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AHC Media

Fluids and Electrolyte Management Part 2: Electrolyte Disturbances and Acid-Base Disorders

Disorders of Potassium Homeostasis

Hypokalemia

Definition. Normal potassium levels vary by age. (*See Table 1.*) Hypokalemia is defined by serum potassium < 3.5 mEq/L. Mild hypokalemia is a potassium level between 3-3.5 mEq/L; moderate hypokalemia is a potassium level between 2.5-3 mEq/L; and severe hypokalemia is a potassium level < 2.5 mEq/L. Hypokalemia can be acute or chronic, depending on the etiology.

Etiology. Gastroenteritis is the most common cause of pediatric hypokalemia.[1]

Pathophysiology. Potassium is an intracellular ion whose concentration is regulated by multiple mechanisms:

- Alkalosis shifts potassium into cells and acidosis shifts it out. For every increase in pH by 0.1 unit, serum potassium drops by 1 mEq/L.
- Insulin shifts potassium into cells via a sodium-potassium ATPase pump.
- Potassium excretion from the kidneys is regulated by aldosterone, mineralocorticoids, antidiuretic hormone, urinary flow rate, metabolic alkalosis, and sodium delivery to the distal tubules.

Specific illnesses will lower the serum potassium in different ways. Diarrhea results in the loss of potassium through the gastrointestinal tract. However, vomiting does not directly cause hypokalemia through gastrointestinal losses, but results in alkalosis secondary to the loss of gastric fluids and volume loss, and the alkalosis increases potassium excretion from the kidneys. Hypovolemia (releasing aldosterone), diuretics, genetic renal tubular disorders, and osmotic diuresis (e.g., glucosuria) all increase the secretion of potassium via the renal tubules. (*See Table 2.*)[1,2,3]

Hypokalemia affects many organs since it causes cellular dysfunction. The main organs affected are the muscles (rhabdomyolysis), heart, nervous system, and kidneys.

Clinical Features. *History.* Once hypokalemia is established, a detailed history to identify the potential cause is important. A history of diarrhea or vomiting can easily establish the cause without having to do an extensive workup. Ask about medication use and changes in enteral or parenteral formulation, such as total parenteral nutrition (TPN). Symptoms of hypokalemia typically are not seen at a serum level of > 3 mEq/L. Clinical effects may include muscle weakness, respiratory distress, palpitations or chest pain from arrhythmia, confusion, lethargy, polydipsia, and polyuria.

Physical Exam. Evaluate the vital signs and complete a rapid assessment, identifying signs of shock, respiratory failure, or dysrhythmia. Neurologic signs of hypokalemia may include confusion, lethargy, hyporeflexia, and flaccid paralysis. Hypoactive bowel sounds and a distended abdomen can be seen with ileus secondary to hypokalemia.

EXECUTIVE SUMMARY

- Symptomatic or severe hyperkalemia is an emergency treated in three steps: providing cardiac protection with calcium gluconate; promoting intracellular shifts with insulin and glucose; and enhancing its excretion via sodium polystyrene sulfonate, fluids, and diuretics.
- Preferably, hypokalemia is treated slowly with oral potassium chloride or intravenously if symptomatic or severe.
- Calcium, phosphorus, and magnesium disorders are rare, interlinked, and typically secondary to an underlying chronic disease. Typically, presenting symptoms are vague and affect the neuromuscular system. As in adults, hypercalcemia may be a harbinger of an underlying malignancy requiring further investigation.
- Metabolic acidosis is the most common acid-base disorder. A stepwise approach to evaluating a child is the most efficient way to tackle this presentation.
- When and how to treat metabolic acidosis is still controversial. However, consensus has been reached for the following: avoid treating diabetic ketoacidosis with bicarbonate, treat the underlying disease for lactic acidosis, and aggressively hydrate acidosis secondary to dehydration and diarrhea.
- Always evaluate for appropriate respiratory compensation in metabolic acid-base disorders to identify a mixed disorder.

Table 1. Normal Potassium Levels[1]

Age	Potassium (mEq/L)
Preterm	3-6
Newborn	3.7-5.9
Infant	4.1-5.3
Child	3.4-4.7
Adult	3.5-5.1

Source: Author adapted.

Generalized muscle weakness and pain are seen in rhabdomyolysis.

Diagnostic Studies. Serum electrolytes will establish the hypokalemia. When the etiology of the hypokalemia can be determined by the history (e.g., gastroenteritis, diuretic use, diabetic ketoacidosis, or an already known chronic disease), no further studies are needed. However, if there is a diagnostic dilemma, a full set of electrolytes, urine potassium to creatinine ratio, a blood gas to evaluate for acidosis or alkalosis, serum blood urea nitrogen (BUN), creatinine, magnesium and glucose, and a urine chloride are indicated:[3]

• A urine potassium to creatinine ratio < 1.5 mEq/mmoL indicates possible gastrointestinal losses, decreased potassium intake, or loop diuretic use.

• A urine potassium to creatinine ratio > 1.5 mEq/mmoL requires further investigation, for example:

- If hypertension is present, consider hyperaldosteronism, Liddle syndrome, or adrenal hyperplasia, and check renin and aldosterone levels, although these most probably will not change the emergency department (ED) care of this child.

- If metabolic acidosis is present, consider Fanconi syndrome, cystinosis, RTA 1 and 2, diabetic ketoacidosis, and diarrhea.

- If metabolic alkalosis is present, consider emesis, diuretic use, nasogastric drainage, and Bartter or Gitelman syndromes.

• Magnesium levels are important for several reasons: hypomagnesemia can cause hypokalemia, and in addition, it helps differentiate Gitelman syndrome from Bartter syndrome, as Gitelman presents with hypomagnesemia and Bartter does not.

Look for potential complications of hypokalemia if the child is symptomatic. An elevated creatine phosphokinase (CPK) and urinary myoglobin reflect an acute rhabdomyolysis secondary to the hypokalemia. An electrocardiogram (ECG) should be obtained on all children with hypokalemia < 3 mEq/L. The following ECG changes appear sequentially with worsening hypokalemia; however, they do not correlate with a specific potassium level: prolonged PR interval, flattened T waves, depressed ST segment, U waves, ventricular fibrillation, and torsade de pointes.[4,5]

Management. Shock, respiratory failure, or dysrhythmia should be treated as per Pediatric Advanced Life Support (PALS) algorithms.[6] Hypokalemia in a stable patient that is secondary to vomiting, diarrhea, or dehydration usually can be treated with maintenance intravenous (IV) fluid rehydration that includes potassium (such as 5% dextrose with normal saline and an additional 20-40 mEq/L of potassium chloride [KCl]), rather than a KCl bolus. Aim for a KCl rate of 0.25 mEq/kg/hr.[2,5]

Stable patients with chronic hypokalemia, for example secondary to medications or chronic disease, preferably are treated with oral potassium.[7] Particularly when renal disease is present, excess potassium is difficult to clear and places the patient at risk of hyperkalemia. A potassium-sparing diuretic also can be used to correct serum potassium slowly in conjunction with a nephrologist.[4]

In cases in which more rapid correction is required, such as with cardiac dysrhythmias or a potassium level < 2.5 mEq/L, intravenous replacement is recommended.[4] Typically, IV KCl at 0.5-1 mEq/kg/dose (max of 10 mEq) infused over 1-2 hours is used. Repeat potassium levels after the infusion. Potassium phosphate and potassium bicarbonate also can be used if the hypokalemia is associated with hypophosphatemia and alkalosis, respectively. Note that potassium infusions may cause phlebitis. Therefore, use a maximal rate of 0.5 mEq/kg/hr in peripheral veins; higher rates can be infused via intraosseous or central venous lines but need constant ECG monitoring because of the risk of hyperkalemia, ventricular fibrillation, and cardiac arrest.[7]

Additional Aspects. If present, always treat hypomagnesemia and hypochloremia concomitantly, as they may exacerbate the symptoms of hypokalemia. Treat hypomagnesemia with magnesium supplementation, and hypochloremia with normal saline.[5]

Disposition.[5] Deciding on inpatient or pediatric intensive care unit (PICU) admission often varies by hospital. The following are recommendations, not strict guidelines.

Criteria to Discharge Home:

• Well-appearing, asymptomatic patient with a potassium level > 3 mEq/L.

• Patient can be treated with oral supplements.

• The underlying etiology is known and patient is not at risk for a further drop in potassium.

• Parents understand the instructions for further care at home and are able and committed to follow through with care.

• Available primary care physician or

Table 2. Etiology of Pediatric Hypokalemia[2,3]

Gastrointestinal Loss	Renal Loss	Decreased Intake (rare)	Intracellular Shift (normal total body potassium)
Diarrhea Vomiting Laxatives Short gut syndrome	Alkalosis Renal tubular acidosis type 1 or 2 Aldosterone secreting adenomas Glucocorticoid/mineralocorticoid excess (e.g., congenital adrenal hyperplasia) Hypovolemia Bartter and Gitelman syndromes Diuretics	Malnutrition Anorexia Errors in total parenteral nutrition	Insulin Beta-adrenergic medications (e.g., albuterol) Hypokalemic periodic paralysis (rare and familial)

Source: Author adapted.

Table 3. Common Causes of Hyperkalemia in Children[4,8]

Increased Intake (increased total body potassium)	Decreased Excretion (decreased total body potassium)	Intracellular Shift (normal total body potassium)
Iatrogenic causes (e.g., total parenteral nutrition, intravenous fluids) Medication use (e.g., supplements, potassium-sparing diuretics)	Renal insufficiency or failure (acute or chronic) Severe hypovolemia Adrenal insufficiency	Rhabdomyolysis (e.g., crush injury, exercise) Massive hemolysis or transfusion Tumor lysis syndrome Acidosis (e.g., diabetic ketoacidosis)

Source: Author adapted.

specialist follow-up.

Criteria to Admit to the Inpatient Pediatric Ward:

• Patient with expectant further acute losses due to the underlying disease.

• Patient with underlying renal disease requiring electrolyte monitoring.

• The etiology for the hypokalemia is unknown.

Criteria to Admit to the PICU:

• Hemodynamic instability, dysrhythmia, or an altered mental status.

• Significant electrolyte derangements requiring frequent monitoring, laboratory evaluations, and intervention at a PICU level.

