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ACID BASE BALANCE AND IMBALANCE

1. INTRODUCTION:

Acid–base homeostasis is the part of human homeostasis concerning the proper balance between acids and bases, in other words, the pH. The body is very sensitive to its pH level, so strong mechanisms exist to maintain it. Outside the acceptable range of pH, proteins are denatured and digested, enzymes lose their ability to function, and death may occur.

Acid–base disturbances are commonly encountered in clinical practice. Identification of the specific acid–base imbalance is important in identifying the underlying cause of the disorder and in determining appropriate treatment.

Plasma pH is an indicator of hydrogen ion (H□) concentration. Homeostatic mechanisms keep pH within a normal range (7.35–7.45). These mechanisms consist of buffer systems, the kidneys, and the lungs. The H□□concentration is extremely important: the greater the concentration, the more acidic the solution and the lower the pH. The lower the H□□ concentration, the more alkaline the solution and the higher the pH. The pH range compatible with life (6.8–7.8) represents a tenfold difference in H□□ concentration in plasma.

2. ACID BASE BALANCE:

2.1. DEFINITION:

Acid-base balance can be defined as homeostasis of the body fluids at a normal arterial blood pH ranging between 7.37 and 7.43.

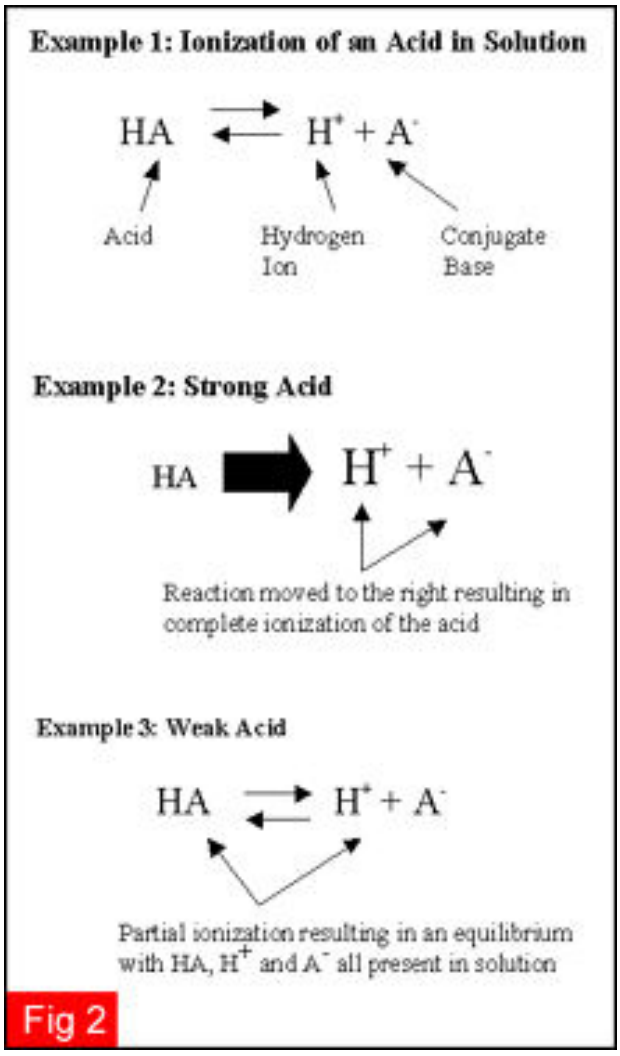
2.2. KEY TERMS:

Acids: An acid is defined as any compound, which forms hydrogen ions in solution. For this reason acids are sometimes referred to as "proton donors".

Bases: A base is a compound that combines with hydrogen ions in solution. Therefore, bases can be referred to as "proton acceptors".

Strong Acids: A strong acid is a compound that ionizes completely in solution to form hydrogen ions and a base.

Weak Acids and Bases: these are compounds that are only partially ionised in solution.



2.3. BUFFER SYSTEMS:

- Buffer systems prevent major changes in the pH of body fluids by removing or releasing H□; they can act quickly to prevent excessive changes in H□□concentration. Hydrogen ions are buffered by both intracellular and extracellular buffers.

- The body's major extracellular buffer system is the bicarbonate-carbonic acid buffer system. This is the system that is assessed when arterial blood gases are measured. Normally, there are 20 parts of bicarbonate (HCO_3^-) to one part of carbonic acid (H_2CO_3). If this ratio is altered, the pH will change.
- It is the ratio of HCO_3^- to H_2CO_3 that is important in maintaining pH, not absolute values. Carbon dioxide (CO_2) is a potential acid; when dissolved in water, it becomes carbonic acid ($CO_2 + H_2O \rightleftharpoons H_2CO_3$).
- Thus, when CO_2 is increased, the carbonic acid content is also increased, and vice versa. If either bicarbonate or carbonic acid is increased or decreased so that the 20:1 ratio is no longer maintained, acid–base imbalance results.
- Less important buffer systems in the ECF include the inorganic phosphates and the plasma proteins. Intracellular buffers include proteins, organic and inorganic phosphates, and, in red blood cells, hemoglobin.

