration has profound effects on neurological, gastrointestinal, and renal function. Maintenance of the normal serum calcium is a result of tightly regulated ion transport by the kidney, intestinal tract, and bone, mediated by calcemic hormones, especially parathyroid hormone (PTH) and 1,25-dihydroxyvitamin D[1,25(OH)2 D].[52,53] Abnormalities in calcium transport that result in uncompensated influx into, or efflux from, the extracellular fluid, will result in hypercalcemia or hypocalcemia, respectively.

Hypocalcemia

Hypocalcemia generally is defined as an ionized calcium level less than 4 mg/dL (1 mmol/L). Hypocalcemia occurs when there is a net efflux of calcium from the ECF; calcium is lost from the ECF, often through renal mechanisms, in greater quantities than can be replaced by intestinal transport or bone. Falsely low levels of calcium due to hypoalbuminemia should be excluded by measuring ionized calcium.

In many cases, hypocalcemia is a result of an inability to mobilize calcium from the skeletal system. This is secondary to decreased secretion of PTH (hypoparathyroidism, hypomagnesemia), impaired synthesis of 1,25(OH)2 D (renal failure, vitamin D-dependent rickets), or inadequate responsiveness of target organs to PTH (pseudohypoparathyroidism, vitamin D deficiency, osteomalacia, renal failure, hypomagnesemia).[53]

Hypocalcemia, both total and ionized, is common in critically ill children.[54-57] The cause of hypocalcemia is uncertain and likely to be multifactorial. In some critically ill children with ionized hypocalcemia, the PTH concentrations are raised whereas in others it is not.[54] This suggests the etiology of hypocalcemia is twofold: in some children, a failure to increase PTH concentrations is responsible, and in others, a failure of PTH to elevate calcium levels is the culprit. Low magnesium concentrations may prevent PTH secretion and interfere with its peripheral action leading to hypocalcemia.[52] Hypocalcemia may also occur during administration of citrate-buffered blood products or plasma expanders due to free calcium binding with citrate and protein, respectively. Trauma, especially with crush injuries to major muscle groups causing rhabdomyolysis, releases cellular phosphorous which complexes with calcium and lowers serum calcium. Pancreatitis leads to the release of pancreatic lipase, degradation of retroperitoneal omental fat, and binding of calcium in the peritoneum – and this loss of extracellular calcium results in hypocalcemia.

The manifestations of hypocalcemia may be ascribed to increased neuromuscular excitability including numbness and tingling of lips, hands, and toes, carpopedal spasms, irritability, laryngeal stridor, apnea, and generalized tonic clonic seizures. Trousseau's sign (contractions of the hand muscles induced by decreased blood flow to the extremity), and Chvostek's sign (spasm of the facial muscles evoked by tapping the facial nerve anterior to the ear) may be present. Decreases in cardiac contractility and systemic vascular resistance result in hypotension. Cardiac manifestations also may consist of a prolonged QT interval which may progress to ventricular fibrillation or heart block.

Severe, symptomatic hypocalcemia should be treated immediately.[36] Calcium may be given intravenously as 10% calcium chloride (10-20 mg/kg/dose) or 10% calcium gluconate (50-100 mg/kg/dose) by slow infusion. The slow intravenous administration of calcium supplementation (10-15 minutes) and continuous ECG recording are critical to monitor for bradycardia or ventricular irritability. Intravenous access must be secure, as calcium infiltration can result in phlebitis and tissue necrosis. Except in the setting of life-threatening hypocalcemia, calcium salts are generally best administered into a central vein. Multiple doses must be guided by frequent ionized calcium determinations.

Several general principles apply to the management of a hypocalcemic patient. The magnesium level should be

checked and, if low, corrected. In a setting of sepsis or renal failure, metabolic acidosis may accompany hypocalcemia and calcium must be replaced before the acidosis is corrected. Calcium and hydrogen ions compete for protein-binding sites so an increase in pH with alkali therapy will increase the binding sites for calcium, leading to a rapid fall in ionized calcium, potentially resulting in cardiac arrest—unless the calcium is corrected first. Sodium bicarbonate and calcium salts must be infused in separate lines to avoid precipitation of calcium carbonate. Patients on digoxin should be monitored carefully because administration of calcium may potentiate digitalis toxicity and cause death. Intravenous calcium should be given cautiously in the presence of hyperphosphatemia; a total calcium times phosphate product of greater than 70 mg/dL may lead to soft-tissue calcification. Similarly, aggressive replacement of phosphorus may precipitate tetany.