Hyperkalemia

Definition. Hyperkalemia is defined by a serum potassium > 5.5 mEq/L. Moderate hyperkalemia is a level between 6 -7 mEq/L and severe is > 7 mEq/L.[4] One exception to this is in the newborn period. In infants younger than 1 month of age, normal serum potassium levels may reach 6 mEq/L. In this age group, hyperkalemia is defined as serum potassium > 6.5 mEq/L.[1,8]

Etiology. The most common cause of hyperkalemia is pseudohyperkalemia, followed by renal or adrenal diseases.[4] (*See Table 3.*)Pseudohyperkalemia is a falsely elevated serum potassium level. This is quite common in children secondary to hemolyzed blood. When suspected, always draw another sample, while ensuring that it is as free-flowing as possible. Another cause of pseudohyperkalemia is leukocytosis.[4]

Pathophysiology. As described above, potassium is an intracellular ion whose concentration is regulated by multiple mechanisms:

• Alkalosis shifts potassium into cells and acidosis shifts it out. For every drop in pH by 0.1 unit, serum potassium increases by 1 mEq/L.

• Insulin shifts potassium into cells via a sodium-potassium ATPase pump.

• Potassium excretion from the kidneys is regulated by aldosterone, mineralocorticoids, antidiuretic hormone, urinary flow rate, metabolic alkalosis, and sodium delivery to the distal tubules.

Specific illnesses will affect these mechanisms differently. (*See Table 3.*) Severe hypovolemia causes poor tissue perfusion and metabolic acidosis and decreased potassium excretion from the kidneys. One of the most emergent complications of hyperkalemia is cardiac instability resulting in dysrhythmias and potential death.

Clinical Features. *History.* Identifying the cause of hyperkalemia is crucial to its management. Before further diagnostic workup is started, ask about chronic diseases (e.g., renal disease), medication intake, and recent illnesses. A new diagnosis of leukemia or Burkitt lymphoma puts the patient at a very high risk for hyperkalemia secondary to tumor lysis, even before chemotherapy is started.

Symptoms of hyperkalemia are uncommon, but if present include paresthesias, myalgias, weakness, and ascending flaccid paralysis sparing the respiratory muscles.[4] Cardiovascular symptoms of palpitations and syncope could happen in severe hyperkalemia.

Physical Exam. As with all potentially sick children, look for signs of shock, respiratory failure, or dysrhythmia. A thorough neurological exam will identify the specific findings of hyperkalemia described above.

Diagnostic Studies. For patients with a dysrhythmia or neuromuscular symptoms, check a serum potassium level. Once true hyperkalemia is established, check a full set of electrolytes. For rhabdomyolysis, check serum creatine phosphokinase and urine myoglobin. For tumor lysis, add a complete blood count, uric acid, and lactate dehydrogenase. For possible renal disease, order a urinalysis, urine electrolytes, and serum and urine osmolality. Check an ECG on all patients with hyperkalemia, whether symptomatic or not. Specific ECG changes appear sequentially and depend on the serum potassium level. (*See Table 4.*)

Management. Hyperkalemia > 7 mEq/L or with significant ECG changes is an emergency. Once initial stabilization is performed following the PALS algorithms, focus on managing the hyperkalemia, irrespective of the underlying cause.[6] Once the hyperkalemia is verified (i.e., pseudohyperkalemia is ruled out), this treatment consists of three steps.[4]

Step 1: Cardiac Protection: The increase in extracellular potassium changes the

Table 4. ECG Changes[6,7]

Serum K (mEq/L)	5.5	6.5		7.5	8	9	>10
ECG changes	Tall peaked T waves with short QT interval	Prolonged PR interval	Decreased or disappearing P waves	Wide QRS and amplified R wave	Absent P wave	Bundle branch block	Ventricular fibrillation and asystole

membrane potential of cardiac cells, putting the heart at risk for dysrhythmias. This is counteracted by infusing 10% calcium gluconate to stabilize the cardiac membrane. Calcium chloride can also be used; however, it poses the risk of tissue necrosis during infusion. Repeat the dose if needed based on ECG changes. The effect is immediate but also transient; therefore, steps 2 and 3 should be started concomitantly.

Step 2: Shifting Extracellular Potassium into the Cells: While cardiac protection is taking place, the fastest way to decrease serum potassium is via an intracellular shift. This can be accomplished by several means. First, infuse insulin and glucose concomitantly. Insulin shifts potassium into cells, but puts the child at risk for hypoglycemia, hence the need for the glucose. Second, start inhaled albuterol via a nebulizer or a metered-dose inhaler. In addition, sodium bicarbonate also may be used. However, its effect is unpredictable and should not be used as a first-line or sole therapy.

Step 3: Increasing the Elimination of Potassium: Start with a loop diuretic (e.g., furosemide) and sodium polystyrene sulfonate (Kayexalate). The former promotes potassium excretion through the kidneys and the latter through the gastrointestinal tract by binding potassium. Hydrate if renal function allows. Finally, hemodialysis in consultation with a nephrologist may be required for recalcitrant hyperkalemia or renal failure. (*See Table 5 for medication doses.*)

Potassium levels < 7 mEq/L or with only early ECG changes (peaked T waves) do not need the rapid initial treatments (steps 1 and 2). Focus on step 3 and treat the underlying disease, usually in consultation with a specialist, as well as stopping potassium intake (e.g., IV fluids and medications) and treating any acidosis.[9]

Note that patients with rhabdomyolysis, tumor lysis, and renal failure may have rapid rises in potassium. Therefore, a lower threshold than described above may be needed in these clinical scenarios. (*See Table 5 for medication doses.*)

Disposition.[8] Deciding on inpatient or PICU admission often varies by hospital. The following are recommendations, not strict guidelines.

Criteria to Admit to the Inpatient Pediatric Ward:

- Patients with hyperkalemia requiring further treatment.
- Etiology for the hyperkalemia is unknown or the patient is still at risk of hyperkalemia.

Criteria to Admit to the PICU:

- Hemodynamic instability, dysrhythmia, or an altered mental status.
- Significant electrolyte derangements requiring frequent monitoring, laboratory evaluations, and intervention at a PICU level.

Disorders of Calcium Homeostasis

Hypocalcemia

Definition. In the ED, hypocalcemia, especially when symptomatic, is mostly encountered in the newborn period. Normal calcium levels vary by age. (*See Table 6.*) Therefore, the definition of hypocalcemia also varies. In newborns, hypocalcemia is a total calcium level < 7 mg/dL; in older children, it is < 8.5 mg/L.[1,10] It is also important to differentiate total serum calcium from ionized calcium. The former reflects the bound calcium. However, the latter is the active and physiologically important ion.

Etiology. The causes of hypocalcemia vary and depend on the patient's age. (*See Table 7.*) Some of these etiologies are associated with an underlying genetic syndrome. The most common, DiGeorge syndrome (chromosome 22q11.2 microdeletion syndrome), has typical craniofacial malformations, cardiac defects, and thymic hypoplasia. The thymic hypoplasia includes parathyroid hypoplasia and, hence, hypoparathyroidism, which causes hypocalcemia.[11]

Pathophysiology. Ninety-nine percent of the total body calcium is found in the bone as calcium phosphate. Of the circulating calcium, half is free and the rest is bound to albumin, bicarbonate, or citrate. Calcium is closely linked to phosphorous (*see Table 8*) and the intertwining of several factors regulates calcium homeostasis. These include the parathyroid hormone (PTH), vitamin D, calcitonin, and calcium-sensing receptors on end organs, as well as the pH of the blood, level of magnesium, and the function of the liver and the kidneys. Alkalosis increases the binding of calcium to albumin; PTH recruits calcium from bones; and the active form of vitamin D enhances the absorption of calcium and phosphorus from the intestines and stimulates PTH. Vitamin D deficiency is often due to lack of exposure to sunlight and low dietary intake. It is important to know that exclusively breastfed children require oral vitamin D supplements.[12]

Clinical Features. *History.* Newborns will typically present with lethargy, decreased feeding, vomiting, or, more significantly, tetany, twitching, or seizures. Hypocalcemia is on the differential of every child with abnormal movements or seizures. A recent history of vomiting, diarrhea, and weight loss may suggest malabsorption as a cause of hypocalcemia. A past medical history of anxiety in a child or adolescent presenting with tetany and paresthesia of the upper extremities suggests the diagnosis of hyperventilation or panic attack as the cause of the symptoms. Review the medical history for other chronic diseases and drug therapies, as well as accidental or intentional drug ingestions, which may lead to hypocalcemia.

Physical Exam. The most frequent physical exam findings are neuromuscular. These include non-specific changes such as an altered mental status, cramping, fatigue, irritability, and lethargy; others are more specific, such as tetany, hyperreflexia, paresthesia, seizures, cardiac dysrhythmias, and laryngospasm. The latter is a rare and emergent presentation of hypocalcemia that can rapidly lead to respiratory failure and arrest. The Trousseau (carpopedal spasm after arterial occlusion of the extremity for 3 min) and Chvostek (muscle twitching after tapping the facial nerve) signs are specific

Table 5. Medications Used to Treat Hyperkalemia[6,7]

	10% Calcium Gluconate (10% = 100 mg/mL = 9 mg/L elemental Ca)	Regular Insulin and Glucose	Albuterol	Sodium Bicarbonate	Furosemide	Sodium Polystyrene Sulfonate
Dosage	For hyperkalemia or hypermagnesemia with ECG changes or cardiac arrest: 100 mg/kg/dose (1 mL/kg/dose) slow IVP. May repeat in 10 min. Maximum rates: IVP 100 mg/min; Infusion 120-240 mg/kg/hr For hypocalcemia: 200-500 mg/kg/24 hours divided every 6 hours, IV	0.1 unit/kg IV (max 10 units) over 30 min Mix with D25W as 2 mL/kg Repeat in 30-60 min	Nebulizer: < 25 kg: 2.5 mg 25-50 kg: 5 mg > 50 kg: 10 mg OR 4-8 puffs of MDI	1 mEq/kg (max 50 mEq) over 5-10 min In infants use the 4.2% concentration	1 mg/kg (max 80 mg)	1 g/kg (max 50 g) every 6 hours
Mode	IV/IO through a large vein or central line (preferably)	IV/IO	Inhaled	IV	IV	PO/NG/PR
Onset/Duration	1-2 min/30-60 min	10-20 min/ 1-4 hours	20-30 min/ 2-4 hr	15 min/1-4 hr	1-2 hr/4-6 hr	1-2 hr/ 4-6 hr
Effect on K	—	Drops by 0.5-1 mEq/L	Drops by 0.5-1 mEq/L	Unpredictable	—	1 g binds 1mEq of K
Side Effects	Hypercalcemia Bradycardia Arrhythmia with digitalis Extravasation into tissue	Hypoglycemia or hyperglycemia	Tachycardia	Hypernatremia Volume overload CO_2 (ensure adequate ventilation) Tissue irritation	Hypovolemia Electrolyte abnormalities	Electrolyte abnormalities, constipation, NEC
Warnings	CI in ventricular fibrillation; Caution in renal impairment; Precipitates if infused in the same line as sodium bicarbonate		Mix in 2 mL of saline for the nebulizer	Do not infuse in the same line as calcium Flush IV tube before and after	Requires good renal and liver function	CI in preterm, term neonates with intestinal dysfunctions
Monitor	Serial EKG Calcium	Glucose		Sodium	Fluid status Electrolytes	Electrolytes

Ca = calcium; K = potassium; IVP = intravenous push; IO = intraosseous; CI = contraindicated; D25W: 25% dextrose in water; MDI = metered-dose inhaler; NG = nasogastric; NEC = necrotizing enterocolitis

Source: Author Created

for hypocalcemia. Finally, take note of any abnormal facies or findings suggestive of an underlying genetic disorder.

