

CHAPTER 35

Sodium Disorders

The kidney regulates sodium balance and is the principal site of sodium excretion. Sodium is unique among electrolytes because **water balance**, not sodium balance, usually determines its concentration. When the sodium concentration increases,

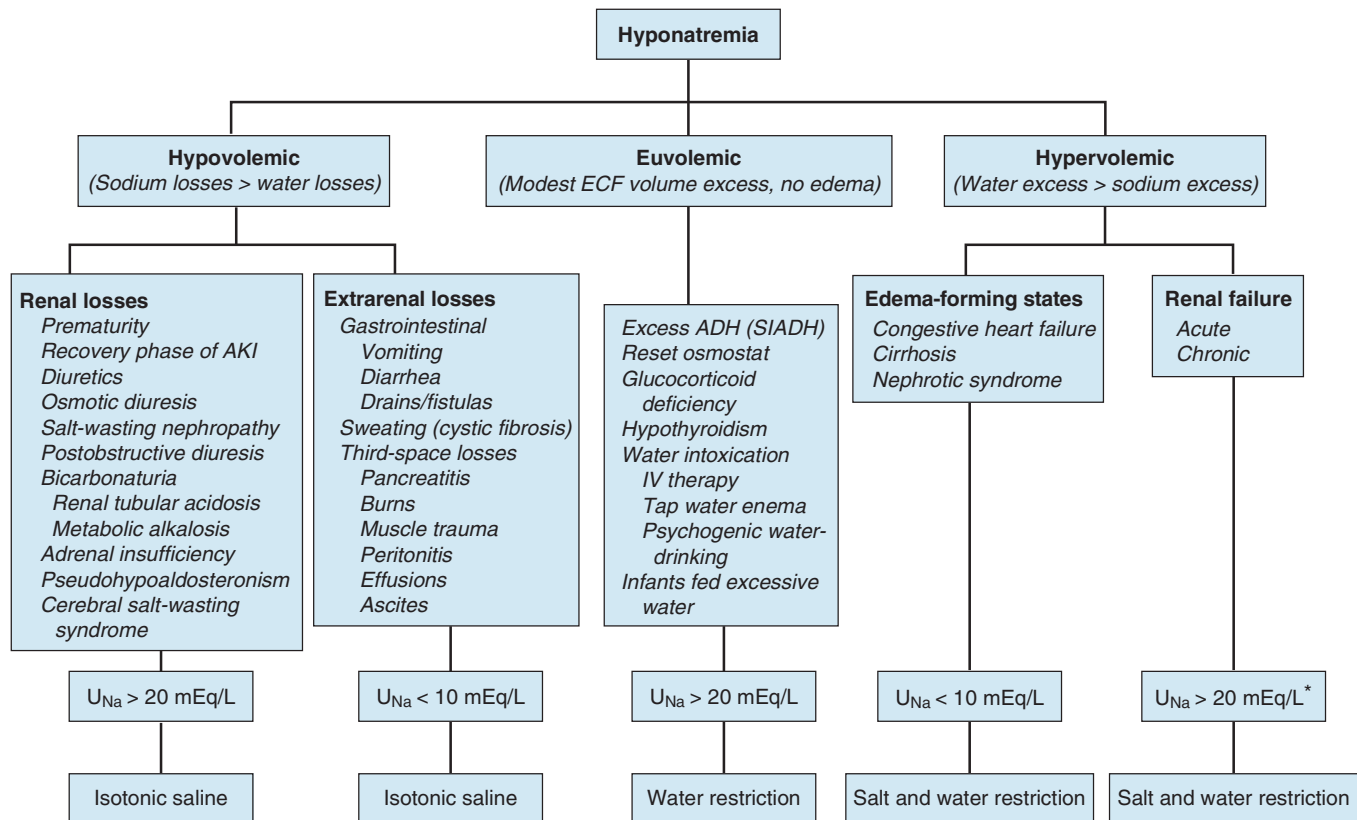


FIGURE 35.1 Classification, diagnosis, and treatment of hyponatremic states. *In water intoxication the urine sodium is often <20mEq/L. †Urinary sodium is <10mEq/L in acute renal failure secondary to glomerular disease. ADH, Antidiuretic hormone; AKI, acute kidney injury; ECF, extracellular fluid; IV, intravenous; SIADH, syndrome of inappropriate antidiuretic hormone secretion. (Modified from Berl T, Anderson RJ, McDonald KM, et al. Clinical disorders of water metabolism. *Kidney Int.* 1976;10:117–132 [fig. 2].)

the resultant higher plasma osmolality causes increased thirst and increased secretion of antidiuretic hormone (ADH), which leads to renal conservation of water. Both of these mechanisms increase the water content of the body, and the sodium concentration returns to normal. During hyponatremia, the fall in plasma osmolality decreases ADH secretion, and consequent renal water excretion leads to an increase in the sodium concentration. Although water balance is usually regulated by osmolality, volume depletion also stimulates thirst, ADH secretion, and renal conservation of water. In fact, volume depletion takes precedence over osmolality; volume depletion stimulates ADH secretion, even if a patient has hyponatremia.

The excretion of sodium by the kidney is not determined by the plasma osmolality. The patient's effective plasma volume regulates the amount of sodium in the urine through a variety of regulatory systems, including the renin-angiotensin-aldosterone system. In hyponatremia or hypernatremia, the underlying pathophysiology determines the urinary sodium concentration, not the serum sodium concentration.

HYPONATREMIA

Etiology

Different mechanisms can cause hyponatremia (Fig. 35.1). **Pseudohyponatremia** is a laboratory artifact that is present when the plasma contains high concentrations of protein or

lipid. It does not occur when a direct ion-selective electrode determines the sodium concentration, a technique that is increasingly used in clinical laboratories. In true hyponatremia, the *measured* osmolality is low, whereas it is normal in pseudohyponatremia. **Hyperosmolality**, resulting from mannitol infusion or hyperglycemia, causes a low serum sodium concentration, because water moves down its osmotic gradient from the intracellular space into the extracellular space, diluting the sodium concentration. For every 100mg/dL increment of the serum glucose, the serum sodium decreases by 1.6mEq/L. Because the manifestations of hyponatremia are due to the low plasma osmolality, patients with hyponatremia caused by hyperosmolality do not have symptoms of hyponatremia and do not require the correction of hyponatremia.

Classification of true hyponatremia is based on the patient's volume status (see Fig. 35.1). In **hypovolemic hyponatremia**, the child has lost sodium from the body. Water balance may be positive or negative, but there has been a higher net sodium loss than water loss; this is often due to oral or intravenous (IV) water intake, with water retention by the kidneys to compensate for the intravascular volume depletion. If the sodium loss is due to a nonrenal disease (e.g., diarrhea), the urine sodium concentration is very low, as the kidneys attempt to preserve the intravascular volume by conserving sodium. In renal diseases, the urine sodium is inappropriately elevated.

Patients with hyponatremia and no evidence of volume overload or volume depletion have **euvolemic hyponatremia**.

These patients typically have an excess of total body water and a slight decrease in total body sodium. Some of these patients have an increase in weight, implying that they are volume overloaded. Nevertheless, they usually appear normal or have only subtle signs of fluid overload. In the **syndrome of inappropriate ADH (SIADH)**, there is secretion of ADH that is not inhibited by either low serum osmolality or expanded intravascular volume. Retention of water causes hyponatremia, and the expansion of the intravascular volume results in an increase in renal sodium excretion. SIADH is associated with physiologic stress, pneumonia, mechanical ventilation, meningitis, and other central nervous system disorders (trauma). Ectopic (tumor) production of ADH is rare in children. SIADH should be distinguished from **cerebral salt wasting**, which is a form of hypovolemic hyponatremia often associated with tuberculosis meningitis or intracranial hemorrhage. Infants can develop euvolemic hyponatremia as a result of excessive water consumption or inappropriately diluted formula.

