CHAPTER 70

Respiratory Acid-Base Disorders

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OBJECTIVES

This chapter will:

1. Analyze the biologic origin and chemical characteristics of carbon dioxide, explaining the key role of this molecule in acid-base equilibrium.
2. Briefly summarize the mechanisms regulating spontaneous breathing activity fundamental to understand the pathophysiology of respiratory acid-base disorders.
3. Summarize the physiologic compensatory mechanisms of respiratory acid-base derangements.
4. Analyze signs and symptoms of hypercapnia and hypocapnia.
5. Discuss causes of and treatment options for acute and chronic respiratory acid base disorders.

Carbon dioxide (CO_2) is a linear, symmetric, nonpolar molecule composed of a carbon atom covalently double-bonded to two oxygen atoms. At standard temperature and pressure, CO_2 is found in its gaseous state. Depending on the circumstances, CO_2 has very different, opposite roles in nature: it can be either the primary source of carbon atoms necessary for the storage of light energy into carbohydrate molecules (photosynthesis, mainly in plants) or the waste product of cellular metabolism for aerobic organisms. Although in unicellular organisms the excretion of CO_2 occurs simply through a passive transfer down an electrochemical gradient to the environment, a convective movement becomes necessary in more complex organisms, such as humans, to transport CO_2 from the site of production (i.e., the cells) to the site of elimination (i.e., the lungs). For this purpose, CO_2 must be stored in blood (mainly as

bicarbonate ion [HCO_3^-]) and transported by its flow (cardiac output).

In Earth's atmosphere, CO_2 is a trace gas, currently accounting for 0.04% of the atmosphere, whereas it reaches 125 to 150 times higher concentrations in gases expired from the lungs (5% to 6%). Cellular metabolism of an average 70-kg human produces approximately 290 to 360 L of CO_2 per day (13,000 to 16,000 mmol/day), which must be eliminated through pulmonary ventilation to maintain constant CO_2 and pH within the body. Indeed, although CO_2 is not an acid, it combines with water when added to aqueous solutions such as body fluids, reversibly forming carbonic acid (H_2CO_3), which, being a weak acid, dissociates to hydrogen ions (H^+) and HCO_3^-.

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

Equation 1

For the above-mentioned behavior in body fluids, CO_2 plays a key role in acid-base equilibrium, and its partial pressure (PCO_2) was identified by the Canadian physiologist Peter Stewart as being one of the three independent variables (along with the strong ion difference [SID] and total amount of weak acids [A_{TOT}]) regulating pH of biologic solutions.[1,2]

An acute increase in PCO_2 above its normal values (40–45 mm Hg) causes a reduction in pH (or increase in H^+ concentration), which is termed *hypercapnic* (respiratory) *acidosis*. On the other hand, an acute decrease in CO_2 causes an increase in pH (or decrease in H^+ concentration), which is termed *hypocapnic* (respiratory) *alkalosis*. Compensatory mechanisms may be quick or slower (buffering systems and renal electrolyte handling, respectively, see later in chapter) and significantly contribute to the reduction of the consequent pH swings, especially in chronic respiratory disorders. In this chapter, we (1) summarize the mechanisms regulating spontaneous breathing activity, fundamental to understand the pathophysiology of respiratory acid-base disorders, (2) summarize the compensatory mechanisms, (3) analyze signs and symptoms of hypercapnia and hypocapnia, and (4) discuss causes of and treatment options for acute and chronic respiratory acid-base disorders.