Diagnostic Studies. When the history is not enough to narrow down the differential, a more extensive workup is recommended. This includes a serum electrolyte panel including phosphorus and magnesium, a liver function panel, renal function panel, alkaline phosphatase (reflects bone resorption), lipase (for pancreatitis), and venous blood gas (looking for alkalosis). Specifically, check the ionized calcium (for the degree of hypocalcemia) and albumin levels (for pseudohypocalcemia). A chest X-ray may reveal an absent thymus in chromosome 22q11.2 microdeletion syndrome. If hyperventilation is suspected, then no further workup is needed, although a blood gas will show respiratory alkalosis. Finally, a PTH and vitamin D level would be helpful for the final diagnosis, but those results most probably will not help in the immediate care of the child in the ED. In addition, hypocalcemia may cause the following ECG changes: prolonged QT, prolonged ST, and T wave changes.[10]

Management. For hemodynamically unstable patients, follow the PALS algorithms.[6] Treat acute hypocalcemia, especially if symptomatic, with IV calcium. As with hyperkalemia, the infusion of choice is 10% calcium gluconate. Providers may use 10% calcium chloride as a last resort if calcium gluconate is not available or if more rapid infusion is required.[9,10,13] (*See Table 5.*) If possible, place a central venous line for calcium chloride or if repeated dosing is expected, such as for cases of ongoing calcium loss (e.g., calcium channel blocker overdose or a rattlesnake bite). Seizures secondary to hypocalcemia are refractory to anticonvulsants.[13] Treat the underlying disease in consultation with the specialist.

Chronic hypocalcemia can be treated with oral calcium and vitamin D in conjunction with the specialist's recommendations.[13] Identifying the underlying disease will help determine which specialist to consult (endocrinology, nephrology, gastroenterology, and toxicology for drug overdoses).

Additional Aspects. Hyperphosphatemia, hypomagnesemia, and acidosis are closely intertwined with hypocalcemia. Treat hyperphosphatemia before hypocalcemia (unless symptomatic) to avoid soft tissue calcium phosphate deposits.[9,13] Acidosis will increase ionized calcium, falsely elevating the serum calcium level, although the stores still may be low. Therefore, treat hypocalcemia before or concomitantly with the acidosis.[13] Treat

Table 6. Normal Total Calcium Levels by Age[1]

Age	Total Calcium (mg/dL)
Premature neonate	6.1-11
0-10 days	7.6-10.4
10 days -24 months	9-11
24 months -12 years	8.8-10.8
12-18 years	8.4-10.2
Source: Author adapted.	

Table 7. Most Common Causes of Hypocalcemia in Children[10]

Neonatal Period	Beyond the Neonate
Prematurity Perinatal asphyxia Maternal gestational diabetes Intrauterine growth retardation Phosphorous intake Hypomagnesemia Hypoparathyroidism Gentamycin toxicity	Hypoparathyroidism Hypomagnesemia Hyperphosphatemia Malabsorption Vitamin D deficiency Pancreatitis Drugs (e.g., antiepileptics, calcium channel blockers) Tumor lysis syndrome Renal failure Respiratory alkalosis (e.g., hyperventilation from anxiety, tachypnea, respiratory distress, pneumonia) Rattlesnake bite
Source: Author adapted.	

hypomagnesemia in conjunction with hypocalcemia, if the former is not corrected; its effect on PTH resistance will hinder the elevation of serum calcium.[13]

Disposition.[10] Deciding on inpatient or PICU admission often varies by hospital. The following are recommendations, not strict guidelines.

Criteria to Admit to the Inpatient Pediatric Ward:

• All patients with symptomatic hypocalcemia.

• The etiology is unknown and the patient requires further workup.

Criteria to Admit to the PICU:

• Hemodynamic instability, dysrhythmia, or an altered mental status.

• Significant electrolyte derangements requiring frequent monitoring, laboratory evaluations, and intervention at a PICU level.

Hypercalcemia

Definition. Hypercalcemia, a rare finding in children, is defined as serum calcium > 11 mg/dL. It is considered severe if > 14 mg/dL.[2,14]

Etiology. In mild cases, hypercalcemia is an incidental finding with no clear etiology that does not require further workup but does require close follow-up with a primary care provider. More significant elevations could be a harbinger for a malignancy.

Pathophysiology. Serum calcium is increased by two main routes: bone and gut. (*See Table 9.*) Calcium regulation is reviewed in the section on hypocalcemia. Hypercalcemia hyperpolarizes the cell membranes of smooth muscles, which affects multiple end organs such as the nervous system, intestines, and heart.

Clinical Features. *History.* Similar to adults, the main symptoms consist of "bones, groans, moans, and stones."[15] This reflects all the systems involved: bone pain (and pathologic fractures), abdominal pain (with vomiting, constipation, nausea, and anorexia), depression/psychosis, and kidney stones (secondary to hypercalciuria). Cardiac symptoms consist of chest pain and palpitations. Non-specific constitutional symptoms consist of fatigue, weakness, polyuria, and weight loss.

Physical Exam. Look for signs reflecting the above symptoms and end organ dysfunctions: dehydration and shock, bony tenderness, anxiety, depression, hallucinations, lethargy, hypotonia, and hyporeflexia. Hepatosplenomegaly, diffuse lymphadenopathy, pallor, and petechiae may be the signs of an underlying malignancy.[15]

Diagnostic Studies. A full electrolyte panel, including phosphorus and magnesium, total and ionized calcium, a renal function panel, alkaline phosphatase (reflects bone resorption), PTH, calcitriol, and vitamin D, is essential to narrow the differential diagnosis of hypercalcemia. (*See Table 10.*) Primary hyperparathyroidism and malignancy are the most common causes of hypercalcemia in children. Therefore, additional workup may include a CBC with a blood smear, a chest X-ray to evaluate for a mediastinal mass, and a skeletal survey for pathologic fractures. Consult with a specialist early to determine the necessary evaluation.

ECG changes of hypercalcemia include a short QT and ST segment, prolonged PR and QRS, and second- or third-degree heart block.[14]

Management. For hemodynamically unstable patients, follow the PALS algorithms.[6] The first line of treatment for symptomatic or asymptomatic patients with total serum calcium > 14 mg/dL is IV fluid hydration with 0.9% normal saline. This helps treat any dehydration and increases calcium delivery to the kidneys and, hence, the excretion of calcium. Start with normal saline bolus then infuse it at two to three times maintenance over 1-2 days, rechecking calcium regularly.[9] If renal insufficiency is present, fluid must be given with caution and dialysis should be considered. Diuresis with furosemide in addition to the hydration can help with the calcium excretion.[15] (*See Table 5 for dosing.*)

Disposition. Admit all patients with hypercalcemia for monitoring and further workup. PICU is recommended for any patient with dysrhythmias, hemodynamic instability, or renal insufficiency that may require dialysis and a rapidly rising calcium level. The rest can be safely managed on an inpatient unit.[14]

Disorders of Phosphorus Homeostasis

Hypophosphatemia

Definition. Normal phosphorus levels vary by age.[1] (*See Table 11.*) Hypophosphatemia is defined as serum phosphorus < 2.5 mg/dL. It may be mild (2-2.5 mg/dL), moderate (1-1.9 mg/dL), or severe (< 1 mg/dL).[16]

Etiology. Hypophosphatemia is a rare finding in healthy children; it is seen more commonly in critically ill inpatients.[17,18] In the ED, it may be found in children with malabsorption (e.g., short gut syndrome) and adolescents with anorexia nervosa. (*See Table 12.*)

Pathophysiology. Phosphorus is mainly found intracellularly in the bone (as is calcium) and in smooth muscle. Less than 1% is circulating in the blood. The main causes of hypophosphatemia are decreased intake, increased excretion, or intracellular shifts.

Clinical Features. *History.* A detailed

Table 8. Etiology of Hypocalcemia in Relation to the Serum Phosphate[10,13]

Serum phosphate low	Serum phosphate normal	Serum phosphate high
Primary and secondary vitamin D deficiencies or resistance (e.g., malabsorption, anticonvulsant therapy, chronic renal failure) X-linked hypophosphatemic rickets	Malabsorption Anticonvulsants Renal tubular acidosis Primary vitamin D dependence types I and II	True hypoparathyroidism Iatrogenic causes Renal insufficiency

Source: Author adapted.

Table 9. Common Causes of Hypercalcemia[14,15]

Increased bone resorption	Increased intestinal absorption	Miscellaneous
Immobilization Bony metastases Hyperparathyroidism (e.g., primary, malignancy, secondary to renal failure) Hypervitaminosis A	Vitamin D intoxication Hypervitaminosis D Milk alkali syndrome Lymphoma Tuberculosis Sarcoidosis	Infantile hypercalcemia Thiazide diuretics (decrease renal excretion) Dietary intake

Source: Author adapted.

feeding history, including quantity and type of food, is important. A history of vomiting, diarrhea, or abdominal pain may point to a malabsorption process. Review the past medical history and drug therapies. Symptoms of hypophosphatemia are usually seen with a phosphate level < 1 mg/dL. They are non-specific and include irritability, paresthesias, confusion, seizures, coma, and myocardial depression.[20] In severely malnourished children, watch for signs and symptoms of infection and sepsis.

Physical Exam. Look for signs of malnutrition and nutrition deficiency. Bradycardia may be noted because of the hypophosphatemia and malnutrition. Typical features of rickets include a large head and a protruding forehead, a pigeon chest, a protruding abdomen, and curved long bones such as the legs that appear bowing.

