Simple and mixed acid-base disorders

INTRODUCTION — Each day, adults generate large amounts of acids that must be expired, excreted, metabolized to non-charged neutral molecules, and/or buffered to avoid fatal acidemia. These acids are of three major classes:

- Approximately 15,000 mmol (considerably more with exercise) of carbon dioxide (CO2) is produced each day, which combines with water to form carbonic acid (H2CO3).
- Metabolic reactions generate several thousand mmol per day of organic acids, such as lactic acid and citric acid. These acids are metabolized to neutral products (such as glucose) and to CO2 and water. Normally, the generation and utilization rates of these organic acids are equal so that their steady state concentration in the extracellular fluid is relatively low and stable.
- Approximately 50 to 100 meq of nonvolatile acid is produced each day (mostly sulfuric acid derived from the metabolism of sulfur-containing amino acids in the diet).

Acid-base balance is maintained by normal pulmonary excretion of carbon dioxide, metabolic utilization of organic acids, and renal excretion of nonvolatile acids.

Renal excretion of acid is achieved by combining hydrogen ions with either urinary buffers to form titratable acid, such as phosphate (HPO42- + H+ → H2PO4-), urate, and creatinine, or with ammonia to form ammonium (NH3 + H+ → NH4+) [1]. When increased quantities of acid must be excreted by the kidney, the major adaptive response is an increase in ammonia production (derived from the metabolism of glutamine) with a resultant increase in ammonium excretion into the urine.

Acid-base status is usually assessed by measuring the components of the bicarbonate-carbon dioxide buffer system in blood:

Dissolved CO2 + H2O ↔ H2CO3 ↔ HCO3- + H+

When blood gas analysis is carried out, the partial pressure of CO2 (PCO2) and the pH are each measured using analytical electrodes. The serum bicarbonate (HCO3-) concentration is then calculated with the Henderson-Hasselbalch equation. Generally, the PCO2 is reported in mmHg, and HCO3- in meq/L:

\[
\text{pH} = 6.10 + \log \left( \frac{[\text{HCO}_3^-]}{0.03 \times \text{PCO}_2} \right)
\]

where the pH is equal to (-log [H+]); 6.10 is the negative log of Ka (-log Ka), which is the dissociation constant for this reaction; 0.03 is the solubility coefficient for CO2 in blood; and the PCO2 is the partial pressure of carbon dioxide in blood [2].

When the HCO3 is measured in venous blood, it is usually measured directly as "total CO2" with an ion-selective electrode. The directly measured venous "total CO2" is generally about 2 meq/L greater than the simultaneously calculated arterial HCO3.

NORMAL VALUES ACCORDING TO SITE OF SAMPLING — The range of normal values for acid-base parameters is different for arterial and venous samples and also varies among laboratories. These issues are discussed in detail elsewhere but will be briefly summarized here. (See "Arterial blood gases" and "Venous blood gases and other alternatives to arterial blood gases".)

Arterial blood gas sample — For an arterial blood gas sample, the normal range for pH is 7.36 to 7.44; for bicarbonate (HCO3-) concentration, 21 to 27 meq/L; and for PCO2, 36 to 44 mmHg (4.8 to 5.9 kPa).

Peripheral venous blood gas sample — Normal values for peripheral venous blood gases differ from those of arterial blood due to the uptake and buffering of metabolically produced CO2 in the capillary circulation and the addition of organic acids produced by the tissue bed drained by the vein. If a tourniquet is used to facilitate phlebotomy, it should be released about one minute before the sample is drawn to avoid changes induced by

Approximately 15,000 mmol (considerably more with exercise) of carbon dioxide (CO2) is produced each day, which combines with water to form carbonic acid (H2CO3). Metabolic reactions generate several thousand mmol per day of organic acids, such as lactic acid and citric acid. These acids are metabolized to neutral products (such as glucose) and to CO2 and water. Normally, the generation and utilization rates of these organic acids are equal so that their steady state concentration in the extracellular fluid is relatively low and stable. Approximately 50 to 100 meq of nonvolatile acid is produced each day (mostly sulfuric acid derived from the metabolism of sulfur-containing amino acids in the diet).
In different studies, the range for peripheral venous pH is approximately 0.02 to 0.04 pH units lower than in arterial blood, the HCO3 concentration is approximately 1 to 2 meq/L higher, and the PCO2 is approximately 3 to 8 mmHg (0.4 to 1.1 kPa) higher [4-6]. If venous measurements are used for serial monitoring, periodic correlation with arterial measurements should be performed. (See "Arterial blood gases").