PATHOPHYSIOLOGY OF THE CONTROL OF BREATHING

Breathing has the ultimate purpose of (1) delivering oxygen (O_2) to every cell of the organism to produce energy from the oxidation of substrates and (2) eliminating CO_2, the waste product of cellular respiration. Accordingly, the principal stimuli for breathing are a reduction in the partial pressure of O_2 (PO_2), that is, hypoxemia, acting mainly on peripheral chemoreceptors (type 1 glomus cells of carotid bodies), and variations in PCO_2, acting as variations in pH mainly on central chemoreceptors (located at the ventral surface of the medulla, within the central nervous system).[3,4] Hypoxemia causes a significant increase in alveolar ventilation only for values of PO_2 below 50 mm Hg[5]; nevertheless, the initial hyperventilation will lower PCO_2 and increase pH, reducing their input stimuli and therefore limiting the hypoxic ventilatory response.[6] This phenomenon clearly indicates that PCO_2 variations are the principal respiratory stimulus: if PCO_2 rises, with consequent fall in pH, the central chemoreceptors will increase the signal strength (input) to the central controller, causing an augmented output signal that, transduced through the peripheral nervous system, will activate the "effectors" (respiratory muscles), with the consequent increase in alveolar ventilation.

The opposite occurs in case of PCO_2 reduction with consequent increase in pH.[7,8] These complex regulatory mechanisms of respiration have the final purpose of maintaining PCO_2 constant despite wide variations in CO_2 production (e.g., during exercise or fever). Finally, also lung receptors, such as C-fiber receptors and slowly adapting receptors, may play a role in the pattern of respiration.[9–11] These receptors, however, have a minor role, because they are usually not active in physiologic conditions.

The above-mentioned mechanisms observed during spontaneous breathing are influenced profoundly by pharmacologic sedation, which may turn off the central controller, as well as by paralysis, which blocks the respiratory muscles, that is, the effectors of the control of breathing. In these circumstances, the control of breathing must be taken over by the attending physician, who regulates the settings of the mechanical ventilator to increase or decrease alveolar ventilation.

COMPENSATORY MECHANISMS

The development of acute hypercapnia (i.e., the mismatch between CO_2 production and elimination, in favor of the first) leads to accumulation of CO_2 in the body. Two major compensatory mechanisms occur: a first, quick compensation (buffering), and a second, slower compensation (renal electrolyte handling).

Buffering

When PCO_2 increases acutely, the equilibrium of Eq. 1 is shifted to the right, that is, the tendency is increased for CO_2 to hydrate to H_2CO_3 and thereafter to dissociate to HCO_3^- and H^+. It is important to underline that these two elements have extremely different concentrations in body fluids, ranging HCO_3^- within the milliequivalent (10^{-3} Eq/L) and H^+ within the nanoequivalent (10^{-9} Eq/L) interval. It is therefore evident that the increase in the products of the reaction is not equivalent. For example, an increase of PCO_2 in normal, isolated plasma from 40 to 80 mm Hg will cause an increase of HCO_3^- from 24 to 26.5 mEq/L, approximately. Nevertheless, the increase in H^+ will be from 40 to 72 nEq/L (i.e., from 0.000000040 to 0.000000072 mEq/L), corresponding to a reduction in pH from 7.40 to 7.14. Therefore, despite its clinical importance, the increase in H^+ is negligible from a quantitative point of view. With this in mind, it is straightforward that the increase in negative charges deriving from the hydration of CO_2 (i.e., HCO_3^-) is not paralleled by an equivalent increase in H^+, and that, to fulfill the law of electroneutrality, another anion must be reduced. In other words, the remaining part of the H^+ deriving from the hydration of CO_2 bonds to the dissociated form of the nonvolatile buffers (A^-), shifting therefore the equilibrium toward the undissociated form (AH), as summarized in Eq. 2. In the example mentioned earlier (increased PCO_2 from 40 to 80 mm Hg), the decrease in A^- would be around 2.5 mEq/L (i.e., it would parallel the increase in HCO_3^-).

$$A^- + H^+ \leftrightarrows AH$$

Equation 2

Within the *extracellular fluid space*, nonvolatile buffers (A_{TOT}) can be divided into extracellular (i.e., proteins, mainly albumin, and phosphates) and intracellular (i.e.,