Finally, the administration of calcium to critically ill patients is controversial. Available data suggests that decreased ionized calcium levels are protective during critical illness, especially shock states. Administration of calcium to animals with infection increases ionized calcium levels into the normal range and improves blood pressure; however, it also causes increased mortality.[54] A variety of mechanisms by which calcium may be detrimental have been suggested.[36] Free intracellular calcium concentrations are elevated during critical illness. Unregulated increases in intracellular calcium levels cause cell dysfunction. There is activation of intracellular digestive enzymes (i.e., proteases, lipases, nucleases), increased membrane permeability, impaired mitrochondrial function and ATP production, lysosomal destabilization, impaired cardiac contractility, catecholamine resistance, free radical production, and activated apoptosis. Exogenous calcium administration aggravates these processes.

Hypercalcemia

In pediatrics, hypercalcemia is an uncommon occurrence. This discussion excludes hypercalcemia in the newborn. Hypercalcemia is defined as a measured total serum calcium concentration of greater than 11.0 mg/dL. Hypercalcemia can result from increased calcium absorption from the gut or increased calcium resorption from bone. Hypercalcemia occasionally results from a massive increase in dietary calcium intake or a reduction in the renal excretion of calcium. In hyperparathyroidism, increased bone resorption of calcium results in hypercalcemia, and decreased renal reabsorption of phosphorus results in hypophosphatemia.[52,53] Because PTH stimulates bone turnover, alkaline phosphatase is elevated. PTH is inappropriately elevated for the level of serum calcium and confirms the diagnosis.

The vitamin D toxicity syndromes usually can be suspected from the history; hypercalcemia is the result of increased calcium absorption. If the intoxicating compound is conventional vitamin D, then hypercalcemia may be prolonged because of the storage of this compound in adipose tissue.

Symptoms of hypercalcemia may be attributed to its depressive effects on neuromuscular function.[52] These include anorexia, nausea, vomiting, lethargy, muscular weakness, confusion, and stupor. Electrocardiographic changes (shortening of the QT interval) may be seen.

Treatment of hypercalcemia is facilitated by knowing the underlying cause of the derangement. The choice of therapy depends on whether the kidneys are functioning normally. The initial emergency treatment of symptomatic hypercalcemia is designed to enhance calcium excretion by saline infusion at a rate of twice maintenance followed by bolus injections of furosemide, 1-2 mg/kg every 6-8 hours. The subsequent amount and rate of saline to be administered depends on the state of hydration and presence or absence of hypertension or preexisting cardiac disease, but in an otherwise normal patient, saline flow rates of two to three times daily maintenance would be appropriate until the serum calcium returns to normal. Treatment of a hypercalcemic crisis depends on the underlying cause, the level of serum calcium, and the severity of signs and symptoms. It always requires hospitalization in an intensive care setting. In acute oliguric renal failure, peritoneal or hemodialysis against a low calcium dialysate is usually effective.

For hypercalcemia that is poorly responsive to conventional treatment, treatment with biphosphonates should be considered.[58] Most pediatric experience is with pamidronate: a single dose of 0.5-1 mg/kg IV should normalize the serum calcium in 2-5 days. Hypersensitivity to the drug or its components is the only contraindication to IV administration. It should be used cautiously in renal insufficiency and adequate hydration and urinary output should be ensured during treatment.

Magnesium

Magnesium is the fourth most abundant cation in the body and the second most abundant intracellular electrolyte. Ninety-nine percent is found in the intracellular compartment, and the remaining 1% is in ECF. This important ion is a dependent cofactor in the function of more than 300 enzyme systems.[59,60] It is an obligatory cofactor in reactions involving adenosine triphosphate, including maintenance of normal intracellular potassium by the sodium-potassium adenosine triphosphatase pump. It is essential to oxidative phosphorylation, protein synthesis, amino acid activation, and glucose use.[59,60] Serum magnesium levels are regulated by the kidneys. The normal serum magnesium ranges between 1.7-2.2 mg/dL (0.75-0.95 mmol/L; 1.5-1.9 mEq/L).