In **hypervolemic hyponatremia**, there is an excess of total body water and sodium, although the increase in water is greater than the increase in sodium. In renal failure, there is an inability to excrete sodium or water; the urine sodium may be low or high, depending on the cause of the renal insufficiency. In other causes of hypervolemic hyponatremia, there is a decrease in the effective blood volume because of either third space fluid loss or poor cardiac output (see Chapter 145). In response to the low effective blood volume, ADH causes renal water retention, and the kidneys also retain sodium, which leads to a low urine sodium concentration. The patient's serum sodium concentration decreases when water intake exceeds sodium intake, and ADH prevents the normal loss of excess water.

Clinical Manifestations

Hyponatremia causes a fall in the osmolality of the extracellular space. Because the intracellular space then has a higher osmolality, water moves from the extracellular space to the intracellular space to maintain osmotic equilibrium. The increase in intracellular water may cause cells to swell. **Brain cell swelling** is responsible for most of the symptoms of hyponatremia. Neurologic symptoms of hyponatremia include anorexia, nausea, emesis, malaise, lethargy, confusion, agitation, headache, seizures, coma, and decreased reflexes. Patients may develop hypothermia, Cheyne-Stokes respirations, muscle cramps, and weakness. Symptoms are more severe when hyponatremia develops rapidly; chronic hyponatremia can be asymptomatic because of a compensatory decrease in brain cell osmolality, which limits cerebral swelling.

Treatment

Rapid correction of hyponatremia can produce **central pontine myelinolysis**. Avoiding more than a 10 mEq/L increase in the serum sodium every 24 hours is prudent, especially in chronic hyponatremia. Treatment of hypovolemic hyponatremia requires administration of IV fluids with sodium to provide maintenance requirements and deficit correction, and to replace ongoing losses (see Chapter 33). For children with SIADH, water restriction is the cornerstone of therapy, although vaptan drugs, which are ADH antagonists, have a role in some patients. Children with hyponatremia secondary to hypothyroidism or cortisol deficiency need specific

hormone replacement. **Acute water intoxication** rapidly self-corrects with the transient restriction of water intake, which is followed by introduction of a normal diet. Treatment of hypervolemic hyponatremia centers on restriction of water and sodium intake, but disease-specific measures, such as dialysis in renal failure, may also be necessary.

Emergency treatment of **symptomatic hyponatremia**, such as seizures, uses IV hypertonic saline to rapidly increase the serum sodium concentration, which leads to a decrease in brain edema. One milliliter per kilogram of 3% sodium chloride increases the serum sodium by approximately 1 mEq/L. A child often improves after receiving 4–6 mL/kg of 3% sodium chloride.

HYPERNATREMIA

Etiology

There are three basic mechanisms of hypernatremia (Fig. 35.2). **Sodium intoxication** is frequently iatrogenic in a hospital setting, resulting from correction of metabolic acidosis with sodium bicarbonate. In hyperaldosteronism, there is renal retention of sodium and resultant hypertension; the hypernatremia is mild.

Hypernatremia resulting from water losses develops only if the patient does not have access to water or cannot drink adequately because of neurologic impairment (adipsia), emesis, or anorexia. Infants are at high risk because of their inability to control their own water intake. Ineffective breast-feeding, often in a primiparous mother, can cause severe hypernatremic dehydration. High insensible losses of water are especially common in premature infants; the losses increase further as a result of radiant warmers or phototherapy for hyperbilirubinemia. Children with extrarenal causes of water loss have high levels of ADH and very concentrated urine.

Children with diabetes insipidus have inappropriately diluted urine. Hereditary **nephrogenic diabetes insipidus** causes massive urinary water losses. Because it is most commonly an X-linked disorder due to a mutation in the gene for the ADH receptor, it usually occurs in males, who may have episodes of severe hypernatremic dehydration and failure to thrive. *Acquired nephrogenic diabetes insipidus* may be secondary to interstitial nephritis, sickle cell disease, hypercalcemia, hypokalemia, or medications (lithium). If the defect is due to **central diabetes insipidus**, urine output decreases and urine osmolality increases in response to administration of an ADH analog. Central causes of ADH deficiency include tumor, infarction, or trauma. There is no response to an ADH analog in a child with nephrogenic diabetes insipidus.

Diarrhea results in sodium and water depletion. Most children with gastroenteritis do not develop hypernatremia because they drink enough hypotonic fluid to compensate at least partially for stool water losses. Hypernatremia is most likely in a child with diarrhea who has inadequate intake because of emesis, lack of access to water, or anorexia. Some renal diseases, including obstructive uropathy, renal dysplasia, and juvenile nephronophthisis, can cause losses of sodium and water, potentially producing hypernatremia if the patient consumes insufficient water.

In situations with combined sodium and water deficits, analysis of the urine differentiates renal and nonrenal etiologies. When the losses are extrarenal, the kidney responds to volume depletion with low urine volume, a concentrated

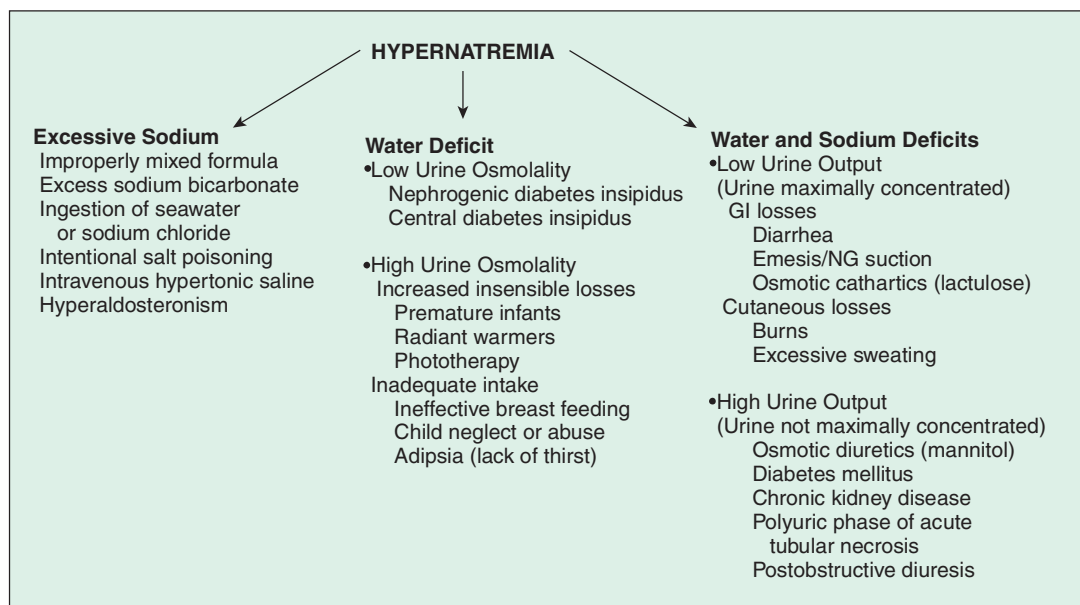


FIGURE 35.2 Differential diagnosis of hypernatremia by mechanism. GI, Gastrointestinal; NG, nasogastric.

urine, and sodium retention (urine sodium <10 mEq/L). With renal causes, the urine volume is usually high, the urine is not maximally concentrated, and the urine sodium may be inappropriately elevated.