Diagnostic Studies. Obtain a full set of electrolytes, including calcium and magnesium, a renal function panel, PTH, vitamin D levels, and urine electrolytes. Plain radiographs of the wrists may show typical epiphyseal widening seen in rickets; however, this is not essential to obtain in the ED setting.

Management. Treat severe, symptomatic hypophosphatemia with IV potassium phosphate or sodium phosphate and chronic or mild asymptomatic hypophosphatemia with the oral forms. (*See Table 13.*) Treat the underlying disease early, and consult a specialist if needed.[16,20]

Disposition.[20] Deciding on inpatient or PICU admission often varies by hospital. The following are recommendations, not strict guidelines.

Criteria to Admit to the Inpatient Pediatric Ward:

- Patients with symptomatic or severe hypophosphatemia.
- Etiology for the hypophosphatemia is unknown and inpatient workup is recommended.
- Management of the underlying disease requires inpatient care (e.g., severe acute malnutrition and anorexia nervosa).

Criteria to Admit to the PICU:

- Hemodynamic instability or an altered mental status.
- Additional significant electrolyte derangements requiring frequent monitoring, laboratory evaluations, and intervention at a PICU level.

Hyperphosphatemia

Definition. Normal phosphorus levels are shown in Table 11.[1] Hyperphosphatemia is a serum phosphate level > 4.5 mg/dL. Hyperphosphatemia is usually not symptomatic in and of itself, and is not an emergency. However, it may reflect an underlying disorder that may be symptomatic and will need to be addressed emergently (e.g., tumor lysis syndrome).

Etiology. The most common cause of hyperphosphatemia is renal failure; the most emergent is tumor lysis syndrome. (*See Table 12.*)[9] Case reports of hyperphosphatemia in children secondary to sodium-phosphate laxatives also have been reported.[21]

Pathophysiology. Phosphorus, like calcium, is mainly found intracellularly, in the bone. Less than 1% is circulating in the blood. Hyperphosphatemia is a result of increased intake (usually in association with renal insufficiency, rarely secondary to vitamin D intoxication), decreased renal excretion (e.g., hypoparathyroidism), or intracellular shifts (e.g., tumor lysis syndrome). (*See Table 12.*)

Clinical Features. As mentioned above, hyperphosphatemia does not cause signs and symptoms. However, the underlying cause and its consequences do. For example, hyperphosphatemia is usually associated with hypocalcemia, which may be symptomatic and requires more urgent therapy.[9] (*See section on hypocalcemia.*)

Diagnostic Studies. Order studies that will help diagnose the underlying disease: full electrolyte panel including total and ionized calcium, magnesium, a renal function panel, PTH, vitamin D, uric acid, lactate dehydrogenase, CBC, and urine electrolytes.

Management. In emergent cases such as with tumor lysis syndrome, IV normal saline is the treatment of choice. Typically start at twice maintenance with a goal of at least 4 mL/kg/hour of urine output.[22]

Otherwise, treat the underlying cause in consultation with a specialist as needed. This may include decreasing or stopping phosphate intake as well as prescribing available drugs to excrete phosphorus, usually phosphorus binders. The most common ones are used orally and bind phosphorus in the gut and excrete it through the feces. (*See Table 14.*)

Disposition. The underlying disorder and associated electrolyte abnormalities determine the disposition of the patient with hyperphosphatemia; for example, all children with tumor lysis syndrome require admission. The choice of inpatient unit or PICU varies by hospital.

Table 10. Etiology of Hypercalcemia in Relation to the Serum Phosphate[14]

Serum phosphate low	Serum phosphate normal	Serum phosphate high
Primary hyperparathyroidism	Infantile hypercalcemia Vitamin D intoxication Malignancy Immobilization Sarcoidosis Thiazide diuretics Hypervitaminosis A	Vitamin D intoxication

Source: Author adapted.

Disorders of Magnesium Homeostasis

Hypomagnesemia

Definition. Normal serum magnesium levels range from 1.2-2.1 mEq/L.[1] Hypomagnesemia is a serum magnesium level < 1.5 mEq/L. Severe forms are < 1 mEq/L.

Epidemiology. Disorders of magnesium are rare. Hypomagnesemia, however, is seen more commonly in children with malignancies.

Etiology/Pathophysiology. Magnesium is regulated by the gastrointestinal, renal, and endocrine systems.[23] Diseases affecting those organs may result in hypomagnesemia. Diarrhea, malabsorption, and short gut syndrome will increase gastrointestinal losses; hypercalcemia, chronic renal disease, and certain drugs, such as diuretics, cause proximal tubular injury, while others, like amphotericin B and cisplatin, increase renal excretion. Diabetes, primary aldosteronism, and parathyroid disorders cause hypomagnesemia via endocrine dysregulation. Finally, hospitalization associated with prolonged IV fluid therapy and nasogastric suctioning with limited enteral feeds is a common cause of hypomagnesemia in children. Similar findings are noted in adolescents with eating disorders.[24]

Clinical Features. *History.* Ask about chronic diseases, drug therapy, surgeries, and TPN. Errors in the latter are a common cause of electrolyte abnormalities. Symptoms of hypomagnesemia are similar to hypocalcemia and affect the neuromuscular system, including ataxia, vertigo, athetoid and choreiform movements, tremors, nystagmus, Trousseau and Chvostek signs, and psychiatric symptoms such as depression and cardiac dysrhythmias.

Physical Exam. Look for an abnormal neurological exam, muscle weakness, and muscle atrophy (chronic hypomagnesemia).

Diagnostic Studies. As noted in calcium homeostasis, magnesium and calcium are closely related. Always check a total and ionized calcium with the magnesium level. A full electrolyte panel may help determine other gastrointestinal or renal losses, and a renal function panel will help determine any renal insufficiency.

Obtain an ECG in all cases of severe hypomagnesemia. Changes include prolonged PR and QT intervals, atrial and ventricular ectopy, and torsade de pointes.[9]

Management. Treatment of hypomagnesemia consists of treating the underlying disorder and replacing magnesium through IV or oral supplements. Oral supplements are preferred.[23] Use magnesium oxide for oral replacements. However, in a hemodynamically unstable patient with seizures or torsade de pointes, infuse magnesium sulfate at 25-50 mg/kg/dose IV every 4-6 hours. Although adults may tolerate intramuscular doses, children report these injections to be extremely painful and should be avoided. Watch for hypotension, respiratory depression, and heart block when infusing. Calcium gluconate is the recommended antidote.[7]

Disposition. Deciding on inpatient or PICU admission often varies by hospital. The following are recommendations, not strict guidelines.

Criteria to Admit to the Inpatient Pediatric Ward:

• Patients with symptomatic or severe hypomagnesemia.

• Management of the underlying disease requires inpatient care (e.g., profuse diarrhea, hypercalcemia).

Criteria to Admit to the PICU:

• Hemodynamic instability, arrhythmias, or an altered mental status.

• Additional significant electrolyte derangements requiring frequent monitoring, laboratory evaluations, and intervention at a PICU level.

Table 11. Normal Phosphorus Levels[1]

Age	Phosphorus (mg/dL)
0-9 days	4.5-9
10 days -24 months	4-6.5
3-9 years	3.2-5.8
10-15 years	3.3-5.4
>15 years	2.4-4.4

Source: Author adapted.

Hypermagnesemia

Definition. Hypermagnesemia, a serum magnesium level > 2.2 mEq/L,[1] is quite uncommon in children and is usually related to iatrogenic overdosing (e.g., Epsom salts) or from renal failure.[25] Medications that may cause hypermagnesemia include antacids, enemas, cathartics, or IV medications such as magnesium sulfate infusion in severe status asthmaticus.

Clinical Features. Symptoms of hypermagnesemia worsen as the level of magnesium increases: hypotension, followed by respiratory depression, apnea, and cardiac arrhythmias as the levels increase beyond 8 -10 mEq/L. Depressed deep tendon reflexes, lethargy, and confusion are also part of the constellation of symptoms.[25] ECG findings for severe hypermagnesemia progress with increased levels and include prolonged PR and QT intervals, widened QRS, and severe bradycardia followed by a complete heart block at levels > 10 mEq/L.[26]

Diagnostic Studies. Obtain a full serum electrolyte panel including total and ionized calcium, phosphorus, BUN, and creatinine to ensure no concomitant electrolyte abnormalities and a normal renal function.[9]

Management. Hypermagnesemia is an emergency. Treat hemodynamic instability as per PALS algorithms.[6] Stop any magnesium intake, oral and intravenous. If the etiology is not renal failure, continue treatment with IV fluid hydration and diuresis. A 10% calcium gluconate solution is recommended to treat symptomatic hypermagnesemia. (*See Table 5 for dosing.*) Calcium opposes the effect of magnesium on the membranes to reverse respiratory and cardiac depression. Finally, dialysis may be needed for refractory hypermagnesemia or renal failure.[9,25]

Disposition. Deciding on inpatient or PICU admission often varies by hospital.

The following are recommendations, not strict guidelines.

Criteria to Admit to the Inpatient Pediatric Ward:

• Patients with symptomatic or severe hypermagnesemia.

• Management of the underlying disease requires inpatient care (e.g., status asthmaticus or renal failure).

Criteria to Admit to the PICU:

• Hemodynamic instability or respiratory depression.

• Additional significant electrolyte derangements requiring frequent monitoring, laboratory evaluations, and intervention at a PICU level.

Acid-Base Disorders

Acid-base disorders are caused by changes in the extracellular fluid (ECF) levels of hydrogen (H+) and bicarbonate (HCO_3-) ions. (*See Table 15.*)

This discussion will focus on acute rather than chronic disorders.

In practice, the bicarbonate level is used, not the hydrogen. This is reported in a blood gas or serum. In the former, HCO_3- is calculated from the pH and PCO_2, not measured, by using the Henderson-Hasselbalch equation. However, serum HCO_3- is measured, but as the total serum CO_2, which is typically 2 mEq/L greater than arterial HCO_3-. In this text, we will refer to serum HCO_3- and serum CO_2 interchangeably.

Normal HCO_3- is 20-28 mEq/L.[1] The units mmoL/L may also be used and, in this case, they are equivalent.

