Chapter 76: Electrolyte Homeostasis

INTRODUCTION

- *Fluid and electrolyte homeostasis* is maintained by feedback mechanisms, hormones, and many organ systems, and is necessary for the body's normal physiologic functions. Disorders of sodium and water, calcium, phosphorus, potassium, and magnesium homeostasis are addressed separately in this chapter.

DISORDERS OF SODIUM AND WATER HOMEOSTASIS

- Total body water (TBW) ranges from 45% to 60% of body weight depending on sex and age and is distributed primarily into two compartments: intracellularly (ICF; two-thirds [67%] of TBW), and one-third (33%) is contained in the extracellular space.
- *Effective osmoles* are solutes that cannot freely cross cell membranes, such as sodium and potassium. Addition of an isotonic solution to the extracellular fluid (ECF) does not change ICF volume because there is no change in effective ECF osmolality. Adding a hypertonic solution to the ECF decreases ICF volume, whereas adding a hypotonic solution increases it. **Table 76-1** summarizes the composition of commonly used IV solutions and their expected distribution into the ECF and ICF compartments.
- Hypernatremia and hyponatremia can be associated with conditions of high, low, or normal ECF sodium and volume. Both conditions are most commonly the result of abnormalities of water metabolism. It's important to understand the difference between *dehydration* (loss of TBW producing hypertonicity) and *hypovolemia* (volume depletion due to a symptomatic deficit in ECF volume).

TABLE 76-1

Composition of Common IV Solutions

								Distribution		
Solution	Dextrose g/dL (kcal/L)	[Na^+] (mEq/L or mmol/L)	[K^+] (mEq/L or mmol/L)	[Cl^-] (mEq/L or mmol/L)	Other (mEq/L or mmol/L)	Osmolality (mOsm/kg or mmol/kg)	Tonicity	% ECF	% ICF	Free water (mL/L)
Dextrose 5% in water	5 (170)	0	0	0	—	253	Hypotonic	33	67	1000 mL
0.2% NaCl[a]	0	34	0	34	—	68	Hypotonic	50	50	750 mL
0.45% NaCl[b]	0	77	0	77	—	154	Hypotonic	67	33	500 mL
0.9% NaCl[c]	0	154	0	154	—	308	Isotonic	100	0	0 mL
Lactated Ringer's[d]	0	130	4	105	Lactate 28 Ca 4.8	273	Isotonic	97	3	0 mL
Plasma-Lyte A[e]	0.44 (21)	140	5	98	Acetate 27 Mg 3	294	Isotonic	100	0	0 mL
Plasma-Lyte 148[e]										
Normosol-R (pH 6.6)	0	140	5	98	Acetate 27 Mg 3	294	Isotonic	100	0	0 mL
Normosol-R (pH 7.4)										
3% NaCl[f]	0	513	0	513	—	1026	Hypertonic	100	0	–2331 mL

[a]Also referred to as *quarter normal saline*.

[b]Also referred to as *half normal saline*.

[c]Also referred to as *normal saline*.

[d]Also referred to as LR; also available commercially as Dextrose 5% LR.

[e]Plasma-Lyte A pH 7.4; Plasma-Lyte 148 pH 5.5.

[f]Hypertonic solution; results in osmotic removal of water from the ICF.

One g/dL is equivalent to 0.1 g/L; one kcal/L is equivalent to 4.18 kJ/L; Ca, calcium; Cl^-, chloride; ECF, extracellular fluid; ICF, intracellular fluid; IV, intravenous; K^+, potassium; Mg, magnesium; NA, not applicable; Na^+, sodium; NaCl, sodium chloride.

Hyponatremia (Serum Sodium <135 mEq/L [mmol/L])

Pathophysiology

- Results from an excess of extracellular water relative to sodium because of impaired water excretion.
- Causes of nonosmotic release of arginine vasopressin (AVP), commonly known as *antidiuretic hormone*, include hypovolemia and decreased effective circulating volume as seen in patients with congestive heart failure (CHF), nephrotic syndrome, cirrhosis, and syndrome of inappropriate antidiuretic hormone (SIADH).
- Hyponatremia is classified as isotonic, hypertonic, or hypotonic depending on serum osmolity (**Figure 76-1**).
- Hypotonic hyponatremia, the most common form of hyponatremia, can be further classified as hypovolemic, euvolemic, or hypervolemic.
- Hypovolemic hypotonic hyponatremia is associated with a loss of ECF volume and sodium, with the loss of more sodium than water. It is seen in patients with diarrhea or in those taking thiazide diuretics.
- Euvolemic hyponatremia is associated with a normal or slightly decreased ECF sodium content and increased TBW and ECF volume. It is most commonly caused by SIADH.
- Hypervolemic hyponatremia is associated with an increase in ECF volume in conditions with impaired renal sodium and water excretion, such as cirrhosis, CHF, and kidney failure.