Central venous sample — Central venous samples may be analyzed in patients with central venous catheters. The central venous pH is usually 0.03 to 0.05 pH units lower than in arterial blood and the PCO2 is 4 to 5 mmHg (0.5 to 0.7 kPa) higher, with little or no increase in serum HCO3 [7,8].

DEFINITIONS OF ACID-BASE DISORDERS — The following definitions of acid-base disorders are based upon principles of the Henderson-Hasselbalch equation:

- Acidemia – An arterial pH below the normal range (less than 7.36).
- Alkalemia – An arterial pH above the normal range (greater than 7.44).
- Acidosis – A process that tends to lower the extracellular fluid pH (hydrogen ion concentration increases). This can be caused by a fall in the serum bicarbonate (HCO3) concentration and/or an elevation in PCO2.
- Alkalosis – A process that tends to raise the extracellular fluid pH (hydrogen ion concentration decreases). This can be caused by an elevation in the serum HCO3 concentration and/or a fall in PCO2.
- Metabolic acidosis – A disorder that reduces the serum HCO3 concentration and pH. (See "Approach to the adult with metabolic acidosis").
- Metabolic alkalosis – A disorder that elevates the serum HCO3 concentration and pH. (See "Pathogenesis of metabolic alkalosis" and "Causes of metabolic alkalosis".)
- Respiratory acidosis – A disorder that elevates the arterial PCO2 and reduces the pH.
- Respiratory alkalosis – A disorder that reduces the arterial PCO2 and elevates the pH.
- Simple acid-base disorder – The presence of one of the above disorders with the appropriate respiratory or renal compensation for that disorder. (See 'Compensatory respiratory and renal responses' below.)
- Mixed acid-base disorder – The simultaneous presence of more than one acid-base disorder. Mixed acid-base disorders can be suspected from the patient's history, from a lesser- or greater-than-expected compensatory respiratory or renal response, and from analysis of the serum electrolytes and anion gap. As an example, a patient with severe vomiting would be expected to develop a metabolic alkalosis due to the loss of acidic gastric fluid. If, however, the patient also developed hypovolemic shock from the fluid loss, the ensuing lactic acidosis would lower the elevated serum HCO3 possibly to below normal values, resulting in acidemia. (See 'Mixed acid-base disorders' below.)

COMPENSATORY RESPIRATORY AND RENAL RESPONSES

General principles — The Henderson-Hasselbalch equation described above shows that the pH is determined by the ratio of the serum bicarbonate (HCO3) concentration and the PCO2, not by the value of either one alone. Each of the simple acid-base disorders is associated with a compensatory respiratory or renal response that limits the change in ratio and therefore in pH (figure 1) [9].

- When a metabolic acid-base disorder reduces the serum HCO3 (metabolic acidosis) or increases the HCO3 (metabolic alkalosis), there should be an appropriate degree of respiratory compensation moving the PCO2 in the same direction as the serum HCO3 (falling in metabolic acidosis and rising in metabolic alkalosis). The respiratory compensation mitigates the change in the ratio of the serum HCO3 to PCO2 and therefore in the pH. Respiratory compensation in metabolic acidosis or alkalosis is a rapid response. With metabolic acidosis, for example, the response begins within 30 minutes [10] and is complete within 12 to 24 hours [11].