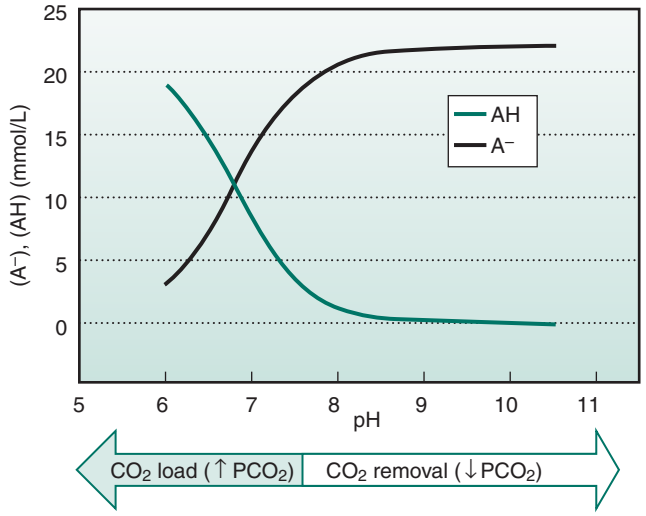

FIGURE 70.1 Plasma nonvolatile buffers (A_{TOT}), consisting mainly of albumin and phosphates, are weak acids with a reported pK around 6.8. The relationship of the dissociated *(A⁻)* and undissociated *(AH)* from of a fixed amount of A_{TOT} in response to respiratory acid-base disorders is expressed. In case of addition of CO_2 to the system (CO_2 load), PCO_2 will increase, leading to respiratory acidosis (reduction in pH). On the contrary, the removal of CO_2 from the system (CO_2 removal) will reduce PCO_2, causing respiratory alkalosis (increase in pH). When pH is equal to pK, the concentration of the dissociated and undissociated form are equal.

hemoglobin). All these substances have, allegedly, a similar acid dissociation constant (pK) of 6.8. As can be noted in Fig. 70.1, A^- has the same concentration as AH when pH is equal to pK. The efficiency of the buffering system is therefore maximal in this particular scenario. The buffer system includes also volatile, or carbonic, buffers (i.e., the HCO_3^-/CO_2 system [pK = 6.1]). Nevertheless, despite playing a crucial role in metabolic acid-base disturbances, it does not contribute in buffering respiratory acid-base disorders. Finally, when considering whole blood, clinicians must take into account the role of red blood cells in compensating respiratory acid-base disorders. Red blood cells, besides containing a quantitatively important nonvolatile buffer (hemoglobin), constitute an important electrolyte reservoir that allows the shift of electrolytes between plasma and red blood cells, therefore increasing the HCO_3^- variations (1 mEq/L for every 10 mm Hg of PCO_2 above 40 mm Hg for whole blood) while reducing the pH shifts resulting from CO_2 variations.[12,13] Two additional considerations regarding the buffering system are valid: (1) the pK value of volatile and nonvolatile buffers is below the physiologic pH, meaning that humans are more protected against acidosis than against alkalosis, and (2) critically ill patients, typically having low albumin and hemoglobin levels, have likely a lower buffer power and therefore are exposed to higher pH variations as compared with normal subjects.

Finally, the opposite mechanisms of what has been described earlier take place in case of respiratory (hypocapnic) alkalosis (i.e., the equilibrium of Eq. 1 is shifted to the left) followed by all the consequences described earlier acting in the opposite direction.

Renal Electrolyte Handling

According to the traditional approach, the kidney contributes to the regulation of acid-base equilibrium through its ability to (1) excrete about 100 mEq of nonvolatile H^+ per day and (2) maintain constant plasma HCO_3^-.[14] These objectives are achieved through (1) the excretion of H^+, as urinary buffer molecules (titratable acidity) or associated with ammonia (NH_3) as urinary NH_4^+, and (2) the reabsorption/regeneration of most of the filtered/consumed HCO_3^-, respectively.

