and less negative at the base. The normal difference in pleural pressure from apex to base in an adult is about 8 cm H_2O (Fig. 15-10). Because the apical alveoli are more stretched at FRC, they are operating on a stiffer, less compliant region of their volume-pressure curve than the alveoli at the bases, making them more difficult to inflate than the basilar alveoli. Therefore, at the beginning of inspiration, more volume is directed toward the base than to the apex of the lung.

Control of Ventilation

Maintenance of adequate oxygenation and acid-base balance is accomplished through the respiratory control system. This system consists of the neurologic respiratory control centers, the respiratory effectors (muscles that provide the power to inflate the lungs), and the respiratory sensors. The respiratory center that automatically controls inspiration and expiration is located in the medulla of the brain stem. The respiratory center in the brain stem has an intrinsic rhythm generator (pacemaker) that drives breathing. The output of this center is modulated by inputs from peripheral and central chemoreceptors, from mechanoreceptors in the lungs, and from higher centers in the brain, including conscious control from the cerebral cortex. The respiratory center in the medulla is primarily responsible for determining the level of ventilation.

Carbon dioxide is the primary factor controlling ventilation. Carbon dioxide in the arterial blood diffuses across the blood-brain barrier, thereby reducing the pH of the cerebral spinal fluid and stimulating the central chemoreceptors. A change in Pa_{CO_2} above or below normal will increase or decrease ventilation, respectively. During quiet, resting breathing, the level of Pa_{CO_2} is thought to be the major factor controlling breathing. Only when the Pa_{O_2} (i.e., the partial pressure of oxygen dissolved in the blood that is not bound to hemoglobin) falls substantially does ventilation respond significantly. Typically, Pa_{O_2} needs to fall to less than 50 mm Hg before ventilation dramatically increases (Fig. 15-11). Low oxygen levels in the blood are not sensed by the respiratory center in the brain but are sensed by receptors in the carotid body. These vascular receptors are located between the internal and external branches of the carotid artery. Changes in Pa_{O_2} are sensed by the carotid sinus nerve. Neural traffic projects to the respiratory center through the glossopharyngeal nerve, which serves to modulate ventilation. The carotid body also senses changes in Pa_{CO_2} and pH. Nonvolatile acids (e.g., ketoacids) stimulate ventilation through their effects on the carotid body.

The outcome of this complex respiratory control system is that variables such as Pa_{O_2}, Pa_{CO_2}, and pH are held within narrow limits under most circumstances. The respiratory control center also can adjust tidal volume and frequency of breathing to minimize the energetic cost of breathing and can adapt to special circumstances such as speaking, swimming, eating, and exercise. Breathing can be stimulated by artificial manipulation of the P_{CO_2}, P_{O_2}, and pH. For example, ventilation is increased by rebreathing of carbon dioxide, inhalation of a concentration of low oxygen, or infusion of acid into the bloodstream.

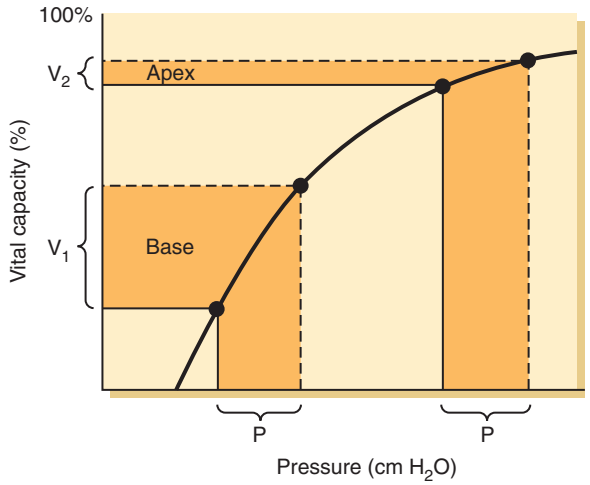

FIGURE 15-10 Transpulmonary pressure and volume for lung units at the base and apex of the lung. Because pleural pressure is more negative at the apex of the lung. Therefore, the alveoli in that region are stretched, placing them on a less compliant part of the volume-pressure curve. For a given change *(P)* in transpulmonary pressure during inspiration, the more compliant base inflates to a greater degree than the apex (V_1 and V_2, respectively).

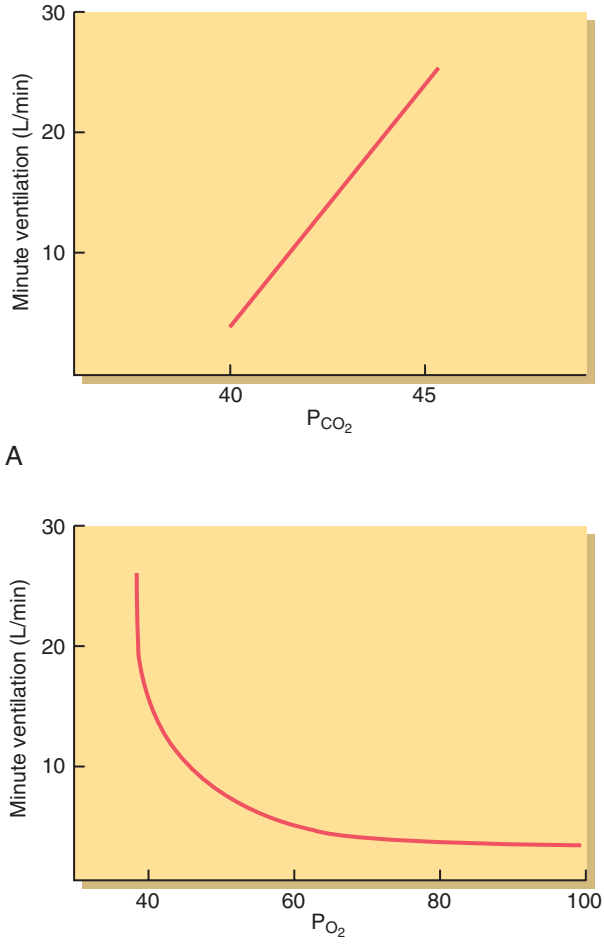

FIGURE 15-11 **A**, A rising partial pressure of carbon dioxide (P_{CO_2}) leads to a linear increase in minute ventilation. **B**, The ventilatory response to hypoxemia is less sensitive and is clinically relevant only when the partial pressure of oxygen (P_{O_2}) has dropped significantly.