Clinical Manifestations

Most children with hypernatremia are dehydrated and have the typical signs and symptoms of dehydration (see [Chapter 33](#)). Children with hypernatremic dehydration tend to have better preservation of intravascular volume owing to the shift of water from the intracellular space to the extracellular space. Hypernatremic infants potentially become more dehydrated before seeking medical attention. Probably because of intracellular water loss, the pinched abdominal skin of a dehydrated, hypernatremic infant has a *doughy* feel.

Hypernatremia, even without dehydration, causes central nervous system symptoms that tend to parallel the degree of sodium elevation and the acuity of the increase. Patients are irritable, restless, weak, and lethargic. Some infants have a high-pitched cry and hyperpnea; hypernatremia may cause fever. Alert patients are very thirsty, although nausea may be present.

Brain hemorrhage is the most devastating consequence of hypernatremia. As the extracellular osmolality increases, water moves out of brain cells, resulting in a decrease in brain volume. This decrease in volume can result in tearing of intracerebral veins and bridging blood vessels as the brain moves away from the skull and the meninges. Patients may have subarachnoid, subdural, and parenchymal hemorrhage. Seizures and coma are possible sequelae of the hemorrhage.

Treatment

As hypernatremia develops, the brain generates idiogenic osmoles to increase the intracellular osmolality and prevent the loss of brain water. This mechanism is not instantaneous and is most prominent when hypernatremia has developed gradually. If the serum sodium concentration is lowered

rapidly, there is movement of water from the serum into the brain cells to equalize the osmolality in the two compartments. The resultant brain swelling manifests as seizures or coma. Because of these dangers, hypernatremia should be corrected slowly. The goal is to decrease the serum sodium by less than 12 mEq/L every 24 hours (see [Fig. 33.1](#)). The most important components of correcting moderate or severe hypernatremia are restoring the effective intravascular volume and then frequently monitoring the serum sodium to allow adjustment of fluid therapy and to provide adequate correction that is neither too slow nor too fast.

In a child with hypernatremic dehydration, as in any child with dehydration, the first priority is restoration of intravascular volume with isotonic fluid. [Fig. 33.1](#) outlines a general approach for correcting hypernatremic dehydration secondary to gastroenteritis. If the hypernatremia and dehydration are secondary to water loss, as occurs with diabetes insipidus, a more hypotonic IV fluid is appropriate. A child with central diabetes insipidus should receive an ADH analog to prevent further excessive water loss. A child with nephrogenic diabetes insipidus requires a urine replacement solution to offset ongoing water losses. Chronically, reduced sodium intake, thiazide diuretics, and nonsteroidal antiinflammatory drugs can decrease water losses in nephrogenic diabetes insipidus.

Acute, severe hypernatremia, usually secondary to sodium administration, can be corrected more rapidly because idiogenic osmoles have not had time to accumulate; this balances the high morbidity and mortality from severe, acute hypernatremia with the dangers of overly rapid correction. When hypernatremia is due to sodium intoxication, and the hypernatremia is severe, it may be impossible to administer enough water to rapidly correct the hypernatremia without worsening volume overload. Some patients require the use of a loop diuretic or dialysis.

PEARLS FOR PRACTITIONERS

See *Fluids and Electrolytes: Pearls for Practitioners* at the end of this section.

CHAPTER 36

Potassium Disorders

The kidneys are the principal regulator of potassium balance, adjusting excretion based on intake. Factors affecting renal potassium excretion include aldosterone, acid-base status, serum potassium concentration, and renal function. The intracellular potassium concentration is approximately 30 times the extracellular potassium concentration. A variety of conditions alter the distribution of potassium between the intracellular and extracellular compartments, potentially causing either hypokalemia or hyperkalemia. The plasma concentration does not always reflect the total body potassium content.

HYPOKALEMIA

Etiology

Hypokalemia is common in children, with most cases related to gastroenteritis. Spurious hypokalemia occurs in

patients with leukemia and elevated white blood cell counts if plasma for analysis is left at room temperature, permitting the white blood cells to take up potassium from the plasma. There are four basic mechanisms of hypokalemia (Table 36.1). Low intake, nonrenal losses, and renal losses all are associated with total body potassium depletion. With a **transcellular shift**, total body potassium is normal unless there is concomitant potassium depletion secondary to other factors.

The transcellular shift of potassium after initiation of insulin therapy in children with diabetic ketoacidosis (see Chapter 171) can be dramatic. These patients have reduced total body potassium because of urinary losses, but they often have a normal serum potassium level before insulin therapy from a transcellular shift into the extracellular space secondary to insulin deficiency and metabolic acidosis. Children receiving aggressive doses of β -adrenergic agonists (albuterol) for asthma can develop hypokalemia resulting from the intracellular movement of potassium. Poor intake is an unusual cause of hypokalemia, unless it is also associated with significant weight loss (anorexia nervosa).

TABLE 36.1 Causes of Hypokalemia

Spurious	With metabolic alkalosis
High white blood cell count	Low urine chloride
Transcellular shifts	Emesis/nasogastric suction
Alkalemia	Pyloric stenosis
Insulin	Chloride-losing diarrhea
β -adrenergic agonists	Cystic fibrosis
Drugs/toxins (theophylline, barium, toluene)	Low-chloride formula
Hypokalemic periodic paralysis	Posthypercapnia
Refeeding syndrome	Previous loop or thiazide diuretic use
Decreased intake	High urine chloride and normal blood pressure
Extrarenal losses	Gitelman syndrome
Diarrhea	Bartter syndrome
Laxative abuse	Loop and thiazide diuretics
Sweating	High urine chloride and high blood pressure
Renal losses	Adrenal adenoma or hyperplasia
With metabolic acidosis	Glucocorticoid-remediable aldosteronism
Distal RTA	Renovascular disease
Proximal RTA	Renin-secreting tumor
Ureterosigmoidostomy	17 α -hydroxylase deficiency
Diabetic ketoacidosis	11 β -hydroxylase deficiency
Without specific acid-base disturbance	Cushing syndrome
Tubular toxins (amphotericin, cisplatin, aminoglycosides)	11 β -hydroxysteroid dehydrogenase deficiency
Interstitial nephritis	Licorice ingestion
Diuretic phase of acute tubular necrosis	Liddle syndrome
Postobstructive diuresis	
Hypomagnesemia	
High urine anions (e.g., penicillin or penicillin derivatives)	

RTA, Renal tubular acidosis.

TABLE 36.2 Bartter and Gitelman Syndromes

	TYPE 1 BARTTER SYNDROME	TYPE 2 BARTTER SYNDROME	TYPE 3 BARTTER SYNDROME	TYPE 4 BARTTER SYNDROME	TYPE 5 BARTTER SYNDROME	GITELMAN SYNDROME
Inheritance	AR	AR	AR	AR	X-linked	AR
Gene	<i>SLC12A1</i>	<i>KCNJ1</i>	<i>CLCNKB</i>	<i>BSND</i> (type 4a) or <i>CLCNKA</i> and <i>CLCNKB</i> (type 4b)	<i>MAGED2</i>	<i>SLC12A3</i>
Onset	Prenatal, postnatal	Prenatal, postnatal	Postnatal (prenatal less commonly)	Prenatal, postnatal	Prenatal	Adolescent, adult
Features	Polyhydramnios, prematurity, nephrocalcinosis	Polyhydramnios, prematurity, nephrocalcinosis, transient postnatal hyperkalemia	Term birth (polyhydramnios and premature less commonly), variable nephrocalcinosis and hypomagnesemia	Polyhydramnios, prematurity, sensorineural hearing loss, variable nephrocalcinosis and hypomagnesemia	Massive polyhydramnios, nephrocalcinosis, transient: resolves in infancy	Hypomagnesemia and hypocalciuria

AR, Autosomal recessive.

