Back to Basics: Acidosis and Alkalosis

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Pediatr. Rev. 2004;25;350-357
DOI: 10.1542/pir.25-10-350

BACK TO BASICS

A review of the scientific foundations of current clinical practice

Acidosis and Alkalosis

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Objectives

After completing this article, readers should be able to:

1. Plan initial therapy for severe acidosis (metabolic).
2. Know the differential diagnosis of acidosis associated with a high anion gap.
3. Discuss the consequences of chronic volume contraction.
4. Describe the pulmonary compensatory changes seen in primary metabolic alkalosis.
5. Describe the renal compensatory changes seen in primary respiratory acidosis and in primary respiratory alkalosis.
6. Delineate which diuretics produce metabolic alkalosis and which produce metabolic acidosis.

Case Study

A 20-kg child presents with the primary complaints of several days of diarrhea, poor intake, and decreased urine output. On physical examination, the patient has a respiratory rate of 30 breaths/min and mildly dry mucous membranes. Laboratory evaluation demonstrates: sodium, 135 mEq/L (135 mmol/L); potassium, 4.0 mEq/L (4.0 mmol/L); chloride, 120 mEq/L (120 mmol/L); bicarbonate, 4 mEq/L (4 mmol/L); blood urea nitrogen, 10 mg/dL (3.6 mmol/L); creatinine, 0.5 mg/dL (44.2 mcmol/L); glucose, 100 mg/dL (5.6 mmol/L); arterial pH, 7.02; and P_{CO_2}, 16 mm Hg. What needs to be considered in the differential diagnosis? Is intravenous hydration alone adequate for therapy?

Introduction

Acid-base disorders, which may be caused by a variety of underlying conditions, are encountered frequently in both inpatient and outpatient settings. Because many variables are involved in the regulation of acid-base homeostasis, the clinical approach to these disturbances may seem confusing. A basic understanding of the physiology, evaluation, and treatment of acid-base disorders can help the pediatrician to prevent the consequences of altered acid-base homeostasis.

An acid is a substance capable of donating protons (hydrogen ions), and a base is a substance capable of receiving protons. The body's extracellular hydrogen ion (H^+) concentration is extremely small, less than *one-millionth* the concentration of sodium (Na^+). The negative logarithm of the hydrogen ion concentration is the pH, and this determination is clinically most useful.

The normal pH of arterial blood is 7.4 and is maintained within narrow limits, due to acid being highly reactive, particularly with proteins. Acidemia is defined as an arterial pH less than 7.36, and alkalemia occurs when the pH is greater than 7.44. The process of acid-base regulation involves: 1) buffering by extracellular

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and intracellular buffers, 2) controlling the partial pressure of carbon dioxide (P_{CO_2}) by means of the respiratory rate, and 3) controlling the plasma bicarbonate by changes in renal acid excretion. The most important extracellular buffer is bicarbonate (HCO_3^-), which can be combined with hydrogen ions according to the following reaction: $H^+ + HCO_3^- \leftrightarrow H_2CO_3 \leftrightarrow H_2O + CO_2$. The patient's acid-base status is determined by the ratio of bicarbonate to carbon dioxide (CO_2) concentrations, as expressed by the Henderson-Hasselbalch equation: $pH = 6.1 + \log (HCO_3^-/(0.03 \times P_{CO_2}))$. Volatile carbon dioxide, which is produced by the metabolism of carbohydrates and fats, is not an acid but combines with water to form carbonic acid. The loss of carbon dioxide via respiration prevents a progressive accumulation of carbonic acid. Nonvolatile acids (acids other than carbonic acid) are derived from the metabolism of proteins and are excreted in the urine.

Control of the plasma bicarbonate by changes in renal acid excretion occurs primarily in the tubules. The proximal tubule reabsorbs 85% of filtered bicarbonate, and the thick ascending limb reabsorbs 10%. The remaining bicarbonate is reabsorbed in the collecting duct, and excreted acid combines with buffers in the tubular lumen, primarily phosphate and ammonia, allowing the regeneration of additional bicarbonate. Acid secretion causes a rise in serum bicarbonate, and acid retention causes a fall in serum bicarbonate. Acidosis refers to processes that cause acid to accumulate, and alkalosis refers to processes that cause base to accumulate.

