pneumonia) leading to respiratory acidosis or alkalosis. Patients with underlying pulmonary disease (e.g., chronic obstructive pulmonary disease) may not respond to metabolic acidosis with an appropriate ventilatory response because of insufficient respiratory reserve. Such imposition of respiratory acidosis on metabolic acidosis can lead to severe acidemia. When metabolic acidosis and metabolic alkalosis coexist in the same patient, the pH may be normal or near normal. When the pH is normal, an elevated anion gap (AG; see below) reliably denotes the presence of an AG metabolic acidosis at a normal serum albumin of 4.5 g/dL. Assuming a normal AG of 10 mmol/L, a discrepancy in the ΔAG (prevailing minus normal AG) and the ΔHCO_3^- (normal value of 25 mmol/L minus abnormal HCO_3^- in the patient) indicates the presence of a mixed high-gap acidosis—metabolic alkalosis (see example below). A diabetic patient with ketoacidosis may have renal dysfunction resulting in simultaneous metabolic acidosis. Patients who have ingested an overdose of drug combinations such as sedatives and salicylates may have mixed disturbances as a result of the acid-base response to the individual drugs (metabolic acidosis mixed with respiratory acidosis or respiratory alkalosis, respectively). Triple acid-base disturbances are more complex. For example, patients with metabolic acidosis due to alcoholic ketoacidosis may develop metabolic alkalosis due to vomiting and superimposed respiratory alkalosis due to the hyperventilation of hepatic dysfunction or alcohol withdrawal.

APPROACH TO THE PATIENT: Acid-Base Disorders

A stepwise approach to the diagnosis of acid-base disorders follows (Table 66-3). Care should be taken when measuring blood gases to obtain the arterial blood sample without using excessive heparin. Blood for electrolytes and arterial blood gases should be drawn simultaneously prior to therapy, because an increase in $[HCO_3^-]$ occurs with metabolic alkalosis and respiratory acidosis. Conversely, a decrease in $[HCO_3^-]$ occurs in metabolic acidosis and respiratory alkalosis. In the determination of arterial blood gases by the clinical laboratory, both pH and $Paco_2$ are measured, and the $[HCO_3^-]$ is calculated from the Henderson-Hasselbalch equation. This calculated value should be compared with the measured $[HCO_3^-]$ (total CO_2) on the electrolyte panel. These two values should agree within 2 mmol/L. If they do not, the values may not have been drawn simultaneously, a laboratory error may be present, or an error could have been made in calculating the $[HCO_3^-]$. After verifying the blood acid-base values, the precise acid-base disorder can then be identified.

CALCULATE THE ANION GAP

All evaluations of acid-base disorders should include a simple calculation of the AG; it represents those unmeasured anions in plasma (normally 8–10 mmol/L) and is calculated as follows: $AG = Na^+ - (Cl^- + HCO_3^-)$. The unmeasured anions include anionic proteins (e.g., albumin), phosphate, sulfate, and organic anions. When acid anions, such as acetoacetate and lactate, accumulate in extracellular fluid, the AG increases, causing a high-AG acidosis. An increase in the AG is most often due to an increase in unmeasured anions and, less commonly, is due to a decrease in unmeasured cations (calcium, magnesium, potassium). In addition, the AG may increase with an increase in anionic albumin, because of either increased albumin concentration or alkalosis, which alters albumin charge. A decrease in the AG can be due to (1) an increase in unmeasured cations; (2) the addition to the blood of abnormal cations, such as lithium (lithium intoxication) or cationic immunoglobulins (plasma cell dyscrasias); (3) a reduction in the major plasma anion albumin concentration (nephrotic syndrome); (4) a decrease in the effective anionic charge on albumin by acidosis; or (5) hyperviscosity and severe hyperlipidemia, which can lead to an underestimation of sodium and chloride concentrations. A fall in serum albumin by 1 g/dL from the normal value (4.5 g/dL) decreases the AG by 2.5 meq/L. Know the common causes of a high-AG acidosis (Table 66-3).