The plasma magnesium concentration is composed of bound and unbound fractions in a manner that is similar to that of calcium; approximately 50% of the circulating magnesium is free (i.e., ionized). In critically ill patients the total magnesium concentration may poorly reflect the physiological (ionized) concentration, the latter can be measured with ion-selective electrodes.[61]

Particularly in pharmacological concentrations, magnesium can inhibit calcium channels, which represents some of the potentially therapeutic effects of magnesium. Through inhibition of calcium channels and the subsequent reduction of intracellular calcium concentration, magnesium causes smooth muscle relaxation, which has been used in the treatment of acute severe asthma.[62] In addition, the effects of magnesium on calcium channels, and perhaps other membrane effects, have been

useful in the treatment of torsades de pointes VT.[36,60]

Hypomagnesemia

In critically ill patients, estimates of magnesium deficiency range from 20%-65% and have been associated with increased mortality rates.[60,63] Because magnesium deficiency is common and may lead to life-threatening complications, total serum magnesium concentration has been viewed as the "fifth electrolyte" needed in every patient, in addition to sodium, potassium, chloride, and bicarbonate.[63] The usual cause of hypomagnesemia is loss of magnesium from the gastrointestinal tract or the kidney.

Most of the symptoms of moderate to severe hypomagnesemia are non-specific and symptomatic magnesium depletion usually is associated with additional ion abnormalities such as hypocalcemia, hypokalemia, and metabolic alkalosis.[64]

Hypocalcemia is typical in severe hypomagnesemia, and its degree seems to be related to the severity of the magnesium depletion, usually appearing at a serum below 1.0 mEq/L (0.5 mmol/L.)[60] Patients may present with evidence of neuromuscular hyperexcitability, with positive Chvostek and Trousseau signs or spontaneous carpopedal spasm. Most hypocalcemic/hypomagnesemic patients have a low or normal PTH concentration, suggesting impaired synthesis or secretion of PTH. Magnesium supplementation leads to a rapid rise in plasma PTH. Many observations are compatible with a primary role for PTH resistance, where severe hypomagnesemia may alter signal transduction from the PTH receptor to catalytic adenylate cyclase.[65]

Hypokalemia also is a frequent feature of magnesium deficiency (40-60% of cases). In magnesium deficiency potassium secretion in the loop of Henle and the cortical collecting tubule increases. The hypokalemia here does not respond to potassium replacement, and the magnesium deficit itself has to be corrected.[66]

Magnesium is vital to carbohydrate metabolism and the generation of both anaerobic and aerobic energy, and it influences glucose catabolism and insulin sensitivity.

Magnesium depletion may produce acute electrocardiographic changes such as widening of the QRS complex and the appearance of peak T waves. In severe depletion the PR interval is prolonged, with progressive widening of the QRS, T wave inversion, and the appearance of U waves. Hypomagnesemia has been implicated in severe ventricular arrhythmias, especially during myocardial ischemia and cardiopulmonary bypass procedures. There also is an association between hypomagnesemia and sensitivity to cardiac glycosides.

The use of intravenous magnesium should be considered for refractory arrhythmias, even in the presence of normal serum magnesium levels, particularly if the patient is on digoxin and diuretics.[67] According to numerous case reports, magnesium sulfate has proven effective in treating a wide range of cardiac arrhythmias, especially ventricular arrhythmias, after conventional therapies have failed.[68] *(See Table 2.)*

The choice of route of magnesium repletion varies with the severity of the clinical findings. An acute infusion of magnesium could decrease magnesium reabsorption in the loop of Henle, most of the infused magnesium ending up in the urine. For this reason, oral replacement is preferred, especially in symptom-free patients.

Table 2. Cardiac Arrhythmias Terminated by Administration of IV Magnesium Sulfate

- Torsade de pointes
- Refractory ventricular fibrillation
- Refractory ventricular tachycardia
- Refractory PVCs
- Ventricular arrhythmia associated with digitalis overdose
- Multifocal atrial tachycardia

Symptomatic magnesium deficiency should be treated parenterally. Magnesium sulfate can be supplemented at an IV dose of 25-50 mg/kg/dose (maximum single dose 2 grams) infused over 3-4 hours. Electrocardiographic monitoring is required during intravenous administration of magnesium because hypotension, arrhythmias and skeletal muscle weakness with respiratory failure have been reported (see section on hypermagnesium). Calcium should be readily available as an antidote. Concomitant hypocalcemia and hypokalemia should be corrected separately.

Hypermagnesemia

Hypermagnesemia is uncommon in pediatrics but, as in adults, usually is related to accidental overdose.[59,69,70] This is particularly true in patients with impaired renal function. Magnesium-containing over-the-counter medications, particularly antacids and cathartics, may result in hypermagnesium in infants and small children.[69] Measurement of serum magnesium concentration is appropriate in the child with unexplained lethargy, hypotonia, respiratory depression, or hypotension.