Metabolic Acidosis

Definition

Metabolic acidosis is defined as a net loss of bicarbonate or gain of hydrogen ions that results in an arterial pH below 7.36, accumulation of nonvolatile acid, and usually a decrease in the serum bicarbonate.

Causes, Pathogenesis, and Clinical Aspects

Metabolic acidosis may be caused by several mechanisms, including increased acid production, increased acid intake, decreased renal acid excretion, or increased bicarbonate loss from the gastrointestinal tract or the kidney. As a result of respiratory compensation, by the means of increased ventilation, each 1 mEq/L (1 mmol/L) reduction in plasma bicarbonate concentration results in a 1.2-mm Hg fall in the P_{CO_2}. This response begins rapidly, usually within 1 hour, and is complete within 24 hours. The patient in the case study has the expected low P_{CO_2} that indicates a compensated metabolic acidosis. In the absence of an associated respiratory disorder, the patient's tachypnea is explained adequately by the respiratory compensation. The conditions that cause a metabolic acidosis (Table 1) are divided into normal anion gap acidosis and elevated anion gap acidosis.

NORMAL ANION GAP

Normal anion gap acidosis is caused by the inability to excrete hydrogen or the loss of bicarbonate from the gastrointestinal or urinary tracts. An anion gap, which may be estimated from the following formula—$Na^+ - (Cl^- + HCO_3^-)$—is defined as elevated when the difference is greater than 12 mEq/L. The normal value for an anion gap may be higher for children younger than 2 years of age, with some authors using 16±4 mEq/L as the normal range. In the case report, a normal anion gap of 11 mEq/L (135 – (120+4)) is present.

Diarrhea is the leading cause of such an acidosis among children. Surgical procedures that expose urine to ileal mucosa result in chloride-bicarbonate exchange, as does the use of cationic exchange resins such as cholestyramine. Both conditions result in an increased gastrointestinal loss of bicarbonate. Renal tubular acidosis (RTA) also is associated with a normal gap metabolic

Table 1. Causes of Metabolic Acidosis

Normal Anion Gap

- Gastrointestinal loss of bicarbonate
  - –Diarrhea
  - –Pancreatic fistula
  - –Ureteroenterostomy
  - –Ureterosigmoidostomy
- Drugs
  - –Acidifying agents
  - –Cholestyramine
  - –Magnesium chloride
  - –Sulfamylon
- Hyperalimentation
- Rapid intravenous hydration with 0.9% NaCl
- Renal loss of bicarbonate
  - –Renal tubular acidosis
  - –Carbonic anhydrase inhibitor
  - –Hyperparathyroidism
- Posthypocapnea
- Hypoaldosteronism

Elevated Anion Gap

- Renal failure
- Ketoacidosis
  - –Starvation or fasting
  - –Diabetic ketoacidosis
  - –Ethanol intoxication
- Lactic acidosis
  - –Tissue hypoxia
  - –Muscular exercise
  - –Ethanol ingestion
  - –Systemic diseases
  - –Inborn errors of metabolism
- Toxins
  - –Methanol
  - –Ethylene glycol
  - –Salicylates
  - –Paraldehyde

Adapted from Hanna et al, 1995; Narins and Emmett, 1980; and Chabali, 1997.

acidosis. In type II (proximal) RTA and with the use of carbonic anhydrase inhibitors such as acetazolamide, reabsorption of filtered bicarbonate is impaired. Distal (type I) RTA is characterized by a defect in distal acid secretion resulting in decreased urinary levels of acid and ammonium. The urine net charge [(urine Na^+ + urine K^+) - (urine Cl^-)] can be used to identify a type II RTA. Because ammonium (an unmeasured cation) accompanies chloride, the concentration of chloride should be greater than the sum of the sodium and potassium, and the net charge should be negative. A positive net charge indicates impaired ammonium secretion and, therefore, impaired distal acidification. The use of potassium-sparing agents may reduce distal proton secretion. Treatment of patients who have cirrhosis with spironolactone has caused metabolic acidosis, which resolves with discontinuation of the spironolactone.

ELEVATED ANION GAP

When an elevated anion gap occurs with an acidosis, the cause usually is increased organic acid production or ingestion, inborn errors of metabolism, or decreased excretion of acid due to renal failure. Increased production of acid may result in ketoacidosis and lactic acidosis. The overproduction of ketoacids, such as acetoacetic and hydroxybutyric acids, causes the elevated anion gap.