- When a respiratory acid-base disorder causes the PCO2 to increase (respiratory acidosis) or decrease (respiratory alkalosis), compensation occurs in two phases. There is an immediate, small change in serum HCO3 (in the same direction as the PCO2 change), which is due to whole body buffering mechanisms. If the respiratory disorder persists for more than minutes to hours, the kidneys respond by producing larger changes in serum HCO3 (again, in the same direction as the PCO2). These HCO3 changes mitigate the change in pH. Renal compensations are mediated by increased hydrogen ion secretion (which raises the serum HCO3
concentration) in respiratory acidosis and decreased hydrogen ion secretion and urinary HCO3 loss in respiratory alkalosis. The renal compensation takes three to five days for completion. As a result, the expected findings are very different in acute (whole body buffering without significant renal compensation) and chronic (full renal compensation) respiratory acid-base disorders. (See 'Respiratory acid-base disorders' below.)

The compensatory renal and respiratory responses are thought to be mediated, at least in part, by parallel pH changes within sensory and regulatory cells including renal tubule cells and cells in the respiratory center [12]. The magnitude of the compensatory response is proportional to the severity of the primary acid-base disturbance.

It follows from the above discussion that a high HCO3 concentration may be due to metabolic alkalosis or compensation for chronic respiratory acidosis. Conversely, a low HCO3 may be due to metabolic acidosis or compensation for chronic respiratory alkalosis. Analogous issues apply to a high or low PCO2. At least two of the three variables in the Henderson-Hasselbalch equation (pH, HCO3, PCO2) must be measured to assess an acid-base disorder (and if two are measured, the third can be deduced).

The expected degree of compensation for each acid-base disorder has been determined empirically by observations in humans with either spontaneous or experimentally induced simple acid-base disorders (figure 1). The degree of compensation is usually defined by the decrease or increase in arterial PCO2 from its normal range (in metabolic acid-base disorders) or the decrease or increase in serum HCO3 from its normal range (in respiratory acid-base disorders). This approach presumes that the patient had normal values prior to the onset of the acid-base disorder. Thus, in the absence of known baseline values, there is the potential for error if the patient's acid-base status was not normal at the onset of the disorder.

**Metabolic acid-base disorders**

**Metabolic acidosis** — Respiratory compensation for metabolic acidosis causes the arterial PCO2 to fall approximately 1.2 mmHg (0.16 kPa) for every 1 meq/L reduction in the serum HCO3 concentration [9,13]. The respiratory response to metabolic acidosis begins within 30 minutes [10] and is complete within 12 to 24 hours [11]. There is no lag in respiratory compensation when metabolic acidosis develops slowly (eg, 4 meq/L fall in serum HCO3 over 15 hours) [11]. An inability to generate the expected respiratory response is usually indicative of significant underlying respiratory or neurologic disease, but can also occur at the onset of acute metabolic acidosis before there has been adequate time for respiratory compensation to fully develop [14].

Several other predictive relationships have been proposed to determine the appropriate respiratory compensation to metabolic acidosis. These include:

- Arterial PCO2 = 1.5 x serum HCO3 + 8 ± 2 (Winters' equation) [15]
- Arterial PCO2 = Serum HCO3 + 15
- Arterial PCO2 should be similar to the decimal digits of the arterial pH (eg, 25 mmHg when the arterial pH is 7.25, a setting in which the serum HCO3 concentration would be approximately 11 meq/L) [16]

These formulas and rules generally give similar results. Because there are no data on comparative accuracy (see 'Case 2' below), the reader may use the relationship rule he or she finds easiest to remember and implement.

There is a limit to the maximum respiratory compensation that can be attained. With severe metabolic acidosis (eg, serum HCO3 concentration less than 6 meq/L), the PCO2 can fall no lower than 8 to 12 mmHg (1.1 to 1.6 kPa). In addition, the duration that such compensation can be maintained is limited due to respiratory muscle fatigue.