Manifestations of hypermagnesemia are based on this ion's affect on the central nervous system (CNS), cardiovascular system, and neuromuscular junction.[60] CNS manifestations include drowsiness, confusion, lethargy, and coma. Effects on the cardiovascular system include hypotension and dysrhythmias. These effects are caused by the calcium channel-blocking properties of magnesium, which decreases entry of calcium into cells and enhances egress of calcium from cells. At the neuromuscular junction, magnesium sulfate decreases the amount of acetylcholine liberated, diminishes the sensitivity of the endplate to acetylcholine, and depresses the excitability of the muscle membrane. This results in skeletal muscle weakness and respiratory distress. Clinical signs and symptoms correlate with plasma concentrations.[60,69] EKG changes (prolongation of the PR interval, increased duration of the QRS complex, and increased height of the T waves) are noted with concentrations of 6-12 mg/dL (5-10 mEq/L), deep tendon reflexes are lost when serum concentrations reach 12 mg/dL (10 mEq/L), respiratory paralysis and sinoatrial and atrioventricular block occurs at 18 mg/dL (15 mEq/L), and cardiac arrest occurs at 30 mg/dL (25 mEq/L).

Management of hypermagnesemia is dictated by the cardiovascular, CNS, and neuromuscular changes that occur. Treatment consists of stopping the source of magnesium, respiratory and cardiovascular support, calcium, diuresis, and dialysis. Indications for dialysis include: kidney failure, increasing magnesium levels despite diuresis, dysrhythmias, and persistent hemo-

dynamic instability.

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CME Questions

1. Which one of the following is *not* a direct result of hyponatremia?
   A. Convulsions
   B. Muscle cramps
   C. Coma
   D. Osmotic demyelination
   E. Cerebral edema

2. Patients presenting with hypovolemic hypernatremia should initially be treated with which one of the following?
   A. 0.9% NaCl
   B. 0.45% NaCl
   C. 5% dextrose and water
   D. Enteral free water

3. Among the following, the most common etiology of status epilepticus in an afebrile 6-month-old is:
   A. benzodiazepine ingestion.
   B. hyponatremia.
   C. medulloblastoma.
   D. Reye syndrome.
   E. ruptured cerebral aneurysm.

4. A 3-month-old boy who has diarrhea is fed only apple juice for three days. Because of increasing lethargy, he is brought to the hospital where he has a generalized tonic-clonic seizure lasting 10 minutes. He is treated with lorazepam and Phenobarbital and intubated for apnea. He is noted to be well hydrated and afebrile. All other find-

ings are normal. The serum glucose level is 80 mg/dL. Of the following, the *most* likely diagnosis is

A. bacterial meningitis.
B. fructose intolerance.
C. hypocalcemia.
D. hyponatremia.
E. Viral meningoencephalitis.

5. Which one of the following ECG changes is *not* associated with hyperkalemia?
   A. Narrow peaked T waves
   B. Inverted P wave
   C. Wide QRS
   D. Elevated ST segment

6. Of the following therapies for symptomatic hyperkalemia, the one that has the most rapid effect on stabilizing resting membrane potential is:
   A. Intravenous bicarbonate therapy
   B. Intravenous glucose
   C. Intravenous calcium therapy
   D. Kayexalate – oral

7. Which one of the following statements concerning the syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is correct?
   A. SIADH is characterized by volume depletion and an "inappropriate" volume stimulus to ADH despite hypotonicity.
   B. SIADH is best treated by administration of hypertonic saline.
   C. SIADH results in both increased total body sodium and increased total body water.
   D. SIADH may complicate acute central nervous system or pulmonary infections.

8. Which one of the following statements is true? Hypernatremic dehydration:

CME Objectives

The CME objectives for Pediatric Emergency Medicine Reports are to help physicians:

a.) Quickly recognize or increase index of suspicion for specific conditions;

b.) Understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;

c.) Be educated about how to correctly perform necessary diagnostic tests;

d.) Take a meaningful patient history that will reveal the most important details about the particular medical problem discussed;

e.) Apply state-of-the-art therapeutic techniques (including the implications of pharmaceutical therapy discussed) to patients with the particular medical problems discussed;

f.) Understand the differential diagnosis of the entity discussed;

g.) Understand both likely and rare complications that may occur; and

h.) Provide patients with any necessary discharge instructions.

A. results in a urine sodium greater than 20 mEq/L.
B. may be seen in infants with diarrhea and high insensible water losses.
C. should be treated with rapid hypotonic fluid administration to minimize the effects of brain cell shrinkage.
D. is a common complication of exogenous ADH administration.