On the other hand, considering Stewart's approach, the kidney actively regulates pH through modifications of extracellular SID, which are achieved through the regulation of excretion/reabsorption of plasma electrolytes.[15] Because electrical neutrality must hold true also for urine, it follows that every time a cation is excreted with urine, it must be associated with an anion. Furthermore, as long as a strong cation (such as Na^+) is excreted associated with a strong anion (such as Cl^-), the ability of the kidney to modify the plasma SID will be limited. Consequently, the renal system has developed two strategies to enhance its efficiency in modifying extracellular SID: (1) the elimination (or reabsorption) of a strong cation (such as Na^+) associated with a weak anion (such as HCO_3^-) and (2) the exchange of a strong anion (such as Cl^-) with a weak anion (such as HCO_3^-). Because the kidney handles Na^+ and Cl^- excretion almost entirely as associated with each other,[16] two specific segments of the nephron gain particular importance in the regulation of acid-base equilibrium (i.e., where Na^+ excretion/reabsorption is dissociated from that of Cl^-). The first one is located at the proximal tubule, where, thanks to a different permeability of tubular cells to Cl^-, an HCO_3^-–dependent Na^+ reabsorption takes place. The second one, more important for the compensatory mechanisms of respiratory acid-base disorders, is located at the distal collecting tubules, specifically in the A- and B-type intercalated cells. A-type intercalated cells excrete H^+ into the tubular lumen and reabsorb HCO_3^- into the peritubular capillaries (because of the Cl^-/HCO_3^- pendrin); B-type intercalated cells, having a reverse polarity, allow the reabsorption of Cl^- in exchange with HCO_3^-.

Therefore, in case of *hypercapnia*, the tubular cells of the distal collecting tubules will increase the excretion of H^+ in form of NH_4^+. The associated reduced activity of the luminal Cl^-/HCO_3^- exchanger will determine a net increase in Cl^- elimination that will preserve urinary electrical neutrality.[15] Furthermore, the elimination of one molecule of NH_4^+ with Cl^- will lead necessarily to the net reabsorption of one positive ion (either Na^+ or K^+) with HCO_3^-. These processes explain how the kidney actively reduces plasma Cl^- and increases plasma pH in response to protracted hypercapnia. The opposite phenomena generally occur during *hypocapnia*.

CAUSES OF RESPIRATORY ACID-BASE DISORDERS

Tables 70.1 and 70.2 list the major causes of chronic and acute alveolar hypoventilation leading to respiratory acidosis. Schematically, the causes of respiratory acidosis can be divided into three categories: (1) defects in the respiratory drive, (2) neuromuscular defects and, (3) derangement of pulmonary parenchyma, including alterations of respiratory mechanics or alveolar gas exchange. Of course, alveolar hypoventilation may be absolute or relative in relation to CO_2 production. For example, a patient with chronic respiratory failure may be able to exhale 200 mL/min of CO_2. However, this patient may not be able to increase alveolar ventilation in case of increased CO_2 load (e.g., during fever) because of the underlying disease,[17] therefore developing

TABLE 70.1

Causes of Chronic Alveolar Hypoventilation/Respiratory Acidosis

	SITE OF DEFECT	CONDITION
Defects in respiratory drive	Central and peripheral chemoreceptors	Brainstem lesions Primary alveolar hypoventilation syndrome (Ondine's curse) Extreme obesity (Pickwickian syndrome)
Neuromuscular defects	Neuromuscular transmission	Spinal cord lesions *Motor neuron disease:* critical illness polyneuropathy, multiple sclerosis, amyotrophic lateral sclerosis
	Muscular disease	Myasthenia gravis, critical illness myopathy
Defects in respiratory mechanics and gas exchange	Lung	*Increased dead space:* chronic obstructive pulmonary disease, chronic pulmonary embolism *Increased lung elastance*: pulmonary fibrosis
	Chest wall	*Increased chest wall elastance:* extreme obesity, fibrothorax, kyphoscoliosis
	Airways	*Increased respiratory resistance*: airway stenosis, chronic obstructive pulmonary disease