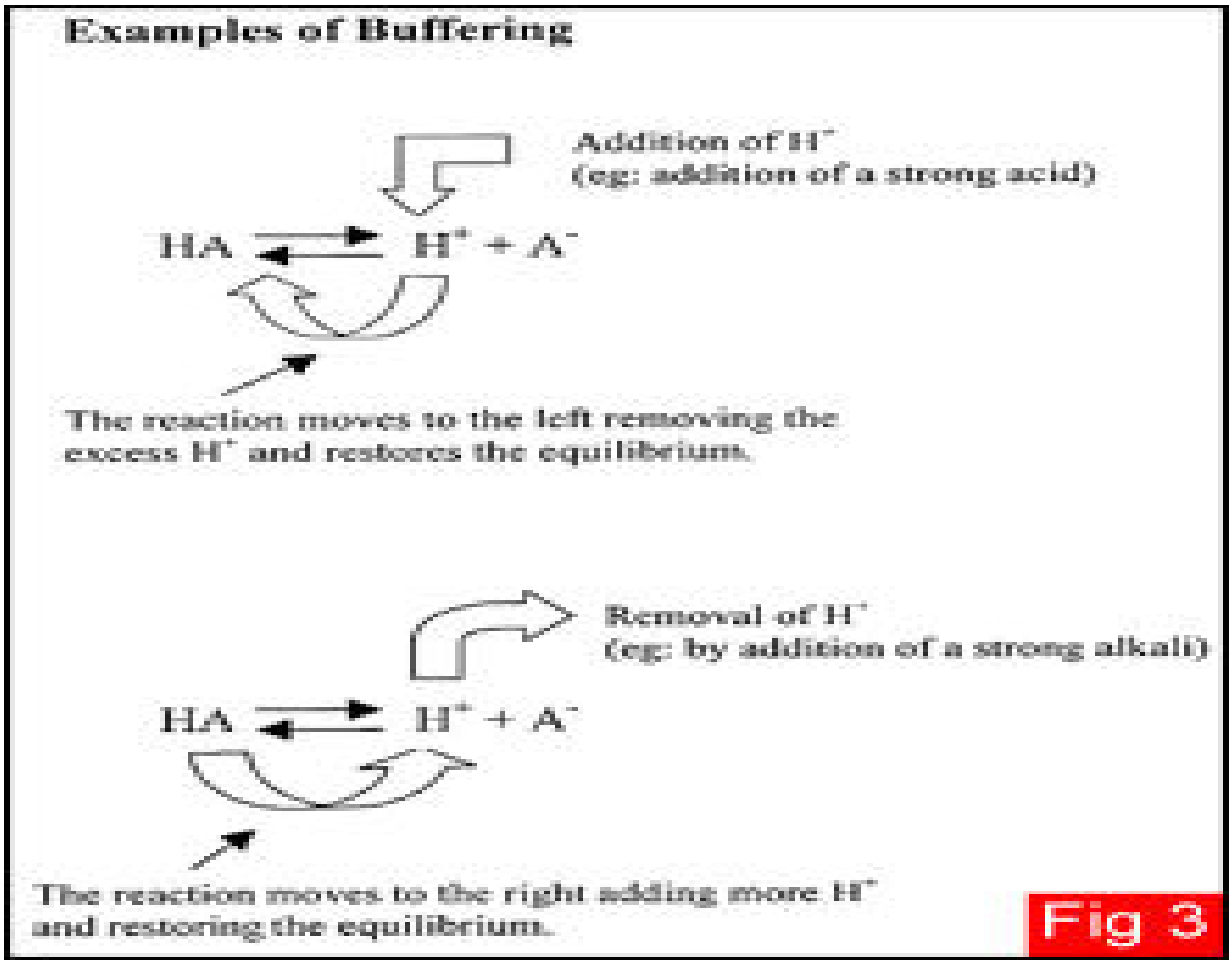
Kidneys

- The kidneys regulate the bicarbonate level in the ECF; they can regenerate bicarbonate ions as well as reabsorb them from the renal tubular cells.
- In respiratory acidosis and most cases of metabolic acidosis, the kidneys excrete hydrogen ions and conserve bicarbonate ions to help restore balance.
- In respiratory and metabolic alkalosis, the kidneys retain hydrogen ions and excrete bicarbonate ions to help restore balance.
- The kidneys obviously cannot compensate for the metabolic acidosis created by renal failure. Renal compensation for imbalances is relatively slow (a matter of hours or days).

Lungs

- The lungs, under the control of the medulla, control the CO_2 and thus the carbonic acid content of the ECF. They do so by adjusting ventilation in response to the amount of CO_2 in the blood.
- A rise in the partial pressure of CO_2 in arterial blood ($PaCO_2$) is a powerful stimulant to respiration.
- Of course, the partial pressure of oxygen in arterial blood (PaO_2) also influences respiration.
- Its effect, however, is not as marked as that produced by the $PaCO_2$.
- In metabolic acidosis, the respiratory rate increases, causing greater elimination of CO_2 (to reduce the acid load).

- In metabolic alkalosis, the respiratory rate decreases, causing CO2 to be retained (to increase the acid load).



2.4. DESCRIPTION:

- An acid is a substance that acts as a proton donor.
- In contrast, a base, also known as an alkali, is frequently defined as a substance that combines with a proton to form a chemical bond.
- Acid solutions have a sour taste and produce a burning sensation with skin contact.
- A base is any chemical compound that produces hydroxide ions when dissolved in water. Base solutions have a bitter taste and a slippery feel.
- Despite variations in metabolism, diet, and environmental factors, the body's acid-base balance, fluid volume, and electrolyte concentration are maintained within a narrow range.

2.5. FUNCTION:

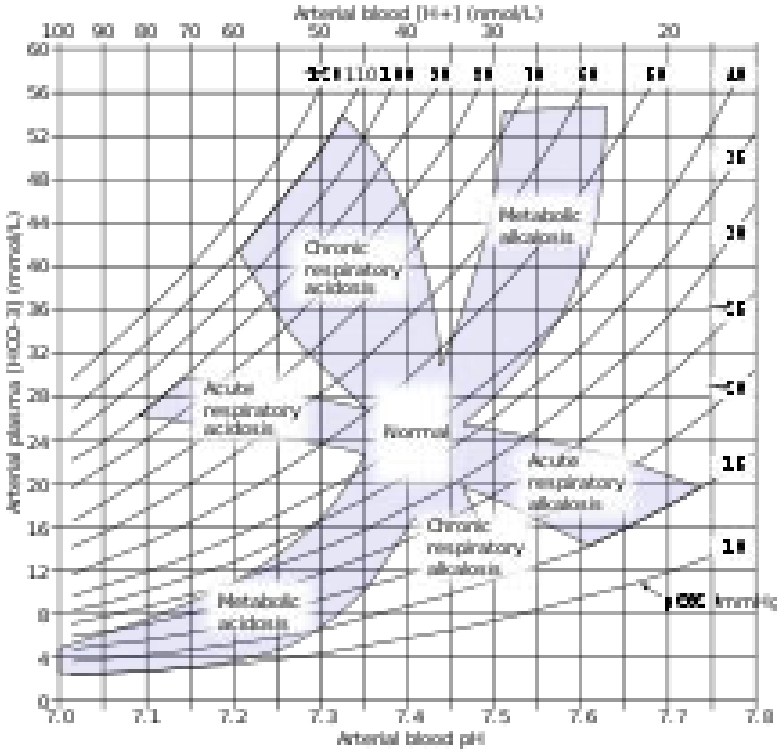
- Many naturally occurring acids are necessary for life.
- For example, hydrochloric acid is secreted by the stomach to assist with digestion. The chemical composition of food in the diet can have an effect on the body's acid-base production.
- Components that affect acid-base balance include protein, chloride, phosphorus, sodium, potassium, calcium, and magnesium. In addition, the rate at which nutrients are absorbed in the intestine will alter acid-base balance.
- Cells and body fluids contain acid-base buffers, which help prevent rapid changes in body fluid pH over short periods of time, until the kidneys pulmonary systems can make appropriate adjustments.
- The kidneys and pulmonary system then work to maintain acid-base balance through excretion in the urine or respiration.
- The partial pressure of carbon dioxide gas (PCO_2) in the pulmonary system can be measured with a blood sample and correlates with blood carbon dioxide (CO_2) levels. PCO_2 can then be used as an indicator of the concentration of acid in the body.
- The concentration of base in the body can be determined by measuring plasma bicarbonate (HCO_{3-}) concentration.
- When the acid-base balance is disturbed, the respiratory system can alter PCO_2 quickly, thus changing the blood pH and correcting imbalances.
- Excess acid or base is then excreted in the urine by the renal system to control plasma bicarbonate concentration.
- Changes in respiration occur primarily in minutes to hours, while renal function works to alter blood pH within several days.