9. Which of the following correlates with the severity of signs and symptoms in a patient with hyponatremia?
A. A sodium of 131 mEq/L
B. Rapidity of development of hyponatremia
C. Chronic hyponatremia
D. Hypomagnesemia

10. What is the most common cause of an increased serum potassium?
A. Acute renal failure
B. Chronic renal failure
C. Spironolactone
D. Pseudohyperkalemia secondary to hemolysis

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In Future Issues: Crush Injuries

BIOTERRORISM WATCH

Preparing for and responding to biological, chemical and natural disasters

Clinicians must be voice of reason, reassurance now that bioterrorism battle has been joined

The threat is real, but we are far from defenseless

A new era of bioterrorism has begun with the intentional anthrax scares that have left several people dead and many more exposed as this issue went to press.

But amid the shrill coverage of the widening anthrax investigations, the scramble for gas masks and the expected hoarding of Cipro, there must be a voice of calm and reason. That voice must be your own.

Infection control professionals, hospital epidemiologists, and other key clinicians involved in health care bioterrorism readiness and response must set the tone for a panicky public and an uneasy health care work force, emphasizes veteran epidemiologist **William Schaffner**, MD, chairman of preventive medicine at Vanderbilt University School of Medicine in Nashville.

"We have to re-instill a sense of confidence for people who work in the health care system," he says. "Start with the doctors. They are the ones who are going to be more panicked than the nurses."

Restoring calm to health care community

The current situation is reminiscent of the early stages of the HIV epidemic, when there was much anxiety about the communicability of the disease and whether even casual contact would spell a death sentence for health care workers.

In that chilling time of alarmist reactions and burning mattresses, Schaffner recalls that ICPs, epidemiologists, and other clinicians, stepped into the fray to provide calming confidence and accurate risk data.

"I'm beginning to think that we may be in a similar position now," he says. "We could have a very powerful educational and reassuring effect. Everybody's anxious about this, but I think we can diminish the level of anxiety," Schaffner adds.

Infection control methods in place

Health care workers must be educated about bioterrorism agents and provided reassurance that the patient isolation precautions developed by the Centers for Disease Control and Prevention (CDC) are extremely effective, urges Schaffner.[1]

"The barrier precautions are going to work for bioterrorism. Once you get to chemical [weapons] then you get into the whole 'moon suit' issue. But for bioterrorism, we don't need that," he says.

For example, systems of barrier precautions such as gloves, gowns, and masks to isolate patients infected with all manner of infectious diseases are already in place in virtually all U.S. hospitals.

"They work," he says. "Look, we all know pulmonary tuberculosis is communicable. I'm an infectious disease doctor, have been for 30 years. I've seen a lot of patients with tuberculosis, but I have also been meticulous about my use of [face masks and respirators]. My tuberculin test continues to be negative."

This supplement was prepared by Gary Evans, editor of *Hospital Infection Control*. Telephone: (706) 742-2515. E-mail: gary.evans@ahcpub.com.

A Bioterrorism Time Line

1155 Barbarossa uses the bodies of dead soldiers to poison the wells at the battle of Tortona.

1346 Mongols catapult corpses of plague victims into the city of Kaffa to infect the defenders.

1763 British commander Sir Jeffrey Amherst ordered the transfers of blankets used by British smallpox victims to Native American tribes, ostensibly as a gesture of goodwill, with the intention of inducing illness.

1970 The United States ends its programs of developing biological agents for use in warfare. The offensive use of such weapons was forbidden by U.S. policy under executive orders of President Richard Nixon.

1972 Soviet Union signs off on Biological and Toxin Weapons Convention, but continues a high-intensity program to develop and produce biological weapons at least through the early 1990s. Hundreds of tons of weaponized anthrax spores are stockpiled, along with dozens of tons of smallpox and plague. Many of these agents are reputed to have been specifically designed to be resistant to common antibiotics.

1984 Members of the Rajneesh cult contaminated salad bars in Oregon with salmonella, resulting in the infection of 751 people. The Paris Police raided a residence suspected of being a safe house for the German Red Army Faction. During the search, they found documentation and a bathtub filled with flasks containing *Clostridium Botulinum.*

1990s Japan's Aum Shinrykyo cult plans attacks using biological agents, specifically, anthrax and botulinum toxin. While these biological attacks were not successful, cult members later implemented the release of sarin nerve gas in the Tokyo subway system.

1995 A U.S. microbiologist with right-wing ties orders bubonic plague cultures by mail. The ease with which he obtained these cultures prompts new legislation to ensure that biologic materials are destined for legitimate medical and scientific purposes.

1998 A variety of feigned exposures to anthrax spores occurred in several U.S. cities including Indianapolis, where a full-scale response by emergency services and public health occurred before the episode was found to be a hoax.

