Disorders of Acid-Base Balance

Horacio J. Adrogué
Nicolaos E. Madias

Maintenance of acid-base homeostasis is a vital function of the living organism. Deviations of systemic acidity in either direction can impose adverse consequences and when severe can threaten life itself. Acid-base disorders frequently are encountered in the outpatient and especially in the inpatient setting. Effective management of acid-base disturbances, commonly a challenging task, rests with accurate diagnosis, sound understanding of the underlying pathophysiology and impact on organ function, and familiarity with treatment and attendant complications [1].

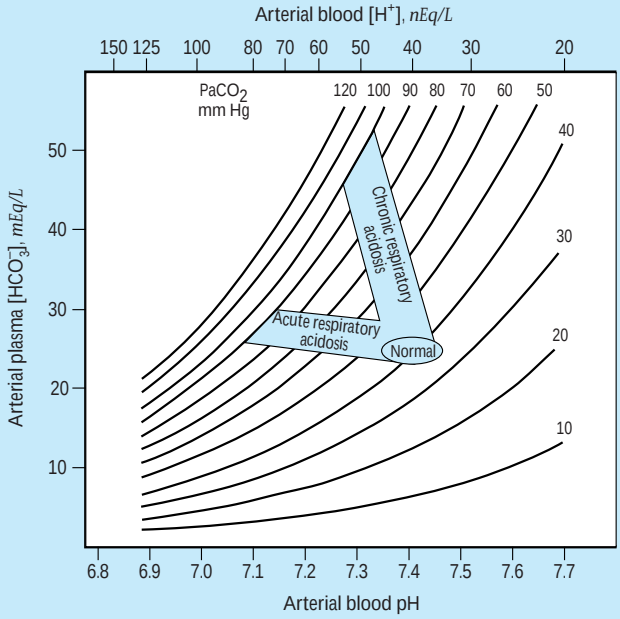
Clinical acid-base disorders are conventionally defined from the vantage point of their impact on the carbonic acid-bicarbonate buffer system. This approach is justified by the abundance of this buffer pair in body fluids; its physiologic preeminence; and the validity of the isohydric principle in the living organism, which specifies that all the other buffer systems are in equilibrium with the carbonic acid-bicarbonate buffer pair. Thus, as indicated by the Henderson equation, $[H^+] = 24 \times PaCO_2/[HCO_3^-]$ (the equilibrium relationship of the carbonic acid-bicarbonate system), the hydrogen ion concentration of blood ($[H^+]$, expressed in nEq/L) at any moment is a function of the prevailing ratio of the arterial carbon dioxide tension ($PaCO_2$, expressed in mm Hg) and the plasma bicarbonate concentration ($[HCO_3^-]$, expressed in mEq/L). As a corollary, changes in systemic acidity can occur only through changes in the values of its two determinants, $PaCO_2$ and the plasma bicarbonate concentration. Those acid-base disorders initiated by a change in $PaCO_2$ are referred to as respiratory disorders; those initiated by a change in plasma bicarbonate concentration are known as metabolic disorders. There are four cardinal acid-base disturbances: respiratory acidosis, respiratory alkalosis, metabolic acidosis, and metabolic alkalosis. Each can be encountered alone, as a simple disorder, or can be a part of a mixed-disorder, defined as the simultaneous presence of two or more simple

CHAPTER 6

acid-base disturbances. Mixed acid-base disorders are frequently observed in hospitalized patients, especially in the critically ill.

The clinical aspects of the four cardinal acid-base disorders are depicted. For each disorder the following are illustrated: the underlying pathophysiology, secondary adjustments in acid-base equilibrium in response to the initiating disturbance, clinical manifestations, causes, and therapeutic principles.