2.6. ROLE IN HUMAN HEALTH:

- Production of CO_2 is a result of normal body metabolism.
- Exercise or serious infections will increase the production of CO_2 through increased respiration in the lungs.
- When oxygen (O_2) is inhaled and CO_2 is exhaled, the blood transports these gases to the lungs and body tissues.

- The body's metabolism produces acids that are buffered and then excreted by the lungs and kidneys to maintain body fluids at a neutral pH.
- Disruptions in CO_2 levels and HCO_3-create acid-base imbalances. When acid-base imbalances occur, the disturbances can be broadly divided into either acidosis (excess acid) or alkalosis (excess base/alkali).

2.7. MECHANISM:



- The body's acid–base balance is tightly regulated.
- Several buffering agents that reversibly bind hydrogen ions and impede any change in pH exist.
- Extracellular buffers include bicarbonate and ammonia, whereas proteins and phosphate act as intracellular buffers.
- The bicarbonate buffering system is especially key, as carbon dioxide (CO_2) can be shifted through carbonic acid (H_2CO_3) to hydrogen ions and bicarbonate (HCO_3^-) as shown below.

$$H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

- Acid–base imbalances that overcome the buffer system can be compensated in the short term by changing the rate of ventilation.
- This alters the concentration of carbon dioxide in the blood, shifting the above reaction according to Le Chatelier's principle, which in turn alters the pH.
- For instance, if the blood pH drops too low (acidemia), the body will compensate by increasing breathing, expelling CO_2, and shifting the above reaction to the left such that less hydrogen ions are free; thus the pH will rise back to normal.
- For alkalemia, the opposite occurs.
- The kidneys are slower to compensate, but renal physiology has several powerful mechanisms to control pH by the excretion of excess acid or base.
- In responses to acidosis, tubular cells reabsorb more bicarbonate from the tubular fluid, collecting duct cells secrete more hydrogen and generate more bicarbonate, and ammoniagenesis leads to increased formation of the NH_3 buffer.
- In responses to alkalosis, the kidney may excrete more bicarbonate by decreasing hydrogen ion secretion from the tubular epithelial cells, and lowering rates of glutamine metabolism and ammonia excretion.

2.8. COMMON DISEASES AND DISORDERS:

Acid-base metabolism imbalances are often characterized in terms of the HCO_3-/CO_2 buffer system. Acid-base imbalances result primarily from metabolic or respiratory failures. An increase in HCO_3-is called metabolic alkalosis, while a decrease in the same substance is called metabolic acidosis. An increase in PCO_2, on the other hand, is known as respiratory acidosis, and a decrease in the same substance is called respiratory alkalosis.

Acidosis

- Acidosis is a condition resulting from higher than normal acid levels in the body fluids. It is not a disease, but may be an indicator of disease.
- Metabolic acidosis is related to processes that transform food into energy and body tissues. Conditions such as diabetes, kidney failure, severe diarrhea, and poisoning can result in metabolic acidosis.
- Mild acidosis is often compensated by the body in a number of ways. However, prolonged acidosis can result in heavy or rapid breathing, weakness, and headache.

- Acidemia (arterial pH < 7.35) is an accumulation of acids in the bloodstream that may occur with severe acidosis when the acid load exceeds respiratory capacity.
- This condition can sometimes result in comaand, if the pH falls below 6.80, it will lead to death. Diabetic ketoacidosis is a condition where excessive glucagon and a lack of insulin contribute to the production of ketoacids in the liver.
- This condition can be caused by chronic alcoholism and poor carbohydrate utilization.

Acid-base disturbances, causes, and compensatory mechanisms		
Acid-base disturbance	Common cause	Mode of compensation
Respiratory acidosis	Respiratory depression (drugs, central nervous system trauma)	Kidneys will retain increased amounts of $HCO_{3/sub>}$ to increase pH
	Pulmonary disease (pneumonia, chronic obstructive pulmonary disease, respiratory underventilation)	
Respiratory alkalosis	Hyperventilation (emotions, pain, respirator overventilation)	Kidneys will excrete increased amounts of $HCO_{3/sub>}$ to lower pH
Metabolic acidosis	Diabetes, shock, renal failure, intestinal fistula	Lungs "blow off" CO_2 to raise pH
Metabolic alkalosis	Sodium bicarbonate overdose, prolonged vomiting, nasogastric drainage	Lungs retain CO_2 to lower pH

- Respiratory acidosis is caused by the lungs's failure to remove excess carbon dioxide from the body, reducing the pH in the body.
- Several conditions, including chest injury, blockage of the upper air passages, and severe lung disease, may lead to respiratory acidosis.
- Blockage of the air passages may be caused by bronchitis, asthma, or airway obstruction, resulting in mild or severe acidosis.

- Regular, consistent retention of carbon dioxide in the lungs is referred to as chronic respiratory acidosis.
- This disorder results in only mild acidosis because it is balanced by increased bicarbonate production.
- The predominant symptoms of acidosis are sometimes difficult to distinguish from symptoms of an underlying disease or disorder.
- Mild conditions of acidosis may be asymptomatic or may be accompanied by weakness or listlessness, nausea, and vomiting.
- Most often, severe metabolic acidosis (pH < 7.20) is associated with increased respiration to compensate for a shortage of HCO_3-.
- This is followed by a secondary decrease in PCO_2 that occurs as part of respiratory compensation process.
- Treatment options for acidosis typically require correction of the underlying condition by venous administration of sodium bicarbonate or another alkaline substance.

