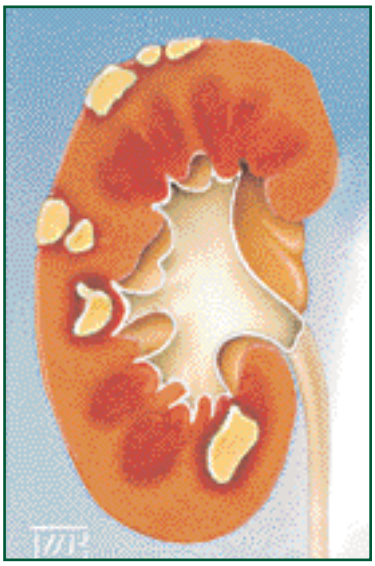

Practical Approach To Patients With Electrolyte Disorders

When dealing with hospitalized patients, electrolyte disorders, such as hypernatremia, hyponatremia, hyperkalemia and hypokalemia, can cause complications and should be guarded against.

By André Gougoux, MD, FRCPC

Electrolyte disorders are common clinical problems, especially in hospitalized patients. Since these disorders are accompanied by significant morbidity and mortality, an appropriate and rapid treatment is mandatory.

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Stability of the extracellular fluid. Indeed, the ionic composition of the extracellular fluid surrounding our cells must be maintained within physiologic limits by the homeostatic mechanisms of the body. For example, it is important to keep plasma sodium concentration around 140 milliequivalents per litre (mEq/L) and potassium concentration around 4 mEq/L.

Hypernatremia and hyponatremia. When natremia is too far from the normal value, the induced osmotic shift of water across the cell membrane markedly changes the cell volume. This volume decreases when hypernatremia and hyperosmolality shift water from the cells to the extracellular compartment. In contrast, cell vol-

Table 1

Clinical Manifestations of Electrolyte Disorders

- Hypernatremia/hyponatremia
  - -Seizures, coma
- Hyperkalemia/hypokalemia
  - -Paralysis
  - -Cardiac arrhythmias

ume increases when hyponatremia and hypo-osmolality shift water into cells. These changes in cell volume are especially important in the central nervous system and produce seizures, coma and various other neurologic signs and symptoms (Table 1).[1]

Hypernatremia occurs when plasma sodium concentration exceeds 145 mEq/L, reflecting a deficit of water for the amount of sodium in the extracellular fluid.

Hyperkalemia and hypokalemia. The normal ratio of around 30 of the intracellular (Ki) over the extracellular (Ke) potassium concentration is increased by hypokalemia or decreased by hyperkalemia. The resting membrane potential of -90 millivolts becomes more negative when hypokalemia increases the Ki/Ke ratio and less negative when hyperkalemia decreases this ratio. Because hyperpolarization and hypopolarization modify the excitability of nerve and muscle cells, they induce paralysis and life-threatening cardiac arrythmias, including cardiac arrest (Table 1).

Table 2

Etiology of Hypernatremia

- Decreased water intake
  - -Decreased thirst
  - -No water available
  - -Drinking impossible
- Increased urinary excretion of water
  - -Diabetes insipidus (central or nephrogenic)
  - -Osmotic diuresis (glucose, mannitol)

Hypernatremia

Definition. Hypernatremia occurs when plasma sodium concentration exceeds 145 mEq/L,[2] reflecting a deficit of water for the amount of sodium in the extracellular fluid.

Etiology. In most cases, hypernatremia results from a negative water balance when the water intake is lower than its urinary excretion. Two categories are observed according to the volume and the aspect of the urine:

1. *Water intake is decreased* when only a small volume of concentrated urine is excreted. This is observed when: thirst is reduced in various neurologic conditions; when water is not available (*e.g.*, in a desert; and when the patient is unable to drink for a variety of reasons) (Table 2).
2. *Urinary excretion of water is increased* when a large volume of dilute urine is obtained in patients with central (lack of vasopressin) or nephrogenic (renal resistance to vasopressin) diabetes insipidus. Osmotic diuresis is characterized by the increased urinary excretion of osmoles, such as glucose, when diabetic patients have a marked hyperglycemia, or by the increased urinary excretion of mannitol, an osmotic diuretic. In this condition, hypernatremia results from the uri-

nary excretion of an approximately half-isotonic saline solution.