FIGURE 76-1

Algorithm for the assessment and treatment of hyponatremia.

(AI, adrenal insufficiency; EABV, effective arterial blood volume; GI, gastrointestinal; HF, heart failure; LR, lactated Ringers; NaCl, sodium chloride; SIADH, syndrome of inappropriate antidiuretic hormone; UNa, urine sodium concentration [values in mEq/L are numerically equivalent to mmol/L]; Uosm, urine osmolality [values in mOsm/kg are numerically equivalent to mmol/kg]; VRA, vasopressin receptor antagonist.)

image

Clinical Presentation

- Most patients with hyponatremia are asymptomatic.
- Presence and severity of symptoms are related to the magnitude and rapidity of onset of hyponatremia. Hyponatremia that is severe or develops rapidly is associated with symptoms that progress from nausea and malaise to headache and lethargy and, eventually, to seizures, coma, and death.
- Patients with hypovolemic hyponatremia present with neurologic symptoms and also symptoms of hypovolemia, including decreased skin turgor, orthostatic hypotension, tachycardia, and dry mucous membranes.

Treatment

- Goals of Treatment: Resolve underlying cause of the sodium and ECF volume imbalance and safely correct the sodium and water derangements. Too rapid correction of serum sodium concentration can lead to an acute decrease in brain cell volume, contributing to the development of osmotic demyelination syndrome (ODS).

Acute or Severely Symptomatic Hypotonic Hyponatremia

- Symptomatic patients, regardless of fluid status, should initially be treated with 3% NaCl (513 mEq/L [mmol/L]) until symptoms resolve. Resolution of severe symptoms may require only a 5% increase in serum sodium; some clinicians suggest an initial target serum sodium of ~120 mEq/L (mmol/L).
- Treat SIADH with 3% saline plus, if the urine osmolality exceeds 300 mOsm/kg (mmol/kg), a loop diuretic (**furosemide**, 20–40 mg IV every 6 hours or **bumetanide**, 0.5–1 mg IV every 2–3 hours for several doses). Consider a continuous infusion if intermittent doses are not sufficient to manage edema.
- Treat hypovolemic hypotonic hyponatremia with 0.9% NaCl.
- Treat hypervolemic hypotonic hyponatremia with 3% NaCl and prompt initiation of fluid restriction. Loop diuretic therapy or **arginine vasopressin receptor antagonist (VRA)** is often required to facilitate urinary excretion of free water.

Nonemergent Hypotonic Hyponatremia

- Treatment of SIADH involves water restriction and correction of the underlying cause; discontinue drugs that could be a contributing factor. Restrict water intake to approximately 1000–1200 mL/day. Treat patients unable to restrict water sufficiently with NaCl tablets and a loop diuretic or **demeclocycline** (300 mg orally two to four times daily; onset of action in 3–6 days).
- VRAs or "vaptans" (eg, **conivaptan** [available IV only] and **tolvaptan** [15 mg orally daily]) can be used to treat SIADH as well as other causes of euvolemic and hypervolemic hypotonic hyponatremia that has been nonresponsive to other therapeutic interventions in patients with heart failure and SIADH. Fluid restriction should be avoided for the first 24–48 hours of starting VRA therapy when active sodium correction is occurring. Tolvaptan labeling currently includes a warning to NOT use it for more than 30 days and should not be used in patients with liver disease, including cirrhosis. The vaptans have dramatic effects on water excretion and represent a breakthrough in the therapy of hyponatremia and disorders of fluid homeostasis.
- Treatment of asymptomatic hypervolemic hypotonic hyponatremia involves correction of the underlying cause and restriction of water intake to less than 1000–1200 mL/day. Dietary intake of sodium chloride should be restricted to 1000–2000 mg/day.

Hypernatremia (Serum Sodium >145 mEq/L [mmol/L])

Pathophysiology and Clinical Presentation

- Hypernatremia results from insensible water loss (evaporative water loss through skin and lungs), from hypotonic GI losses, or when patients are exposed to high temperatures. Diabetes insipidus (DI) causes a water diuresis. Hypernatremia may also result from hypertonic NaCl administration or from excess sodium intake from IV and enteral fluids and medications.
- Increase in serum sodium concentration and osmolality causes acute water movement from the ICF to the ECF. Symptoms are primarily caused by decreased brain cell volume and can include weakness, lethargy, restlessness, irritability, twitching, and confusion. Symptoms of a more rapidly developing hypernatremia include seizures, coma, and death.