Alkalosis

- Alkalosis is a condition resulting from a higher than normal level of base/alkali in the body fluids. An excessive loss of HCO_3-in the blood causes metabolic alkalosis.
- The body can compensate for mild alkalinity, but prolonged alkalosis can result in convulsions, muscular weakness, and even death if the pH rises above 7.80.
- Alkalosis can be caused by drugs or disorders that upset the normal acid-base balance. Prolonged vomiting and hyperventilation (abnormally fast, deep breathing) can result in alkalosis.
- The predominant symptoms of alkalosis are neuromuscular hyperexcitability and irritability.
- Alkalemia (abnormal blood alkalinity) increases protein binding of ionized calcium even though plasma total calcium does not change.
- Severe cases may induce hypocalcemia (a low level of plasma calcium). Low plasma potassium leads to a condition called hypokalemic alkalosis.
- It is frequently accompanied by metabolic alkalosis, resulting in cramping, muscle weakness, polyuria, and ileus (obstruction of the intestines). Diuretic medications may cause hypokalemic alkalosis.

- Prolonged vomiting may induce hypochloremic alkalosis (a large loss of chloride). The kidneys may conserve bicarbonate in order to compensate for the chloride reduction.
- Compensated alkalosis results when the body has partially compensated for alkalosis, and has restored normal acid-base balances.
- However, in compensated alkalosis, abnormal bicarbonate and carbon dioxide levels persist.
- Alkalosis requires correction of the underlying condition and may involve venous administration of a weak acid to restore normal balance.
- If the source of alkalosis is excessive drug intake, it may be appropriate to reduce intake to restore the normal acid-base balance.

Respiratory alkalosis results from decreased CO_2 levels caused by conditions such as hyperventilation (a faster breathing rate), anxiety, and fever. The pH is elevated in the body. Hyperventilation causes the body to lose excess carbon dioxide in expired air and can be triggered by altitude or a disease that reduces the amount of oxygen in the blood. Symptoms of respiratory alkalosis may include dizziness, lightheadedness, and numbing of the hands and feet. Treatments include breathing into a paper bag or a mask that induces rebreathing of carbon dioxide.

3. ACID-BASE IMBALANCE:

Acid–base imbalance occurs when a significant insult causes the blood pH to shift out of the normal range (7.35 to 7.45). In the fetus, the normal range differs based on which umbilical vessel is sampled (umbilical vein pH is normally 7.25 to 7.45; umbilical artery pH is normally 7.18 to 7.38). An excess of acid in the blood is called acidemia and an excess of base is called alkalemia. The process that causes the imbalance is classified based on the etiology of the disturbance (respiratory or metabolic) and the direction of change in pH (acidosis or alkalosis). There are four basic processes: metabolic acidosis, respiratory acidosis, metabolic alkalosis, and respiratory alkalosis. One or a combination may occur at any given time.

3.1. DEFINITIONS:

When pH_a (arterial blood pH) differs from 7.4 +/- 0.02 (or the $[H^+]$ differs from 40 +/- 2 nEq/L) there occurs acidemia (pH_a < 7.38, $[H^+]$ > 42 nEq/L) or alkalemia (pH_a > 7.42, $[H^+]$ < 38 nEq/L).

If the pH_a change is due primarily to a change in P_{aCO2}, there is respiratory acidosis (P_{aCO2} > 42 mmHg) or respiratory alkalosis (P_{aCO2} < 38 mmHg).

When the pH_a change is due primarily to a change in $[HCO_3^-]$ from its normal value of 24 mM, there is metabolic acidosis ($[HCO_3^-]$ < 22 mM) or metabolic alkalosis ($[HCO_3^-]$ > 26 mM).

3.2. ACUTE AND CHRONIC METABOLIC ACIDOSIS (BASE BICARBONATE DEFICIT)

Metabolic acidosis: pH < 7.38; HCO_3^- < 22 mM; P_{aCO2} 1 mmHg decrease per 1 mM decrease in HCO_3^- (acute or chronic)

Metabolic acidosis is a clinical disturbance characterized by a low pH (increased H□□concentration) and a low plasma bicarbonate concentration. It can be produced by a gain of hydrogen ion or a loss of bicarbonate.

It can be divided clinically into two forms, according to the values of the serum anion gap: high anion gap acidosis and normal anion gap acidosis.

The anion gap reflects normally unmeasured anions (phosphates, sulfates, and proteins) in plasma. Measuring the anion gap is essential in analyzing acid–base disorders correctly.

The anion gap can be calculated by either one of the following equations:

Anion gap □□Na□□□□K□□−□(Cl−□□□HCO3 −)

Anion gap □□Na□□−□(Cl−□□□HCO3 −)

Potassium is often omitted from the equation because of its low level in the plasma; thus, the second equation is used more often than the first.

The normal value for an anion gap is 8 to 12 mEq/L (8–12 mmol/L) without potassium in the equation. The normal value for the anion gap if including potassium in the equation is 12 to 16 mEq/L (12–16 mmol/L). The unmeasured anions in the serum normally account for less than 16 mEq/L of the anion production.

An anion gap greater than 16 mEq (16 mmol/L) suggests excessive accumulation of unmeasured anions. An anion gap occurs because not all electrolytes are measured. More anions are left unmeasured than cations.

Normal anion gap acidosis results from the direct loss of bicarbonate, as in diarrhea, lower intestinal fistulas, ureterostomies, and use of diuretics; early renal insufficiency; excessive administration of chloride; and the administration of parenteral nutrition without bicarbonate or bicarbonate-producing solutes (eg, lactate).

Causes:

Metabolic acidosis is the most frequent acid-base imbalance and may be due to:

(1) Extra renal loss of bicarbonate, with hyperchloremia and increased urinary excretion of NH_4^+ (evident as high urinary cation gap: $[Cl^-] - [Na^+] - [K^+] >> 0$)

(2) Urinary loss of HCO_3^- (alkaline urine, with high bicarbonate, and little NH_4^+ and thus no urine cation gap)

(3) Accumulation of organic anions (lactacidosis, ketoacidosis) with large plasma anion gap (due to organic anions, $[Na^+]+[K^+]-[Cl^-]-[HCO_3^-]>>15$), abundant urinary NH_4^+ but no urinary cation gap (NH_4^+ is excreted with organic anions so that there is a large urinary osmolar gap: $U_{osm} - 2([Na^+]+[K^+]) - [urea] - [glucose] >>0$. Only lactacidosis can develop in minutes (as in shock).