Diabetic ketoacidosis often is seen in children. Alcoholic ketoacidosis is more common in adults, but can occur at any age. Alcoholic ketoacidosis develops a few days after a prolonged alcoholic binge (when serum ethanol levels frequently are normal). Ketoacidosis also results from vomiting-induced starvation, often presenting as abdominal pain. Lactic acidosis causes an elevated anion gap, when the kidney or liver underuses excess lactate. Type A lactic acidosis occurs from tissue hypoxia or hypoperfusion. Type B lactic acidosis results from systemic disease, drugs, toxins, and inborn errors of metabolism.

Inborn errors of metabolism in the newborn period can be divided into urea cycle abnormalities or errors in amino acid, carbohydrate, or organic acid metabolism. Symptoms often include poor feeding, failure to thrive, seizures, and vomiting. Ingestion of salicylates is another cause of an elevated anion gap acidosis in children, although in adults and older children, stimulation of the respiratory center causes primary respiratory alkalosis.

Overdoses of ibuprofen (a nonsteroidal anti-inflammatory agent and a weak acid) and toluene inhalations have been associated with a high anion gap metabolic acidosis. Ethylene glycol (antifreeze), methanol (wood alcohol), and paraldehyde produce acidic byproducts that cause a metabolic acidosis. These substances produce an osmolar gap in addition to an anion gap. Serum osmolality is approximated by the formula: Calculated serum osmolality=2 x [Na^+] + glucose/18 + BUN/2.8. Unmeasured solutes such as ethylene glycol and methanol are not included in this formula and would account for an osmolar gap (osmolal gap = measured osmolality − calculated osmolality). Exogenous osmolal substances such as sulfates and phosphates result in a normal osmolal gap of 10 mOsm/L. The osmolal gap must be used cautiously because a normal gap has an inadequate negative predictive value. Massive ingestion of creams containing propylene glycol, such as silver sulfadiazine, may cause an increased anion gap metabolic acidosis. The inability to excrete hydrogen ions in acute or chronic renal failure results in an elevated anion gap metabolic acidosis. When the glomerular filtration rate falls below 25 mL/min per 1.73 m^2, insufficient excretion of ammonium and acids prevents bicarbonate regeneration.

Management

Management of metabolic acidosis usually is directed toward addressing the underlying condition. Correction of the underlying insulin, volume, and electrolyte deficiencies treats diabetic ketoacidosis. Administration of saline generally is adequate treatment for alcoholic ketoacidosis. Therapy for lactic acidosis focuses on restoring adequate tissue oxygenation and identifying and treating the underlying cause. Treatment of salicylate ingestion involves treating the underlying acidosis and promoting an alkaline diuresis to enhance renal acid and salicylate excretion. In severe cases, dialysis may be required. Management of ethylene glycol toxicity consists of hemodialysis, which removes both the substance and metabolites from the serum, and ethanol administration, which competes for alcohol dehydrogenase, resulting in increased renal excretion. Recently, fomepizole, a potent inhibitor of alcohol dehydrogenase that reduces the generation of toxic metabolites, has become available.

Assuming an adequate ventilatory response, a metabolic acidosis is severe when the serum bicarbonate concentration is 8 mEq/L (8 mmol/L) or less. With an increased anion gap acidosis, treatment of the underlying disorder may correct the acidosis within hours. In a normal anion gap acidosis (hyperchloremic), several days may be required for correction. With the low serum bicarbonate of 4 mEq/L (4 mmol/L) described in the case report, hydration alone would be inadequate treatment. Exogenous sodium bicar-

Table 2. Adverse Consequences of Severe Acidemia

Cardiovascular
- Impairment of cardiac contractility
- Arteriole dilation, venoconstriction, and centralization of blood volume
- Increased pulmonary vascular resistance
- Reductions in cardiac output, arterial blood pressure, and hepatic and renal blood flow
- Sensitization to re-entrant arrhythmias and reduction in threshold of ventricular fibrillation
- Attenuation of cardiovascular responsiveness to catecholamines

Respiratory
- Hyperventilation
- Decreased strength of respiratory muscles and promotion of muscle fatigue
- Dyspnea