Treatment

- Goals of Treatment: Correct serum sodium concentration at a rate that restores and maintains brain cell volume.
- Begin treatment of hypovolemic hypernatremia with 0.9% NaCl. After hemodynamic stability is restored and intravascular volume is replaced, replace free-water deficit with 5% dextrose or 0.45% NaCl.
- The correction rate should be approximately 1 mEq/L (1 mmol/L) per hour for hypernatremia that developed over a few hours and 0.5 mEq/L (0.5 mmol/L) per hour for hypernatremia that developed more slowly.
- Treat central DI with intranasal **desmopressin**, beginning with 10 mcg once daily. Titrate to 20 mcg twice daily based on serum sodium concentration. Oral tablets are available; poor bioavailability contributes to unpredictable response when transitioning between dosage forms.

- Treat nephrogenic DI by decreasing ECF volume with a thiazide diuretic and dietary sodium restriction (2000 mg/day), which can decrease urine volume by as much as 50%. Other treatment options include drugs with antidiuretic properties (**Table 76-2**).
- Treat sodium overload with loop diuretics (furosemide, 20–40 mg IV every 6 hours) and 5% dextrose at an appropriate rate.

TABLE 76-2

Drugs Used in Central and Nephrogenic Diabetes Insipidus

Drug	Indication	Dose
Desmopressin acetate	Central and nephrogenic	5–20 mcg intranasally q12–24 hr
Chlorpropamide	Central	125–250 mg orally daily
Carbamazepine	Central	100–300 mg orally twice daily
Clofibrate	Central	500 mg orally four times daily
Hydrochlorothiazide	Central and nephrogenic	25 mg orally q12–24 hr
Amiloride	Nephrogenic	5–10 mg orally daily
Indomethacin	Central and nephrogenic	50 mg orally q8–12 hr

Edema

Pathophysiology and Clinical Presentation

- Edema, defined as a clinically detectable increase in interstitial fluid volume, develops when excess sodium is retained either as a primary defect in renal sodium excretion or as a response to a decrease in the effective circulating volume despite an already expanded or normal ECF volume.
- Edema is usually due to heart, kidney, or liver failure, or a combination of these conditions.
- Edema is initially detected in the feet or pretibial area in ambulatory patients and in the presacral area in bed-bound individuals, and is described as “pitting” when a depression caused by briefly exerting pressure over a bony prominence does not rapidly refill.

Treatment

- Diuretics are the primary pharmacologic therapy for edema. Loop diuretics are the most potent, followed by thiazide diuretics and then potassium-sparing diuretics.

Disorders of Calcium Homeostasis

- ECF calcium is moderately bound to plasma proteins (40%), primarily albumin. Ionized or free calcium is the physiologically active form that is homeostatically regulated.
- Each 1 g/dL (10 g/L) drop in serum albumin concentration less than 4 g/dL (40 g/L) decreases total serum calcium concentration by 0.8 mg/dL (0.20 mmol/L).

Hypercalcemia (Total Serum Calcium >10.2 mg/dL [>2.55 mmol/L])

Pathophysiology and Clinical Presentation

- Cancer and hyperparathyroidism are the most common causes of hypercalcemia. Primary mechanisms include increased bone resorption, increased GI absorption, and increased tubular reabsorption by the kidneys.
- Clinical presentation depends on the degree of hypercalcemia and rate of onset. Mild-to-moderate hypercalcemia (serum calcium concentration <13 mg/dL [<3.25 mmol/L] or ionized calcium concentration <6 mg/dL [<1.50 mmol/L]) can be asymptomatic.
- Hypercalcemia of malignancy develops quickly and is associated with anorexia, nausea and vomiting, constipation, polyuria, polydipsia, and nocturia. Hypercalcemic crisis is characterized by acute elevation of serum calcium to greater than 15 mg/dL (>3.75 mmol/L), acute kidney injury, and obtundation. Untreated hypercalcemic crisis can progress to oliguric acute kidney injury, coma, and life-threatening ventricular arrhythmias.
- Chronic hypercalcemia (ie, hyperparathyroidism) is associated with metastatic calcification, hypercalciuria, and chronic kidney disease secondary to interstitial nephrocalcinosis.
- Electrocardiographic (ECG) changes include shortening of the QT interval and coving of the ST-T wave.