(4) Decreased kidney production of HCO_3^- (hyperchloremia, no plasma anion gap, and low urinary excretion of ammonium, (urinary cation gap =0); severe chronic renal failure may result in metabolic acidosis with increased plasma anion gap (due to high plasma $[P_i]$) and low urinary NH_4^+ excretion.

Normal anion gap acidosis is also referred to as hyperchloremic acidosis. A reduced or negative anion gap is primarily caused by hypoproteinemia. Disorders that cause a decreased or negative anion gap are rare compared to those related to an increased or high anion gap.

High anion gap acidosis results from excessive accumulation of fixed acid. If it is increased to 30 mEq/L (30 mmol/L) or more, then a high anion gap metabolic acidosis is present regardless of what the pH and the HCO3 −□are. High ion gap occurs in ketoacidosis,

lactic acidosis, the late phase of salicylate poisoning, uremia, methanol or ethylene glycol toxicity, and ketoacidosis with starvation. The hydrogen is buffered by $HCO3^-$, causing the bicarbonate concentration to fall. In all of these instances, abnormally high levels of anions flood the system, increasing the anion gap above normal limits.

Clinical Manifestations

Signs and symptoms of metabolic acidosis vary with the severity of the acidosis. They may include headache, confusion, drowsiness, increased respiratory rate and depth, nausea, and vomiting.

Peripheral vasodilation and decreased cardiac output occur when the pH falls below 7. Additional physical assessment findings include decreased blood pressure, cold and clammy skin, dysrhythmias, and shock.

Chronic metabolic acidosis is usually seen with chronic renal failure. The bicarbonate and pH decrease slowly; thus, the patient is asymptomatic until the bicarbonate is approximately 15 mEq/L or less.

Assessment and Diagnostic Findings

Arterial blood gas measurements are valuable in diagnosing metabolic acidosis.

Expected blood gas changes include a low bicarbonate level (less than 22 mEq/L) and a low pH (less than 7.35). The cardinal feature of metabolic acidosis is a decrease in the serum bicarbonate level.

Hyperkalemia may accompany metabolic acidosis as a result of the shift of potassium out of the cells. Later, as the acidosis is corrected, potassium moves back into the cells and hypokalemia may occur.

Hyperventilation decreases the CO_2 level as a compensatory action.

As stated previously, calculation of the anion gap is helpful in determining the cause of metabolic acidosis. An ECG will detect dysrhythmias caused by the increased potassium.

Medical Management

Treatment is directed at correcting the metabolic defect. If the problem results from excessive intake of chloride, treatment is aimed at eliminating the source of the chloride.

When necessary, bicarbonate is administered if the pH is less than 7.1 and the bicarbonate level is less than 10. Although hyperkalemia occurs with acidosis, hypokalemia may occur with reversal of the acidosis and subsequent movement of potassium back into the cells.

Therefore, the serum potassium level is monitored closely and hypokalemia is corrected as acidosis is reversed.

In chronic metabolic acidosis, low serum calcium levels are treated before treating chronic metabolic acidosis to avoid tetany resulting from an increase in pH and a decrease in ionized calcium.

Alkalyzing agents may be given if the serum bicarbonate level is less than 12 mEq/L. Treatment modalities may also include hemodialysis or peritoneal dialysis.

Compensations:

(1) Immediate buffering by reaction with ECF HCO_3^- represents ~40% of rapid (~2 hrs) buffering of acid. $HCl + NaHCO_3 \Rightarrow NaCl + H_2CO_3 + CO_2 + H_2O$

(2) Respiratory compensation. A low pH_a stimulates V_A, so P_{aC02} decreases minimizing the decrease in pH_a. For each 1 mM decrease in $[HCO_3^-]$ a 1 mmHg drop in P_{aC02} is expected.

Note: Because of respiratory compensation for metabolic acidosis, P_{aCO2} is expected to be below its normal range or ($P_{aCO2} < 38$ mmHg). If , because of disease, there is no respiratory compensation, then P_{aCO2} will be normal or elevated, and the respiratory system is contributing to the acidemia (see Respiratory Acidosis below)..

(3) Tissue phase. Entry of H^+ into cells accounts for ~60% of rapid (~2 h) buffering of poorly permeable acids (HCl or H_2SO_4). This phase is capable of buffering 100% of the acid by 24 h, and is due to the following ion exchanges and buffering of H^+ by cell proteins and HCO_3^-:

(a) Na^+ in the ICF for H^+ from the ECF; occurs in most tissues including bone; accounts for 65% of the entry of protons into the ICF (and bone).

(b) ICF K^+ for ECF H^+; accounts for 25% of the entry of H^+ into the ICF. May result in hyperkalemia (6-7 mEq/L) that affects muscle and nerve cells and induces cardiac

arrythmias.

(c) ECF Cl^- for ICF $HC0_3^-$; accounts for 10% of the ICF buffering of H^+; reduces ICF $HC0_3^-$ and intracellular pH; occurs mostly in red cells where Hb buffers excess H^+.

(4) Renal phase. Generation of bicarbonate through urinary excretion of ammonium and titratable acids, restores the depleted cell HCO_3^- and buffer base reserves over 2-3 days. Manifest only in chronic stage.

3.3. ACUTE AND CHRONICMETABOLIC ALKALOSIS (BASE BICARBONATE EXCESS)

Metabolic alkalosis: pH_a > 7.42; $[HCO_3^-]$ > 26 mM; P_aCO_2 0.75 mmHg increase for each 1 mM increase in $[HCO_3^-]$ (chronic or acute)

- Metabolic alkalosis is a clinical disturbance characterized by a high pH (decreased H□ □concentration) and a high plasma bicarbonate concentration. It can be produced by a gain of bicarbonate or a loss of H.
- Probably the most common cause of metabolic alkalosis is vomiting or gastric suction with loss of hydrogen and chloride ions. The disorder also occurs in pyloric stenosis, in which only gastric fluid is lost.
- Gastric fluid has an acid pH (usually 1–3); therefore, loss of this highly acidic fluid increases the alkalinity of body fluids.
- Other situations predisposing to metabolic alkalosis include those associated with loss of potassium, such as diuretic therapy that promotes excretion of potassium (eg, thiazides, furosemide), and excessive adrenocorticoid hormones (as in hyperaldosteronism and Cushing's syndrome).
- Hypokalemia produces alkalosis in two ways: (1) the kidneys conserve potassium, and thus H□ □excretion increases; and (2) cellular potassium moves out of the cells into the ECF in an attempt to maintain near-normal serum levels (as potassium ions leave the cells, hydrogen ions must enter to maintain electroneutrality).
- Excessive alkali ingestion from antacids containing bicarbonate or from using sodium bicarbonate during cardiopulmonary resuscitation can also cause metabolic alkalosis.