TABLE 70.2

Causes of Acute Alveolar Hypoventilation/Respiratory Acidosis

	SITE OF DEFECT	CONDITION
Defects in respiratory drive	Central and peripheral chemoreceptors	*Drugs:* opiates, sedatives, anesthetics Brainstem lesions
Neuromuscular defects	Neuromuscular transmission	Spinal cord lesions Neuromuscular blocking agents Elapid snake venom
	Muscular disease	Myasthenia gravis crisis, Guillain-Barré syndrome
Defects in respiratory mechanics and gas exchange	Lung	*Increased dead space:* acute respiratory distress syndrome, exacerbation of chronic obstructive pulmonary disease, pulmonary embolism *Increased venous admixture:* acute cardiogenic pulmonary edema, atelectasis, pneumonia *Mixed mechanisms*: pneumothorax
	Chest wall	*Increased chest wall elastance*, e.g., obesity, fibrothorax
	Airways	*Upper airway obstruction*, e.g., laryngospasm, obstructive sleep apnea, trauma
Iatrogenic	Mechanical ventilation	Insufficient ventilation

respiratory acidosis. Furthermore, a sedated and paralyzed patient cannot actively increase alveolar ventilation, because his or her breathing activity is controlled by the attending physician. Therefore, in this situation, a mismatch between CO_2 production and elimination easily can occur. Finally, hypercapnia also can develop because of an increased CO_2 fraction in inspiratory gas (e.g., as with an increase in instrumental dead space, use of gas mixtures containing higher than normal CO_2 concentrations, exhaustion of soda lime during general anesthesia. Table 70.3 summarizes the main causes of respiratory alkalosis, which can be divided schematically into (1) primary increase in respiratory drive, arising either from central or peripheral chemoreceptors and (2) iatrogenic, resulting from either excessive mechanical ventilation or excessive extracorporeal CO_2 removal.

SIGNS AND SYMPTOMS OF RESPIRATORY ACID-BASE DISORDERS

This section summarizes schematically signs and symptoms deriving from hypercapnia and hypocapnia, without taking into account signs and symptoms of the underlying pathologic condition resulting in the imbalance between CO_2 production and elimination. First, as stated above, efficient compensatory mechanisms take place rapidly, limiting therefore the pH shifts resulting from respiratory disorders. As most effects of hypercapnia/hypocapnia result from variations in pH rather than from variations in PCO_2,[18] it is not surprising that chronic respiratory disorders, conditions in which pH of body fluids essentially has been restored, may be well tolerated, whereas acute conditions may have dramatic and life-threatening consequences.

Carbon dioxide is a lipid-soluble, nonpolar substance that freely crosses cellular membranes, the blood-brain and blood-cerebrospinal fluid barriers, therefore quickly equilibrating with the intracellular and cerebral milieu. Consequently, neurologic symptoms are a major characteristic of acute respiratory acid-base disorders and are likely a result of cerebral pH derangements.[19] Typical signs and symptoms, such as paresthesia, tetany, and seizures, can be observed in cases of acute hypocapnic alkalosis, whereas headache, somnolence, and lethargy can characterize acute hypercapnia.[20] Furthermore, cerebral perfusion is regulated physiologically by the pH/CO_2 relationship, with acute increases in CO_2 causing increased cerebral perfusion, and acute reductions having the opposite effect. This physiologic mechanism is exploited to transiently reduce intracranial pressure in cases of expanding space-occupying lesions and brain swelling. In addition to neurologic alterations,

TABLE 70.3

Causes of Alveolar Hyperventilation/Respiratory Alkalosis

	SITE OF DEFECT	CONDITION
Defects in respiratory drive	Central chemoreceptors	*Voluntary hyperventilation* *Psychogenic*: pain, panic attack *Central neurogenic hyperventilation:* brainstem injuries, brain tumors *Hormonal:* increased progesterone levels in pregnancy and liver cirrhosis *Infectious:* meningitis, encephalitis *Thermal hyperpnea:* fever, hyperthermia *Intoxication:* salicylate, topiramate *Therapeutic:* doxapram
	Peripheral chemoreceptors	*Increased activity of peripheral chemoreceptors:* hypoxic pulmonary disease, high altitude *Increased activity of lung receptors*, e.g., pulmonary edema, pneumonia, pulmonary embolism, interstitial fibrosis
Iatrogenic		*Mechanical ventilation:* excessive mechanical ventilation (accidental, or therapeutic for traumatic brain injury) *Extracorporeal gas exchange:* excessive extracorporeal CO_2 removal