Sources

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2. Bosker G. Bioterrorism: An update for clinicians, pharmacists, and emergency management planners. *Emergency Medicine Reports* (in press) 2001. ■

And anthrax, of course, is not communicable from person to person, reminds Schaffner, who investigated a case of occupational anthrax in an animal-hide worker when he was a epidemiologist for the CDC in the late 1960s.

"The bacteria do not cause a conventional pneumonia," he says. "They replicate locally and then release toxins. Because the bacteria never replicate to very high numbers the person is not communicable. It is not so much an infection as it is an intoxication."

Inordinate fear of anthrax could cause another problem — hoarding and misuse of Ciprofloxacin and other antibiotics. That tactic eventually could contribute to emerging resistance in pathogens such as *Streptococcus pneumoniae,* Schaffner notes.

"It is one thing for a hospital and the health department to develop an inventory in the event of an emergency," he says. "I do not recommend that individuals do that. I'm quite concerned that with antibiotics in their medicine cabinets there will be a temptation to just use it now and again for inadequate reasons in inadequate doses. If there was a recipe for antibiotic resistance — that's it."

More terror than toll

While the anthrax mailing campaign now under way sends out another shock wave with every news report, the tactic will likely result in more terror than actual toll. The rapid administration of antibiotics has offset illness following exposures, the disease is not communicable from those actually infected, and everyone is now on high alert for suspicious mailings.

Indeed, if the wave of anthrax mailings continues, postal-treatment technologies may become a growth industry.

Regardless, anthrax is problematic as a bioweapon because only a certain micron size of the inhaled spore will lodge in the upper lungs where it can release its toxins, says **Allan J. Morrison Jr.**, MD, MSc, FACP, a bioterrorism expert and health care epidemiologist for the Inova Health System in Washington, DC.

"If it is too large, it won't go in," says Morrison, a former member of the U.S. Army Special Forces. "If it's too small, it goes in and moves about freely without ever lodging. This is not as easy as getting a culture, growing it in your home, and the next day having infectious microbes.

"The sizing, preparation, and ability to deliver such a weapon are extremely difficult," he adds.

The Aum Shinrykyo cult in Tokyo attempted at least eight releases of anthrax or botulism during 1990 to 1995 without getting any casualties, he recalls. **(See time line, p. 2.)** Variables such as humidity can come into play, clumping up spores even if they are perfectly sized for inhalation. Anthrax spores bound for human targets are also at the whims of ultraviolet light, rain, and wind dispersal patterns, Morrison says.

"It is a very hostile climate for microbes on planet earth." Morrison says. "The intent may be widespread, but the ability to deliver weapons grade agents is going to be restricted to a very small subgroup. And even among them, they still will require optimal climatic conditions to carry it out. There will be causalities, as in war, but the distinction here is that there has not been widespread infection."

While anthrax is the current weapon of choice, the direst scenarios usually turn to the most feared weapon in the potential arsenal of bioterrorism: smallpox.

"Invariably, I have seen smallpox described as 'highly infectious,'" Schaffner says. "It's not. That is erroneous." For example, during the global eradication efforts in the 1960s, African natives infected with smallpox were often found living with extended families in huts, he adds. "It would usually take two to three incubation periods for smallpox to move through an extended family."

"It doesn't happen all it once. This was a critical concept in the strategy to eradicate smallpox. If you could find smallpox, you could vaccinate around that case and prevent further transmission. If it had been a frighteningly [rapid] communicable disease, that strategy would never have worked," Schaffner explains.

In addition, some medical observers question the certitude of the general consensus that all those vaccinated decades ago are again susceptible to smallpox. They argue that those immunized during the eradication campaign may at least have some greater protection against fatal infection.[2]

Regardless, rather than dropping like flies, as many as 70% of those infected with smallpox actually survive and then have lifelong immunity.

While there are many other agents to discuss and prevention plans to outline in the weeks and months ahead, perhaps the greatest protective factor is the unprecedented level of awareness in the health care system. The world has changed so much since Sept. 11th that hospitals are probably more prepared for bioterrorism than they have ever been. Everywhere, lines of communication have been opened with health departments and affiliated clinics, emergency plans have been reviewed and hot-button phone numbers posted on the wall.

"We're on alert," says **Fran Slater**, RN, MBA, CIC, CPHQ administrative director of performance improvement at Methodist Hospital in Houston. "We are *all* on alert."

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Should clinicians get smallpox vaccinations?

Questions arise, stockpile expansion fast-tracked

The recent decision to accelerate production of a new smallpox vaccine is raising the complex question of whether health care workers — front-line soldiers in the war against bioterrorism — should be immunized against the disease.