- Chronic metabolic alkalosis can occur with long-term diuretic therapy (thiazides or furosemide), villous adenoma, external drainage of gastric fluids, significant potassium depletion, cystic fibrosis, and the chronic ingestion of milk and calcium carbonate.

Causes:

(1) Loss of gastric juice (vomiting, suction)

(2) Side effect of diuretics and other forms of ECFV contraction.

(3) Hyperaldosteronism of volume depletion promotes renal H^+ secretion, generation and retention of HCO_3^-.

(4) In hypokalemia, K^+ shifts out of cells in exchange for H^+, inducing extracellular alkalosis and intracellular acidosis.

Clinical Manifestations

- Alkalosis is primarily manifested by symptoms related to decreased calcium ionization, such as tingling of the fingers and toes, dizziness, and hypertonic muscles.
- The ionized fraction of serum calcium decreases in alkalosis as more calcium combines with serum proteins. Because it is the ionized fraction of calcium that influences neuromuscular activity, symptoms of hypocalcemia are often the predominant symptoms of alkalosis.
- Respirations are depressed as a compensatory action by the lungs. Atrial tachycardia may occur. As the pH increases above 7.6 and hypokalemia develops, ventricular disturbances may occur.
- Decreased motility and paralytic ileus may also occur.
- Symptoms of chronic metabolic alkalosis are the same as for acute metabolic alkalosis, and as potassium decreases, frequent premature ventricular contractions or U waves are seen on the ECG.

Assessment and Diagnostic Findings

- Evaluation of arterial blood gases reveals a pH greater than 7.45 and a serum bicarbonate concentration greater than 26 mEq/L.

- The PaCO2 increases as the lungs attempt to compensate for the excess bicarbonate by retaining CO2. This hypoventilation is more pronounced in semiconscious, unconscious, or debilitated patients than in alert patients.
- The former may develop marked hypoxemia as a result of hypoventilation. Hypokalemia may accompany metabolic alkalosis.
- Urinary chloride levels may help to identify the cause of metabolic alkalosis if the patient's history provides inadequate information.
- Metabolic alkalosis is the setting in which urine chloride concentration may be a more accurate estimate of volume than is the urine sodium concentration.
- Urine chloride concentrations help to differentiate between vomiting or diuretic ingestion or one of the causes of mineralocorticoid excess.
- Hypovolemia and hypochloremia in patients with vomiting or cystic fibrosis, those receiving nutritional repletion, or those taking diuretics produce urine chloride concentrations less than 25 mEq/L.
- Signs of hypovolemia are not present and the urine chloride concentration exceeds 40 mEq/L in patients with mineralocorticoid excess or alkali loading; these patients usually have expanded fluid volume.
- The urine chloride concentration should be less than 15 mEq/L when decreased chloride levels and hypovolemia occur.

Medical Management

✦ Treatment of metabolic alkalosis is aimed at reversing the underlying disorder.

✦ Sufficient chloride must be supplied for the kidney to absorb sodium with chloride (allowing the excretion of excess bicarbonate).

✦ Treatment also includes restoring normal fluid volume by administering sodium chloride fluids (because continued volume depletion serves to maintain the alkalosis). In patients with hypokalemia, potassium is administered as KCl to replace both K□ and Cl−□losses.

✦ Histamine-2 receptor antagonists, such as cimetidine (Tagamet), reduce the production of gastric HCl, thereby decreasing the metabolic alkalosis associated with gastric suction.

✦ Carbonic anhydrase inhibitors are useful in treating metabolic alkalosis in patients who cannot tolerate rapid volume expansion (eg, patients with heart failure). Because of volume depletion from GI loss, the patient's fluid intake and output must be

monitored carefully. Management of chronic metabolic alkalosis is aimed at correcting the underlying acid–base disorder.

Compensations:

(1) Respiratory. As pH_a increases, V_A is depressed and P_{aCO2} increases (P_{aCO2} > 42 mmHg). This normalizes blood pH but is limited by ensuing hypoxia. For each 1 mM rise in HCO_3^- there is expected a 0.75 mmHg rise in P_{aCO2}; if this does not occur, there is a respiratory tendency to alkalosis.

(2) Cell ionic exchanges. Some 25% of the bicarbonate load is neutralized by H^+ derived from intracellular buffers that exchange the H^+ for extracellular Na^+. In addition, ~2% of extracellular HCO_3^- enters red cells in exchange for Cl^-.

(3) Metabolic. Increases in endogenous organic acid production neutralize ~5 % of an acute $HCO_3^{-\,load}$. High pH_a increases production of lactic and citric acids which decrease $[HCO_3^-]$. High blood pH stimulates glycolysis and inhibits the citric acid cycle.

(4) Renal excretion of HCO_3^- rises when its concentration in plasma increases. Lowering of $[HCO_3^-]_{pl}$ is limited by high renal reabsorption rate stimulated by high P_{aCO2}, by ECF volume contraction, by hyperaldosteronism, by K^+ depletion, and by hypochloremia. These tend to perpetuate the high $[HCO_3^-]_{pl}$. Beta-intercalated cells in CCD secrete bicarbonate, increasing its urinary excretion.

3.4. ACUTE AND CHRONIC RESPIRATORY ALKALOSIS (CARBONIC ACID DEFICIT)

Respiratory alkalosis: pH > 7.44; P_{aCO2} < 38 mm Hg; $[HCO_3^-]$ decreases (<24 mM) by 0.5 mM (chronic) or 0.1 mM (acute) per each 1 mmHg drop in P_{aC02}

Respiratory alkalosis is a clinical condition in which the arterial pH is greater than 7.45 and the PaCO2 is less than 38 mm Hg. As with respiratory acidosis, acute and chronic conditions can occur.