The pH and PCO_2 are usually measured via a blood gas. A venous blood gas (VBG), an arterial blood gas (ABG), or a capillary blood gas (CBG) in neonates may be used to determine these with minor variations that are not clinically significant for acid-base disorders. The main difference to acknowledge is the pH difference. Normal arterial pH is 7.35-7.45, and the normal venous pH is 7.3-7.4. It is recommended to use a central VBG for sick patients, as it reflects the state of tissue perfusion.[27] In theory and for definitions, typically the pH and PCO_2 from ABGs are used.

Metabolic Acid-Base Disorders

Metabolic Acidosis

Definition. Metabolic acidosis is defined by an arterial pH < 7 .35 with a serum bicarbonate (CO_2) < 22 mEq/L.[9]

Table 12. Etiologies of Hypophosphatemia and Hyperphosphatemia[9,19,20]

Hypophosphatemia		
Decreased Intake	**Increased Excretion**	**Decreased Intracellular Shifts**
Starvation Protein-energy malnutrition Malabsorption Rickets Very low birth weight infants	Renal disease Diuretic therapy	Alkalosis (moves phosphorus into the cell) Recovering diabetic ketoacidosis
Hyperphosphatemia		
Increased Intake	**Decreased Excretion**	**Increased Intracellular Shifts**
Hypoparathyroidism Iatrogenic administration (e.g., laxatives)	Renal failure	Tumor lysis syndrome

Source: Author adapted.

Table 13. Phosphorus Replacement Therapies[7]

	Potassium Phosphate/ Sodium Phosphate
Dosing	Acute/symptomatic: 5-10 mg/kg/dose IV over 6 hours Chronic/asymptomatic: 30-90 mg/kg/24 hr PO ÷ every 6-8 hours
Contraindications	Caution in renal insufficiency
Side effects	Tetany, hyperphosphatemia, hyperkalemia, hypocalcemia. Hypotension, renal failure, arrhythmias, heart block, cardiac arrest with IV potassium phosphate
Warnings	Do not co-infuse with calcium Monitor electrolytes regularly

IV = intravenous; PO = per os

Source: Author adapted.

Although the following definitions are arbitrary and may vary slightly, generally, mild metabolic acidosis is defined by an arterial pH 7.30-7.36 and/or a CO_2 > 20 mEq/L; moderate metabolic acidosis a pH 7.20-7.29 and/or CO_2 10-19 mEq/L; and severe metabolic acidosis a pH < 7.20 and/or CO_2 < 10 mEq/L.[27]

Acute metabolic acidosis develops within minutes to days, and chronic metabolic acidosis develops over weeks to years. In itself, metabolic acidosis is not a disease, but rather is a non-specific finding that indicates an underlying disease. However, it still may have dire consequences on the organs of the body, including but not limited to decreased cardiac contractility and output, cardiac arrhythmias, peripheral vasodilation, hypotension, decreased tissue oxygen delivery, stimulation of inflammatory mediators, and phagocytosis.[27]

Epidemiology. The most emergent causes are sepsis, diabetic ketoacidosis, and inborn errors of metabolism (these include the lactic acidosis and ketoacidosis, which in fact have been the most studied).

Etiology. Metabolic acidosis can be divided into two groups based on the anion gap. (*See Table 15*). The anion gap is calculated from serum electrolytes (in mEq/L) as follows:

Anion gap (AG) = [Na+] – [Cl- + HCO_3-]

A normal AG is 12 ± 2 mEq/L.[9]

Note that some formulas include the potassium as another cation; however, the number is usually insignificant and does not affect the anion gap. A normal anion gap metabolic acidosis is also called hyperchloremic metabolic acidosis, and typically presents with elevated serum chloride levels too.

The osmolar gap and lactic acid level help differentiate increased anion gap metabolic acidosis further. (*See Table 16.*) The osmolar gap is the difference between the measured and the calculated serum osmolality. It is calculated as follows:

Calculated osmolarity:

2 (Na) + (BUN/2.8) + (Glucose/18)

Normal osmolar gap is ≤ 10 mOsm/L.[28]

Clinically, osmolality and osmolarity,

Table 14. Dosing of Oral Phosphate Binders[7]

	Aluminum Hydroxide	Calcium Carbonate	Calcium Acetate
Dosing	50-150 mL/kg/24 hrs ÷ every 4-6 hours, PO	125-375 mg/kg/24 hrs ÷ every 4-6 hours, PO	Only for adolescents and adults 1334 mg PO with each meal
Advantages	First drug used	Ubiquitous and cheap	Safest
Contraindications	Renal failure or gastrointestinal hemorrhage	Ventricular fibrillation Caution in renal failure	Ventricular fibrillation Caution in renal failure
Side effects	Constipation, encephalopathy, hypophosphatemia, aluminum intoxication with chronic use	High risk of hypocalcemia Constipation, hypophosphatemia, hypomagnesemia, nausea, vomiting, headache and confusion	Hypercalcemia Nausea
Warnings	Do not take other oral medications within 1-2 hours of ingestion	Increase fluid intake	Reduces absorption of certain medications; increases effect of digoxin Administer with meals and increase fluid intake

*PO = per os

Source: Author adapted.

although based on different units, are practically the same and often are used interchangeably. Osmolality is the number of particles per kilogram, and osmolarity is the number of particles per liter.[29]

Remember the mnemonic MUDPILES when a child presents with an increased anion gap metabolic acidosis of unknown cause: Methanol, Uremia, Diabetic ketoacidosis, Phenformin/metformin, Iron/isoniazid, Lactic acidemia (cyanide and carbon monoxide poisoning), Ethylene glycol, and Salicylates.

Lactic acidosis and ketoacidosis are the most common causes of metabolic acidosis. Etiologies of lactic acidosis include sepsis, tissue hypoxia, shock, generalized tonic-clonic seizures that are usually self-limiting, and ketoacidosis includes diabetic ketoacidosis and starvation/severe dehydration.

Pathophysiology. Metabolic acidosis is caused by a net gain of H+ or loss of HCO_3- in the ECF. H+ is typically gained by increased delivery to the ECF or decreased excretion from the kidneys. HCO_3- is lost via the gastrointestinal or the renal systems. The body will naturally attempt to compensate for the metabolic acidosis via two mechanisms that will also affect the final pH (this is also called buffering):

Respiratory compensation: As a primary metabolic acidosis starts, the $PaCO_2$ is normal. However, the respiratory system begins compensating within minutes by hyperventilation, causing a respiratory alkalosis, and a drop in the $PaCO_2$ (typically < 40 mmHg). This buffering can be predicted by using Winter's formula: $PaCO_2 = 1.5 \times (HCO_3\text{-}) + 8 \pm 2$.[28]

Another quick way of determining the appropriate compensation is to know the following: $PaCO_2$ will decrease by 1.2 mmHg for every 1 mEq/L decrease in serum HCO_3-. Knowing this prediction helps determine if there is an additional acid-base disorder in place (i.e., a mixed disorder).

Example: A 3-year-old boy with severe dehydration secondary to diarrhea presents with metabolic acidosis. His measured CO_2 is 11 mEq/L. What is the expected PCO_2 if the body is adequately compensating for this metabolic acidosis?

Using Winter's formula, $1.5 \times 11 + 8 \pm 2 = 24.5 \pm 2$. Therefore, the PCO_2 in an ABG or VBG is expected to be between 22.5 and 26.5 mmHg.

If the PCO_2 is not within that range (i.e., much lower), then a mixed disorder (respiratory alkalosis) is present and should be investigated further.

Renal compensation: The kidneys will excrete H+ in the urine and increase HCO_3- absorption. This compensation is slower (over days), but allows for full correction of the metabolic acidosis and near normalization of the pH.[28]

It is important to note that infants are more prone to metabolic acidosis and its complications than older children and adults. At baseline, they have a higher acid load secondary to decreased renal bicarbonate absorption and acid excretion, and increased acid production from growing bones. This makes it more difficult for them to compensate for acid-base disturbances such as with acute diarrhea.

Clinical Features. The presenting signs and symptoms of metabolic acidosis depend largely on the underlying disorder as well as on the degree of acidosis.

Table 15. Acid-Base Disorders[9]

Metabolic acidosis: arterial of pH < 7.35 with a serum HCO_3- < 22 mEq/L.
Metabolic alkalosis: arterial of pH > 7.45 with a serum HCO_3- > 26 mEq/L.
Respiratory acidosis: arterial of pH < 7.35 with a PCO_2 > 45 mmHg.
Respiratory alkalosis: arterial of pH > 7.45 with a PCO_2 < 35 mmHg
Source: Author adapted.

History. Ask about presenting symptoms, including severity and duration, such as fever, vomiting, and diarrhea; decreased oral intake and urine output (signs of dehydration); and polydipsia, polyuria, and weight loss (signs of diabetes). A past medical history significant for abdominal surgeries, renal disease, total parenteral nutrition, diabetes, and chronic medications is important. Attempting to determine intentional or accidental ingestions also may offer clues to the cause of the acidosis. There may not be an evident history of ingestion; therefore, it is important to ask about what medications, drugs, or toxins are present in the household. A history of chronic weight loss or failure to thrive may suggest chronic renal failure. The presence of developmental delay is concerning for inborn errors of metabolism.

Physical Exam. In clinically significant metabolic acidosis, a child will appear sick; vital signs may be abnormal; and mental status depressed. Depending on the underlying disorder, more specific signs may be present: dry mucous membranes, sunken eyes, poor capillary

refill, tachycardia, hypotension in severe dehydration, or sepsis. Signs of metabolic acidosis include Kussmaul breathing or, more commonly, just tachypnea (from the respiratory compensation), tachycardia, and hypotension secondary to myocardial depression. Plotting the child's weight (especially if previous weights are available) can help determine failure to thrive. Signs of chronic wasting, dysmorphic features, and hypotonia may suggest a possible inborn error of metabolism.

Diagnostic Studies (*see Figure 1*). When the history clearly identifies a predisposing etiology for the metabolic acidosis, then the studies can be geared toward that disease entity. For example, in a child with diarrhea and dehydration, electrolytes are the only laboratory measurements warranted to look for glucose, sodium, or potassium abnormalities if the child is severely dehydrated.

