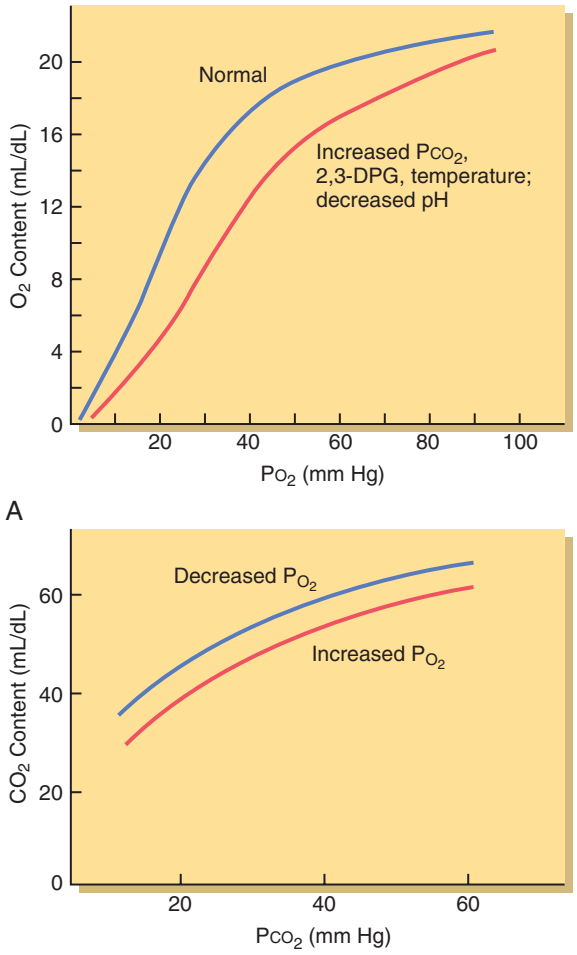

FIGURE 15-15 **A**, The various factors that decrease the oxygen affinity of hemoglobin are shown shifting the curve to the right. **B**, The carbon dioxide dissociation curve is more linear than the oxyhemoglobin curve throughout the physiologic range. Increased partial pressure of oxygen in the arteries (Pao_2) shifts the curve to the right, decreasing the carbon dioxide content for any given arterial partial pressure of carbon dioxide ($Paco_2$) and thereby facilitating carbon dioxide off-loading in the lungs. The shift to the left at a lower Pao_2 facilitates carbon dioxide on-loading at the tissues. 2,3-DPG, 2,3-Diphosphoglycerate.

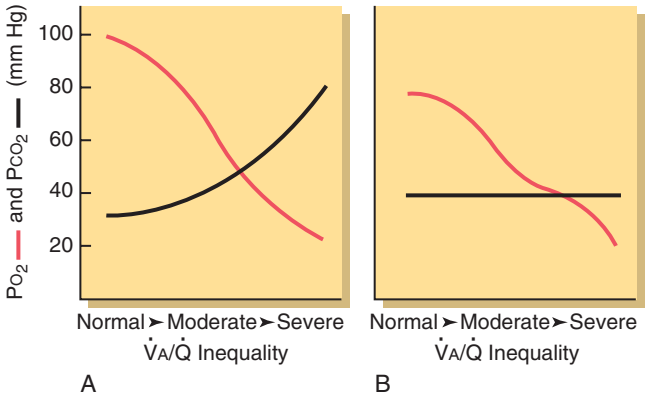

FIGURE 15-16 **A**, The effects of increasing inequality of alveolar ventilation and perfusion (decreasing $\dot{V}_A/\dot{Q}$) on the arterial partial pressures of oxygen (P_{O_2}) and carbon dioxide (P_{CO_2}) when cardiac output and minute ventilation are held constant. **B**, The gas tensions change when minute ventilation is allowed to increase. Increased ventilation can maintain a normal arterial P_{CO_2} but can only partially correct the hypoxemia. (Modified from Dantzker DR: Gas exchange abnormalities. In Montenegro H, editor: Chronic obstructive pulmonary disease, New York, 1984, Churchill Livingstone, pp 141–160.)

Hypoventilation is defined as ventilation that is inadequate to keep P_{CO_2} from increasing above normal. Hypoxemia may occur when increased carbon dioxide in the alveoli displaces alveolar oxygen. As alveolar ventilation falls and $Paco_2$ rises, P_{AO_2} will have to fall. Administration of supplemental oxygen (i.e., increasing the F_{IO_2}) can reverse hypoventilation-induced hypoxemia. When one is breathing room air, the difference between alveolar oxygen and arterial oxygen (A-a gradient) is normally about 10 mm Hg. Typically, this difference increases when hypoxemia is present. However, if the hypoxemia is caused by hypoventilation, the A-a gradient will be within normal limits. Causes of hypoventilation are varied and range from diseases or drugs that depress the respiratory control center to disorders of the chest wall or respiratory muscles that impair respiratory pump function. Disorders associated with hypoventilation include inflammation, trauma, or hemorrhage in the brain stem; spinal cord pathology; anterior horn cell disease; peripheral neuropathies; myopathies; abnormalities of the chest wall such as kyphoscoliosis; and upper airway obstruction. Administration of a higher F_{IO_2} alleviates the hypoxemia but does little to improve the elevated $Paco_2$.

The most common cause of hypoxemia in disease states is ventilation-perfusion mismatch. In regions where the ratio of ventilation $\dot{V}$ to perfusion $\dot{Q}$ is low, the blood receives little oxygen from the poorly ventilated alveoli. By contrast, in regions where $\dot{V}/\dot{Q}$ is high, the blood is well oxygenated but receives little additional oxygen despite the higher ventilation because the shape of the oxyhemoglobin dissociation curve plateaus at levels of high Pao_2. As a result, lung units with high $\dot{V}/\dot{Q}$ cannot completely correct for the low oxygen content of blood flowing past units with low $\dot{V}/\dot{Q}$. Thus, the oxygen uptake of the whole lung is lowered, causing hypoxemia. In the ideal lung, ventilation and perfusion would be perfectly matched (i.e., $\dot{V}/\dot{Q} = 1$). However, the $\dot{V}/\dot{Q}$ normally ranges from 0.5 at the base to 3 at the apex, with an overall value of 0.8. If lung disease develops, ventilation-perfusion inequality may be amplified. If the $\dot{V}/\dot{Q}$ is less than 0.8, the A-a gradient is increased and hypoxia ensues. The $Paco_2$ is usually within the normal range but increases slightly at extremely low $\dot{V}/\dot{Q}$ ratios (Fig. 15-16). Typically, hypoxemia in diseases that affect the airways, such as chronic obstructive pulmonary disease (COPD), is caused by ventilation-perfusion mismatch. As with hypoxemia due to hypoventilation, administration of a higher F_{IO_2} improves hypoxemia by improving the P_{AO_2} in areas of *low* $\dot{V}/\dot{Q}$.

The third cause of hypoxemia is shunt. A right-to-left shunt occurs when a portion of blood travels from the right side to the left side of the heart without the opportunity to exchange oxygen and carbon dioxide in the lung. Right-to-left shunts can be classified as anatomic or physiologic. With an anatomic shunt, a portion of the blood bypasses the lung by traversing through an anatomic canal. In all healthy individuals, there is a small fraction of blood in the bronchial circulation that passes to the pulmonary veins and empties into the left atrium, thereby reducing the Pao_2