also the cardiovascular system may be affected by respiratory acid-base disorders, with hypercapnia being associated with an increased sympathetic tone, a decreased cardiac contractility, and a decreased systemic vascular resistance, and hypocapnia having the opposite effect. Carbon dioxide has also an effect on pulmonary vascular resistance, although controversial results have been reported.[21] On the contrary, the role of carbon dioxide on bronchial smooth muscle tone appears clear: hypercapnia favors bronchodilation, whereas hypocapnia fosters bronchoconstriction. Two additional effects must be mentioned: (1) the role of PCO_2 on the oxyhemoglobin dissociation curve, with hypercapnia shifting the curve rightward and hypocapnia causing a leftward shift, and (2) the effect of CO_2 variations on electrolyte concentrations, with acute hypercapnia favoring the movement of cations from cells to plasma and of anions in the opposite direction.

THERAPEUTIC OPTIONS

Respiratory Acidosis

As already mentioned, respiratory acidosis is a condition characterized by a mismatch between CO_2 production and elimination, resulting in the accumulation of CO_2 and a consequent reduction in pH. Available therapeutic options to counteract this phenomenon can be summarized as follows: (1) increase CO_2 elimination, (2) reduce CO_2 production, and (3) correct pH while tolerating hypercapnia.

Increase Carbon Dioxide Elimination

To outline strategies to increase CO_2 elimination, it is useful to analyze the simplified equation of motion (Eq. 3), describing the force that must be exerted by the respiratory muscles to move air from the atmosphere to the lungs.

$$P_{mus} = (V_A + V_D) * E + \dot{V} * R$$

Equation 3

where P_{mus} represents the pressure exerted by the respiratory muscles, E and R represent respiratory system elastance and resistance, respectively, V_A and V_D alveolar and dead space ventilation, and $\dot{V}$ the flow of gas entering the respiratory system. In patients with normal respiratory system the respiratory muscular effort varies in parallel with CO_2 production (e.g., it increases during exercise, with consequent increase in ventilation [V_A+V_D and $\dot{V}$] at fairly constant mechanical characteristics of the lung [E and R]). In patients with lung pathology, E can be worsened because of the accumulation of edema causing a reduction of the ventilable lung,[22] airway hyperreactivity and inflammation may lead to an increase in R, and, finally, V_D can be increased because of the presence of ventilation-perfusion mismatch. In conditions of respiratory acidosis resulting from reduced respiratory drive or neuromuscular defects (see Tables 70.1 and 70.2), in patients with healthy lungs, the application of mechanical ventilation is straightforward: in this case the pressure generated by the ventilator (P_{vent}) replaces, or is added to P_{mus}, therefore acting on the left side of Eq. 3. Theoretically, the application of P_{vent} has a sound rationale also in cases of respiratory acidosis resulting from an isolated increase in chest wall elastance (normal lungs). On the other hand, in cases of lung pathology, mechanical ventilation tries to increase CO_2 elimination by exploiting the part of the lung still viable for gas exchange, with the potential, however, of worsening the underlying pulmonary pathology (ventilator-induced lung injury, VILI). In selected cases, therefore, extracorporeal CO_2 removal can be applied. This strategy acts on the right side of Eq. 3, lowering the need to breathe (V_A+ V_D and $\dot{V}$). Furthermore, therapy should aim at reducing R in cases of respiratory acidosis resulted from increased respiratory resistance (e.g., through bronchodilators). Finally, also lung elastance (E) can be influenced by therapy (e.g., through the use of antibiotics and the resolution of the underlying infection).

