Fig. 10.1. Schematic representation of the basic concepts of the bicarbonate buffering system in health and in acid-base disorders. Respiratory disorders involve removal of CO_2 from pulmonary arterial (capillary) blood. Metabolic disorders cause abnormal concentrations of H^+ and HCO_3^- in systemic venous blood.

A. In health, H^+ from metabolism is buffered by HCO_3^- to form H_2CO_3, which dissociates to H_2O and $CO_{2(g)}$. The $CO_{2(g)}$ is expired via the respiratory system. In the presence of carbonic anhydrase (*CA*), the reactions are reversible but the net flow is to the right (toward $CO_{2(g)}$ expiration). The approximate molar concentrations of H^+, HCO_3^-, H_2CO_3, and dissolved $CO_{2(g)}$ in plasma show that a large excess of HCO_3^- is available to buffer H^+.

B. In a metabolic acidosis, acidosis occurs because of one of two basic processes. Without compensation, P_{CO_2} remains WRI. However, ↑ $[H^+]$ will stimulate respiration and result in increased removal of CO_2 from pulmonary blood and thus a ↓ P_{CO_2}.

1. Excess H^+ accumulates because of increased production of organic acids, increased H^+ release from ATP usage, or decreased renal excretion of H^+. The excess H^+ drives the equation to the right and thus leads to consumption of HCO_3^-.
2. Excess loss of HCO_3^- via the alimentary or urinary system reduces the buffering capacity and allows H^+ to accumulate.

C. In a respiratory acidosis, hypoventilation causes reduced expiration of $CO_{2(g)}$, which leads to an ↑ P_aCO_2 and an ↑ $[H^+]$ (↓ pH). Without compensation, $[HCO_3^-]$ is insignificantly increased and remains WRI. Given time, the kidneys will compensate for acidemia and conserve HCO_3^-.

D. In a metabolic alkalosis, alkalosis occurs because of one of two basic processes. Without compensation, P_{CO_2} remains WRI.

1. Excess H^+ is lost via gastric or renal secretion. The secretion of H^+ results in a generation of HCO_3^- that accumulates in plasma.
2. Excess HCO_3^- is formed, conserved, or administered and results in more removal of H^+ from blood and thus an alkalemia.

E. In a respiratory alkalosis, hyperventilation causes excessive expiration of $CO_{2(g)}$, which leads to a ↓ P_aCO_2 and a ↓ $[H^+]$ (↑ pH). Without compensation, $[HCO_3^-]$ remains WRI.

Fig. 10.2. Schematic drawing of the exchange of O_2 and CO_2 at the alveolus-capillary junction. Pressure values are included in the figure to illustrate the magnitude of changes that occur. Actual pressures will vary because of several factors (e.g., total atmospheric pressure is 760 mmHg at sea level but near 735 mmHg at 1000 ft elevation).

- Atmosphere to alveolus: Inspired air has a P_{O_2} (PI_{O_2}) of 159 mmHg. With the contribution of P_{H_2O} (47 mmHg) in the warm trachea, the P_{O_2} drops to 149 mmHg [0.209(760 − 47)]. In the alveolus, the P_AO_2 is lower, near 100 mmHg, because of the interchange of O_2 with the blood and because of the increased P_ACO_2 (50 mmHg) from the blood.
- Alveolus to blood: In health, O_2 quickly diffuses from the alveolus to the capillary blood (P_{O_2} near 40 mmHg) to give a P_{O_2} of 100 mmHg, which represents the pressure exerted by the dissolved O_2 in plasma. The O_2 also diffuses into erythrocytes and binds to Hgb (O_2Hgb) to saturate the oxygen-binding sites of ferrous heme (S_{O_2} = 100 %). With a normal [Hgb], 1 L of blood contains about 200 mL O_2 bound to Hgb (i.e., 1.31 mL O_2/g Hgb) and 3 mL of dissolved O_2.
- Blood to alveolus: Reversal of the carbonic anhydrase reaction produces CO_2 (not shown) which quickly diffuses from blood to alveolus and thus lowers the P_vCO_2 to P_aCO_2 near 40 mmHg. The $[H^+]$ decreases slightly because it combines with HCO_3^- to form CO_2 and H_2O. In the healthy lung, CO_2 diffuses from blood to alveoli at 20 times the rate that O_2 diffuses from alveoli to blood.
- Alveolus to atmosphere: When breathing air, the PE_{CO_2} will be less than the P_ACO_2 because the PE_{CO_2} represents a mixture of alveolar gases and the gases in the airways. During anesthesia, measuring the expired P_{CO_2} (capnography) provides information to assess CO_2 production, pulmonary gas exchange, and elimination of CO_2 by the anesthetic equipment.