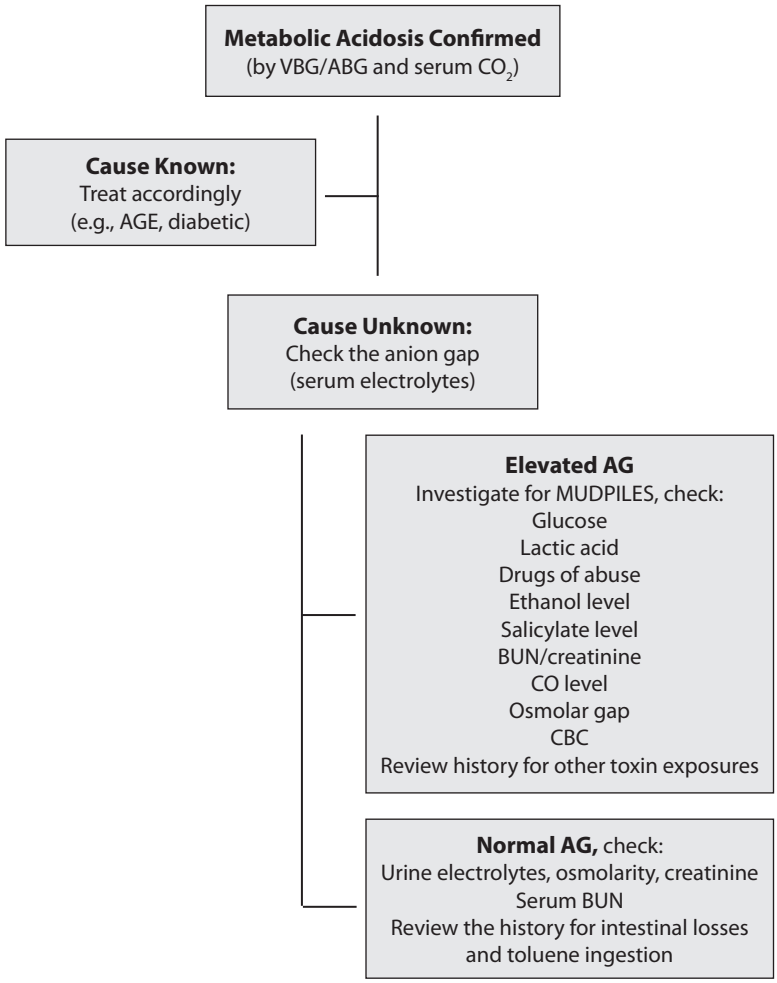
However, a child may present with an altered mental status, poor perfusion, and sick appearing but without a clear etiology. In such scenarios, if metabolic acidosis is identified, then the cause needs to be determined and treated.

Steps for the workup of metabolic acidosis of unknown origin:[9,28,30]

• First, if the metabolic acidosis is identified via the CO_2 in the electrolytes, obtain a VBG or ABG to document the pH, the $PaCO_2$, and the presence or absence of an appropriate respiratory compensation or a mixed disorder.

• Then, calculate the anion gap by ordering a full set of electrolytes: Hyperkalemia and hyperphosphatemia are common in certain disorders causing metabolic acidosis.

Figure 1. Metabolic Acidosis: Causes and Workup[9, 28,30]



VBG: venous blood gas, ABG: arterial blood gas, AGE: acute gastroenteritis; AG: anion gap; CO: carbon monoxide, BUN: blood urea nitrogen

Source: Author created

Table 16. Causes of Metabolic Acidosis[28,30]

Normal Anion Gap	Increased Anion Gap	
Renal tubular acidosis	Diarrhea/dehydration	
Early renal failure	Ketoacidosis (diabetic ketoacidosis or starvation)	
Hypernatremic dehydration	Renal failure	
Hyperalimentation	Inborn errors of metabolism	
Enteric fistulae or enterostomies	Poisoning/toxin	
Ureterosigmoidostomies	Metabolic diseases (seizures, lethargy, coma)	
Drugs (sulfamylon, amphoterecin, ammonium chloride, diamox)	Lactic acidosis: Hypoxia/tissue ischemia/shock (trauma or medical)	Increased serum lactate
Rapid volume expansion	Sepsis	
	Idiopathic	
	Toxic alcohol ingestions (methanol, ethylene glycol, "antifreeze")	Increased osmolar gap

Source: Author adapted.

• Finally, depending on the anion gap, target your investigation further (*see Figure 1 and Table 16*). Additional studies include serum osmolarity, lactic acid, CBC, toxins, liver function tests, and urine tests for creatinine, pH, and osmolarity. Work up all infants with an unexplained metabolic acidosis for inborn errors of metabolism. Consult with a geneticist early to determine the best laboratory tests to order and, hence, to avoid multiple blood draws on a small baby.

In children with an altered mental status and metabolic acidosis, consider non-accidental trauma and work up as indicated; also consider a post-ictal state from an unwitnessed seizure (this metabolic acidosis is transient).

Consider an ECG to detect any arrhythmias secondary to myocardial dysfunction from the metabolic acidosis.

Management. In a hemodynamically unstable patient, PALS algorithms should be followed.[3] Recognize shock emergently and treat immediately. Treat the underlying disease rapidly to minimize progression of the metabolic acidosis. In stable patients, or once resuscitation has begun in unstable patients, treatment targeting the metabolic acidosis remains controversial, and data for best practices, especially in children, are still poor with the exception of diabetic ketoacidosis.[27,31-34]

Three modalities of therapy are available for use in acute metabolic acidosis: sodium bicarbonate ($NaHCO_3$-) infusions, tromethamine (THAM), and dialysis; $NaHCO_3$- is the first line.[27]

Treatment with $NaHCO_3$-: Although very tempting to use immediately, the guidelines for $NaHCO_3$- infusions in acute metabolic acidosis remain controversial.[27,31,32] For non-anion gap metabolic acidosis, there appears to be more consensus on the advantages of $NaHCO_3$- therapy, and, therefore, it is recommended, although strong evidence is still lacking.[27,33,34] However, for elevated anion gap metabolic acidosis, typically from lactic acidosis or ketoacidosis, the evidence for the use of $NaHCO_3$- remains poor, especially in children, and depends on the severity of the acidosis and underlying illness. The rationale behind this is that in these clinical scenarios, there is no actual loss of bicarbonate from the body, but a conversion of bicarbonate into another organic acid, which, with the appropriate treatment, can be converted back.[31]

$NaHCO_3$- is inexpensive, widely available, and easy to use. However, it may increase intracellular acidosis, decrease cardiac contractility (by decreasing serum calcium), cause volume overload, hypernatremia, and a hyperosmolar state, and therefore should be used judiciously.

The following is used to treat a non-anion gap metabolic acidosis in the ED to calculate the bicarbonate deficit, with a goal to reach a serum HCO_3- of 15-18 and pH ≥ 7.25.[2,32,35] However, realistically this goal may not be reached in the ED. (*See Table 17.*)

It is important to recheck electrolytes every 2 hours to evaluate the anion gap, HCO_3-, as well as the potassium and calcium levels that can be complications of bicarbonate therapy. Consult with a specialist early to help guide the therapy. It is important to note that clinically and practically, during a busy ED shift, giving 0.5-1 mEq/kg of $NaHCO_3$- with a goal to reach a pH ≥ 7.2 would be sufficient.[2]

Treatment with THAM: THAM is a sodium-free alkalinizing agent. It has not yet been extensively studied in children, but it is thought to be advantageous over $NaHCO_3$- because it does not cause intracellular acidosis. However, it may cause respiratory depression and hypoglycemia.[27,35] It is recommended for use in patients with CO_2 retention.[27] Note that a child should have an intact kidney function or be on dialysis to use THAM to allow clearance. (*See Table 17.*)

Scenarios in which alkali treatment is not required or is contraindicated:

1. Metabolic acidosis secondary to hypovolemia (dehydration, diarrhea) can be treated solely with fluid resuscitation. Use normal saline or lactated Ringer's at 20 mL/kg over 30-60 min (or faster if in shock) with repetition as needed to ensure appropriate hydration.

2. Treat diabetic ketoacidosis with IV hydration and an insulin drip rather than bicarbonate. $NaHCO_3$- infusions are not recommended and may be harmful as they are associated with cerebral edema.[36 37]

3. Ingestion of ethylene glycol, methanol, or isopropyl alcohol may benefit from specific treatments such as IV fomepizole, ethanol (competes with the other alcohols), or hemodialysis.

Table 17. Management of Acute Metabolic Acidosis

Treatment with $NaHCO_3$
For a pH 7.2-7.37:
HCO_3- (mEq) = [normal serum HCO_3- – patient's serum HCO_3-] x 20% of TBW (kg or L)
pH < 7.2: HCO_3- (mEq) = [normal serum HCO_3- – patient's serum HCO_3-] x 50% of TBW (kg or L)
Serum HCO_3: measured total CO_2 in the serum; TBW: total body weight.
Normal serum HCO_3- is 20-28 mEq/L. We recommend using 20 mEq/L in these formulas as it would be the lower level to reach for correction of the acidosis. In practice, the typical $NaHCO_3$ solution present in the ED would be the $NaHCO_3$- 1 mEq/L (8.4%) concentration, available in 10 mL and 50 mL. It should be diluted (with the use of dextrose 5% or sterile water) to a concentration of 0.5 mEq/L and infused over 2 hours at a maximal rate of 1 mEq/kg/hr.[7]
Example: A 2-year-old, 14 kg child presents with a pH of 7.23 and an HCO_3- of 14 mEq/L.
The HCO_3- deficit is: [normal serum HCO_3- – patient's serum HCO_3-] x 20% of TBW (kg)
[20-14] x (20 x 14/100) = 6 x 2.8 = 16.8 mEq
Example: A 5-year-old boy weighing 25 kg has a pH of 7.05 and an HCO_3- of 8 meq/L.
The HCO_3- deficit is: [normal serum HCO_3- – patient's serum HCO_3-] x 50% of TBW (kg)
[20-8] x (50 x 25/100) = 150 mEq
Treatment with THAM[35]
Amount in mL of (3 mmol/L of THAM) = TBW (kg) x [desired serum HCO_3- – patient's serum HCO_3-] (mEq/L) x 1.1
Serum HCO_3: measured total CO_2 in the serum; TBW: total body weight
Example: A 2-year-old 14 kg child presents with a pH of 7.23 and an HCO_3- of 14 mEq/L. Creatinine 0.3 mg/dL. How much THAM is needed to correct the acidosis?
TBW (kg) x [desired serum HCO_3- – patient's serum HCO_3-] (mEq/L) x 1.1
14 x [20-14] x 1.1 = 99 mL of THAM (3 mmol/L)
Source: Author adapted.