Respiratory Acidosis



Steady-state relationships in respiratory acidosis: average increase per mm Hg rise in $PaCO_2$

	$[HCO_3^-]$ mEq/L	$[H^+]$ nEq/L
Acute adaptation	0.1	0.75
Chronic adaptation	0.3	0.3

FIGURE 6-1

Quantitative aspects of adaptation to respiratory acidosis. Respiratory acidosis, or primary hypercapnia, is the acid-base disturbance initiated by an increase in arterial carbon dioxide tension ($PaCO_2$) and entails acidification of body fluids. Hypercapnia elicits adaptive increments in plasma bicarbonate concentration that should be viewed as an integral part of respiratory acidosis. An immediate increment in plasma bicarbonate occurs in response to hypercapnia. This acute adaptation is complete within 5 to 10 minutes from the onset of hypercapnia and originates exclusively from acidic titration of the nonbicarbonate buffers of the body (hemoglobin, intracellular proteins and phosphates, and to a lesser extent plasma proteins). When hypercapnia is sustained, renal adjustments markedly amplify the secondary increase in plasma bicarbonate, further ameliorating the resulting acidemia. This chronic adaptation requires 3 to 5 days for completion and reflects generation of new bicarbonate by the kidneys as a result of upregulation of renal acidification [2]. Average increases in plasma bicarbonate and hydrogen ion concentrations per mm Hg increase in $PaCO_2$ after completion of the acute or chronic adaptation to respiratory acidosis are shown. Empiric observations on these adaptations have been used for construction of 95% confidence intervals for graded degrees of acute or chronic respiratory acidosis represented by the areas in color in the acid-base template. The black ellipse near the center of the figure indicates the normal range for the acid-base parameters [3]. Note that for the same level of $PaCO_2$, the degree of acidemia is considerably lower in chronic respiratory acidosis than it is in acute respiratory acidosis. Assuming a steady state is present, values falling within the areas in color are consistent with but not diagnostic of the corresponding simple disorders. Acid-base values falling outside the areas in color denote the presence of a mixed acid-base disturbance [4].

