

alveolar membrane. Therefore, the oxygen and CO₂ tensions in capillary blood leaving a normal alveolus are essentially equal to those in alveolar gas. Only in rare circumstances (e.g., at high altitude or in high-performance athletes exerting maximal effort) is oxygen uptake from normal lungs diffusion limited. Diffusion limitation can also occur in interstitial lung disease if substantially thickened alveolar walls remain perfused.

Ventilation/Perfusion Heterogeneity As noted above, for gas exchange to be most efficient, ventilation to each individual alveolus (among the millions of alveoli) should match perfusion to its accompanying capillaries. Because of the differential effects of gravity on lung mechanics and blood flow throughout the lung and because of differences in airway and vascular architecture among various respiratory paths, there is minor ventilation/perfusion heterogeneity even in the normal lung; however, $\dot{V}/\dot{Q}$ heterogeneity can be particularly marked in disease. Two extreme examples are (1) ventilation of unperfused lung distal to a pulmonary embolus, in which ventilation of the physiologic dead space is “wasted” in the sense that it does not contribute to gas exchange; and (2) perfusion of nonventilated lung (a “shunt”), which allows venous blood to pass through the lung unaltered. When mixed with fully oxygenated blood leaving other well-ventilated lung units, shunted venous blood disproportionately lowers the mixed arterial PaO₂ as a result of the nonlinear oxygen content versus PO₂ relationship of hemoglobin (**Fig. 285-5**). Furthermore, the resulting arterial hypoxemia is refractory to supplemental inspired oxygen. The reason is that (1) raising the inspired F_{IO₂} has no effect on alveolar gas tensions in nonventilated alveoli and (2) while raising inspired F_{IO₂} increases Paco₂ in ventilated alveoli, the oxygen content of blood exiting ventilated units increases only slightly, as hemoglobin will already have been nearly fully saturated and the solubility of oxygen in plasma is quite small.