Diarrhea has a high concentration of potassium, and the resulting hypokalemia is usually associated with a metabolic acidosis secondary to stool losses of bicarbonate. With emesis or nasogastric suction, there is gastric loss of potassium, but this is fairly minimal given the low potassium content of gastric fluid (~10 mEq/L). More important is the gastric loss of hydrochloride, leading to a metabolic alkalosis and a state of volume depletion. Metabolic alkalosis and volume depletion increase urinary losses of potassium.

Urinary potassium wasting may be accompanied by a metabolic acidosis (proximal or distal renal tubular acidosis; see Chapter 37). Loop and thiazide diuretics lead to hypokalemia and a metabolic alkalosis. **Bartter syndrome** and **Gitelman syndrome** are autosomal recessive disorders resulting from defects in tubular transporters and are associated with hypokalemia and a metabolic alkalosis. Bartter syndrome is usually associated with hypercalciuria, often with nephrocalcinosis; children with Gitelman syndrome have low urinary calcium losses, but hypomagnesemia secondary to urinary losses (Table 36.2).

In the presence of a high aldosterone level, there is urinary loss of potassium, hypokalemia, and a metabolic alkalosis. There also is renal retention of sodium, leading to hypertension. A variety of genetic and acquired disorders can cause high aldosterone levels. **Liddle syndrome**, an autosomal dominant disorder caused by constitutively active sodium channels, has the same clinical features as hyperaldosteronism, but the serum aldosterone level is low.

Clinical Manifestations

The heart and skeletal muscle are especially vulnerable to hypokalemia. **Electrocardiographic (ECG) changes** include a flattened T wave, a depressed ST segment, and the appearance of a U wave, which is located between the T wave (if still visible) and P wave. Ventricular fibrillation and torsades de pointes may occur, although usually only in the context of underlying heart disease.

The clinical consequences in skeletal muscle include muscle weakness and cramps. **Paralysis** is a possible complication

(generally only at potassium levels <2.5 mEq/L). Paralysis usually starts with the legs, followed by the arms. Respiratory paralysis may require mechanical ventilation.

Some hypokalemic patients develop **rhabdomyolysis**, especially following exercise. Hypokalemia slows gastrointestinal motility; potassium levels less than 2.5 mEq/L may cause an ileus. Hypokalemia impairs bladder function, potentially leading to urinary retention. Hypokalemia causes polyuria by producing secondary nephrogenic diabetes insipidus. Chronic hypokalemia may cause kidney damage, including interstitial nephritis and renal cysts.

Diagnosis

It is important to review the child's diet, history of gastrointestinal losses, and medications. Emesis and diuretic use can be surreptitious. The presence of hypertension suggests excess mineralocorticoids. Concomitant electrolyte abnormalities are useful clues. The combination of hypokalemia and metabolic acidosis is characteristic of diarrhea, and proximal or distal renal tubular acidosis. A concurrent metabolic alkalosis is characteristic of gastric losses, aldosterone excess, diuretics, Bartter syndrome, or Gitelman syndrome.

Treatment

Factors that influence the therapy of hypokalemia include the potassium level, clinical symptoms, renal function, presence of transcellular shifts of potassium, ongoing losses, and the patient's ability to tolerate oral potassium. Severe, symptomatic hypokalemia requires aggressive treatment. Supplementation is more cautious if renal function is decreased because of the kidney's limited ability to excrete excessive potassium. The plasma potassium level does not always provide an accurate estimation of the total body potassium deficit because there may be shifts of potassium from the intracellular space to the plasma. Clinically, this shift occurs most commonly with metabolic acidosis and as a result of the insulin deficiency of diabetic ketoacidosis; the plasma potassium underestimates the degree of total body potassium depletion. When these

TABLE 36.3 Causes of Hyperkalemia

Spurious laboratory value	Acquired Addison disease
Hemolysis	21-hydroxylase deficiency
Tissue ischemia during blood drawing	3 β -hydroxysteroid-dehydrogenase deficiency
Thrombocytosis	Lipoid congenital adrenal hyperplasia
Leukocytosis	Adrenal hypoplasia congenita
Increased intake	Aldosterone synthase deficiency
IV or PO	Adrenoleukodystrophy
Blood transfusions	Hyporeninemic hypoaldosteronism
Transcellular shifts	Urinary tract obstruction
Acidemia	Sickle cell disease
Rhabdomyolysis	Kidney transplant
Tumor lysis syndrome	Lupus nephritis
Tissue necrosis	Renal tubular disease
Hemolysis/hematomas/gastrointestinal bleeding	Pseudohypoaldosteronism type 1
Succinylcholine	Pseudohypoaldosteronism type 2
Digitalis intoxication	Urinary tract obstruction
Fluoride intoxication	Sickle cell disease
β -adrenergic blockers	Kidney transplant
Exercise	Medications
Hyperosmolality	ACE inhibitors
Insulin deficiency	Angiotensin II blockers
Malignant hyperthermia	Potassium-sparing diuretics
Hyperkalemic periodic paralysis	Cyclosporine
Decreased excretion	NSAIDs
Renal failure	Trimethoprim
Primary adrenal disease	

ACE, Angiotensin-converting enzyme; IV, intravenous; NSAIDs, nonsteroidal antiinflammatory drugs; PO, oral.

problems are corrected, potassium moves into the intracellular space, and these patients require more potassium supplementation to correct the hypokalemia. Patients who have ongoing losses of potassium need correction of the deficit and replacement of the ongoing losses.

Because of the risk of hyperkalemia, intravenous (IV) potassium should be used cautiously. Oral potassium is safer in nonurgent situations. The dose of IV potassium is 0.5–1 mEq/kg, usually given over 1 hour. The adult maximum dose is 40 mEq. Conservative dosing is generally preferred. For patients with excessive urinary losses, potassium-sparing diuretics are effective. When hypokalemia, metabolic alkalosis, and volume depletion are present, restoration of intravascular volume decreases urinary potassium losses.

HYPERKALEMIA

Etiology

Three basic mechanisms cause hyperkalemia (Table 36.3). In the individual patient, the etiology is sometimes multifactorial.

Factitious hyperkalemia is usually due to hemolysis during phlebotomy, but it can be the result of prolonged tourniquet application or fist clenching during phlebotomy, which causes local potassium release from muscle. Falsely elevated serum potassium levels can occur when serum levels are measured in patients with markedly elevated white blood cell or platelet counts; a promptly analyzed plasma sample usually provides an accurate result.

Because of the kidney's ability to excrete potassium, it is unusual for excessive intake, by itself, to cause hyperkalemia. This mechanism can occur in a patient who is receiving large quantities of IV or oral potassium for excessive losses that are no longer present. Frequent or rapid blood transfusions can increase the potassium level acutely secondary to the high potassium content of stored blood. Increased intake may precipitate hyperkalemia if there is an underlying defect in potassium excretion.

The intracellular space has a high potassium concentration, so a **shift of potassium from the intracellular space** to the extracellular space can have a significant impact on the plasma

potassium. This shift occurs with acidosis, cell destruction (rhabdomyolysis or tumor lysis syndrome), insulin deficiency, medications (succinylcholine, β blockers), malignant hyperthermia, and hyperkalemic periodic paralysis.

Hyperkalemia secondary to decreased excretion occurs with renal insufficiency. The risk of hyperkalemia secondary to medications that decrease renal potassium excretion is greatest in patients with underlying renal insufficiency.

Aldosterone deficiency or unresponsiveness to aldosterone causes hyperkalemia, often with associated metabolic acidosis (see [Chapter 37](#)) and hyponatremia. A form of congenital adrenal hyperplasia, **21-hydroxylase deficiency**, is the most frequent cause of aldosterone deficiency in children. Untreated patients have hyperkalemia, metabolic acidosis, hyponatremia, and volume depletion.