Respiratory alkalosis is always due to hyperventilation, which causes excessive "blowing off" of CO2 and, hence, a decrease in the plasma carbonic acid concentration. Causes can include extreme anxiety, hypoxemia, and the early phase of salicylate intoxication, gram-negative bacteremia, and inappropriate ventilator settings that do not match the patient's requirements.

Chronic respiratory alkalosis results from chronic hypocapnia, and decreased serum bicarbonate levels are the consequence.

Chronic hepatic insufficiency and cerebral tumors are predisposing factors.

Cause: Alveolar hyperventilation (altitude, hysteria, aspirin excess)

Clinical Manifestations

Clinical signs consist of lightheadedness due to vasoconstriction and decreased cerebral blood flow, inability to concentrate, numbness and tingling from decreased calcium ionization, tinnitus, and at times loss of consciousness. Cardiac effects of respiratory alkalosis include tachycardia and ventricular and atrial dysrhythmias.

Assessment and Diagnostic Findings

- Analysis of arterial blood gases assists in the diagnosis of respiratory alkalosis. In the acute state, the pH is elevated above normal as a result of a low PaCO2 and a normal bicarbonate level.
- (The kidneys cannot alter the bicarbonate level quickly.) In the compensated state, the kidneys have had sufficient time to lower the bicarbonate level to a near-normal level.
- Evaluation of serum electrolytes is indicated to identify any decrease in potassium as hydrogen is pulled out of the cells in exchange for potassium; decreased calcium, as severe alkalosis inhibits calcium ionization, resulting in carpopedal spasms and tetany; or decreased phosphate due to alkalosis, causing an increased uptake of phosphate by the cells.
- A toxicology screen should be performed to rule out salicylate intoxication.
- Patients with chronic respiratory alkalosis are usually asymptomatic, and the diagnostic evaluation and plan of care are the same as for acute respiratory alkalosis.

Medical Management

Treatment depends on the underlying cause of respiratory alkalosis. If the cause is anxiety, the patient is instructed to breathe more slowly to allow CO2 to accumulate or to

breathe into a closed system (such as a paper bag). A sedative may be required to relieve hyperventilation in very anxious patients.

Treatment for other causes of respiratory alkalosis is directed at correcting the underlying problem.

Compensations

(1) Cell buffers. In the acute state there is a 0.1 mM decrease in $[HCO_3^-]$ for each mmHg decrease in P_{aCO2}. This decrease is due to enhanced dissociation of H^+ from cell buffers when the $[H^+]_i$ decreases due to the low P_{aCO2}. Cell H^+ exchange for ECF Na^+ and K^+ and react with the ECF HCO_3^-, reducing its concentration. Some extracellular HCO_3^- enters cells in exchange for Cl^- and is titrated by H^+ dissociating from the cell buffers.

In the chronic state, there is a 0.5 mM decrease in $[HCO_3^-]$ for each one mmHg decrease in $PaCO_2$. This is due to:

(2) Renal compensation due to increased HCO_3^- excretion associated with the low P_{aCO2}, which decreases HCO_3^- reabsorption. Urinary excretion of NH_4^+ and titratable acid are transiently reduced, leading to accumulation of metabolic and dietary acids which help reduce ECF $[HCO_3^-]$ ($[HCO_3^-] < 22$ mM). Eventually urinary HCO_3^- excretion ceases and excretion of $NH4^+$ and titratable acid resumes.

(3) Metabolic compensation by increased production of lactic and citric acids that react with and reduce $[HCO_3^-]_{ecf}$

3.5. ACUTE AND CHRONIC RESPIRATORY ACIDOSIS (CARBONIC ACID EXCESS)

Respiratory acidosis: pH < 7.38; $P_{aC02} > 42$ mm Hg; $[HCO_3^-]$ increases (>24 mM) by 0.25 mM (chronic) or 0.05 mM (acute) per each 1 mmHg rise in P_{aC02}

Respiratory acidosis is a clinical disorder in which the pH is less than 7.35 and the PaCO2 is greater than 42 mm Hg. It may be either acute or chronic.

Respiratory acidosis is always due to inadequate excretion of CO2 with inadequate ventilation, resulting in elevated plasma CO2 levels and thus elevated carbonic

acid (H_2CO_3) levels. In addition to an elevated $PaCO_2$, hypoventilation usually causes a decrease in PaO_2.

Acute respiratory acidosis occurs in emergency situations, such as acute pulmonary edema, aspiration of a foreign object, atelectasis, pneumothorax, overdose of sedatives, sleep apnea syndrome, administration of oxygen to a patient with chronic hypercapnia (excessive CO_2 in the blood), severe pneumonia, and acute respiratory distress syndrome. Respiratory acidosis can also occur in diseases that impair respiratory muscles, such as muscular dystrophy, myasthenia gravis, and Guillain-Barre syndrome.

Mechanical ventilation can be associated with hypercapnia if the rate of effective alveolar ventilation is inadequate. Ventilation is fixed in these patients, and CO_2 may be retained if the rate of CO_2 production is increased.

Cause: Alveolar hypoventilation

Clinical Manifestations

- Clinical signs in acute and chronic respiratory acidosis vary.
- Sudden hypercapnia (elevated $PaCO_2$) can cause increased pulse and respiratory rate, increased blood pressure, mental cloudiness, and feeling of fullness in the head. An elevated $PaCO_2$ causes cerebrovascular vasodilation and increased cerebral blood flow, particularly when it is higher than 60 mm Hg.
- Ventricular fibrillation may be the first sign of respiratory acidosis in anesthetized patients.
- If respiratory acidosis is severe, intracranial pressure may increase, resulting in papilledema and dilated conjunctival blood vessels.
- Hyperkalemia may result as hydrogen concentration overwhelms the compensatory mechanisms and moves into cells, causing a shift of potassium out of the cell.
- Chronic respiratory acidosis occurs with pulmonary diseases such as chronic emphysema and bronchitis, obstructive sleep apnea, and obesity. As long as the $PaCO_2$ does not exceed the body's ability to compensate, the patient will be asymptomatic.
- However, if the $PaCO_2$ rises rapidly, cerebral vasodilation will increase intracranial pressure; cyanosis and tachypnea will develop.
- Patients with chronic obstructive pulmonary disease who gradually accumulate CO_2 over a prolonged period (days to months) may not develop symptoms of hypercapnia because compensatory renal changes have had time to occur.

