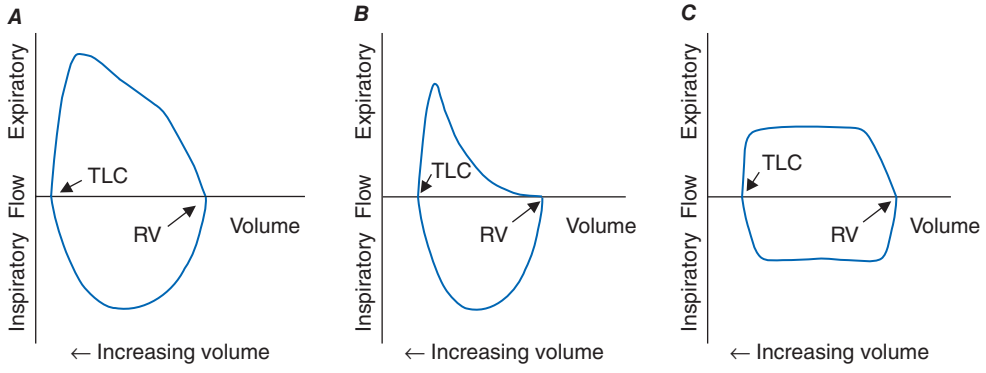

FIGURE 306e-4 **Flow-volume loops.** ***A.*** Normal. ***B.*** Airflow obstruction. ***C.*** Fixed central airway obstruction. RV, residual volume; TLC, total lung capacity.

increase considerably due to a metabolic requirement for substantially increased ventilation, an abnormally increased mechanical load, or both. As discussed below, the rate of ventilation is primarily set by the need to eliminate carbon dioxide, and thus ventilation increases during exercise (sometimes by more than twentyfold) and during metabolic acidosis as a compensatory response. Naturally, the work rate required to overcome the elasticity of the respiratory system increases with both the depth and the frequency of tidal breaths, while the work required to overcome the dynamic load increases with total ventilation. A modest increase of ventilation is most efficiently achieved by increasing tidal volume but not respiratory rate, which is the normal ventilatory response to lower-level exercise. At high levels of exercise, deep breathing persists, but respiratory rate also increases. The pattern chosen by the respiratory controller minimizes the work of breathing.

The work of breathing also increases when disease reduces the compliance of the respiratory system or increases the resistance to airflow. The former occurs commonly in diseases of the lung parenchyma (interstitial processes or fibrosis, alveolar filling diseases such as pulmonary edema or pneumonia, or substantial lung resection), and the latter occurs in obstructive airway diseases such as asthma, chronic bronchitis, emphysema, and cystic fibrosis. Furthermore, severe airflow obstruction can functionally reduce the compliance of the respiratory system by leading to dynamic hyperinflation. In this scenario, expiratory flows slowed by the obstructive airways disease may be insufficient to allow complete exhalation during the expiratory phase of tidal breathing; as a result, the "functional residual capacity" from which the next breath is inhaled is greater than the static FRC. With repetition of incomplete exhalations of each tidal breath, the operating FRC becomes dynamically elevated, sometimes to a level that approaches TLC. At these high lung volumes, the respiratory system is much less compliant than at normal breathing volumes, and thus the elastic work of each tidal breath is also increased. The dynamic pulmonary hyperinflation that accompanies severe airflow obstruction causes patients to sense difficulty in inhaling—even though the root cause of this pathophysiologic abnormality is expiratory airflow obstruction.

Adequacy of Ventilation As noted above, the respiratory control system that sets the rate of ventilation responds to chemical signals, including arterial CO_2 and oxygen tensions and blood pH, and to volitional needs, such as the need to inhale deeply before playing a long phrase on the trumpet. Disturbances in ventilation are discussed in Chap. 318. The focus of this chapter is on the relationship between ventilation of the lung and CO_2 elimination.