Renin, via angiotensin II, stimulates aldosterone production. A deficiency in renin, resulting from kidney damage, can lead to decreased aldosterone production. These patients typically have hyperkalemia and a metabolic acidosis, without hyponatremia. Some patients have impaired renal function, partially accounting for the hyperkalemia, but the impairment in potassium excretion is more extreme than expected for the degree of renal insufficiency.

Children with **pseudohypoaldosteronism (PHA) type 1** have hyperkalemia, metabolic acidosis, and salt wasting, leading to hyponatremia and volume depletion; aldosterone levels are elevated. In the autosomal recessive variant, there is a defect in the renal sodium channel that is normally activated by aldosterone. In the autosomal dominant form, patients have a defect in the aldosterone receptor, and the disease is milder, often remitting in adulthood. **PHA type 2**, also called **Gordon syndrome**, is an autosomal dominant disorder characterized by hypertension secondary to salt retention and impaired excretion of potassium and acid, leading to hyperkalemia and metabolic acidosis. PHA type 2 responds to a thiazide diuretic.

Clinical Manifestations

The most important effects of hyperkalemia are due to the role of potassium in membrane polarization. The cardiac conduction system is usually the dominant concern. **ECG changes** begin with peaking of the T waves. As the potassium level increases, an increased P-R interval, flattening of the P wave, and widening of the QRS complex occur; this eventually can progress to ventricular fibrillation. Asystole also may occur. Some patients have paresthesias, weakness, and tingling, but cardiac toxicity usually precedes these clinical symptoms.

Diagnosis

The etiology of hyperkalemia is often readily apparent. Spurious hyperkalemia is common in children, so a repeat potassium level is often appropriate. If there is a significant elevation of the white blood cells or platelets, the repeat sample should be from plasma that is evaluated promptly. Initially, the history should focus on potassium intake, risk factors for transcellular shifts of potassium, medications that cause hyperkalemia, and the presence of signs of renal insufficiency, such as oliguria or an abnormal urinalysis. Initial laboratory evaluation should include serum creatinine and assessment of acid-base status. Many causes of hyperkalemia, such as renal insufficiency and

TABLE 36.4 Treatment of Hyperkalemia

Rapidly decrease the risk of life-threatening arrhythmias
Shift potassium intracellularly
Sodium bicarbonate administration (IV)
Insulin and glucose (IV)
β -agonist (albuterol via nebulizer)
Cardiac membrane stabilization
IV calcium
Remove potassium from the body
Loop diuretic (IV or PO)
Sodium polystyrene and other potassium binding agents (PO or rectal)
Dialysis

IV, Intravenous; PO, oral.

aldosterone insufficiency or resistance, cause a metabolic acidosis. Cell destruction, as seen in rhabdomyolysis or tumor lysis syndrome, can cause concomitant hyperphosphatemia, hyperuricemia, and an elevated serum lactate dehydrogenase.

Treatment

The plasma potassium level, the ECG, and the risk of the problem worsening determine the aggressiveness of the therapeutic approach. A high serum potassium level with ECG changes requires more vigorous treatment. An additional source of concern is a patient with increasing plasma potassium despite minimal intake. This situation can occur if there is cellular release of potassium (tumor lysis syndrome), especially in the setting of diminished excretion (renal failure).

The first action in a child with a concerning elevation of plasma potassium is to stop all sources of additional potassium (oral and IV). If the potassium level is greater than 6.5 mEq/L, an ECG should be obtained to help assess the urgency of the situation. Therapy of hyperkalemia has two basic goals:

1. Prevent life-threatening arrhythmias
2. Remove potassium from the body ([Table 36.4](#))

Treatments that acutely prevent arrhythmias all work quickly (within minutes), but do not remove potassium from the body.

Long-term management of hyperkalemia includes reducing intake via dietary changes and eliminating or reducing medications that cause hyperkalemia. Some patients require medications, such as sodium polystyrene sulfonate and loop or thiazide diuretics, to increase potassium losses. The disorders that are due to a deficiency in aldosterone respond to replacement therapy with fludrocortisone, which is a mineralocorticoid.

PEARLS FOR PRACTITIONERS

See *Fluids and Electrolytes: Pearls for Practitioners* at the end of this section.

CHAPTER 37

Acid-Base Disorders

Close regulation of pH is necessary for cellular enzymes and other metabolic processes, which function optimally at a normal pH (7.35–7.45). Chronic, mild derangements in acid-base status may interfere with normal growth and development, whereas acute, severe changes in pH can be fatal. Control of acid-base balance depends on the kidneys, the lungs, and the intracellular and extracellular buffers.

The lungs and kidneys maintain a normal acid-base balance. Carbon dioxide (CO_2) generated during normal metabolism is a weak acid. The lungs prevent an increase in the partial pressure of CO_2 (PCO_2) in the blood by excreting the CO_2 . Production of CO_2 varies depending on the body's metabolic needs. The rapid pulmonary response to changes in CO_2 concentration occurs via central sensing of the PCO_2 , and a subsequent increase or decrease in ventilation to maintain a normal PCO_2 (35–45 mm Hg).

The kidneys excrete endogenous acids. An adult normally produces about 1–2 mEq/kg per day of hydrogen ions, whereas a child produces 2–3 mEq/kg per day. The hydrogen ions from endogenous acid production are neutralized by bicarbonate, potentially causing the bicarbonate concentration to fall. The kidneys regenerate this bicarbonate by secreting hydrogen ions, maintaining the serum bicarbonate concentration in the normal range (20–28 mEq/L).

CLINICAL ASSESSMENT OF ACID-BASE DISORDERS

Acidemia is a pH below normal (<7.35), and **alkalemia** is a pH above normal (>7.45). **Acidosis** is a pathologic process that causes an increase in the hydrogen ion concentration, and **alkalosis** is a pathologic process that causes a decrease in the hydrogen ion concentration. A **simple acid-base disorder** is a single primary disturbance. During a simple metabolic disorder, there is respiratory compensation; the PCO_2 decreases during metabolic acidosis and increases during metabolic alkalosis. With metabolic acidosis, the decrease in the pH increases the ventilatory drive, causing a decrease in the PCO_2 . The fall in the CO_2 concentration leads to an increase in the pH. This **appropriate respiratory compensation** for a metabolic process happens quickly and is complete within 12–24 hours.

During a primary respiratory process, there is metabolic compensation mediated by the kidneys. The kidneys respond to a respiratory acidosis by increasing hydrogen ion excretion, increasing bicarbonate generation, and raising the serum bicarbonate concentration. The kidneys increase bicarbonate excretion to compensate for a respiratory alkalosis; the serum bicarbonate concentration decreases. In contrast to a rapid respiratory compensation, it takes 3–4 days for the kidneys to complete **appropriate metabolic compensation**. However, there is a small and rapid compensatory change in the bicarbonate concentration during a primary respiratory process. The expected appropriate metabolic compensation for a respiratory disorder depends on whether the process is acute or chronic.

A **mixed acid-base disorder** is present when there is more than one primary acid-base disturbance. An infant with bronchopulmonary dysplasia may have respiratory acidosis from chronic lung disease and metabolic alkalosis from a diuretic used to treat the chronic lung disease. Formulas are available for calculating the appropriate metabolic or respiratory compensation for the six primary simple acid-base disorders (Table 37.1). Appropriate compensation is expected in a simple disorder; it is not optional. If a patient does not have appropriate compensation, a mixed acid-base disorder is present.

METABOLIC ACIDOSIS

Metabolic acidosis occurs frequently in hospitalized children; diarrhea is the most common cause. For a patient with an unknown medical problem, the presence of metabolic acidosis is often diagnostically helpful because it suggests a relatively narrow differential diagnosis (Table 37.2).