Treatment. The first step is to minimize, if present, the large ongoing loss of water. For example, vasopressin must be given in central diabetes insipidus or insulin must be given to markedly hyperglycemic patients.

The next step is to replace the water loss by the ingestion of water, if possible, or by the intravenous administration of 5% dextrose in water. In order to calculate the amount of electrolyte-free water required to correct the hypernatremia, the volume of the total body water, or 60% of body weight, is utilized. For example, before any loss of water, a 70-kg patient has 42 L of body fluids. If his/her plasma sodium concentration is 154 mEq/L or 10% higher than the normal value of 140 mEq/L, the patient's water deficit equals 10% of the volume of 42 L. This patient needs, over the next 24 hours, 4 L of water by mouth or the same quantity of 5% dextrose in water intravenously (Table 3). Of course, the water losses expected during this period also must be replaced.

When osmotic diuresis induces hypernatremia, however, a half-isotonic saline solution should be administered to correct the loss in the urine. Finally, if a severe contraction of the extracellular fluid volume produces significant hypotension, a 0.9% sodium chloride solution must first be rapidly administered to correct, at least in part, this volume contraction.

A chronic hypernatremia cannot be corrected at a rate faster than 0.5 mEq/L/hour to prevent cerebral edema, intracranial hypertension and herniation of the brain. In acute hypernatremia, the intravenous administration of 5% dextrose (or glucose) in water cannot exceed the rate of its metabolism (around 300 ml/hour) to avoid a severe hyperglycemia that is unresponsive to insulin.[3]

Table 3

Example of Hypernatremia Treatment

- Total body water (TBW) = 42 L (60% of body weight)
- Natremia = 154 mEq/L (10% rise)
- Rx: 4 L (10% of TBW) of water or 5% dextrose in water

Table 4

Etiology of Hyponatremia

- With marked expansion and edema
  - -Congestive heart failure
  - -Hepatic cirrhosis
  - -Acute or chronic renal failure
- With slight expansion (no edema): SIADH
- With contraction and sodium loss
  - -Renal losses: diuretics
  - -Gastrointestinal losses

SIADH = syndrome of inappropriate secretion of antidiuretic hormone

Hyponatremia

Definition. Hyponatremia is present when plasma sodium concentration is lower than 135 mEq/L, representing an excess of water for the quantity of sodium in the extracellular fluid.

Facing Chronic Non-Cancer-Related Pain

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Table 5

Water and Sodium Balances in Hyponatremia

Etiology	Water balance	Sodium balance
• Marked expansion	+	+
• SIADH	+	—
• Contraction	—	—

Table 6

Treatment of Hyponatremia

- With marked expansion and edema
  - -Reduce the ingestion of sodium chloride and water
  - -Diuretics
- With slight expansion (no edema): SIADH
  - -Reduce the ingestion of water
  - -Adequate amounts of sodium chloride
- With contraction and sodium loss
  - -0.9% NaCl i.v. 100-125 ml/hour

NaCl = sodium chloride

Etiology. Hyponatremia is the most common electrolyte disorder encountered in clinical practice and usually one of the following three categories can be identified (Table 4):

1. *Hyponatremia with marked expansion and edema.* The obvious presence of edema indicates a significant expansion of the extracellular fluid volume and is observed in congestive heart failure, hepatic cirrhosis, and acute or chronic renal failure.
2. *Hyponatremia with slight expansion (no edema) or syndrome of inappropriate secretion of antidiuretic hormone (SIADH).* The absence of clinically detectable edema reflects a slight expansion of the extracellular fluid volume, and is found in SIADH. The inappropriate release of antidiuretic hormone (ADH) is encountered with: various diseases of the central nervous system; malignant tumors, such as the oat cell lung carcinoma; several drugs; and during the pre- and post-operative periods. For that reason, intravenous hypotonic fluids should be avoided in post-operative patients.[4]
3. *Hyponatremia with contraction and sodium loss.* Clinical signs of contraction of the extracellular fluid volume include weakness, dizziness and orthostatic hypotension (postural drop in arterial pressure). Diuretic-induced renal losses and gastrointestinal losses from vomiting or diarrhea are the most frequent causes.