Table 18. Causes of Metabolic Alkalosis

Chloride-responsive metabolic alkalosis (Ur Cl < 10 mEq/L)	Non-chloride responsive metabolic alkalosis (Ur Cl > 20 mEq/L)
Chronic GI loss: Pyloric stenosis, NG suctioning, vomiting, chronic diarrhea	Renal tubular defects: Bartter and Gitelman syndromes
Cystic fibrosis (sweat loss)	Adrenal disease
Contraction alkalosis secondary to diuretic use	Exogenous steroid use
	Excessive ingestion of $NaHCO_3$-, CaCarb, licorice

Ur Cl: urine chloride; GI: gastrointestinal; NG: nasogastric; $NaHCO_3$-: sodium bicarbonate; CaCarb: calcium carbonate

Source: Author adapted.

4. Attempt to treat the underlying cause of lactic acidosis before using bicarbonate therapy. These therapies include aggressive IV hydration, vasopressors, and antibiotics. However, if metabolic acidosis is severe (pH < 7.1) or the patient is unstable, then consider $NaHCO_3$- therapy as described above.[27] Consult with the appropriate specialist (poison control/toxicology, nephrology, endocrinology) early. Finally, chronic metabolic acidosis, typically caused by renal dysfunction, can be treated with $NaHCO_3$- in conjunction with a nephrologist's recommendations.[38]

Disposition.[29] Deciding on inpatient or PICU admission often varies by hospital. The following are recommendations, not strict guidelines.

Criteria to Admit to the Inpatient Pediatric Ward:

• Patients with metabolic acidosis of unknown etiology.

• Management of the underlying disease requires inpatient care, e.g., severe dehydration, ingestions, mild DKA (in certain institutions), inborn errors of metabolism.

Criteria to Admit to the PICU:

• Hemodynamic instability or mental status changes.

• Metabolic acidosis with pH < 7.1 or worsening metabolic acidosis.

• Underlying disease requires PICU level care (e.g., sepsis, moderate-to-severe DKA, in certain institutions).

Metabolic Alkalosis

Definition. Metabolic alkalosis is defined by an arterial pH > 7.45 with a serum HCO_3- (CO_2) > 26 mEq/L.[9] Secondary metabolic alkalosis, to compensate for respiratory acidosis, is more common than primary. This is typically seen in children with chronic respiratory acidosis secondary to chronic lung disease such as bronchopulmonary dysplasia from prematurity.

Etiology. Causes of metabolic alkalosis can be divided into two groups: chloride-responsive and non-chloride-responsive. (*See Table 18.*) Chloride-responsive metabolic acidosis typically responds to normal saline fluid treatment.[30]

Pathophysiology. Metabolic alkalosis is caused by a net loss of H+ or gain of HCO_3- in the ECF. This can be accomplished by several mechanisms:[9]

1. Intracellular H+ shifts: H+ is combined with potassium pumps. If a child develops hypokalemia secondary to vomiting, potassium will be shifted out of the cells in exchange of H+, resulting in a loss of ECF H+ and alkalosis.

2. Gastrointestinal loss of H+: H+ is part of the gastric fluid, and is lost when excessive gastric fluid is lost, such as with prolonged nasogastric suctioning, or pyloric stenosis. Such gastrointestinal losses are typically associated with potassium and chloride loss too. For example, infants with pyloric stenosis may present with a hypochloremic hypokalemic metabolic alkalosis, especially when the condition has been occurring for several weeks.

3. Renal loss of H+: Metabolic alkalosis secondary to renal losses of H+ only occurs when the kidney is unable to excrete the excess bicarbonate as it would normally do. Infants have immature kidneys and, therefore, are more susceptible to these changes. In addition, conditions affecting renal function will also exacerbate this. Such scenarios include a decrease in the glomerular filtration rate, heart failure, and even dehydration.

4. Contraction alkalosis: In situations in which a child is severely dehydrated but without any initial loss of bicarbonate in the ECF, metabolic alkalosis may ensue. This may be found in children presenting with severe dehydration secondary to decreased oral hydration and fever or from excessive use of diuretics, rather than from acute gastroenteritis.

5. Iatrogenic: Excessive administration of bicarbonate: This may be clinician- or patient-induced. As with metabolic acidosis, the body will naturally attempt to compensate for the metabolic alkalosis, mainly via hypoventilation (respiratory compensation). For every 1 mEq/L increase in serum HCO_3-, there should be a 0.7 mmHg decrease in $PaCO_2$. If this compensation is not appropriate, as with metabolic acidosis, suspect a mixed acid-base disorder

Clinical Features. *History.* As with all electrolyte abnormalities, a detailed history will help reveal the underlying cause. Diseases specific to children include pyloric stenosis, and Bartter and Gitelman syndromes. With pyloric stenosis, the typical history is that of a 4- to 8-week-old baby with immediate (usually within 15 min) postprandial projectile emesis, followed by the baby often being hungry again.

Bartter syndrome may present with failure to thrive and developmental delay in the setting of metabolic alkalosis and hypokalemia,[39,40] and Gitelman syndrome with non-specific signs of weakness and fatigue as well as muscle cramps and polyuria. A review of symptoms for causes of gastrointestinal loss is important, as well as a past medical history of chronic lung disease (e.g., cystic fibrosis or bronchopulmonary dysplasia) and a list of medication use (diuretics and steroids).

Physical Exam. Once again, physical exam findings will depend mostly on the underlying disease and associated electrolyte abnormalities, specifically, hypokalemia. Hypoventilation may be noted in cases of compensation for severe alkalosis. When severe, this may be associated with hypoxia and impending respiratory failure. Hypokalemia and hypocalcemia are commonly associated with metabolic alkalosis, and, therefore, signs and symptoms related to these electrolyte abnormalities also may be present.

Diagnostic Studies. When the history clearly identifies a predisposing etiology for the metabolic alkalosis, then the studies can be geared toward that disease entity.

Table 19. ECG Changes Secondary to Electrolyte Abnormalities

Hypokalemia	Prolonged PR interval	Flattened T waves	Depressed ST segment	U waves	Ventricular fibrillation & torsade de pointes		
Hyperkalemia	Tall peaked T waves with short QT interval	Prolonged PR interval	Decreased or disappearing P waves	Wide QRS and amplified R wave	Absent P wave	Bundle branch block	Ventricular fibrillation & asystole
Hypocalcemia	Prolonged QT	Prolonged ST	T wave changes				
Hypercalcemia	Short QT	Short ST	T wave changes				
Hypomagnesemia	Prolonged PR interval	Long QT	Atrial and ventricular ectopy	Torsade de pointes			
Hypermagnesemia	Prolonged, PR, QT Wide QRS	Severe bradycardia	Complete heart block				

Source: Author Created

For example, for an infant with possible or confirmed pyloric stenosis, serum electrolytes are the only laboratory measurements warranted. Realistically, in such a scenario, a gas is not required unless the infant is ill-appearing. However, often, metabolic alkalosis is an "incidental finding" when a gas or serum electrolyte panel is drawn as part of a workup for an ill-presenting patient with an unknown diagnosis. In such cases, a pH, PCO_2, HCO_3-, full set of electrolytes (specifically for potassium, chloride, calcium, and creatinine) as well as a urine chloride are essential. If hypokalemia or hypocalcemia is noted, obtain an ECG.

Management. The mainstay of treatment is to treat the underlying disease, dehydration, and concomitant electrolyte abnormalities. In the ED, most of the cases of metabolic alkalosis will resolve with adequate hydration (with normal saline or lactated Ringer's) and electrolyte replacement (as described previously). When a more rapid correction is needed, for example for surgery, weaning off respiratory support, or avoiding respiratory failure and mechanical ventilation, more aggressive therapies can be used. Typically, sodium chloride hydration is the treatment of choice for the chloride-responsive metabolic alkalosis. Hydrochloric acid infusions may be recommended for a pH > 7.55 or HCO_3- > 55.[2] If the patient is treated with diuretics, these should be stopped or switched to potassium-sparing ones. New evidence for the use of cimetidine for more rapid correction in pyloric stenosis has been reported.[41] Acetazolamide has also been used with some success for chloride-resistant metabolic alkalosis, as well as for chronic metabolic alkalosis.[42]

Disposition. Deciding on inpatient or PICU admission often varies by hospital. The following are recommendations, not strict guidelines.

Criteria to Admit to the Inpatient Pediatric Ward:

• Patients with metabolic alkalosis of known etiology requiring further inpatient workup or treatment.

• Management of the underlying disease requires inpatient care (e.g., renal failure).

Criteria to Admit to the PICU:

• Hemodynamic instability or hypoventilation severe enough to require respiratory support until the metabolic alkalosis is reversed.

• Underlying disease requires PICU level of care (e.g., renal failure and dialysis in certain institutions).

Summary

Children with disorders of electrolytes and acid-base disorders are frequently encountered in the ED. The history and physical exam are key in identifying clues to the etiology of these disorders. Treatment of electrolyte disorders typically consists of replacing the missing electrolyte or protecting the organs from elevated levels. Arrhythmias are a common finding in electrolyte abnormalities (*see Table 19*) and are often a trigger for aggressive therapy. Benefits of aggressive therapy should be weighed against the potential side effects. Treatment of metabolic acidosis in children remains controversial in many areas, with insufficient data to guide the management in many cases. As a rule of thumb, use sodium bicarbonate judiciously. Treatment of metabolic alkalosis is focused on treating the underlying disease. This review guides clinicians in the management of electrolyte disorders and common metabolic acid-base disorders.

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CME/CE Questions

1. What is the most common cause of hypokalemia in children?
   A. Short gut syndrome
   B. Iatrogenic errors in TPN or IV fluids
   C. Albuterol use
   D. Gastroenteritis

2. In neonates, hyperkalemia is defined as a serum potassium level greater than which of the following?
   A. 4.5 mEq/L
   B. 6.5 mEq/L
   C. 5 mEq/L
   D. 3.5 mEq/L

3. A 16-year-old female presents with paresthesia in her upper extremities after an argument with her boyfriend who was threatening to break up with her. Her symptoms are now slowly resolving. What is the best next step?
   A. Obtain a brain MRI
   B. Order a full serum electrolyte panel including calcium, phosphorus, and magnesium
   C. Do nothing, observe in the emergency department
   D. Consult neurology

4. A 2-day-old presents with a focal seizure. Full septic workup is done, antibiotics are started. A CT head is normal. Electrolytes show a calcium of 6 mg/dL. What would be the most helpful in determining the underlying etiology?
   A. A history of being exclusively breast fed
   B. A full term baby
   C. A history of maternal gestational diabetes
   D. A magnesium level of 1.6 mEq/L

5. What is the most common presentation of hyperphosphatemia?
   A. A 2-month-old with new onset seizures
   B. An asymptomatic finding
   C. A 6-year-old boy with profuse diarrhea
   D. A 16-year-old female with anorexia nervosa

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PEDIATRIC EMERGENCY MEDICINE **REPORTS**

Practical, Evidence-Based Reviews in Pediatric Emergency Care

Fluids and Electrolyte Management, Part 2: Electrolyte Disturbances and Acid-Base Disorders

Etiology of Pediatric Hypokalemia[2,3]

Gastrointestinal Loss	Renal Loss	Decreased Intake (rare)	Intracellular Shift (normal total body potassium)
Diarrhea Vomiting Laxatives Short gut syndrome	Alkalosis Renal tubular acidosis type 1 or 2 Aldosterone secreting adenomas Glucocorticoid/mineralocorticoid excess (e.g., congenital adrenal hyperplasia) Hypovolemia Bartter and Gitelman syndromes Diuretics	Malnutrition Anorexia Errors in total parenteral nutrition	Insulin Beta-adrenergic medications (e.g., albuterol) Hypokalemic periodic paralysis (rare and familial)

Source: Author adapted.