Assessment and Diagnostic Findings

Arterial blood gas evaluation reveals a pH less than 7.35, a $PaCO_2$ greater than 42 mm Hg, and a variation in the bicarbonate level, depending on the duration of the acidosis in acute respiratory acidosis.

When compensation (renal retention of bicarbonate) has fully occurred, the arterial pH may be within the lower limits of normal.

Depending on the cause of respiratory acidosis, other diagnostic measures would include monitoring of serum electrolyte levels, chest x-ray for determining any respiratory disease, and a drug screen if an overdose is suspected.

An ECG to identify any cardiac involvement as a result of chronic obstructive pulmonary disease may be indicated as well.

Medical Management

- Treatment is directed at improving ventilation; exact measures vary with the cause of inadequate ventilation.
- Pharmacologic agents are used as indicated. For example, bronchodilators help reduce bronchial spasm, antibiotics are used for respiratory infections, and thrombolytics or anticoagulants are used for pulmonary emboli.
- Pulmonary hygiene measures are initiated, when necessary, to clear the respiratory tract of mucus and purulent drainage. Adequate hydration (2–3 L/day) is indicated to keep the mucous membranes moist and thereby facilitate the removal of secretions.
- Supplemental oxygen is used as necessary.
- Mechanical ventilation, used appropriately, may improve pulmonary ventilation. Inappropriate mechanical ventilation (eg, increased dead space, insufficient rate or volume settings, high fraction of inspired oxygen [FiO_2] with excessive CO_2 production) may cause such rapid excretion of CO_2 that the kidneys will be unable to eliminate excess bicarbonate quickly enough to prevent alkalosis and seizures.
- For this reason, the elevated $PaCO_2$ must be decreased slowly. Placing the patient in a semi-Fowler's position When the $PaCO_2$ is chronically above 50 mm Hg, the respiratory center becomes relatively insensitive to CO_2 as a respiratory stimulant, leaving hypoxemia as the major drive for respiration. Oxygen administration may remove the stimulus of hypoxemia, and the patient develops "carbon dioxide narcosis" unless the situation is quickly reversed.

- Therefore, oxygen is administered only with extreme caution facilitates expansion of the chest wall. Treatment of chronic respiratory acidosis is the same as for acute respiratory acidosis.

Compensations:

(1) Fast cell ion exchanges. An acute small rise in $[HCO_3^-]_{pl}$ is due to exchange of ECF H^+ for ICF (or bone) Na^+ (37%) or for ICF K^+ (13%) and to exchange of ECF Cl^- for ICF (red cells) HCO_3^- (30%). These rapid ionic exchanges are associated with CO_2 buffering by intracellular proteins. For each 1 mmHg increment in P_{aCO2} there is a small acute 0.06 mM increment in HCO_3^-.

(2) Metabolic. Reduced production of lactic acid contributes about 5% to the acute increase in $[HCO_3^-]_{pl}$.

(3) Renal. Increased HCO_3^- reabsorption stimulated by high P_{aCO2} prevents urinary loss of bicarbonate.

In the transition to the chronic stage (1-3 days), enhanced renal NH_4^+, and titratable acid excretion contribute to further increase $[HCO_3^-]$ in ECF and ICF above normal ($[HCO_3^-] > 26$ mM), returning pH towards normal. As the pH stimulus decreases, renal NH_4^+ and titratable acid excretion subside. Renal reabsorption of bicarbonate remains elevated as long as the P_{aCO2} is high.

3.6. MIXED ACID–BASE DISORDERS:

- At times patients can simultaneously experience two or more independent acid–base disorders.
- A normal pH in the presence of changes in the PaCO2 and plasma HCO3 −□concentration immediately suggests a mixed disorder.
- The only mixed disorder that cannot occur is a mixed respiratory acidosis and alkalosis, because it is impossible to have alveolar hypoventilation and hyperventilation at the same time.

- An example of a mixed disorder is the simultaneous occurrence of metabolic acidosis and respiratory acidosis during respiratory and cardiac arrest.

3.7. BLOOD GAS ANALYSIS

- ✦ Blood gas analysis is often used to identify the specific acid–base disturbance and the degree of compensation that has occurred.
- ✦ The analysis is usually based on an arterial blood sample, but when an arterial sample cannot be obtained, a mixed venous sample may be used.
- ✦ Results of arterial blood gas analysis provide information about alveolar ventilation, oxygenation, and acid–base balance. It is necessary to evaluate the serum electrolytes (sodium, potassium, and chloride) and carbon dioxide along with arterial blood gas data as they are often the first sign of an acid–base disorder.
- ✦ The health history, physical examination, previous blood gas results, and serum electrolytes should always be part of the assessment used to determine the cause of the acid–base disorder.
- ✦ Treatment of the underlying condition usually corrects most acid–base disorders.

Table 14-7 • **Acid–Base Disturbances and Compensation**

DISORDER	INITIAL EVENT	COMPENSATION
Respiratory acidosis	↑ $PaCO_2$, ↑ or normal HCO_3^-, ↓ pH	Kidneys eliminate H^+ and retain HCO_3^-
Respiratory alkalosis	↓ $PaCO_2$, ↓ or normal HCO_3^-, ↑ pH	Kidneys conserve H^+ and excrete HCO_3^-
Metabolic acidosis	↓ or normal $PaCO_2$, ↓ HCO_3^-, ↓ pH	Lungs eliminate CO_2, conserve HCO_3^-
Metabolic alkalosis	↑ or normal $PaCO_2$, ↑ HCO_3^-, ↑ pH	Lungs ↓ ventilation to ↑ PCO_2, kidneys conserve H^+ to excrete HCO_3^-

Table 14-8 • **Normal Values: Arterial and Venous Blood**

PARAMETER	ARTERIAL SAMPLE	VENOUS SAMPLE
pH	7.35–7.45	7.33–7.41
$PaCO_2$	35–45 mm Hg	35–40 mmHg
Oxygen saturation	93–98%	65–75%
Base excess or deficit	+/– 2 mmol/L	+/– 4 mmol/L
HCO_3^-	22–26 mEq/L	24–28 Eq/L

4. CONCLUSION:

Acid–base disturbances are commonly encountered in clinical practice. Identification of the specific acid–base imbalance is important in identifying the underlying cause of the disorder and in determining appropriate treatment.

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