Reduce Carbon Dioxide Production

A reduction in CO_2 production can be attempted through different strategies. The control of temperature in case of fever has a strong rationale.[23] Also the application of hypothermia would reduce further cellular metabolism and therefore CO_2 production, especially in association with deep sedation and paralysis. Furthermore, overfeeding should be avoided, and the use of fat-rich preparations could reduce CO_2 production. Finally, a pharmacologic strategy applying inhaled hydrogen sulfide (H_2S) has been

proposed to induce a suspended animation-like state, similar to hibernation. Nevertheless, despite striking results in mice,[24] its application in larger animals has so far been unsuccessful.

Correct pH While Tolerating Hypercapnia

Although controversial, the most commonly applied treatment aimed at correcting extracellular pH while tolerating hypercapnia is intravenous administration of $NaHCO_3$. According to Stewart's approach, the increase in pH resulting from $NaHCO_3$ infusion is not related to the administration of HCO_3^-, but rather to the administration of Na^+ (associated with a weak anion). In fact, the same increase in pH (and increase in SID and Na^+) could be obtained with the prescription of fluids containing Na^+ in combination with another weak/organic anion (e.g., Na-OH Na-citrate, Na-lactate).

The clarification of the mechanisms by which $NaHCO_3$ administration may correct pH while tolerating hypercapnia allows also an understanding of the limitations of this approach. First, because of the strict association between its efficacy and the necessary increase in Na^+ concentration, its use in cases of hypernatremia is limited. Second, being the distribution volume of $NaHCO_3$ the entire extracellular space (and not just the intravascular compartment), the efficiency of this approach is low, because large amounts of $NaHCO_3$ are necessary even to obtain a small correction of pH. Third, although effective in correcting extracellular pH, $NaHCO_3$ administration can lead rapidly to the development of "paradoxic" intracellular acidosis, because of a CO_2 release and diffusion from the extracellular to the intracellular space.

Despite its widespread use in the clinical setting, no solid evidence is available to support the correction of pH while tolerating hypercapnia. Furthermore, some experimental and preclinical data suggest that this approach may even be deleterious,[25] and that hypercapnia may be protective.

Finally, another therapeutic option theoretically available to correct pH while tolerating hypercapnia is the administration of loop diuretics, which accelerate the compensatory reaction of the renal system to respiratory acidosis. In fact, loop diuretics induce a progressive reduction of Cl^- concentration and an associated increased in extracellular SID, while increasing urinary Cl^- excretion.[26]

Respiratory Alkalosis

Respiratory alkalosis is a condition characterized by a mismatch between production and elimination of CO_2 in favor of the latter. The clinical approach to respiratory alkalosis usually is directed toward the diagnosis and treatment of the underlying clinical disorder. Furthermore, to reduce hypocapnia, available therapeutic options can be summarized as follows: (1) decrease pharmacologically the respiratory drive through the use of sedatives, (2) increase dead space or the fraction of inspired CO_2, and (3) correct pH while tolerating hypocapnia (e.g., through the use of chloride-rich intravenous fluids).

Key Points

1. Approximately 320 L of CO_2, produced daily by the cellular metabolism of an adult, must be eliminated through pulmonary ventilation to maintain constant CO_2 values in the body.
2. CO_2 plays a key role in acid-base equilibrium as, combining with water, it reversibly forms the weak acid carbonic acid, which dissociates to hydrogen ions and bicarbonate.
3. An acute increase in PCO_2 above its normal values (40–45 mm Hg) causes a reduction in pH (or increase in H^+ concentration), which is termed *hypercapnic* (respiratory) *acidosis*, whereas an acute decrease in CO_2 causes an increase in pH (or decrease in H^+ concentration), which is termed *hypocapnic* (respiratory) *alkalosis*.
4. Causes of respiratory acidosis can be divided schematically into three categories: (1) defects in the respiratory drive, (2) neuromuscular defects, and (3) derangement of pulmonary parenchyma.
5. Available therapeutic options for respiratory acidosis include (1) increase CO_2 elimination, (2) reduce CO_2 production, and (3) correct pH while tolerating hypercapnia.

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