In addition to assessing the respiratory compensation, another component in the evaluation of patients with metabolic acidosis is calculation of the serum anion gap to determine whether it is normal or elevated. Metabolic acidosis may be of the high anion gap type, normal anion gap type (hyperchloremic), or combined normal and elevated anion gap acidosis. As an example, with severe diarrhea, loss of bicarbonate in the stool typically generates a normal anion gap metabolic acidosis, but the resulting hypovolemia can also lead to lactic acidosis and renal dysfunction with a high anion gap acidosis. With high anion gap metabolic acidosis, comparing the change in anion gap (or the delta anion gap) with the change in bicarbonate (or the delta bicarbonate) may be helpful. These issues are discussed in detail elsewhere. (See "Approach to the adult with metabolic acidosis", section on 'Physiologic interpretation of the serum anion gap' and "The Δanion gap/ΔHCO3 ratio in patients with a high anion gap metabolic acidosis".)

**Metabolic alkalosis** — The respiratory compensation to metabolic alkalosis should raise the PCO2 by about 0.7 mmHg (0.09 kPa) for every 1 meq/L elevation in the serum HCO3 concentration [9,17,18]. In severe metabolic
alkalosis, the arterial PCO2 usually does not increase above 55 mmHg (7.3 kPa) [17].

Respiratory acid-base disorders — The compensatory response to respiratory acid-base disorders occurs in two stages:

- The initial acute response is generated by a variety of pH buffering molecules present in all of the fluid compartments of the body (ie, total body buffering). Reactions with these molecules cause the serum HCO3 to increase (in respiratory acidosis) or decrease (in respiratory alkalosis) within minutes. The acute response is relatively modest.

- A larger response generated by the kidney is called chronic compensation. This response begins soon after the onset of the primary respiratory disorder but requires three to five days to become complete. Because of this variation with time, different compensatory responses are expected with acute and chronic respiratory disorders:
  - With chronic respiratory acidosis, the kidney increases acid excretion in the form of titratable acid and ammonium that generates additional HCO3; renal tubule HCO3 reabsorption is also increased, which maintains the higher HCO3 concentration (figure 2) [19,20].
  - With chronic respiratory alkalosis, the kidney both reduces acid excretion (which results in a positive acid balance that reduces the serum HCO3 concentration) and excretes some HCO3 (which further reduces the serum HCO3 concentration).
  - These renal responses are carefully regulated. As an example, administering exogenous HCO3 in the setting of chronic respiratory acidosis and relatively normal renal function results in the urinary excretion of the excess alkali without a further elevation in the serum HCO3 concentration [21].

Respiratory acidosis — The compensatory response to acute respiratory acidosis increases the serum HCO3 concentration by about 1 meq/L for every 10 mmHg (1.3 kPa) elevation in the PCO2 (figure 3) [9,22]. If the elevated PCO2 persists, the serum HCO3 will continue to gradually increase and, after three to five days, the disorder is considered chronic. Studies mostly performed in hospitalized patients found that the serum HCO3 increases by 3.5 to 4 meq/L for every 10 mmHg elevation in PCO2 in patients with chronic respiratory acidosis [9,19,20,23]. However, a later study in stable outpatients with chronic respiratory acidosis found a greater compensatory rise in serum HCO3 of about 5 meq/L per 10 mmHg (1.3 kPa) elevation in PCO2 [24]. The compensatory response to mild to moderate chronic respiratory acidosis (PCO2 less than 70 mmHg [9.3 kPa]) results in an arterial pH that is usually modestly reduced [9,19,20,23] or in the low-normal range (figure 2) [24]. Thus, moderate to severe acidemia in a patient with mild to moderate chronic respiratory acidosis is usually indicative of concurrent metabolic acidosis or superimposed acute respiratory acidosis. Conversely, an arterial pH of 7.40 or higher suggests a concurrent metabolic alkalosis or acute respiratory alkalosis.

Respiratory alkalosis — The compensatory response to acute respiratory alkalosis reduces the serum HCO3 concentration by 2 meq/L for every 10 mmHg (1.3 kPa) decline in the PCO2 (figure 3) [9,22]. If the reduced PCO2 persists for more than three to five days, then the disorder is considered chronic and the serum HCO3 concentration should fall by about 4 to 5 meq/L for every 10 mmHg (1.3 kPa) reduction in the PCO2 (figure 4) [9,25].