Treatment. The category of hyponatremia determines the appropriate treatment:[5-7]

1. *Hyponatremia with marked expansion and edema.* In these patients, both sodium and water balances are markedly increased (Table 5). The progressive reduction of these two positive balances, therefore, is the aim of therapy. The intake of sodium chloride and water should be moderately restricted and their urinary excretion increased by loop diuretics (Table 6). Since a reduced effective circulating volume results in the nonosmotic stimulation of ADH, this hyponatremia may be very difficult to treat.[8]
2. *Hyponatremia with slight expansion (no edema) or SIADH.* In this condition, ADH-induced water retention and volume expansion are accompanied by a renal sodium loss. The underlying cause should be corrected if possible (*e.g.*, the surgical removal of a lung carcinoma or the stopping of the drug responsible). The simplest way to correct hyponatremia is water restriction, if the intake of sodium is adequate. If hyponatremia is symptomatic and more severe, a 3%

Table 7

Etiology of Hyperkalemia

- Increased intake of potassium
  - -Orally or intravenously
- Decreased renal excretion of potassium
  - -Renal failure
  - -Hypoaldosteronism
  - -Potassium-sparing diuretics
  - -Other drugs
- Extracellular shift of potassium
  - -Metabolic acidosis
  - -Cell destruction
  - -Drugs
  - -Hormonal deficiency

Table 8

Treatment of Hyperkalemia

- Stop potassium and potassium-sparing diuretics
- Shift potassium into cells
  - -Regular insulin
  - -Sodium bicarbonate
  - -Beta$_2$-adrenergics
- Remove potassium from body fluids
  - -Furosemide
  - -Cation exchange resin
  - -Hemodialysis
- Antagonize the cardiac effects of hyperkalemia
  - -Calcium gluconate

sodium chloride hypertonic solution and small doses of furosemide may be necessary.

3. *Hyponatremia with contraction and sodium loss.* Both sodium and water balances are decreased in these patients. The intravenous administration of a 0.9% sodium chloride saline solution at the rate of 100 ml/hour to 125 ml/hour usually restores the extracellular volume and corrects hyponatremia within 24 hours. When severe hypotension is present, however, the isotonic saline solution should be given as rapidly as possible, with the monitoring of hemodynamic parameters.

Finally, chronic and most often asymptomatic hyponatremia should not be corrected at a rate faster than 0.5 mEq/L/hour in order to avoid osmotic demyelination syndrome, its devastating neurologic sequelae and its high mortality rate.[9-12] By contrast, an acute hyponatremia with brain swelling, seizures and coma is life threatening, and usually requires the intravenous administration of a hypertonic sodium chloride solution (3% sodium chloride, containing 513 mEq of sodium chloride per liter).[1]

Table 9

Etiology of Hypokalemia

- Decreased intake of potassium
  - -orally or intravenously
- Increased excretion of potassium
  - -gastrointestinal: vomiting, gastric suction, diarrhea, laxatives
  - -renal: diuretics, hyperaldosteronism, diabetic ketoacidosis
- Intracellular shift of potassium
  - -metabolic alkalosis
  - -excess of aldosterone, catecholamines, insulin