Metabolic
- Increased metabolic demands
- Insulin resistance
- Inhibition of anaerobic glycolysis
- Reduction in adenosine triphosphate synthesis
- Hyperkalemia
- Increased protein degradation

Cerebral
- Inhibition of metabolism and cell volume regulation
- Obtundation and coma

From Adrogue and Madais, 1998

bonate is used initially to raise the arterial pH to 7.2, with the goal of preventing the adverse effects of severe acidemia (Table 2). The apparent space of distribution of bicarbonate varies, ranging from 100% of body weight when serum bicarbonate values are very low to the normal value of 50% of body weight when less severe acidosis is present. To prevent overtreatment, a bicarbonate space of 50% is recommended and correction only to a pH of 7.2 or serum bicarbonate concentration of 10 to 15 mEq/L (10 to 15 mmol/L) (Table 3). Sodium bicarbonate should be infused over several minutes to a few hours. A bolus should be used only in extreme cases.

Table 3. Calculation of Bicarbonate Dose for Treatment of Severe Acidosis

1. HCO_3^- desired = 10 mEq/L
2. HCO_3^- actual = 4 mEq/L (in the case report patient)
3. Weight = 20 kg (for the case report patient)
4. HCO_3^- space = 0.5 L/kg
5. HCO_3^- needed = (HCO_3^- desired (mEq/L) − HCO_3^- actual (mEq/L)) × weight (kg) × HCO_3^- space (L/kg)
6. Calculated dose = 60 mEq of HCO_3^- [(10 mEq/L −4 mEq/L) × 20 kg × 0.5 L/kg)] required to raise the HCO_3^- to 10 mEq/L.

The need for additional bicarbonate requirements is determined with follow-up monitoring of the patient's acid-base status. The clinical effects of therapy may be judged approximately 30 minutes after completion of the infusion.

Several complications can occur from bicarbonate therapy. Hypernatremia and hyperosmolality can be avoided by diluting 100 mEq/L (100 mmol/L) of sodium bicarbonate in 0.25% NaCl to render a nearly isotonic solution. Volume overload may occur in renal failure or congestive heart failure. Rapid correction can lead to acidification of the cerebrospinal fluid, with aggravation of neurologic symptoms. There also is a risk that overtreatment may transition the patient to a poorly tolerated condition of alkalemia.

Metabolic Alkalosis

Definition

Metabolic alkalosis results when increased plasma bicarbonate causes an increase in the arterial pH above 7.44.

Causes, Pathogenesis, and Clinical Aspects

A metabolic alkalosis may be caused by loss of acid from the extracellular fluid, the functional addition of new bicarbonate (either through increased intake or decreased renal excretion), or volume contraction around a constant amount of extracellular bicarbonate (sometimes referred to as a "contraction alkalosis"). A normal kidney can excrete a large amount of bicarbonate rapidly to correct the alkalosis. Therefore, a metabolic alkalosis must be generated and sustained by impaired renal bicarbonate excretion. Respiratory compensation by means of decreased ventilation tends to raise the P_{CO_2} by 0.7 mm Hg for every 1 mEq/L that the serum HCO_3^- rises.

Impaired renal bicarbonate excretion occurs when proximal tubular bicarbonate reabsorption is increased due to: 1) decreased effective circulating volume, 2) posthypercapnia, or 3) potassium depletion. Whereas hypercapnia stimulates proximal bicarbonate reabsorption, mechanical ventilation decreases P_{CO_2} rapidly, resulting in the development of metabolic alkalosis. Potassium depletion most likely causes intracellular acidosis, which increases bicarbonate reabsorption by stimulating the Na^+/H^+ exchanger. Chloride depletion is a major cause of metabolic alkalosis by causing secondary hyperaldosteronism and stimulating proton secretion in the distal nephron. In addition,

Table 4. Causes of Metabolic Alkalosis

Chloride-responsive (urinary chloride <10 mEq/L [10 mmol/L])

- Gastrointestinal causes
  - –Vomiting
  - –Nasogastric suction
  - –Chloride-wasting diarrhea, including congenital chloridorrhea
  - –Villous adenoma-colon
  - –Laxative abuse
- Diuretic therapy
- Posthypercapnia
- Penicillin
- Cystic fibrosis

Chloride-unresponsive (urinary chloride >10 mEq/L [10 mmol/L])

- Adrenal disorders
  - –Hyperaldosteronism
  - –Cushing syndrome
- Exogenous steroid
  - –Gluco- or mineralocorticoid
  - –Licorice ingestion
  - –Carbenoxalone
- Alkali ingestion
- Refeeding alkalosis
- Bartter syndrome
- Gitelman syndrome

Adapted from Hanna et al, 1980 and Narins and Emmett, 1980

chloride depletion reduces tubular fluid chloride concentration, which inhibits the apical Cl^-/HCO_3^- exchanger of beta-intercalated cells and reduces bicarbonate secretion in the cortical collecting duct.