Diagnosis — There are four primary acid-base disorders: metabolic acidosis, metabolic alkalosis, respiratory acidosis, and respiratory alkalosis. Because the renal compensation to respiratory disorders takes three to five days to complete, the primary respiratory disorders can be further divided into acute and chronic respiratory acidosis and respiratory alkalosis.

Initial evaluation — Accurate diagnosis of an acid-base disorder requires measurement of serum electrolytes to determine the serum HCO3 concentration, the serum potassium (looking for hypokalemia or hyperkalemia which can accompany many metabolic acid-base disorders), and the serum sodium and chloride concentrations to detect possible hyponatremia or hypernatremia and calculation of the serum anion gap. In addition, in patients with a high anion gap metabolic acidosis, analysis of the increase of the anion gap from its baseline divided by the reduction in bicarbonate from normal (ie, the delta anion gap divided by the delta bicarbonate, or "delta/delta") may be helpful. These issues are discussed in detail elsewhere. (See "Approach to the adult with metabolic acidosis", section on 'Physiologic interpretation of the serum anion gap' and "The Δanion gap/ΔHCO3 ratio in patients with a high anion gap metabolic acidosis".) A definitive diagnosis of acid-base disorders requires measurement of the arterial pH and PCO2 as well as the serum chemistries to identify the underlying disorder and to determine whether a mixed acid-base disorder exists.
However, measurement of arterial pH is not always required. When the history and serum electrolytes clearly point toward a particular diagnosis, a presumptive diagnosis can be made. As an example, arterial blood gas analysis might not be required in a previously healthy patient with a recent history of severe diarrhea who has a low serum bicarbonate, hypokalemia, and a normal anion gap. This patient can be assumed to have a non-anion gap metabolic acidosis because there is no reason to suspect chronic respiratory alkalosis (a disorder in which a low serum bicarbonate develops as a compensatory response).

Measurement of peripheral venous pH and PCO2 is an alternative diagnostic procedure that is a less invasive and more convenient approach than arterial measurements. However, venous measurements have some important limitations. As a result, arterial measurements are preferred. If venous measurements are used for serial monitoring, periodic correlation with arterial measurements should be performed. These issues are discussed in detail elsewhere. (See 'Normal values according to site of sampling' above.)

We suggest the following three-step approach in most patients:

- **Step 1: Establish the primary diagnosis:**
  - Metabolic acidosis is characterized by a low serum HCO3 and a low arterial pH; the serum anion gap may be increased or normal.
  - Metabolic alkalosis is characterized by an elevated serum HCO3 and an elevated arterial pH.
  - Respiratory acidosis is characterized by an elevated arterial PCO2 and a low arterial pH.
  - Respiratory alkalosis is characterized by low arterial PCO2 and an elevated arterial pH.
  - With the exception of chronic respiratory alkalosis and mild to moderate respiratory acidosis (see 'Mixed acid-base disorders' below), compensatory responses do not usually return the arterial pH to normal.

  Thus, a normal arterial pH in the presence of substantial changes in both serum HCO3 and arterial PCO2 is usually indicative of a mixed acid-base disorder (which could include an iatrogenic acute respiratory alkalosis if discomfort from the arterial puncture causes the patient to hyperventilate).

- **Step 2: Assess the degree of compensation as defined above for the individual disorders. A substantially reduced or excessive level of compensation is indicative of a mixed acid-base disorder. (See 'Compensatory respiratory and renal responses' above.)**

  The compensatory response must be correlated with the history. This is particularly true in respiratory acid-base disorders since the renal compensation occurs over three to five days. Thus, the expected level of compensation is smaller with acute respiratory disorders compared with chronic respiratory disorders. As noted above, the normal compensatory response to respiratory acidosis is an increase in the serum HCO3 concentration by about 1 meq/L for every 10 mmHg (1.3 kPa) elevation in the PCO2 acutely and about 3.5 to 5 meq/L for every 10 mmHg (1.3 kPa) elevation in the PCO2 if the underlying respiratory problem persists for three to five days or more. (See 'Respiratory acidosis' above.)