Treatment

- Treatment approach depends on the degree of hypercalcemia, acuity of onset, and presence of symptoms requiring emergent treatment (**Figure 76-2**).
- Management of asymptomatic, mild-to-moderate hypercalcemia begins with attention to the underlying condition and correction of fluid and electrolyte abnormalities.
- Hypercalcemic crisis and acute symptomatic hypercalcemia are medical emergencies requiring immediate treatment. Rehydration with normal saline followed by loop diuretics (eg, furosemide, bumetanide) can be used in patients with normal to moderately impaired renal function. Normalization of total calcium may be seen within 24–48 hours.
- Initiate treatment with **calcitonin** in patients in whom saline hydration is contraindicated (**Table 76-3**). Onset of action is seen within 1–2 hours; however, the degree and extent of calcium reduction is often unpredictable.
- **Bisphosphonates** (eg, **pamidronate** and **zoledronic acid**) are indicated for hypercalcemia of malignancy. Total serum calcium decline begins within 2 days and nadirs in 7 days. Duration of normocalcemia varies but usually does not exceed 2–3 weeks, depending on treatment response of underlying malignancy.
- **Denosumab** is a monoclonal antibody approved for treatment of hypercalcemia of malignancy in patients refractory to bisphosphonate therapy.
- **Prednisone** or an equivalent agent is usually effective by reducing GI calcium absorption when hypercalcemia results from multiple myeloma, leukemia, lymphoma, sarcoidosis, and hypervitaminoses A and D. Onset of action is relatively slow.
- **Cinacalcet** is approved for management of parathyroid carcinoma, primary hyperthyroidism where parathyroidectomy is indicated but cannot be undertaken, and secondary hyperparathyroidism in patients with chronic kidney disease on dialysis.

FIGURE 76-2

Pharmacotherapeutic options for the acutely hypercalcemic patient. Serum calcium of 12 mg/dL is equivalent to 3 mmol/L.

image

TABLE 76-3

Drug Dosing Table for Hypercalcemia

Drug/Brand Name	Starting Dosage	Time Frame to Initial Response	Monitoring and Special Population Considerations
0.9% saline ± electrolytes	200–300 mL/hr	24–48 hours	Electrolyte abnormalities, fluid overload, CI in advanced kidney disease, congestive heart failure
Loop diuretics Furosemide/Lasix® Bumetandide/Bumex® Torsemide/Demadex®	40–80 mg IV q 1–4 hr of furosemide or equivalent	N/A	Electrolyte abnormalities (potassium and magnesium), CI in patients with allergy to sulfas (use ethacrynic acid)
Calcitonin/Miacalcin®	4 units/kg q 12 hr SC/IM 10–12 units/hr IV	1–2 hours	Facial flushing, nausea/vomiting, allergic reaction, CI in patients with allergy to calcitonin
Pamidronate/Aredia®	30–90 mg IV over 2–24 hours	2 days	Fever, fatigue, skeletal pain
Zoledronate/Zometa®	4–8 mg IV over 15 minutes	1–2 days	Fever, fatigue, skeletal pain, CI in advanced kidney disease
Glucocorticoids	40–60 mg oral prednisone equivalents daily	3–5 days	Diabetes, osteoporosis, infection, CI in patients with serious infections, hypersensitivity

CI, contraindicated; SC, subcutaneous.

Hypocalcemia (Total Serum Calcium <8.5 mg/dL [<2.13 mmol/L])

Pathophysiology

- Hypocalcemia results from altered effects of parathyroid hormone and vitamin D on the bone, gut, and kidney. Primary causes are postoperative hypoparathyroidism and vitamin D deficiency.
- Hypomagnesemia can be associated with severe symptomatic hypocalcemia that is unresponsive to calcium replacement therapy. Calcium normalization is dependent on magnesium replacement.

Clinical Presentation

- Clinical manifestations are variable and depend on the onset of hypocalcemia. Tetany is the hallmark sign of acute hypocalcemia, which manifests as paresthesias around the mouth and in the extremities; muscle spasms and cramps; carpopedal spasms; and, rarely, laryngospasm and bronchospasm.
- Cardiovascular manifestations result in ECG changes characterized by a prolonged QT interval and symptoms of decreased myocardial contractility often associated with CHF.

Treatment

- Acute, symptomatic hypocalcemia requires IV administration of soluble calcium salts (**Figure 76-3**). Initially, 100–300 mg of elemental calcium (eg, 1 g **calcium chloride**, 2–3 g **calcium gluconate**) should be given IV over 10–30 minutes (≤60 mg of elemental calcium per minute).