As opposed to the current anthrax attacks, a biological release of smallpox would result in incoming patients with an infectious disease. Even health care workers directly exposed to anthrax could be treated with ciprofloxacin and several other antibiotics, so the anthrax vaccine is not a likely candidate for health care.

On the other hand, legitimate questions have been raised about whether health care workers will stay on the job during a smallpox outbreak unless they and their families are rapidly vaccinated. The only known stocks of smallpox virus are held by the United States and Russia, but many bioterrorism experts have warned for years that another nation or group might have secret stocks.

"I think if smallpox [vaccine] became available, we should definitely immunize all the health care workers," says **Martin Evans**, MD, hospital epidemiologist at the University of Kentucky Chandler Medical Center in Lexington. "A lot of people think [health care workers] ought to

be high on the list because they are part of the response team if there was an outbreak in the community. Not to sound self-serving, but I think we ought to immunize the medical community."

But the question currently is somewhat moot because the Centers for Disease Control and Prevention (CDC) is not wavering from its established policy of mobilizing the available vaccine only if smallpox is released. "I'm sure CDC wants to conserve its current stocks for dealing with an outbreak so it could immunize contacts," Evans says. "If [the agency has] already used [its stock] by immunizing all the health care workers in the country, then it won't be able to respond."

15 million doses stockpiled

Currently, there are some 15 million doses of the old smallpox vaccine available, according to Secretary of Health and Human Services **Tommy Thompson,** who recently announced plans to accelerate production of a new smallpox vaccine. Forty million new doses of vaccine are expected to be available by mid-to-late 2002, moving the project up considerably from its original completion date of 2004 or 2005.

The manufacturer of the new vaccine is Acambis Inc. (formerly OraVax) — based in Cambridge, UK, and Cambridge and Canton, MA. The new vaccine will be a purified derivative of the same strain of cowpox virus (vaccinia) that was used in the United States previously, because the old vaccine's efficacy was clearly demonstrated by direct exposures to those infected. While the method of immunization through scarification will be essentially the same, the new vaccine will be produced in a mammalian cell culture that contains no animal protein.

Acambis stated on its web site that it would have no other comment on the project other than to confirm it has "accelerated" its production plans. But when the project was first announced in 2000, company officials said they had the ability to scale up production well beyond the requested 40 million doses. They were even scouting for other global markets. That means the capability to produce smallpox vaccine in abundance is on the horizon, and the question of immunizing health care workers will invariably arise. *Bioterrorism Watch* was unable to get a CDC response on the question as this issue went to press, but CDC director **Jeffrey Koplan**, MD, MPH, outlined the agency's position in an Oct. 2, 2001 Health Alert posted on a CDC web site.

"Smallpox vaccination is not recommended and, as you know, the vaccine is not available to health providers or the public," Koplan said. "In the absence of a confirmed case of smallpox anywhere in the world, there is no need to be vaccinated against smallpox. There also can be severe side effects to the smallpox vaccine, which is another reason we do not recommend vaccination. In the event of an outbreak, the CDC has clear guidelines to swiftly provide vaccine to people exposed to this disease. The vaccine is securely stored for use in the case of an outbreak."

One factor in favor of the CDC's position to rapidly deploy the vaccine — rather than do widespread vaccinations — is that immunization should still be effective several days after a smallpox exposure. In the smallpox global eradication campaign, epidemiologists found they could give vaccine two to three days after an exposure and still protect against the disease. Even at four and five days out, immunization might prevent death. Still, though the new vaccine will be improved in many ways, the hazards and risk factors of introducing cowpox into the human body are expected to be roughly the same as those documented with the old vaccine.

"We are looking at probably about one death per million primary vaccinations," says **D.A. Henderson**, MD, director of the Center for Civilian Biodefense Studies at Johns Hopkins University in Baltimore. "We are looking at one in 300,000 developing post-vaccinal encephalitis — an inflammation of the brain, which occasionally is fatal and sometimes can leave people permanently impaired."

Based on those estimates, if the new stockpile of 40 million doses is eventually rolled out, approximately 40 of those immunized will die, and another 133 will develop encephalitis. In addition to those severe outcomes, the arm lesion created during inoculation can be very large and painful, serving as a reservoir to self-inoculate the eyes or even infect immune-compromised patients.