- **Step 3: Determine whether or not the anion gap is elevated. This is especially important for patients with metabolic acidosis. If the anion gap is increased, then analyze the ratio of the increase in anion gap to the decrease in the HCO3 concentration. This is called the delta anion gap/delta HCO3 ratio. Interpretation of the anion gap and the delta anion gap/delta HCO3 ratio are discussed elsewhere. (See "Approach to the adult with metabolic acidosis", section on 'Physiologic interpretation of the serum anion gap' and "The Δanion gap/ΔHCO3 ratio in patients with a high anion gap metabolic acidosis").**

The final step is to establish the clinical diagnosis. Once the acid-base disorder, or disorders, is identified, the underlying cause or causes of each disorder should be determined and addressed.

**Case 1** — A patient with an unknown past history presents with respiratory distress. Arterial blood shows a pH of 7.32, PCO2 of 70 mmHg (9.3 kPa), and HCO3 of 35 meq/L. The HCO3 is approximately 11 meq/L above the normal range, and the PCO2 is approximately 30 mmHg above the normal range. These values are compatible with a diagnosis of a simple (fully compensated) chronic respiratory acidosis. However, the results are also compatible with a mixed acid-base disorder. As an example, an acute respiratory acidosis causing a rise in PCO2 to 70 mmHg (9.3 kPa) should increase the serum HCO3 by about 3 meq/L to about 27 meq/L. If, before the onset of respiratory acidosis, vomiting (a metabolic alkalosis) had increased the serum bicarbonate by 8 meq/L, the combined effects of acute respiratory acidosis and metabolic alkalosis (a mixed acid-base disorder) would result in identical laboratory values.
findings. The history usually helps to distinguish among these possibilities.

**Case 2** — A patient presents with diarrhea. Arterial blood shows a pH of 7.24, PCO2 of 24 mmHg (3.2 kPa), and HCO3 or 10 meq/L. The low pH indicates acidemia, and the low serum HCO3 concentration indicates metabolic acidosis. The serum HCO3 concentration of 10 meq/L is approximately 14 meq/L below normal. This should stimulate respiratory compensation and a 17 mmHg (2.3 kPa) fall in the PCO2 (14 x 1.2 = 17) from 40 to 23 mmHg (5.3 to 3.1 kPa). These results are consistent with a simple metabolic acidosis. The other estimation equations for the degree of compensation cited above give similar results. Winters' equation predicts a PCO2 of 23 mmHg (1.5 x 10 +8 ± 2); the "HCO3 + 15" rule predicts a PCO2 of 25 mmHg (3.3 kPa). In addition, the PCO2 is the same as the decimal digits of the arterial pH. (See 'Metabolic acidosis' above.)

A PCO2 significantly higher than the expected value would be consistent with a concurrent respiratory acidosis, as might occur, for example, if the patient were obtunded and had respiratory center depression. If, on the other hand, the PCO2 were lower than 20 mmHg (2.7 kPa), then a concurrent respiratory alkalosis would be present. The combination of metabolic acidosis and respiratory alkalosis is often seen with salicylate intoxication or septic shock. (See "Salicylate (aspirin) poisoning in adults", section on 'Acid-base abnormalities'.)  

**Mixed acid-base disorders** — Some patients have two, three, or more relatively independent acid-base disorders. These mixed disorders include combinations of metabolic disorders (eg, vomiting-induced metabolic alkalosis plus hypovolemia-induced lactic acidosis), mixed metabolic and respiratory disorders (eg, metabolic acidosis and respiratory alkalosis in salicylate intoxication), and more complex combinations.

As discussed in the preceding section, the evaluation of patients with acid-base disorders initially requires identification of the major disorder, and then determination of whether or not the degree of compensation is appropriate. If the compensation is not appropriate, then this is indicative of a second acid-base disorder (ie, a mixed acid-base disorder is present). The following examples are illustrative:

- If metabolic acidosis is the primary disorder, an arterial PCO2 substantially higher than the expected compensatory response defines the mixed disorder of metabolic acidosis and respiratory acidosis, while an arterial PCO2 substantially lower than expected defines the mixed disorder of metabolic acidosis and respiratory alkalosis (which could be produced by acute hyperventilation due to the discomfort of obtaining the blood sample).