- The initial bolus dose is effective for only 1–2 hours; therefore, repeat doses should be given hourly as needed until severe, symptomatic patients are stabilized.
- Calcium gluconate is preferred over calcium chloride for peripheral administration because the latter is more irritating to veins.
- After acute hypocalcemia is corrected, the underlying cause and other electrolyte problems should be corrected. Magnesium supplementation is indicated for hypomagnesemia.
- Oral calcium supplementation (eg, 1–3 g/day of elemental calcium initially, then 2–8 g/day in divided doses) is indicated for chronic hypocalcemia due to hypoparathyroidism and vitamin D deficiency. If serum calcium does not normalize, add a vitamin D preparation.

FIGURE 76-3

Hypocalcemia diagnostic and treatment algorithm. Serum calcium of 8.6 mg/dL is equivalent to 2.15 mmol/L. Ionized calcium of 4.4 mg/dL is equivalent to 1.1 mmol/L.

image

DISORDERS OF PHOSPHORUS HOMEOSTASIS

Hyperphosphatemia (Serum Phosphorus >4.5 mg/dL [>1.45 mmol/L])

Pathophysiology

- Most commonly caused by decreased phosphorus excretion, secondary to decreased glomerular filtration rate (GFR).
- Intracellular phosphate release can occur with rhabdomyolysis, hemolysis, and tumor lysis syndrome, a complication of chemotherapy associated with massive cell lysis with highest incidence in patients with acute leukemia and lymphoma.

Clinical Presentation

- Acute symptoms include nausea, vomiting, diarrhea, lethargy, obstruction of the urinary tract, and, rarely, seizures. Calcium phosphate crystals are likely to form when the product of the serum calcium and phosphate concentrations exceeds 50–60 mg^2/dL^2 (4–4.8 $mmol^2/L^2$).
- The major effect is related to the development of hypocalcemia and damage resulting from calcium phosphate crystal precipitation into soft tissues, intrarenal calcification, nephrolithiasis, or obstructive uropathy.
- For more information on hyperphosphatemia and renal failure, see Chapter 75.

Treatment

- The most effective way to treat nonemergent hyperphosphatemia is to decrease phosphate absorption from the GI tract with phosphate binders (see Chapter 75, **Table 75-5**).
- Severe symptomatic hyperphosphatemia manifesting as hypocalcemia and tetany is treated by the IV administration of calcium salts.

Hypophosphatemia (Serum Phosphorus <2.7 mg/dL [<0.9 mmol/L])

Pathophysiology

- Hypophosphatemia results from decreased GI absorption, reduced tubular reabsorption, or extracellular to intracellular redistribution.
- Hypophosphatemia is associated with chronic alcoholism, parenteral nutrition with inadequate phosphate supplementation, chronic ingestion of antacids, diabetic ketoacidosis, and prolonged hyperventilation.

Clinical Presentation

- Severe hypophosphatemia (serum phosphorus <1.5 mg/dL [<0.5 mmol/L]) has diverse clinical manifestations that affect many organ systems, including the following:

  ✔ Neurologic manifestations: Progressive syndrome of irritability, apprehension, weakness, numbness, paresthesias, dysarthria, confusion, obtundation, seizures, and coma.

  ✔ Skeletal muscle dysfunction: Myalgia, bone pain, weakness, and potentially fatal rhabdomyolysis.

  ✔ Respiratory muscle weakness and diaphragmatic contractile dysfunction resulting in acute respiratory failure.

  ✔ Congestive cardiomyopathy, arrhythmias, hemolysis, and increased risk of infection can also occur.

- Chronic hypophosphatemia can cause osteopenia and osteomalacia because of enhanced osteoclastic resorption of bone.

Treatment

- Severe (<1.5 mg/dL; <0.5 mmol/L) or symptomatic hypophosphatemia should be treated with IV phosphorus replacement at a dose of 0.32–0.64 mmol/kg with normal kidney function. In critically ill trauma patients, doses up to 1 mmol/kg have been used.
- Asymptomatic patients or those who exhibit mild-to-moderate hypophosphatemia (1.5–2.7 mg/dL [0.5–0.9 mmol/L]) can be treated with oral phosphorus supplementation in doses of 1–2 g (32–64 mmol) daily in divided doses, with the goal of correcting serum phosphorus concentration in 7–10 days (**Table 76-4**).
- Monitor patients with frequent serum phosphorus and calcium determinations, especially if phosphorus is given IV or if renal dysfunction is present.