TABLE 37.1 Appropriate Compensation During Simple Acid-Base Disorders

DISORDER	EXPECTED COMPENSATION*
Metabolic acidosis	$\text{PCO}_2 = 1.5 \times [\text{HCO}_3^-] + 8 \pm 2$
Metabolic alkalosis	PCO_2 increases by 7 mm Hg for each 10 mEq/L increase in the serum $[\text{HCO}_3^-]$
Respiratory acidosis	
Acute	$[\text{HCO}_3^-]$ increases by 1 for each 10 mm Hg increase in the PCO_2
Chronic	$[\text{HCO}_3^-]$ increases by 3.5 for each 10 mm Hg increase in the PCO_2
Respiratory alkalosis	
Acute	$[\text{HCO}_3^-]$ falls by 2 for each 10 mm Hg decrease in the PCO_2
Chronic	$[\text{HCO}_3^-]$ falls by 4 for each 10 mm Hg decrease in the PCO_2

* $[\text{HCO}_3^-]$ is expressed in mEq/L.

TABLE 37.2 Causes of Metabolic Acidosis

NORMAL ANION GAP
Diarrhea
Renal tubular acidosis
Urinary tract diversions
Posthypocapnia
Ammonium chloride intake
INCREASED ANION GAP
Lactic acidosis (shock or inborn errors of metabolism)
Ketoacidosis (diabetic, starvation, or alcoholic)
Kidney failure
Poisoning (e.g., ethylene glycol, methanol, or salicylates)
Inborn errors of metabolism

Etiology

The plasma **anion gap** is useful for evaluating patients with metabolic acidosis. It divides patients into two diagnostic groups: normal anion gap and increased anion gap. The following formula determines the anion gap:

$$\text{Anion Gap} = \text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$$

A normal anion gap is 9 ± 4 mEq/L.

Normal anion gap metabolic acidosis occurs in the setting of diarrhea and renal tubular acidosis (RTA). Diarrhea causes a loss of bicarbonate from the body. The amount of bicarbonate lost in the stool depends on the volume of diarrhea and the bicarbonate concentration of the stool, which tends to increase with more severe diarrhea. Diarrhea often causes volume depletion because of losses of sodium and water, potentially exacerbating the acidosis by causing hypoperfusion (shock) and a lactic acidosis.

There are three forms of RTA:

1. Distal (type I)
2. Proximal (type II)
3. Hyperkalemic (type IV)

In distal RTA (dRTA), children may have accompanying hypokalemia, hypercalciuria, nephrolithiasis, and nephrocalcinosis; rickets is a less common finding. Failure to thrive, resulting from chronic metabolic acidosis, is the most common presenting complaint. Autosomal dominant (relatively mild) and autosomal recessive (more severe) forms of dRTA exist. Autosomal recessive dRTA is often associated with deafness secondary to a defect in the gene for an H^+ -ATPase that is present in the kidney and the inner ear. dRTA also may be secondary to medications or congenital or acquired renal disease. Patients with dRTA cannot acidify their urine and can have a urine pH greater than 5.5, despite metabolic acidosis.

Proximal RTA is rarely present in isolation. In most patients, proximal RTA is part of **Fanconi syndrome**, a generalized dysfunction of the proximal tubule. Along with renal wasting of bicarbonate, Fanconi syndrome causes glycosuria, aminoaciduria, and excessive urinary losses of phosphate and uric acid. The chronic hypophosphatemia is more clinically significant because it ultimately leads to rickets in children. Rickets or failure to thrive may be the presenting complaint. Fanconi syndrome is rarely an isolated genetic disorder, with pediatric cases usually secondary to an underlying genetic disorder, most commonly **cystinosis**. Medications, such as ifosfamide, deferasirox, or valproate, may cause Fanconi syndrome. The ability to acidify the urine is intact in proximal RTA, and untreated patients have a urine pH less than 5.5.

In **hyperkalemic RTA**, renal excretion of acid and potassium is impaired because of either an absence of aldosterone or an inability of the kidney to respond to aldosterone. In severe aldosterone deficiency, as occurs with congenital adrenal hyperplasia secondary to 21α -hydroxylase deficiency, the hyperkalemia and metabolic acidosis are accompanied by hyponatremia and volume depletion from renal salt wasting. Incomplete aldosterone deficiency causes less severe electrolyte disturbances; children may have isolated hyperkalemic RTA, hyperkalemia without acidosis, or isolated hyponatremia.

Distal and hyperkalemic RTA are similar in that distal tubular acidification is impaired. Conversely, in proximal

RTA, distal tubular acidification is intact, but leads to metabolic acidosis due to bicarbonate wasting.

Increased anion gap metabolic acidosis occurs with lactic acidosis, ketoacidosis, chronic renal failure, and toxic ingestions. Lactic acidosis most commonly occurs when inadequate oxygen delivery to the tissues leads to anaerobic metabolism and excess production of lactic acid. Lactic acidosis may be secondary to shock, severe anemia, or hypoxemia. Inborn errors of carbohydrate metabolism produce a severe lactic acidosis (see [Chapter 52](#)). In diabetes mellitus, inadequate insulin leads to hyperglycemia and diabetic ketoacidosis (see [Chapter 171](#)). Renal failure (see [Chapter 165](#)) causes metabolic acidosis because the kidneys are unable to excrete the acid produced by normal metabolism.

A variety of **toxic ingestions** cause metabolic acidosis. Acute **salicylate** intoxication occurs after a large overdose. Chronic salicylate intoxication is possible because of the gradual buildup of the drug. Patients may also have a respiratory alkalosis. Other symptoms of salicylate intoxication include fever, seizures, lethargy, and coma. Hyperventilation may be particularly marked. Tinnitus, vertigo, and hearing impairment are more likely with chronic salicylate intoxication. **Ethylene glycol**, a component of antifreeze, is converted in the liver to glyoxylic and oxalic acids, causing a severe metabolic acidosis. Excessive oxalate excretion causes calcium oxalate crystals to appear in the urine, and calcium oxalate precipitation in the kidney tubules can cause renal failure. The toxicity of **methanol** ingestion also depends on liver metabolism; formic acid is the toxic end product that causes the metabolic acidosis and other sequelae, which include damage to the optic nerve and central nervous system.

There are many **inborn errors of metabolism** that may cause metabolic acidosis (see [Section 10](#)). Metabolic acidosis may be due to excessive production of ketoacids, lactic acid, or other organic anions. Some patients may have accompanying hyperammonemia. In most patients, acidosis occurs only episodically during acute decompensations, which may be precipitated by the ingestion of specific dietary substrates (proteins), the stress of a mild illness (fasting, catabolism), or poor adherence with dietary or medical therapy.

Clinical Manifestations

The underlying disorder usually produces most of the signs and symptoms in children with a mild or moderate metabolic acidosis. The clinical manifestations of the acidosis are related to the degree of acidemia; patients with appropriate respiratory compensation and less severe acidemia have fewer manifestations than patients with a concomitant respiratory acidosis. At a serum pH less than 7.20, there is impaired cardiac contractility and an increased risk of arrhythmias, especially if underlying heart disease or other predisposing electrolyte disorders are present. With acidemia, there is a decrease in the cardiovascular response to catecholamines, potentially exacerbating hypotension in children with volume depletion or shock. Acidemia causes vasoconstriction of the pulmonary vasculature, which is especially problematic in neonates with primary pulmonary hypertension of the newborn (see [Chapter 61](#)). The normal respiratory response to metabolic acidosis—compensatory hyperventilation—may be subtle with mild metabolic acidosis, but it causes discernible increased respiratory effort with worsening acidemia. Chronic metabolic acidosis causes failure to thrive.