- If respiratory acidosis is the major disorder, then the serum HCO3 should be appropriately increased. If the serum HCO3 is not as high as expected, then metabolic acidosis also exists and the arterial pH may be substantially reduced. In contrast, if the serum HCO3 is higher than expected, then metabolic alkalosis complicates the respiratory acidosis and the arterial pH may be inappropriately "normal."

In patients with a high anion gap metabolic acidosis, a diagnosis of a mixed metabolic acidosis and a metabolic alkalosis is generally suggested by calculation and interpretation of the delta anion gap and the delta HCO3. (See "The Δanion gap/ΔHCO3 ratio in patients with a high anion gap metabolic acidosis".)

**Case 3** — Determining the appropriate compensatory response may be more difficult with respiratory acid-base disorders because compensatory responses differ in acute and chronic disturbances. Consider the following arterial blood values: pH 7.27, PCO2 70 mmHg (9.3 kPa), and HCO3 31 meq/L. The low pH and hypercapnia indicate that the patient has respiratory acidosis. If this is acute hypercapnia, then the 30 mmHg (4 kPa) rise in PCO2 should increase the serum HCO3 concentration by about 3 meq/L (to about 27 meq/L). If this is chronic hypercapnia, the serum HCO3 should increase by about 11 meq/L (to about 35 meq/L). The observed value of 31 meq/L is between these expected levels and could have multiple explanations, including:

- Chronic respiratory acidosis with a superimposed metabolic acidosis that has reduced the serum HCO3 from 35 to 31 meq/L. This might occur in a patient with chronic obstructive pulmonary disease who developed diarrhea due to viral gastroenteritis or lactic acidosis from sepsis.

- Acute respiratory acidosis with a superimposed metabolic alkalosis that has increased the HCO3 from 27 to 31 meq/L. This could occur in a patient with respiratory depression due to a sedating drug who also developed vomiting or was taking diuretics.

- Acute respiratory acidosis superimposed on mild chronic respiratory acidosis. Suppose, for example, that a patient has chronic respiratory acidosis with a PCO2 of 55 mmHg (7.3 kPa) and an appropriate serum HCO3 of 30 meq/L. The patient then develops pneumonia, which acutely increases the PCO2 to 70 mmHg (9.3 kPa). The serum HCO3 would rise further to about 31 meq/L.
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- Acute respiratory acidosis that is evolving into a chronic disorder (between one and three days).

Thus, the correct diagnosis in a primary respiratory acid-base disorder can be established only when correlated with the clinical history and physical examination. This is true even when the arterial blood values appear to represent a simple disorder. If the serum HCO3 concentration had been 35 meq/L in this example, the findings would have been compatible with an uncomplicated chronic respiratory acidosis. However, similar findings could have been induced by acute respiratory acidosis plus metabolic alkalosis. The history usually helps to distinguish among the possibilities. (See 'Respiratory acid-base disorders' above.)

SUMMARY

- Acid-base status is usually assessed by measuring the components of the bicarbonate-carbon dioxide buffer system in blood. When blood gas analysis is carried out, the partial pressure of CO2 (PCO2) and the pH are each measured using electrodes, and the bicarbonate (HCO3) concentration is calculated with the Henderson-Hasselbalch equation. When the HCO3 is measured in venous blood, it is usually measured directly as "total CO2" with an ion-selective electrode. The directly measured venous "total CO2" is generally about 2 meq/L greater than the simultaneously calculated arterial HCO3. (See 'Introduction' above.)