Table 10

Treatment of Hypokalemia

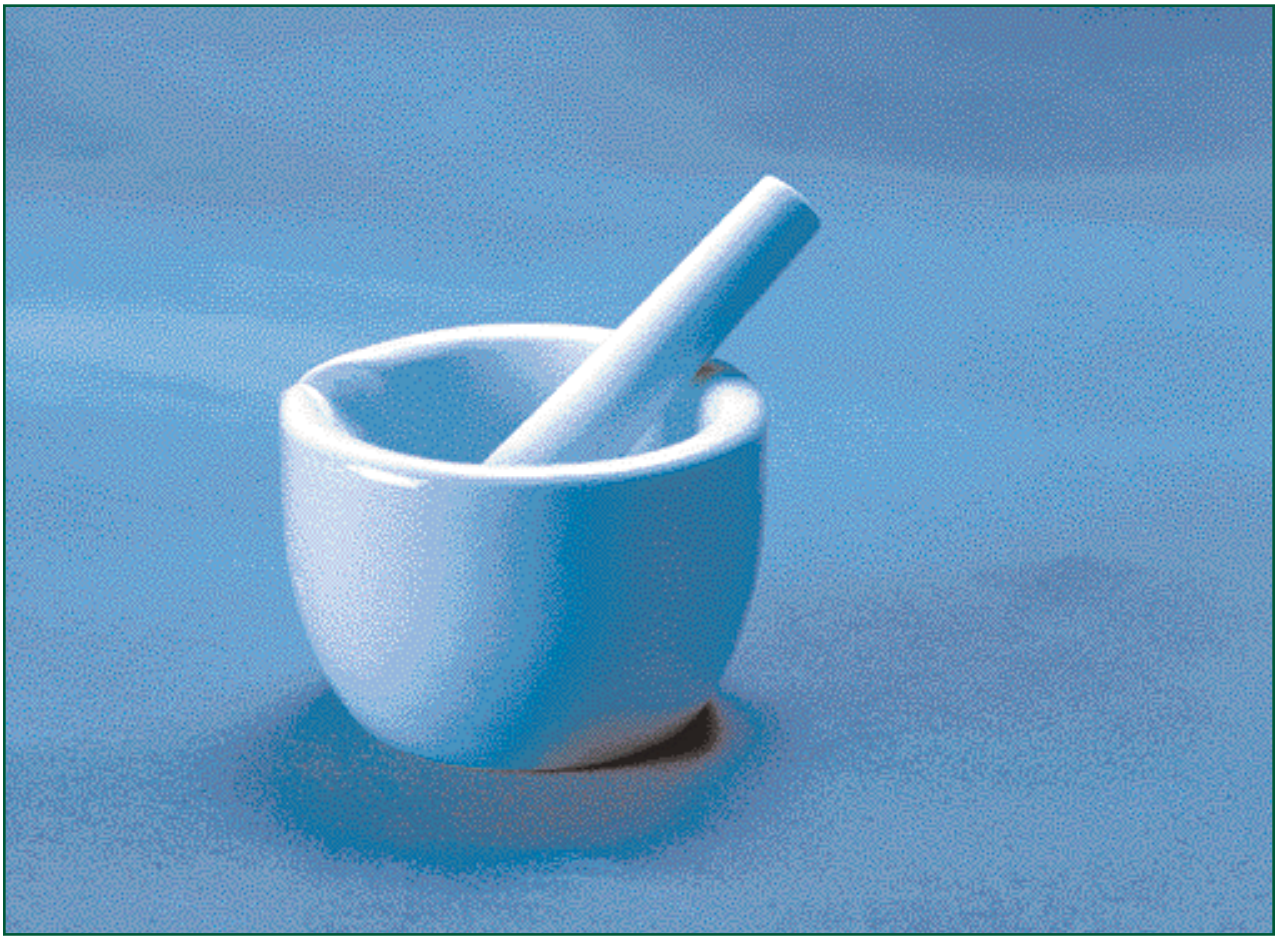
- Potassium chloride (KCl)
  - -20 mEq three to four times a day orally
  - -40 mEq/L i.v.

Hyperkalemia

Definition. Hyperkalemia is characterized by a plasma potassium concentration exceeding 5.0 mEq/L.

Etiology. Hyperkalemia results from changes in the intake of, the excretion of, and from a shift of potassium (Table 7):[13-14]

1. *Increased intake of potassium.* Hyperkalemia is observed with the ingestion of either potassium supplements[15] or salt substitutes, or with the intravenous administration of a bolus of potassium chloride.
2. *Decreased renal excretion of potassium* is the most frequent mechanism involved. Acute or chronic renal failure, hypoaldosteronism and potassium-sparing diuretics (*e.g.*, spironolactone, triamterene, amiloride) reduce the urinary excretion of potassium. Cyclosporin, trimethoprim,[16] angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists also can decrease the renal excretion of potassium. The risk of hyperkalemia is increased by the presence of a significant renal failure, especially when a diabetic nephropathy is accompanied by hyporeninemic hypoaldosteronism.[17]
3. *Extracellular shift of potassium.* Because 98% of the potassium is intracellular, a shift of even small amounts of potassium from the intracellular to the extracellular compartment markedly increases kalemia, but not the total body potassium. Accelerated transfer of potassium from the cells is observed in hyperchloremic metabolic acidosis with an excess of inorganic acids, and with the destruction of red blood cells during hemolysis and of muscle cells during rhabdomyolysis. By contrast, the cellular uptake of potassium is reduced by drugs like succinylcholine during anesthesia and by aldosterone deficiency, insulin deficien-



cy and beta$_2$-adrenergic blockade.