PE_{CO_2}, partial pressure of expired carbon dioxide; P_{H_2O}, partial pressure of water vapor.

Fig. 10.3. Oxygenation and deoxygenation of Hgb.

Erythrocytes in peripheral tissue blood

- Because erythrocytes have their greatest [2,3-DPG] and greatest $[H^+]$ while moving through peripheral capillaries, their Hgb molecules have the lowest affinity for O_2 and thus release O_2 to plasma. The O_2 is then able to diffuse into tissue and participate in metabolic pathways.
- CO_2 (from metabolic pathways) diffuses into plasma and then into erythrocytes. Via the carbonic anhydrase (*CA*) reaction, CO_2 and H_2O are converted to HCO_3^- and H^+. The HCO_3^- moves to plasma in exchange for Cl^-. Most of the H^+ is buffered by the deoxygenated Hgb. The CO_2 produced in tissues is carried in blood in two forms: (1) as dissolved CO_2 with a P_vCO_2 near 45–50 mmHg, and (2) as HCO_3^- in erythrocytes after reacting with H_2O in the presence of carbonic anhydrase.
- Erythrocytes enter in peripheral tissues with high [2,3-DPG], but the more acidic environment (increased $[H^+]$) inhibits phosphofructokinase (*PFK*) in the glycolytic pathway, and thus the rate of 2,3-DPG formation decreases.

Erythrocytes in pulmonary blood

- O_2 diffuses from alveoli to pulmonary plasma and into erythrocytes. Because erythrocytes have their least [2,3-DPG] and least $[H^+]$ in the pulmonary vessels, their Hgb molecules have the greatest affinity for O_2 and thus become saturated with O_2 (S_{O_2} = 100 %) to form O_2Hgb. With a normal [Hgb], 1 L of blood contains about 200 mL O_2 bound to Hgb (i.e., 1.31 mL O_2/g Hgb) and 3 mL of dissolved O_2.
- HCO_3^- moves into erythrocytes (in exchange for Cl^-) and combines with H^+ to form CO_2 and H_2O. The CO_2 diffuses into plasma and then to alveoli from which it is exhaled.
- Most of the H^+ is buffered by the HCO_3^-.
- Erythrocytes enter pulmonary blood with low [2,3-DPG], but the more alkaline environment (lowest $[H^+]$) stimulates PFK in the glycolytic pathway, and thus the rate of 2,3-DPG formation increases.

Fig. 10.4. Oxygen-hemoglobin dissociation curve. With a typical P_aO_2 of 95 mmHg and at a pH of 7.4, the S_{O_2} is near 96 %. Because of the high affinity of Hgb for O_2, S_{O_2} values remain at > 90 % as long as the P_{O_2} remains at > 60 mmHg (dashed arrow). When P_{O_2} values are > 100 mmHg, the S_{O_2} will be near 100 %. Increased $[H^+]$, increased erythrocyte [2,3-DPG], hyperthermia, and hypercarbia will shift the curve to the right. If P_{O_2} stays constant, shifting the curve to the right will result in a lower S_{O_2}. The displayed dissociation curve was constructed from human data. Dissociation curves for other species are slightly different because of differences in Hgb molecules, [2,3-DPG] differences, and other factors. Accordingly, the average P_{50} values (P_aO_2 when hemoglobin is 50 % saturated with oxygen at pH 7.4, 37 °C, and 40 mmHg P_aCO_2) differ: horses ≈ 25 mmHg, cattle ≈ 26 mmHg, people ≈ 27 mmHg, dogs ≈ 30 mmHg, and cats ≈ 34 mmHg.[43,44]

Fig. 10.5. Algorithmic approach to classification of simple (not mixed) acid-base disorders. Refer to Tables 10.7 and 10.8 for expected compensatory responses.