- The range of normal values for acid-base parameters is different for arterial and venous samples and also varies among laboratories (see 'Normal values according to site of sampling' above):
  - For an arterial sample, the normal range for pH is 7.36 to 7.44; for bicarbonate (HCO3) concentration, 21 to 27 meq/L; and for PCO2, 36 to 44 mmHg (4.9 to 5.9 kPa).
  - For a peripheral venous sample, the range for pH is approximately 0.02 to 0.04 pH units lower than in arterial blood; for HCO3 concentration, approximately 1 to 2 meq/L higher; and for PCO2, approximately 3 to 8 mmHg (0.4 to 1.1 kPa) higher.
  - For a central venous sample, the range for pH is usually 0.03 to 0.05 pH units lower than in arterial blood, and the PCO2 is 4 to 5 mmHg (0.5 to 0.7 kPa) higher, with little or no increase in serum HCO3.

- Each simple acid-base disorder is normally associated with a compensatory response that reduces the change in the HCO3/PCO2 ratio and therefore in pH (figure 1). (See 'Metabolic acid-base disorders' above and 'Respiratory acid-base disorders' above.)

- A simple acid-base disorder includes the initial disturbance of acid-base status and the appropriate degree of compensation for that disturbance. (See 'Definitions of acid-base disorders' above.)

- The simultaneous presence of more than one acid-base disturbance is called a mixed acid-base disorder. Mixed acid-base disorders can be suspected from the patient's history, from a lesser- or greater-than-expected compensatory response, and from analysis of the delta anion gap and delta HCO3. (See 'Definitions of acid-base disorders' above.)

- We suggest the following three-step approach for the evaluation of most patients with acid-base disorders (see 'Initial evaluation' above):
  - Establish the primary diagnosis. Metabolic acidosis is characterized by a low serum HCO3 and a low arterial pH; the serum anion gap may be increased or normal. Metabolic alkalosis is characterized by an elevated serum HCO3 and an elevated arterial pH. Respiratory acidosis is characterized by an elevated arterial PCO2 and a low arterial pH. Respiratory alkalosis is characterized by low arterial PCO2 and an elevated arterial pH. (See 'Initial evaluation' above.)
  - Assess the degree of compensation as defined above for the individual disorders. If compensation is inadequate or excessive, this is indicative of a mixed acid-base disorder. (See 'Initial evaluation' above and 'Compensatory respiratory and renal responses' above.)
  - Determine whether or not the anion gap is elevated. If it is, then analyze the ratio of the increase in anion gap to the decrease in the HCO3 concentration. This is the delta anion gap/delta HCO3 ratio. When an anion gap acidosis exists, these changes should be quantitatively similar to one another; that is, the delta anion gap should be of similar magnitude as the delta HCO3. (See 'Initial evaluation' above.)

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REFERENCES


Topic 2352 Version 16.0
Simple and mixed acid-base disorders

Expected compensation ranges for simple acid-base disorders


Graphic 79833 Version 7.0
Compensation to chronic respiratory acidosis

Ninety-five percent significance bands for plasma pH and H+ and HCO3-concentrations in chronic hypercapnia. Because of the compensatory rise in the plasma HCO3- concentration, there is much less change in H+ concentration and pH than in acute hypercapnia.


Graphic 63315 Version 3.0
Compensations to acute respiratory acidosis and alkalosis

Combined significance bands for plasma pH and concentrations of H+ and HCO3- in acute respiratory acidosis and alkalosis in humans. In uncomplicated acute respiratory acid-base disorders, values for the H+ and HCO3- concentrations will, with an estimated 95 percent probability, fall within the band. Values lying outside the band indicate the presence of a complicating metabolic acid-base disturbance.


Graphic 58687 Version 5.0
Compensatory response to chronic respiratory alkalosis

Combined significance bands for plasma pH and concentrations of H+ and HCO3- in chronic respiratory alkalosis in humans. In uncomplicated chronic respiratory alkalosis, values for the H+ and HCO3- concentrations will, with an estimated 95 percent probability, fall within the band. Values lying outside the band indicate the presence of a complicating metabolic acid-base disturbance. Note that the compensatory reduction in the plasma HCO3- concentration is so effective that there is little fall in pH.


Graphic 75327 Version 2.0
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