The downside is real, but as more vaccine becomes available immunization will certainly be discussed at hospitals in previously targeted areas such as New York City and Washington, DC. If they are not immunized in advance, health care workers are going to want vaccine very quickly if they are expected to take care of smallpox patients, says **Allan J. Morrison Jr.**, MD, MSc, FACP, health care epidemiologist for the Inova Health System in Washington, DC. "Forget about smallpox patients. We're talking about taking care of any patients." ■

PEDIATRIC Emergency Medicine Reports
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Electrolyte Disorders

Classification of Hyponatremic States

Pseudohyponatremia	True Hyponatremia	Factitious Hyponatremia
Isotonic Hyponatremia POsm = 280-295	Hypotonic Hyponatremia POsm < 280	Hypertonic Hyponatremia POsm > 295
↓	↓	↓
Hyperlipidemia Hyperproteinemia	See Figure on the Diagnosis and Treatment of True Hyponatremia	Hyperglycemia Mannitol

Diagnosis and Treatment of True Hyponatremia

Hypotonic Hyponatremia POsm < 280

	HYPOVOLEMIC Total Body Sodium		EUVOLEMIC Total Body Sodium Total Body Water	HYPERVOLEMIC Total Body Sodium	
Clinical Volume Status					
Etiologies	**Renal losses** 1. Diuretic excess 2. Osmotic diuresis 3. Salt-wasting nephropathy 4. Adrenal insufficiency 5. Proximal RTA 6. Metabolic alkalosis 7. Pseudohypoaldosteronism 8. Cerebral salt wasting	**Extrarenal losses** 1. Gastrointestinal • Vomiting • Diarrhea • Tubes/Fistula 2. Sweat 3. Third space • Pancreatitis • Burns • Muscle trauma • Peritonitis • Effusions • Ascites • Systemic infections • Intestinal obstruction	1. Excess ADH • SIADH • Drugs, pain 2. Reset osmostat 3. Glucocorticoid deficiency 4. Hypothyroidism 5. Water intoxication • IV therapy • Psychogenic water drinking • Inappropriately diluted formula • Excessive water feeding	**Edema-forming states** 1. Congestive heart failure 2. Cirrhosis; liver failure 3. Nephrotic syndrome	**Renal Failure** 1. Acute 2. Chronic
Urine Sodium	U_{Na} > 20 mEq/L	U_{Na} < 20 mEq/L	U_{Na} > 20 mEq/L	U_{Na} < 20 mEq/L	U_{Na} > 20 mEq/L
Management	Isotonic Saline Volume Expansion	Isotonic Saline Volume Expansion	Water restriction	Sodium and water restriction	Sodium and water restriction

Emergency Treatment of Hyperkalemia Onset/Duration

TECHNIQUE	AGENT	DOSE	ONSET/DURATION OF ACTION	COMMENT
Reversal of membrane effects	10% Calcium gluconate	0.5 mL/kg	Min/30-60 min	ECG monitor; discontinue if pulse rate < 100.
Movement of K into cells	Sodium bicarbonate, 7.5% (1 mEq = 1 mL)	2-3 mL/kg	30 min/1-4 hr	May use in the absence of acidosis.
	Glucose 50% plus insulin (regular)	1 unit for every 5-6 g glucose	Same	Monitor blood glucose.
	Albuterol 0.5% solution	0.01-0.05 mL/kg (max 1 mL) aerosolized with 1-2 mL saline	15-30 min	Monitor heart rate.
Enhanced excretion of K	Kayexalate	1 g/kg	Hours/variable	Can be given PO or by rectum. Give with sorbitol (70%).

Key:
IV = intravenous; ECG = electrocardiogram; K = potassium; PO = orally.

Cardiac Arrhythmias Terminated by Administration of IV Magnesium Sulfate

- Torsade de pointes
- Refractory ventricular fibrillation
- Refractory ventricular tachycardia
- Refractory PVCs
- Ventricular arrhythmia associated with digitalis overdose
- Multifocal atrial tachycardia

Supplement to Pediatric Emergency Medicine Reports, November 2001: "Common Electrolyte Problems in Pediatric Patients Presenting to the ED." Author: **Ronald M. Perkin, MD, MA, FAAP, FCCM**, Professor and Chairman, Department of Pediatrics, Brody School of Medicine at East Carolina University; Medical Director, University Health Systems of Eastern Carolina Children's Hospital, Greenville, NC; **William E. Novotny, MD**, Associate Professor of Pediatrics, Pediatric Critical Care, Brody School of Medicine at East Carolina University; **Glenn D. Harris, MD**, Associate Professor of Pediatrics, Director, Pediatric Diabetology, Brody School of Medicine at East Carolina University; and **Irma Fiordalisi, MD**, Professor of Pediatrics, Pediatric Critical Care, Director, Pediatric Intensive Care Unit, Brody School of Medicine at East Carolina University.