TABLE 76-4

Oral Phosphorus Replacement Therapy with Phosphate, Potassium, and Sodium Content Per Packet or Tablet

Product	Phosphate Content	Potassium Content	Sodium Content
Packet			
Phos-NaK	250 mg (8 mmol)	280 mg (7.1 mEq)	160 mg (6.9 mEq)
Tablet			
Av-Phos 250 Neutral	250 mg (8 mmol)	45 mg (1.1 mEq)	298 mg (13 mEq)
K-Phos Neutral	250 mg (8 mmol)	45 mg (1.1 mEq)	298 mg (13 mEq)
K-Phos No. 2	250 mg (8 mmol)	88 mg (2.3 mEq)	134 mg (5.8 mEq)
Phospha 250 Neutral	250 mg (8 mmol)	45 mg (1.1 mEq)	298 mg (13 mEq)
Phospho-Trin 250 Neutral	250 mg (8 mmol)	45 mg (1.1 mEq)	298 mg (13 mEq)
Virt-Phos 250 Neutral	250 mg (8 mmol)	45 mg (1.1 mEq)	298 mg (13 mEq)

Phosphorus 31 mg = 1 mmol; potassium 39 mg = 1 mEq = 1 mmol; sodium 23 mg = 1 mEq = 1 mmol.

DISORDERS OF POTASSIUM HOMEOSTASIS

Hypokalemia (Serum Potassium <3.5 mEq/L [mmol/L])

Pathophysiology

- Results from a total body potassium deficit or shifting of serum potassium into the intracellular compartment.
- Many drugs can cause hypokalemia (**Table 76-5**), and it is most commonly seen with use of loop and thiazide diuretics. Other causes of hypokalemia include diarrhea, vomiting, and hypomagnesemia.

TABLE 76-5

Mechanism of Drug-Induced Hypokalemia

Transcellular Shift	Enhanced Renal Excretion	Enhanced Fecal Elimination
β_2-Receptor agonists Epinephrine Albuterol Terbutaline Fomoterol Salmeterol Isoproterenol Ephedrine Pseudoephedrine Tocolytic agents Ritodrine Nylidrin Theophylline Levothyroxine Decongestants Caffeine Insulin overdose Verapamil overdose Barium overdose	Diuretics Acetazolamide Thiazides Indapamide Metolazone Furosemide Torsemide Bumetanide Ethacrynic acid High-dose penicillins Nafcillin Ampicillin Penicillin Mineralocorticoids Miscellaneous Aminoglycosides Amphotericin B Cisplatin	Laxatives Sodium polystyrene sulfonate Phenolphthalein Sorbitol Patiromer Sodium zirconium cyclosilicate

Clinical Presentation

- Signs and symptoms are nonspecific and variable and depend on the degree of hypokalemia and rapidity of onset. Mild hypokalemia is often asymptomatic.
- Cardiovascular manifestations include cardiac arrhythmias (eg, heart block, atrial flutter, paroxysmal atrial tachycardia, ventricular fibrillation, and digitalis-induced arrhythmias). In severe hypokalemia (serum concentration <2.5 mEq/L; mmol/L), ECG changes include ST-segment depression or flattening, T-wave inversion, and U-wave elevation.
- Moderate hypokalemia is associated with muscle weakness, cramping, malaise, and myalgias.

Treatment

- In general, every 1 mEq/L (mmol/L) decrease in potassium below 3.5 mEq/L (mmol/L) corresponds with a total body deficit of 100–400 mEq (mmol). To correct mild deficits, patients receiving chronic loop or thiazide diuretics generally need 40–100 mEq (mmol) of potassium.
- Whenever possible, potassium supplementation should be administered by mouth. Of the available salts, potassium chloride is most commonly used because it is the most effective for common causes of potassium depletion, use of diuretics, and with diarrhea.
- Limit IV administration to severe hypokalemia, patients exhibiting signs and symptoms such as ECG changes or muscle spasms, or inability to tolerate oral therapy. IV supplementation is more dangerous than oral therapy due to the potential for hyperkalemia, phlebitis, and pain at the infusion site. Potassium should be administered in saline because dextrose can stimulate insulin secretion and worsen intracellular shifting of

potassium. Generally, 10–20 mEq (mmol) of potassium is diluted in 100 mL of 0.9% NaCl and administered through a peripheral vein over 1 hour. ECG monitoring should be performed to detect cardiac changes.