For diagnostic and therapeutic reasons, the conditions that cause metabolic alkalosis are divided into chloride-responsive and -unresponsive groups (Table 4). A low urine chloride level (<10 mEq/L [10 mmol/L]) characterizes the chloride-responsive group. Loop and thiazide diuretics can prompt a metabolic alkalosis by causing hypovolemia and stimulating secondary hyperaldosteronism, increasing distal urine flow, and generating hypokalemia. The alkalosis is maintained by chloride and volume depletion. A classic example of a sustained metabolic alkalosis in pediatrics is pyloric stenosis in which repeated emesis of gastric acid causes a functional addition of new bicarbonate, while chloride is lost with gastric hydrochloric acid in the emesis. The kidneys respond with a bicarbonate diuresis associated with increased Na^+ and K^+ losses, resulting in hypokalemia and volume depletion, which maintain the alkalosis. The previously mentioned scenario can occur with any type of repetitive emesis, including self-induced surreptitious vomiting. Pediatricians also should be aware that newborns of mothers who have bulimia have alkalosis, reflecting their mother's serum pH. Congenital chloridorrhea is a rare cause of metabolic alkalosis that causes infants to have a watery diarrhea that contains an excessive amount of chloride.

The chloride-unresponsive group is characterized by a normal-to-high urine chloride level (>10 mEq/L [10 mmol/L]). The conditions that lead to a chloride-unresponsive metabolic alkalosis tend to be rare disorders such as Cushing syndrome, congenital adrenal hyperplasia, primary hyperaldosteronism, renin-secreting tumors, Bartter syndrome, Gitelman syndrome, and renal artery stenosis. The patients usually exhibit hypertension, hypokalemia, and volume expansion due to excessive mineralocorticoid activity. Patients who have Bartter syndrome and Gitelman syndrome typically do not have hypertension.

Management

Treatment of metabolic alkalosis is directed at treating the underlying mechanism causing and sustaining the alkalosis, with the goal of avoiding the adverse consequences of severe alkalemia (Table 5). Vomiting can be treated with antiemetics. If continued gastric drainage is required, the loss of gastric acid can be reduced by using histamine$_2$-receptor blockers or proton pump inhibitors. Loop or thiazide diuretic doses may be decreased or coupled with potassium-sparing diuretics. Factors that might worsen the alkalosis should be eliminated or reduced. Administration of bicarbonate and bicarbonate precursors, such as lactate, citrate, and acetate, or drugs that have mineralocorticoid activity should have their indication and dose reassessed.

Table 5. Adverse Consequences of Severe Alkalemia

Cardiovascular

- Arteriole constriction
- Reduction in coronary blood flow
- Reduction in anginal threshold
- Predisposition to refractory supraventricular and ventricular arrhythmias

Respiratory

- Hypoventilation with attendant hypercapnia and hypoxemia

Metabolic

- Stimulation of anaerobic glycolysis and organic acid production
- Hypokalemia
- Decreased plasma ionized calcium
- Hypomagnesemia and hypophosphatemia

Cerebral

- Reduction in cerebral blood flow
- Tetany, seizures, lethargy, delirium, and stupor

From Adrogue and Madias, 1998

If loop and thiazide diuretics cause a hypokalemic, hypochloremic metabolic alkalosis, correction of volume, sodium, and potassium deficits should be initiated. In severe cases or for patients who have renal failure or precarious fluid status, treatments include acetazolamide, dilute hydrochloric acid, arginine hydrochloride, or dialysis using a dialysate that has high chloride and low bicarbonate concentrations to correct the metabolic alkalosis.