Common Causes of Hyperkalemia in Children[4,8]

Increased Intake (increased total body potassium)	Decreased Excretion (decreased total body potassium)	Intracellular Shift (normal total body potassium)
Iatrogenic causes (e.g., total parenteral nutrition, intravenous fluids) Medication use (e.g., supplements, potassium-sparing diuretics)	Renal insufficiency or failure (acute or chronic) Severe hypovolemia Adrenal insufficiency	Rhabdomyolysis (e.g., crush injury, exercise) Massive hemolysis or transfusion Tumor lysis syndrome Acidosis (e.g., diabetic ketoacidosis)

Source: Author adapted.

ECG Changes[6,7]

Serum K (mEq/L)	5.5	6.5		7.5	8	9	>10
ECG changes	Tall peaked T waves with short QT interval	Prolonged PR interval	Decreased or disappearing P waves	Wide QRS and amplified R wave	Absent P wave	Bundle branch block	Ventricular fibrillation and asystole

Medications Used to Treat Hyperkalemia[6,7]

	10% Calcium Gluconate (10% = 100 mg/mL = 9 mg/L elemental Ca)	Regular Insulin and Glucose	Albuterol	Sodium Bicarbonate	Furosemide	Sodium Polystyrene Sulfonate
Dosage	For hyperkalemia or hypermagnesemia with ECG changes or cardiac arrest: 100 mg/kg/dose (1 mL/kg/dose) slow IVP. May repeat in 10 min. Maximum rates: IVP 100 mg/min; Infusion 120-240 mg/kg/hr For hypocalcemia: 200-500 mg/kg/24 hours divided every 6 hours, IV	0.1 unit/kg IV (max 10 units) over 30 min Mix with D25W as 2 mL/kg Repeat in 30-60 min	Nebulizer: < 25 kg: 2.5 mg 25-50 kg: 5 mg > 50 kg: 10 mg OR 4-8 puffs of MDI	1 mEq/kg (max 50 mEq) over 5-10 min In infants use the 4.2% concentration	1 mg/kg (max 80 mg)	1 g/kg (max 50 g) every 6 hours
Mode	IV/IO through a large vein or central line (preferably)	IV/IO	Inhaled	IV	IV	PO/NG/PR
Onset/Duration	1-2 min/30-60 min	10-20 min/ 1-4 hours	20-30 min/ 2-4 hr	15 min/1-4 hr	1-2 hr/4-6 hr	1-2 hr/ 4-6 hr
Effect on K	—	Drops by 0.5-1 mEq/L	Drops by 0.5-1 mEq/L	Unpredictable	—	1 g binds 1mEq of K
Side Effects	Hypercalcemia Bradycardia Arrhythmia with digitalis Extravasation into tissue	Hypoglycemia or hyperglycemia	Tachycardia	Hypernatremia Volume overload CO_2 (ensure adequate ventilation) Tissue irritation	Hypovolemia Electrolyte abnormalities	Electrolyte abnormalities, constipation, NEC
Warnings	CI in ventricular fibrillation; Caution in renal impairment; Precipitates if infused in the same line as sodium bicarbonate		Mix in 2 mL of saline for the nebulizer	Do not infuse in the same line as calcium Flush IV tube before and after	Requires good renal and liver function	CI in preterm, term neonates with intestinal dysfunctions
Monitor	Serial EKG Calcium	Glucose		Sodium	Fluid status Electrolytes	Electrolytes

Ca = calcium; K = potassium; IVP = intravenous push; IO = intraosseous; CI = contraindicated; D25W: 25% dextrose in water; MDI = metered-dose inhaler; NG = nasogastric; NEC = necrotizing enterocolitis

Source: Author Created

Most Common Causes of Hypocalcemia in Children[10]

Neonatal Period	Beyond the Neonate
Prematurity Perinatal asphyxia Maternal gestational diabetes Intrauterine growth retardation Phosphorous intake Hypomagnesemia Hypoparathyroidism Gentamycin toxicity	Hypoparathyroidism Hypomagnesemia Hyperphosphatemia Malabsorption Vitamin D deficiency Pancreatitis Drugs (e.g., antiepileptics, calcium channel blockers) Tumor lysis syndrome Renal failure Respiratory alkalosis (e.g., hyperventilation from anxiety, tachypnea, respiratory distress, pneumonia) Rattlesnake bite

Source: Author adapted.

Acid-Base Disorders[9]

Metabolic acidosis: arterial of pH < 7.35 with a serum HCO_3^- < 22 mEq/L.
Metabolic alkalosis: arterial of pH > 7.45 with a serum HCO_3^- > 26 mEq/L.
Respiratory acidosis: arterial of pH < 7.35 with a PCO_2 > 45 mmHg.
Respiratory alkalosis: arterial of pH > 7.45 with a PCO_2 < 35 mmHg

Source: Author adapted.

Etiology of Hypocalcemia in Relation to the Serum Phosphate[10,13]

Serum phosphate low	Serum phosphate normal	Serum phosphate high
Primary and secondary vitamin D deficiencies or resistance (e.g., malabsorption, anticonvulsant therapy, chronic renal failure) X-linked hypophosphatemic rickets	Malabsorption Anticonvulsants Renal tubular acidosis Primary vitamin D dependence types I and II	True hypoparathyroidism Iatrogenic causes Renal insufficiency

Source: Author adapted.

Common Causes of Hypercalcemia[14,15]

Increased bone resorption	Increased intestinal absorption	Miscellaneous
Immobilization Bony metastases Hyperparathyroidism (e.g., primary, malignancy, secondary to renal failure) Hypervitaminosis A	Vitamin D intoxication Hypervitaminosis D Milk alkali syndrome Lymphoma Tuberculosis Sarcoidosis	Infantile hypercalcemia Thiazide diuretics (decrease renal excretion) Dietary intake

Source: Author adapted.

Dosing of Oral Phosphate Binders[7]

	Aluminum Hydroxide	Calcium Carbonate	Calcium Acetate
Dosing	50-150 mL/kg/24 hrs ÷ every 4-6 hours, PO	125-375 mg/kg/24 hrs ÷ every 4-6 hours, PO	Only for adolescents and adults 1334 mg PO with each meal
Advantages	First drug used	Ubiquitous and cheap	Safest
Contraindications	Renal failure or gastrointestinal hemorrhage	Ventricular fibrillation Caution in renal failure	Ventricular fibrillation Caution in renal failure
Side effects	Constipation, encephalopathy, hypophosphatemia, aluminum intoxication with chronic use	High risk of hypocalcemia Constipation, hypophosphatemia, hypomagnesemia, nausea, vomiting, headache and confusion	Hypercalcemia Nausea
Warnings	Do not take other oral medications within 1-2 hours of ingestion	Increase fluid intake	Reduces absorption of certain medications; increases effect of digoxin Administer with meals and increase fluid intake

*PO = per os

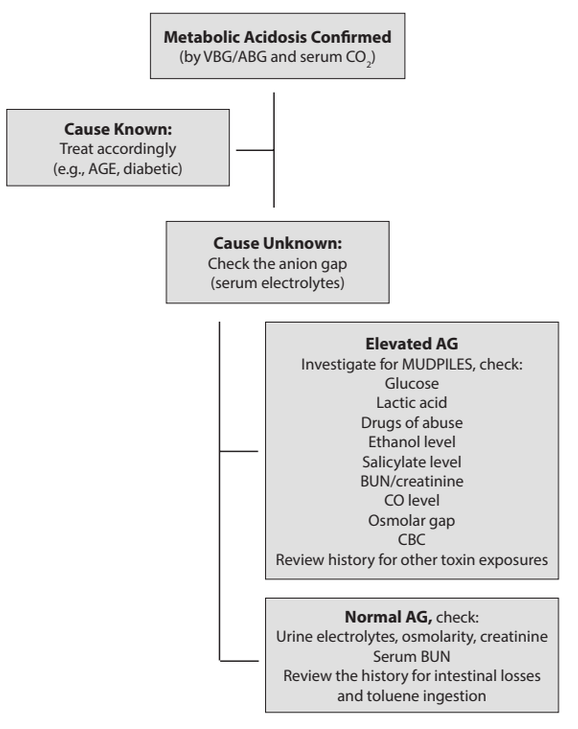
Source: Author adapted.

Causes of Metabolic Acidosis[28,30]

Normal Anion Gap	Increased Anion Gap	
Renal tubular acidosis	Diarrhea/dehydration	
Early renal failure	Ketoacidosis (diabetic ketoacidosis or starvation)	
Hypernatremic dehydration	Renal failure	
Hyperalimentation	Inborn errors of metabolism	
Enteric fistulae or enterostomies	Poisoning/toxin	
Ureterosigmoidostomies	Metabolic diseases (seizures, lethargy, coma)	
Drugs (sulfamylon, amphoterecin, ammonium chloride, diamox)	Lactic acidosis: Hypoxia/tissue ischemia/shock (trauma or medical)	Increased serum lactate
Rapid volume expansion	Sepsis	
	Idiopathic	
	Toxic alcohol ingestions (methanol, ethylene glycol, "antifreeze")	Increased osmolar gap

Source: Author adapted.

Metabolic Acidosis: Causes and Workup[9, 28,30]



VBG: venous blood gas, ABG: arterial blood gas, AGE: acute gastroenteritis; AG: anion gap; CO: carbon monoxide, BUN: blood urea nitrogen

Source: Author created

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