At the end of each tidal exhalation, the conducting airways are filled with alveolar gas that had not reached the mouth when expiratory flow stopped. During the ensuing inhalation, fresh gas immediately enters the airway tree at the mouth, but the gas first entering the alveoli at the start of inhalation is that same alveolar gas in the conducting airways that had just left the alveoli. Accordingly, fresh gas does not enter the alveoli until the volume of the conducting airways has been inspired. This volume is called the *anatomic dead space* (V_D). Quiet breathing with tidal volumes smaller than the anatomic dead space introduces no fresh gas into the alveoli at all; only that part of the inspired tidal volume (V_T) that is greater than the V_D introduces fresh gas into the alveoli. The dead space can be further increased functionally if some of the inspired tidal volume is delivered to a part of the lung that receives no pulmonary blood flow and thus cannot contribute to gas exchange (e.g., the portion of the lung distal to a large pulmonary embolus). In this situation, exhaled minute ventilation ($\dot{V}_E = V_T \times RR$) includes a component of dead space ventilation ($\dot{V}_D = V_D \times RR$) and a component of fresh gas alveolar ventilation ($\dot{V}_A = [V_T - V_D] \times RR$). CO_2 elimination from the alveoli is equal to $\dot{V}_A$ times the difference in CO_2 fraction between inspired air (essentially zero) and alveolar gas (typically ~5.6% after correction for humidification of inspired air, corresponding to 40 mmHg). In the steady state, the alveolar fraction of CO_2 is equal to metabolic CO_2 production divided by alveolar ventilation. Because, as discussed below, alveolar and arterial CO_2 tensions are equal, and because the respiratory controller normally strives to maintain arterial P_{CO_2} (Pa_{CO_2}) at ~40 mmHg, the adequacy of alveolar ventilation is reflected in Pa_{CO_2}. If the Pa_{CO_2} falls much below 40 mmHg, alveolar hyperventilation is present; if the Pa_{CO_2} exceeds 40 mmHg, then alveolar hypoventilation is present. Ventilatory failure is characterized by extreme alveolar hypoventilation.

As a consequence of oxygen uptake of alveolar gas into capillary blood, alveolar oxygen tension falls below that of inspired gas. The rate of oxygen uptake (determined by the body's metabolic oxygen consumption) is related to the average rate of metabolic CO_2 production, and their ratio—the "respiratory quotient" ($R = \dot{V}_{CO_2}/\dot{V}_{O_2}$)—depends largely on the fuel being metabolized. For a typical American diet, R is usually around 0.85, and more oxygen is absorbed than CO_2 is excreted. Together, these phenomena allow the estimation of alveolar oxygen tension, according to the following relationship, known as the *alveolar gas equation*:

$$PA_{O_2} = FI_{O_2} \times (P_{bar} - P_{H_2O}) - PA_{CO_2}/R$$

The alveolar gas equation also highlights the influences of inspired oxygen fraction (FI_{O_2}), barometric pressure (P_{bar}), and vapor pressure of water (P_{H_2O} = 47 mmHg at 37°C) in addition to alveolar ventilation (which sets PA_{CO_2}) in determining PA_{O_2}. An implication of the alveolar gas equation is that severe arterial hypoxemia rarely occurs as a pure consequence of alveolar hypoventilation at sea level while an individual is breathing air. The potential for alveolar hypoventilation to induce severe hypoxemia with otherwise normal lungs increases as P_{bar} falls with increasing altitude.

GAS EXCHANGE

Diffusion For oxygen to be delivered to the peripheral tissues, it must pass from alveolar gas into alveolar capillary blood by diffusing through alveolar membrane. The aggregate alveolar membrane is highly optimized for this process, with a very large surface area and minimal thickness. Diffusion through the alveolar membrane is so efficient in the human lung that in most circumstances a red blood cell's hemoglobin becomes fully oxygen saturated by the time the cell has traveled just one-third the length of the alveolar capillary. Thus the uptake of alveolar oxygen is ordinarily limited by the amount of blood transiting the alveolar capillaries rather than by the rapidity with which oxygen can diffuse across the membrane; consequently, oxygen uptake from the lung is said to be "perfusion limited." CO_2 also equilibrates rapidly across the alveolar membrane. Therefore, the oxygen and CO_2 tensions in capillary blood leaving a normal alveolus are essentially equal to those in alveolar gas. Only in rare circumstances (e.g., at high