In the face of a normal serum albumin, a high AG is usually due to non–chloride-containing acids that contain inorganic (phosphate, sulfate), organic (ketoacids, lactate, uremic organic anions), exogenous (salicylate or ingested toxins with organic acid production), or unidentified anions. The high AG is significant even if an additional acid-base disorder is superimposed to modify the $[HCO_3^-]$ independently. Simultaneous metabolic acidosis of the high-AG variety plus either chronic respiratory acidosis or metabolic alkalosis represents such a situation in which $[HCO_3^-]$ may be normal or even high (Table 66-3). Compare the change in $[HCO_3^-]$ (ΔHCO_3^-) and the change in the AG (ΔAG).

Similarly, normal values for $[HCO_3^-]$, $Paco_2$, and pH do not ensure the absence of an acid-base disturbance. For instance, an alcoholic who has been vomiting may develop a metabolic alkalosis with a pH of 7.55, $Paco_2$ of 47 mmHg, $[HCO_3^-]$ of 40 mmol/L, $[Na^+]$ of 135, $[Cl^-]$ of 80, and $[K^+]$ of 2.8. If such a patient were then to develop a superimposed alcoholic ketoacidosis with a β-hydroxybutyrate concentration of 15 m*M*, arterial pH would fall to 7.40, $[HCO_3^-]$ to 25 mmol/L, and the $Paco_2$ to 40 mmHg. Although these blood gases are normal, the AG is elevated at 30 mmol/L, indicating a mixed metabolic alkalosis and metabolic acidosis. A mixture of high-gap acidosis and metabolic alkalosis is recognized easily by comparing the differences (Δ values) in the normal to prevailing patient values. In this example, the ΔHCO_3^- is 0 (25 – 25 mmol/L), but the ΔAG is 20 (30 – 10 mmol/L). Therefore, 20 mmol/L is unaccounted for in the Δ/Δ value (ΔAG to ΔHCO_3^-).

TABLE 66-3 STEPS IN ACID-BASE DIAGNOSIS

1. Obtain arterial blood gas (ABG) and electrolytes simultaneously.
2. Compare $[HCO_3^-]$ on ABG and electrolytes to verify accuracy.
3. Calculate anion gap (AG).
4. Know four causes of high-AG acidosis (ketoacidosis, lactic acid acidosis, renal failure, and toxins).
5. Know two causes of hyperchloremic or nongap acidosis (bicarbonate loss from gastrointestinal tract, renal tubular acidosis).
6. Estimate compensatory response (Table 66-1).
7. Compare ΔAG and ΔHCO_3^-.
8. Compare change in $[Cl^-]$ with change in $[Na^+]$.

METABOLIC ACIDOSIS

Metabolic acidosis can occur because of an increase in endogenous acid production (such as lactate and ketoacids), loss of bicarbonate (as in diarrhea), or accumulation of endogenous acids (as in renal failure). Metabolic acidosis has profound effects on the respiratory, cardiac, and nervous systems. The fall in blood pH is accompanied by a characteristic increase in ventilation, especially the tidal volume (Kussmaul respiration). Intrinsic cardiac contractility may be depressed, but inotropic function can be normal because of catecholamine release. Both peripheral arterial vasodilation and central venoconstriction can be present; the decrease in central and pulmonary vascular compliance predisposes to pulmonary edema with even minimal volume overload. CNS function is depressed, with headache, lethargy, stupor, and, in some cases, even coma. Glucose intolerance may also occur.

There are two major categories of clinical metabolic acidosis: high-AG and non-AG, or hyperchloremic, acidosis (Table 66-3 and Table 66-4).

TREATMENT METABOLIC ACIDOSIS

Treatment of metabolic acidosis with alkali should be reserved for severe acidemia except when the patient has no "potential HCO_3^-" in plasma. Potential $[HCO_3^-]$ can be estimated from the increment (Δ) in the AG (ΔAG = patient's AG – 10). It must be determined if