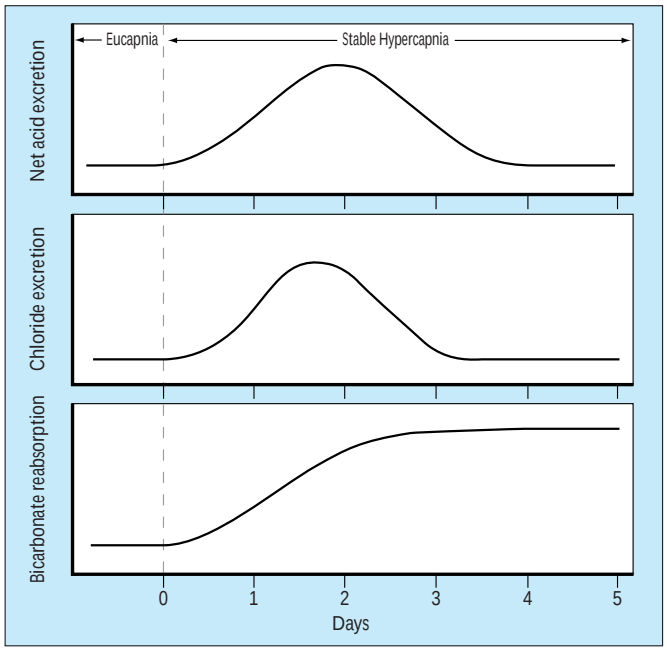


FIGURE 6-2

Renal acidification response to chronic hypercapnia. Sustained hypercapnia entails a persistent increase in the secretory rate of the renal tubule for hydrogen ions (H^+) and a persistent decrease in the reabsorption rate of chloride ions (Cl^-). Consequently, net acid excretion (largely in the form of ammonium) transiently exceeds endogenous acid production, leading to generation of new bicarbonate ions (HCO_3^-) for the body fluids. Conservation of these new bicarbonate ions is ensured by the gradual augmentation in the rate of renal bicarbonate reabsorption, itself a reflection of the hypercapnia-induced increase in the hydrogen ion secretory rate. A new steady state emerges when two things occur: the augmented filtered load of bicarbonate is precisely balanced by the accelerated rate of bicarbonate reabsorption and net acid excretion returns to the level required to offset daily endogenous acid production. The transient increase in net acid excretion is accompanied by a transient increase in chloride excretion. Thus, the resultant ammonium chloride (NH_4Cl) loss generates the hypochloremic hyperbicarbonatemia characteristic of chronic respiratory acidosis. Hypochloremia is sustained by the persistently depressed chloride reabsorption rate. The specific cellular mechanisms mediating the renal acidification response to chronic hypercapnia are under active investigation. Available evidence supports a parallel increase in the rates of the luminal sodium ion–hydrogen ion (Na^+-H^+) exchanger and the basolateral Na^+-$3HCO_3^-$ cotransporter in the proximal tubule. However, the nature of these adaptations remains unknown [5]. The quantity of the H^+-adenosine triphosphatase (ATPase) pumps does not change in either cortex or medulla. However, hypercapnia induces exocytotic insertion of H^+-ATPase–containing subapical vesicles to the luminal membrane of proximal tubule cells as well as type A intercalated cells of the cortical and medullary collecting ducts. New H^+-ATPase pumps thereby are recruited to the luminal membrane for augmented acidification [6,7]. Furthermore, chronic hypercapnia increases the steady-state abundance of mRNA coding for the basolateral $Cl—HCO_3^-$ exchanger (band 3 protein) of type A intercalated cells in rat renal cortex and medulla, likely indicating increased band 3 protein levels and therefore augmented basolateral anion exchanger activity [8].

SIGNS AND SYMPTOMS OF RESPIRATORY ACIDOSIS

Central Nervous System	Respiratory System	Cardiovascular System
Mild to moderate hypercapnia	Breathlessness	Mild to moderate hypercapnia
Cerebral vasodilation	Central and peripheral cyanosis (especially when breathing room air)	Warm and flushed skin
Increased intracranial pressure	Pulmonary hypertension	Bounding pulse
Headache		Well maintained cardiac output and blood pressure
Confusion		Diaphoresis
Combativeness		Severe hypercapnia
Hallucinations		Cor pulmonale
Transient psychosis		Decreased cardiac output
Myoclonic jerks		Systemic hypotension
Flapping tremor		Cardiac arrhythmias
Severe hypercapnia		Prerenal azotemia
Manifestations of pseudotumor cerebri		Peripheral edema
Stupor		
Coma		
Constricted pupils		
Depressed tendon reflexes		
Extensor plantar response		
Seizures		
Papilledema		

FIGURE 6-3

Signs and symptoms of respiratory acidosis. The effects of respiratory acidosis on the central nervous system are collectively known as hypercapnic encephalopathy. Factors responsible for its development include the magnitude and time course of the hypercapnia, severity of the acidemia, and degree of attendant hypoxemia. Progressive narcosis and coma may occur in patients receiving uncontrolled oxygen therapy in whom levels of arterial carbon dioxide tension ($PaCO_2$) may reach or exceed 100 mm Hg. The hemodynamic consequences of carbon dioxide retention reflect several mechanisms, including direct impairment of myocardial contractility, systemic vasodilation caused by direct relaxation of vascular smooth muscle, sympathetic stimulation, and acidosis-induced blunting of receptor responsiveness to catecholamines. The net effect is dilation of systemic vessels, including the cerebral circulation; whereas vasoconstriction might develop in the pulmonary and renal circulations. Salt and water retention commonly occur in chronic hypercapnia, especially in the presence of cor pulmonale. Mechanisms at play include hypercapnia-induced stimulation of the renin-angiotensin-aldosterone axis and the sympathetic nervous system, elevated levels of cortisol and antidiuretic hormone, and increased renal vascular resistance. Of course, coexisting heart failure amplifies most of these mechanisms [1,2].