Hyperkalemia (Serum Potassium >5 mEq/L [mmol/L])

Pathophysiology

- Hyperkalemia develops when potassium intake exceeds excretion or when the transcellular distribution of potassium is disturbed.
- Primary causes of true hyperkalemia include increased potassium intake, decreased potassium excretion, tubular unresponsiveness to aldosterone, and redistribution of potassium to the extracellular space.

Clinical Presentation

- Hyperkalemia is frequently asymptomatic; patients might complain of heart palpitations or skipped heartbeats.
- The earliest ECG change (serum potassium 5.5–6 mEq/L; mmol/L) is peaked T waves. The sequence of changes with further increases in serum potassium concentration is widening of the PR interval, loss of the P wave, widening of the QRS complex, and merging of the QRS complex with the T wave resulting in a sine-wave pattern.

Treatment

- Treatment depends on the desired rapidity and degree of lowering and the patient's clinical condition (**Figure 76-4**, **Table 76-6**).
- Calcium administration rapidly reverses ECG manifestations and arrhythmias, but it does not lower serum potassium concentrations. Calcium is short acting and therefore must be repeated if signs or symptoms recur.
- Rapid correction of hyperkalemia requires administration of drugs that shift potassium intracellularly (eg, insulin and dextrose, sodium bicarbonate, or albuterol).
- **Sodium polystyrene sulfonate** is a cation-exchange resin suitable for asymptomatic patients with mild-to-moderate hyperkalemia. Each gram of resin exchanges 1 mEq (1 mmol) of sodium for 1 mEq (1 mmol) of potassium. The sorbitol component promotes excretion of exchanged potassium by inducing diarrhea. The oral route is better tolerated and more effective than the rectal route.

FIGURE 76-4

Treatment approach for hyperkalemia. Serum potassium of 5.0 mEq/L is equivalent to 5.0 mmol/L.

image

TABLE 76-6

Therapeutic Alternatives for the Management of Hyperkalemia

Medication	Dose	Route of Administration	Onset/Duration of Action	Acuity	Mechanism of Action	Expected Result
Calcium	1 g	IV over 5–10 minutes	1–2 minutes/10–30 minutes	Acute	Raises cardiac threshold potential	Reverses electrocardiographic effects
Furosemide	20–40 mg	IV	5–15 minutes/4–6 hours	Acute	Inhibits renal Na^+ reabsorption	Increased urinary K^+ loss
Regular insulin	5–10 units	IV or SC	30 minutes/2–6 hours	Acute	Stimulates intracellular K^+ uptake	Intracellular K^+ redistribution
Dextrose 10%	1000 mL (100 g)	IV over 1–2 hours	30 minutes/2–6 hours	Acute	Stimulates insulin release	Intracellular K^+ redistribution
Dextrose 50%	50 mL (25 g)	IV over 5 minutes	30 minutes/2–6 hours	Acute	Stimulates insulin release	Intracellular K^+ redistribution
Sodium bicarbonate	50–100 mEq (50–100 mmol)	IV over 2–5 minutes	30 minutes/2–6 hours	Acute	Raises serum pH	Intracellular K^+ redistribution
Albuterol	10–20 mg	Nebulized over 10 minutes	30 minutes/1–2 hours	Acute	Stimulates intracellular K^+ uptake	Intracellular K^+ redistribution
Hemodialysis	4 hours	N/A	Immediate/variable	Acute	Removal from serum	Increased K^+ elimination
Sodium polystyrene sulfonate	15–60 g	Oral or rectal	1 hour/variable	Nonacute	Resin exchanges Na^+ for K^+	Increased K^+ elimination
Patiromer	8.4–25.2 g	Oral	Hours/variable	Nonacute	Resin exchanges Ca^{++} for K^+	Increased K^+ elimination
Sodium zirconium cyclosilicate	5–15 g	Oral	1 hour/variable	Nonacute	Resin exchanges Na^+ for K^+	Increased K^+ elimination

DISORDERS OF MAGNESIUM HOMEOSTASIS

Hypomagnesemia (Serum Magnesium <1.4 mEq/L [<1.7 mg/dL; <0.70 mmol/L])

Pathophysiology

- Hypomagnesemia is usually associated with disorders of the intestinal tract or kidneys. Drugs (eg, aminoglycosides, amphotericin B, cyclosporine, diuretics, digitalis, and cisplatin) or conditions that interfere with intestinal absorption or increase renal excretion of magnesium can cause hypomagnesemia.
- Commonly associated with alcoholism.