Treatment. Hyperkalemia is a life-threatening electrolyte abnormality when it exceeds 6.5 mEq/L to 7.0 mEq/L or induces the characteristic electrocardiogram (ECG) changes:[18] disappearance of P wave; widening of QRS complex; and symmetrical peaking of T wave. Once a laboratory error or pseudohyperkalemia resulting from hemolysis, marked leukocytosis or thrombocytosis has been ruled out, an ECG is obtained (in severe hyperkalemia). The treatment includes four maneuvers (Table 8):[19,20]

1. Discontinue the oral or intravenous administration of potassium supplements, and also discontinue potassium-sparing diuretics and any other drug that induces hyperkalemia.
2. Shift potassium into cells by administering 10 to 20 units of regular insulin with the addition, in the absence of hyperglycemia, of at least 100 grams of glucose: a bolus of 50% dextrose (25 g in 50 ml) is followed by an infusion of 10% dextrose (100 g in a liter). The intravenous administration of 50 mEq to 100 mEq of sodium bicarbonate also is useful and can correct, at least in part, the metabolic acidosis often present. In the absence of acidosis, however, the amount given is too small to induce a significant metabolic alkalosis. Beta$_2$-adrenergic agonists, such as salbutamol, given intravenously or by inhalation also decrease kalemia, but can induce cardiac

arrhythmias.

3. Remove potassium from the body fluids by three possible routes:
   a. The urine by the administration of furosemide—a loop diuretic—increasing the urinary excretion of potassium.
   b. The gastrointestinal tract with the sodium salt of polystyrene sulfonate. This resin, exchanging sodium for potassium in the lumen of the gastrointestinal tract, can be given orally (20-30 g with sorbitol, a non-reabsorbable alcohol, to prevent constipation and fecal impaction) or as a retention enema (50-100 g dissolved in 200 ml of water).
   c. A potassium-free dialysate during an emergency hemodialysis, especially in the presence of renal failure.
4. Antagonize the adverse cardiac effects of hyperkalemia by the intravenous administration in three to five minutes of 10 ml to 20 ml of 10% calcium gluconate under electrocardiographic monitoring, if possible.

Hypokalemia

Definition. Hypokalemia occurs when plasma potassium concentration is lower than 3.5 mEq/L.[21]

Etiology. Changes in the intake, the excretion, and a shift of potassium all act to induce hypokalemia (Table 9):

1. *Decreased intake of potassium.* Hypokalemia occurs with a very low intake of potassium, or in the absence of potassium in the intravenous solutions.
2. *Increased excretion of potassium* through the gastrointestinal or urinary tracts. Excessive gastrointestinal losses are observed with vomiting, nasogastric suction, diarrhea and laxative abuse. Use or abuse of loop (furosemide) or distal (thiazides) diuretics are, by far, the most common causes of hypokalemia,[22,23] especially when the sodium intake is excessive. Renal losses of potassium also are observed with primary or secondary hyperaldosteronism, diabetic ketoacidosis, renal tubular acidosis and drugs, such as amphotericin B, carbenicillin and cisplatin.
3. *Intracellular shift of potassium.* A small shift of potassium from the extracellular to the intracellular compartment decreases kalemia, but without any loss of potassium from the body. This movement of potassium occurs during metabolic alkalosis or with an excess of aldosterone, catecholamines (in stress conditions) and insulin (during the treatment of

diabetic ketoacidosis).

Treatment. Because body potassium is mostly intracellular, a decreased kalemia only provides a crude index of the potassium depletion. The treatment of hypokalemia is mandatory in the following conditions: a kalemia lower than 3.0 mEq/L; a muscle weakness reflecting severe muscle depletion; a cardiac arrhythmia, especially in the presence of digitalis; and during the treatment of diabetic ketoacidosis.

The safest replacement therapy, if possible, is the oral administration of potassium chloride supplements, at the dosage of 20 mEq three to four times a day (Table 10). With a more severe potassium depletion, the administration of potassium chloride in a peripheral vein is necessary, but can induce either thrombophlebitis if the potassium concentration in the solution exceeds 40 mEq/L, or fatal hyperkalemia if the amount exceeds 1 mEq per minute. Potassium bicarbonate or potassium citrate, instead of potassium chloride, should be given if hypokalemia is accompanied by a severe metabolic acidosis. CME

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Put Your Knowledge to the Test

Answer the questions in our quiz found on page 183 and send the response card to the University of Calgary for CME credits.