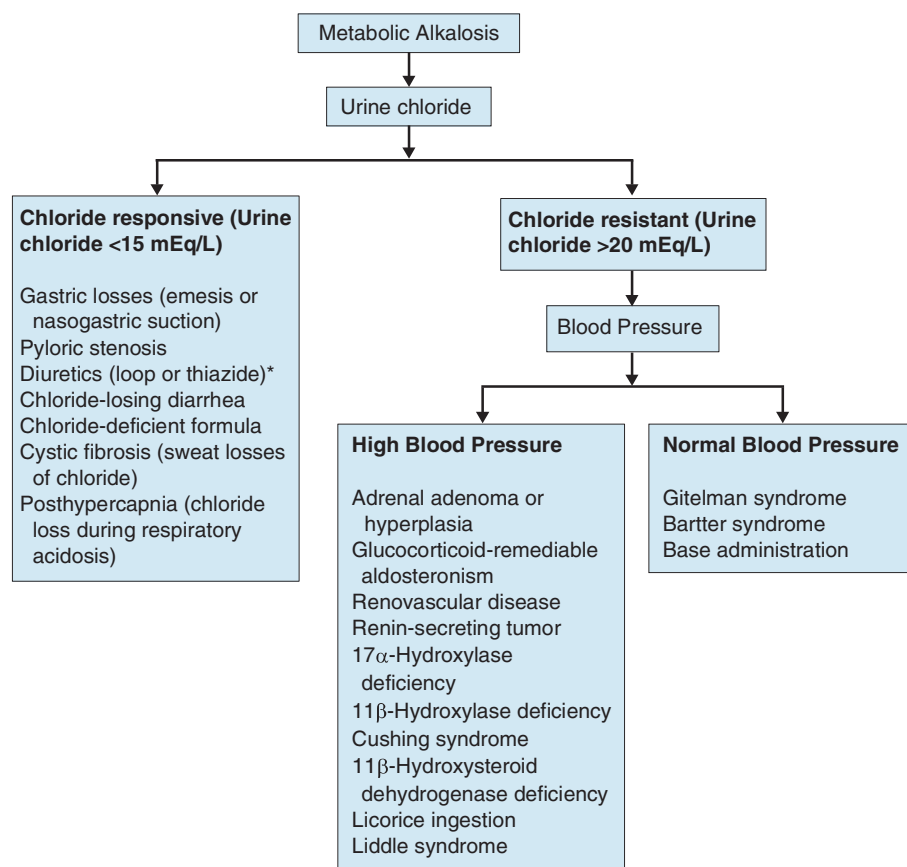


FIGURE 37.1 Causes of a metabolic alkalosis. *Diuretics are associated with an elevated urinary chloride (>20 mEq/L) when the patient is receiving the diuretic, but a low urinary chloride (<15 mEq/L) when the effect has worn off, but are chloride responsive and hence grouped with these disorders.

Diagnosis

Calculating the anion gap can help narrow the differential diagnosis for acidosis. However, the anion gap should not be interpreted in dogmatic isolation; consideration of other laboratory abnormalities and the clinical history improves its diagnostic utility. A decrease in the albumin concentration of 1 g/dL decreases the anion gap by roughly 4 mEq/L. Similarly, albeit less commonly, an increase in unmeasured cations, such as calcium, potassium, or magnesium, decreases the anion gap. Conversely, a decrease in unmeasured cations is a rare cause of an increased anion gap. Because of these variables, the broad range of a normal anion gap and other factors, the presence of a normal or increased anion gap is not always reliable in differentiating the causes of a metabolic acidosis, especially when the metabolic acidosis is mild. Some patients have more than one explanation for their metabolic acidosis, such as a child with diarrhea and lactic acidosis secondary to shock.

Treatment

The most effective therapeutic approach for patients with a metabolic acidosis is correction of the underlying disorder, if possible. The administration of insulin in diabetic ketoacidosis or restoration of adequate perfusion in lactic acidosis from shock eventually results in normalization of acid-base balance. The use of bicarbonate therapy is indicated when the

underlying disorder is irreparable; examples include RTA and chronic renal failure. In salicylate poisoning, alkali administration increases renal clearance of salicylate and decreases the amount of salicylate in brain cells. Short-term base therapy is often necessary in other poisonings and inborn errors of metabolism.

METABOLIC ALKALOSIS

Etiology

The causes of a metabolic alkalosis are divided into two categories based on the urinary chloride (Fig. 37.1). The alkalosis in patients with a low urinary chloride is maintained by volume depletion. They are called **chloride responsive** because volume repletion with fluid containing sodium chloride and potassium chloride is necessary to correct the metabolic alkalosis. Emesis, which causes loss of hydrochloride and volume depletion, is the most common cause of a metabolic alkalosis. Diuretic use increases chloride excretion in the urine. Consequently, while a patient is receiving diuretics, the urinary chloride is typically high (>20 mEq/L). After the diuretic effect resolves, the urinary chloride is low (<15 mEq/L) because of appropriate renal chloride retention in response to volume depletion. Categorization of diuretics based on urinary

chloride depends on the timing of the measurement. The metabolic alkalosis from diuretics is clearly chloride responsive; it corrects after adequate volume repletion. This is the rationale for including it among the chloride-responsive causes of a metabolic alkalosis.

The **chloride-resistant** causes of metabolic alkalosis can be subdivided based on blood pressure. Patients with the rare disorders that cause metabolic alkalosis and hypertension either have increased aldosterone or act as if they have increased aldosterone. Patients with Bartter syndrome or Gitelman syndrome (see [Chapter 36](#)) have metabolic alkalosis, hypokalemia, and normal blood pressure secondary to renal tubular defects, which cause continuous urinary losses of chloride.

Clinical Manifestations

The symptoms in patients with metabolic alkalosis often are related to the underlying disease and associated electrolyte disturbances. Hypokalemia is often present and occasionally severe (see [Chapter 36](#)). Children with chloride-responsive causes of metabolic alkalosis often have symptoms related to volume depletion (see [Chapter 33](#)). In contrast, children with chloride-unresponsive causes may have symptoms related to hypertension. Severe alkalemia may cause arrhythmias, hypoxia secondary to hypoventilation, or decreased cardiac output.

Diagnosis

Measurement of the urinary chloride concentration is the most helpful test in differentiating among the causes of metabolic alkalosis. The history usually suggests a diagnosis, although no obvious explanation may be present in the patient with bulimia or surreptitious diuretic use. Patients with Bartter syndrome or Gitelman syndrome usually have a history of polyuria and may have salt craving.

Treatment

The approach to therapy of metabolic alkalosis depends on the severity of the alkalosis and the underlying etiology. In children with mild metabolic alkalosis ($[\text{HCO}_3^-] < 32 \text{ mEq/L}$), intervention is often unnecessary. Patients with chloride-responsive metabolic alkalosis respond to the correction of hypokalemia and volume repletion with sodium and potassium chloride, but aggressive volume repletion may be contraindicated if mild volume depletion is medically necessary in the child receiving diuretic therapy. In children with chloride-resistant causes of metabolic alkalosis that are associated with hypertension, volume repletion is contraindicated because it exacerbates the hypertension and does not repair the metabolic alkalosis. Treatment focuses on eliminating or blocking the action of the excess mineralocorticoid. In children with Bartter syndrome or Gitelman syndrome, therapy includes oral sodium and potassium supplementation.