Respiratory Acidosis and Alkalosis

Definition

The arterial P_{CO_2} usually is maintained between 39 and 41 mm Hg. Ventilation is controlled by respiratory centers in the pons and medulla. When carbon dioxide production is increased, changes in ventilation result in only small changes in P_{CO_2}. Respiratory acidosis or alkalosis results from a primary increase or decrease in blood P_{CO2} and may coexist with other acid-base disorders.

Causes, Pathogenesis, and Clinical Aspects

A respiratory acidosis may result from increased carbon dioxide production, alveolar hypoventilation, abnormal ventilatory drive, or abnormalities of the chest wall and respiratory muscles (Table 6). With respiratory acidosis, cell buffering begins within minutes; renal compensation requires 3 to 5 days for completion. In respiratory acidosis, for every 10-mm Hg elevation in the P_{CO_2}, the serum bicarbonate increases 1 mEq/L (1 mmol/L) in the acute setting and 3.5 mEq/L (3.5 mmol/L) in the chronic setting. The improvement in renal compensation in the chronic setting is due to renal acid and ammonium secretion.

Respiratory alkalosis is characterized by a reduction in the P_{CO_2} that produces an elevated blood pH and decreased serum bicarbonate concentration. The causes for respiratory alkalosis are multiple and include hypoxia, parenchymal lung disease, central nervous system disorders, metabolic disturbances, and hyperventilation syndrome (Table 7). For every 10-mm Hg decline in the P_{CO_2}, renal compensation reduces the serum bicarbonate 2 mEq/L (2 mmol/L) in the acute setting and 4 mEq/L (4 mmol/L) in the chronic setting.

Table 6. Causes of Acute Respiratory Acidosis

Acute Central Nervous System Depression
- Drug overdose
  - –Benzodiazepines
  - –Narcotics
  - –Barbiturates
  - –Propofol
- Head trauma
- Cerebrovascular accident
- Central nervous system infection

Acute Neuromuscular Disease
- Guillain-Barré syndrome
- Spinal cord injury
- Myasthenic crisis
- Botulism
- Organophosphate poisoning

Acute Airway Disease
- Status asthmaticus
- Upper airway obstruction

Acute Parenchymal and Vascular Disease
- Cardiogenic pulmonary edema
- Acute lung injury
- Multilobar pneumonia

Massive Pulmonary Embolism

Acute Pleural or Chest wall Disease
- Pneumothorax
- Hemothorax
- Flail chest

Adapted from Epstein and Singh, 2001

Table 7. Causes of Respiratory Alkalosis

Hypoxia

Parenchymal Lung Disease
- Pneumonia
- Asthma
- Diffuse interstitial fibrosis
- Pulmonary edema
- Pulmonary embolism

Medications
- Salicylate
- Nicotine
- Xanthine
- Catecholamines
- Analeptics

Mechanical Ventilation

Central Nervous System Disorders
- Meningitis, encephalitis
- Cerebrovascular disease
- Head trauma
- Space-occupying lesion
- Anxiety

Metabolic Disorders
- Sepsis
- Pyrexia
- Hepatic disease

Hyperventilation Syndrome

Adapted from Foster et al, 2001

Management

The treatment for respiratory acidosis is directed at treating the underlying disease. Medications that suppress the respiratory drive, such as opiates, should be avoided. It is important to prevent electrolyte abnormalities that may impair respiratory muscle function, such as hypophosphatemia, hypomagnesemia, and hypokalemia. If diuretic therapy is needed, adequate chloride should be

administered to avoid a concurrent metabolic alkalosis. Supplemental oxygen should be provided if hypoxemia is present. If the respiratory acidosis is severe, ventilatory support may be needed. Alkali therapy is not used to treat a primary respiratory acidosis. Treatment of a respiratory alkalosis also is directed at treatment of the underlying cause. Often, simple observation or use of a rebreathing bag is adequate in hyperventilation syndrome. In the case of high-altitude hypoxia (acute mountain sickness), acetazolamide can be administered prior to ascent to prevent or mitigate symptoms of respiratory alkalosis.

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PIR Quiz

Quiz also available online at www.pedsinreview.org.