Clinical Presentation

- Although typically asymptomatic, the dominant organ systems involved are the neuromuscular and cardiovascular systems. Symptoms include heart palpitations, tetany, twitching, and generalized convulsions.
- Ventricular arrhythmias are the most important and potentially life-threatening cardiovascular effect.
- ECG changes include widened QRS complexes and peaked T waves in mild deficiency. Prolonged PR intervals, progressive widening of the QRS complexes, and flattening of T waves occur in moderate-to-severe deficiency.
- Many electrolyte disturbances occur with hypomagnesemia, including hypokalemia and hypocalcemia.

Treatment

- The severity of magnesium depletion and the presence of symptoms dictate the route of magnesium supplementation. Intramuscular magnesium is painful and should be reserved for patients with severe hypomagnesemia and limited venous access. IV bolus injection is associated with flushing, sweating, and a sensation of warmth.
- The optimal oral magnesium regimen is unknown; 8–12 g of magnesium sulfate in divided doses over 24 hours followed by 4–6 g/day for 3–5 days is one widely accepted regimen when the serum magnesium concentration is greater than 1 mEq/L (1.2 mg/dL [0.5 mmol/L]). Sustained-release products are preferred due to improved patient compliance and less GI side effects (eg, diarrhea).
- Administer IV magnesium if serum concentrations are less than 1 mEq/L (<1.2 mg/dL [<0.5 mmol/L]) or if signs and symptoms are present regardless of serum concentration. Infuse 4–6 g of magnesium over 12–24 hours and repeat as needed to maintain serum concentrations above 1 mEq/L (1.2 mg/dL [0.5 mmol/L]). Continue until signs and symptoms resolve. Reduce magnesium dose by 25%–50% with renal insufficiency.

Hypermagnesemia (Serum Magnesium >1.8 mEq/L [>2.3 mg/dL; >0.9 mmol/L])

Pathophysiology

- Magnesium concentrations steadily increase as the GFR decreases below 30 mL/min/1.73 m^2 and is generally associated with advanced CKD.
- Other causes include magnesium-containing antacids in patients with renal insufficiency, enteral or parenteral nutrition in patients with multiorgan system failure, magnesium for treatment of eclampsia, lithium therapy, hypothyroidism, and Addison disease.

Clinical Presentation

- Symptoms are rare when the serum magnesium concentration is less than 4 mEq/L (<4.9 mg/dL [<2 mmol/L]).
- The sequence of neuromuscular signs as serum magnesium increases from 5 to 12 mEq/L (6.1–14.7 mg/dL [2.5–6 mmol/L]) is sedation, hypotonia, hyporeflexia, somnolence, coma, muscular paralysis, and, ultimately, respiratory depression.
- The sequence of cardiovascular signs as serum magnesium increases from 3 to 15 mEq/L (3.7–18.4 mg/dL [1.5–7.5 mmol/L]) is hypotension, cutaneous vasodilation, QT-interval prolongation, bradycardia, primary heart block, nodal rhythms, bundle branch block, QRS- and then PR-interval prolongation, complete heart block, and asystole.

Treatment

- IV calcium (100–200 mg of elemental calcium; eg, calcium gluconate 2 g IV) is indicated to antagonize the neuromuscular and cardiovascular effects of magnesium. Doses should be repeated as often as hourly in life-threatening situations.
- Forced diuresis with 0.45% NaCl and loop diuretics (eg, furosemide, 40 mg IV) can promote magnesium elimination in patients with normal renal function or stage 1, 2, or 3 CKD. In dialysis patients, change to a magnesium-free dialysate.

EVALUATION OF THERAPEUTIC OUTCOMES

- The primary end point for monitoring treatment of fluid and electrolyte disorders is the correction of the abnormal serum electrolyte. In general, monitoring is initially performed at frequent intervals and, as homeostasis is restored, subsequently performed at less frequent intervals.
- Monitor all electrolytes as individual electrolyte abnormalities typically coexist with another abnormality (eg, hypomagnesemia with hypokalemia and hypocalcemia, or hyperphosphatemia with hypocalcemia).
- Monitor patients for resolution of clinical manifestations of electrolyte disturbances and for treatment-related complications.

See Chapter 66, Disorders of Sodium and Water Homeostasis, authored by Katherine H. Chessman and Jason Haney; Chapter 67, Disorders of Calcium and Phosphorus Homeostasis, authored by Amy Barton Pai and Angela L. Bingham; and Chapter 68, Disorders of Potassium and Magnesium Homeostasis, authored by Rachel W. Flurie, for a more detailed discussion of this topic.