RESPIRATORY ACID-BASE DISTURBANCES

During respiratory acidosis, there is a decrease in the effectiveness of CO_2 removal by the lungs. The causes of respiratory

TABLE 37.3 Causes of Respiratory Acidosis

Central nervous system depression (encephalitis or narcotic overdose)
Disorders of the spinal cord, peripheral nerves, or neuromuscular junction (botulism or Guillain-Barré syndrome)
Respiratory muscle weakness (muscular dystrophy)
Pulmonary disease (pneumonia or asthma)
Upper airway disease (laryngospasm)

TABLE 37.4 Causes of Respiratory Alkalosis

Hypoxemia or tissue hypoxia (carbon monoxide poisoning or cyanotic heart disease)
Lung receptor stimulation (pneumonia or pulmonary embolism)
Central stimulation (anxiety or brain tumor)
Mechanical ventilation
Hyperammonemias

acidosis are either pulmonary or nonpulmonary ([Table 37.3](#)). A respiratory alkalosis is an inappropriate reduction in the blood CO_2 concentration. A variety of stimuli can increase the ventilatory drive and cause respiratory alkalosis ([Table 37.4](#)). Treatment of respiratory acid-base disorders focuses on correction of the underlying disorder. Mechanical ventilation may be necessary in a child with refractory respiratory acidosis.

PEARLS FOR PRACTITIONERS

See *Fluids and Electrolytes: Pearls for Practitioners* at the end of this section.

Suggested Readings

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PEARLS FOR PRACTITIONERS

CHAPTER 32

Maintenance Fluid Therapy

- Maintenance of normal plasma osmolality within the extracellular compartment depends on the regulation of water balance, which is controlled by antidiuretic hormone (ADH); water intake due to thirst has an important role when the osmolality is elevated.
- Control of osmolality is subordinate to the maintenance of an adequate intravascular volume. When significant volume depletion is present, ADH secretion and thirst are stimulated, regardless of the plasma osmolality.
- Control of volume status depends on the regulation of sodium balance. Excretion of sodium by the kidneys is driven by effective plasma volume rather than by serum osmolality or sodium.
- Maintenance intravenous fluids in patients who cannot be fed enterally replace insensible, stool, and urinary losses of water, and urinary and stool losses of electrolytes.
- The glucose in maintenance fluids provides approximately 20% of normal caloric needs to prevent the development of starvation ketoacidosis and diminish the protein degradation that would occur if the patient received no calories, but maintenance fluids are not a long-term replacement for nutrition.
- Maintenance solutions are usually D5 in normal saline plus 20 mEq/L KCl.

CHAPTER 33

Dehydration and Replacement Therapy

- Insensible water losses from the skin and lungs are about 35% of normal water losses.
- An anuric child who is not dehydrated and is not being fed enterally only requires insensible fluids to maintain euvolemia.
- Children with excessive losses (stool, urine, other) may need a replacement solution to avoid volume depletion.
- A 20 mL/kg bolus of an isotonic fluid (normal saline, Ringer lactate) is given over approximately 20 minutes in a child with significant dehydration.
- The blood urea nitrogen (BUN) is elevated out of proportion to the serum creatinine in patients with volume depletion.
- Hyponatremic dehydration occurs when hypotonic fluids such as water or diluted formula are given to a child with gastroenteritis.
- Hypernatremic dehydration occurs in children with poor thirst, poor fluid intake, or excessive urine water losses (diabetes insipidus).

- Mild to moderate diarrheal dehydration can be treated with oral rehydration solution.

CHAPTER 34

Parenteral Nutrition

- Parenteral nutrition (PN) is necessary when enteral feeding is inadequate to meet nutritional needs.
- Short bowel syndrome is a common disorder requiring PN.
- Calories from PN are predominantly from dextrose and fat. Amino acids should mostly be used for protein synthesis.
- Complications of PN include thrombosis and line infection.
- The most concerning complication of long-term PN is cholestatic liver disease, but the risk is reduced by utilization of the gastrointestinal tract even if just for trophic feeds.

CHAPTER 35

Sodium Disorders

- Most disorders of sodium are secondary to abnormalities in water balance.
- The symptoms of hyponatremia, such as seizures, are principally due to water movement into brain cells.
- The symptoms of hypernatremia are due to water movement out of brain cells, which may lead to brain hemorrhage if the hypernatremia is severe.
- Symptoms of hyponatremia are much more likely if the hyponatremia develops rapidly.
- Diagnosing the etiology of hyponatremia should begin by assessing a patient's volume status (hypovolemic, euvolemic, or hypervolemic).
- Most cases of hyponatremia are due to gastroenteritis, but the syndrome of inappropriate antidiuretic hormone secretion (SIADH) or hypervolemic causes (heart failure, cirrhosis) should be considered.
- Most cases of hypernatremia are due to gastroenteritis, but diabetes insipidus must be considered.
- Overly rapid correction of hyponatremia can lead to central pontine myelinolysis; it is optimal to increase the serum sodium less than 10 mEq/L per 24 hours.
- Due to the presence of idiogenic osmoles, overly rapid correction of hypernatremia can lead to cerebral edema, and thus the target decrease in serum sodium is less than 12 mEq/L per 24 hours.
- Acute water intoxication producing hyponatremia often self-corrects once excessive water intake has stopped.
- The emergency treatment of symptomatic hyponatremia involves the use of intravenous hypertonic saline to decrease brain edema.

CHAPTER 36

Potassium Disorders

- The kidneys are the principal regulator of potassium balance.
- Hypokalemia is secondary to renal losses, nonrenal losses (diarrhea), low intake, or transcellular shifts.
- Transcellular potassium shifts are seen in treated diabetic ketoacidosis and patients with asthma treated with albuterol.
- Severe hypokalemia causes muscle cramps and muscle weakness, which may proceed to paralysis.
- Hypokalemia with a metabolic acidosis suggests diarrhea or renal tubular acidosis.
- Hypokalemia with a metabolic alkalosis is most commonly due to emesis or nasogastric losses but may also be due to Bartter or Gitelman syndrome or diuretic use.
- Arrhythmias, which may be fatal, are often the initial clinical manifestation of hyperkalemia.
- Hyperkalemia is most commonly due to decreased excretion or a transcellular shift, although increased intake may cause or contribute.
- Hyperkalemia may be seen in disorders with decreased renin, decreased aldosterone (congenital adrenal hyperplasia), or lack response to aldosterone (decreased aldosterone effect).
- Hyperkalemia is associated with peaked T waves and may produce paresthesia and muscle weakness.
- The two goals of treating hyperkalemia, which require different therapeutic approaches, are to prevent cardiac toxicity and to decrease total body potassium.
- Total body potassium may be reduced by loop or thiazide diuretics, dialysis, or potassium-binding resins.

CHAPTER 37

Acid-Base Disorders

- Acute, severe changes in pH can be fatal, while chronic, mild derangements may interfere with growth and development.
- The lungs and the kidneys maintain normal acid-base balance. The lungs (respiratory) regulate CO_2 concentration, and the kidneys (metabolic) regulate bicarbonate concentration.
- During a primary respiratory process, the kidneys compensate, but full compensation takes a few days.
- During a primary metabolic process, the lungs compensate rapidly (within hours).
- Appropriate compensation is expected in a simple acid-base disorder; it is not optional. If a patient does not have appropriate compensation, a mixed acid-base disorder is present.
- The plasma anion gap divides patients with metabolic acidosis into two categories: normal anion gap and increased anion gap.
- Normal anion gap metabolic acidosis occurs in the setting of diarrhea and renal tubular acidosis.
- Increased anion gap metabolic acidosis occurs with lactic acidosis, ketoacidosis, chronic renal failure, and toxic ingestions.
- The differential diagnosis of metabolic alkalosis begins by measuring the urine chloride and separating patients based on whether the urinary chloride is low or high.
- Patients with a metabolic alkalosis and a low urine chloride are volume depleted, and the alkalosis responds to administration of sodium or potassium chloride (chloride responsive).
- Patients with chloride-resistant metabolic alkalosis (urine chloride not low) are subdivided based on the presence of a normal or elevated blood pressure.