9. An 8-month-old Caucasian infant presents with a history of failure to gain weight for the past 4 months. The infant was born after a term uncomplicated pregnancy. His birthweight was 3.5 kg. He always has been a poor eater and tends to spit up formula frequently after feeding. Physical examination documents the weight below the 3rd percentile, height at the 5th percentile, and head circumference at the 25th percentile. Vital signs include: respiratory rate of 32 breaths/min, heart rate of 110 beats/min, and blood pressure of 80/45 mm Hg. Other than poor subcutaneous fat, no abnormalities are noted. Laboratory studies reveal: hemoglobin, 11 g/dL (110 g/L); sodium, 136 mEq/L (136 mmol/L); potassium, 4.0 mEq/L (4.0 mmol/L); chloride, 112 mEq/L (112 mmol/L); and bicarbonate, 14 mEq/L (14 mmol/L). Venous blood pH is 7.24 and Pco_2 is 26 mm Hg. Blood urea nitrogen and serum creatinine concentrations are normal. Urinalysis shows a pH of 7.0, specific gravity of 1.015, and no protein or glucose. Of the following, the *most* likely diagnosis is:

   A. Cystic fibrosis.
   B. Gastroesophageal reflux.
   C. Obstructive uropathy.
   D. Organic acidemia.
   E. Renal tubular acidosis.

(continued)

10. A 2-year-old girl is brought to the emergency department after being found unconscious in the basement. On physical examination, she is unresponsive to tactile and verbal stimuli except for withdrawal to pain. Pupils are equal and reactive. Respirations are 30 breaths/min and deep, heart rate is 130 beats/min, axillary temperature is 98.2°F (36.8°C), and blood pressure is 90/60 mm Hg. Laboratory studies show: serum sodium, 138 mEq/L (138 mmol/L); potassium, 3.8 mEq/L (3.8 mmol/L); chloride, 94 mEq/L (94 mmol/L); bicarbonate, 10 mEq/L (10 mmol/L); blood urea nitrogen, 14 mg/dL (5 mmol/L); blood glucose, 72 mg/dL (4 mmol/L); serum osmolality, 330 mOsm/kg (330 mmol/kg); venous blood pH, 7.15; and P_{CO_2}, 16 mm Hg. Of the following, the *most* likely diagnosis is:

    A. Carbon monoxide poisoning.
    B. Diabetic ketoacidosis.
    C. Encephalitis.
    D. Ethylene glycol ingestion.
    E. Salicylate poisoning.

11. A 6-week-old male infant presents with vomiting and poor weight gain for the last 2 weeks. The vomiting is described as forceful, and it occurs after every feeding. Physical examination reveals poor subcutaneous fat. You palpate a 2 × 2-cm round mass to the right of the midline in the upper abdominal region. Laboratory studies show: serum sodium, 128 mEq/L (128 mmol/L); potassium, 3.2 mEq/L (3.2 mmol/L); chloride, 86 mEq/L (86 mmol/L); bicarbonate, 34 mEq/L (34 mmol/L); and calcium, 8.2 mg/dL (8.2 mmol/L). Venous blood pH is 7.55. Measurement of urine electrolytes document sodium, 12 mEq/L (12 mmol/L) and chloride, 8 mEq/L (8 mmol/L). Administration of which of the following is *most* likely to correct alkalosis in this child?

    A. Angiotensin-converting enzyme inhibitors.
    B. Calcium chloride.
    C. Hydrochlorothiazide.
    D. Hydrocortisone.
    E. Sodium and potassium chloride.

12. A 12-year-old girl who has steroid-dependent asthma presents with increasing respiratory difficulty for 12 hours. On physical examination, her respiratory rate is 30 breaths/min, heart rate is 160 beats/min, and blood pressure is 80/50 mm Hg. She is unable to speak a full sentence and has severe suprasternal retractions. Her extremities are cool, and capillary refill is poor. Chest auscultation reveals bilateral inspiratory/expiratory wheezing with decreased air entry over the right hemithorax. Arterial blood gases while receiving oxygen via a face mask reveal: pH, 7.1; P_{CO_2}, 50 mm Hg; P_{CO_2}, 50 mm Hg, and HCO_3^-, 15 mEq/L (15 mmol/L). Which of the following *best* describes this child's acid-base disorder?

    A. Combined metabolic and respiratory acidosis.
    B. Metabolic acidosis with compensated respiratory alkalosis.
    C. Metabolic acidosis without respiratory compensation.
    D. Respiratory acidosis with compensated metabolic alkalosis.
    E. Respiratory acidosis without metabolic compensation.

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