Chapter 5

Oxygen Transport and Consumption

S.M. Cain

If a clinician considers them at all, any concern for O₂ transport and consumption will be in terms of whether transport is adequate to meet the demands represented by O₂ consumption. The reason for that concern is tissue hypoxia, which can be insidious and very difficult to detect at the bedside. Arterial hypoxemia is readily recognized when arterial O₂ tension (PₐO₂) falls below acceptable levels or hemoglobin concentration is insufficient to carry the requisite volume of O₂. The advent of reliable apparatus for measuring these descriptors of O₂ transport within the past 20 years has greatly aided critical care of patients who require ventilatory assistance. Similarly, access to mixed venous blood in a pulmonary artery via self-guiding catheters that can also be used to measure cardiac output provides important information about adequacy of O₂ delivery to peripheral tissues. The mixed venous PO₂ gives some indication of the tissue oxygenation achieved by that O₂ delivery.

Determinants of Tissue Oxygen Tension

Very commonly, the physiology of O₂ transport is presented by tracing a molecule of O₂ from the air we breathe to the interior of the mitochondrion, where 80%–90% of resting O₂ uptake occurs [23]. More practically, the care of a critically ill patient mandates that the first concern should be that each organ system is receiving enough O₂ to meet its local demand. From that viewpoint, it might be best to evaluate O₂ transport from the mitochondrion outward. When mitochondria were isolated in a test tube, cytochrome c required only 0.7 μM of O₂ to half-saturate it [18]. In other words, the Pₜ₀ was approximately 66 Pa. If, instead, the hepatocytes that contained the mitochondria were left intact, the Pₜ₀ of cytochrome c increased to 6 μM or more than 530 Pa, nearly an order of magnitude greater. This coincided with the critical level of O₂ in that O₂ uptake of suspended cells, as shown in Fig. 5.1, began to decrease in a linear fashion at lower concentrations [19]. This is therefore a lower limit for adequate O₂ supply to tissues. The difference from the mitochondrial suspension also illustrates how increasing the diffusive pathway for O₂ increases the critical PO₂ necessary to deliver it.

Because O₂ moves primarily by passive diffusion from capillaries to the interior of cells, an additional gradient for PO₂ must exist. A quantitative description of that gradient relative to the cylinder of tissue served by a single capillary was formulated by Krogh with the help of the mathematician Erlang [21]. The equation they derived is:

\[ \Delta P = P_c - P_x = \frac{M}{K} \left( \frac{R^2}{2} \ln \left( \frac{r}{x} \right) - \frac{x^2 - r^2}{4} \right) \]

where Pₗ = POₐ in the capillary; Pₓ = PO₂ at distance x from the capillary; M = O₂ uptake (ml/min per unit of tissue); K = Krogh’s constant for O₂ conductance; R = radius of the tissue cylinder; and r = radius of the capillary. Two adjacent tissue cylinders served by two capillaries are shown in Fig. 5.2. The profile of PO₂ from the capillary wall to the periphery of the cylinders was calculated from the Krogh-Erlang equation and is shown below the repre-
useful as a way to analyze problems in tissue O$_2$ delivery [20]. The diagram in Fig. 5.2 shows that the cell in the worst possible position with respect to O$_2$ delivery is located at the venous end of the capillaries and midway between them. This is sometimes described as the “lethal corner” because it will be the first to become anoxic if O$_2$ supply fails to satisfy demand. Because we cannot readily measure mitochondrial or even tissue PO$_2$, venous PO$_2$ becomes a logical place upon which to base estimates of inadequate tissue oxygenation because it represents the lowest available driving pressure for O$_2$.

The determinants of tissue PO$_2$, as set by venous PO$_2$, are shown in Fig. 5.3. Here the tissue PO$_2$ is indicated to be a function of venous PO$_2$ which, in turn, is a function of the venous concentration of O$_2$ and the oxyhemoglobin dissociation curve (ODC). Concentration or venous O$_2$ content identifies a locus on the ODC once its shape and position are known. Normally, the shape of the relationship between PO$_2$ and O$_2$ content or saturation does not change but the position can. That change can be described by the half-saturation PO$_2$ or P$_{50}$. This thereby becomes a determinant of tissue PO$_2$. Aside from abnormal forms of hemoglobin that can have very different P$_{50}$s, there are four physiological variables that affect P$_{50}$: (1) 2,3-diphosphoglycerate; (2) CO$_2$; (3) hydrogen ion concentration ([H$^+$]); and (4) temperature. The first three actually bind onto the hemoglobin molecule and, in so doing, distort the molecular conformation so that the binding affinity for O$_2$ decreases. Any increase in the four physiological factors increases the P$_{50}$.

The effect of a change in P$_{50}$ can be appreciated by examination of Fig. 5.4. Three different ODCs are shown in which P$_{50}$ was altered by presentation of the tissue cylinders. Because O$_2$ is consumed as it diffuses outward into the tissue cylinder, PO$_2$ falls with distance from the capillary. Admittedly, there were many simplifying assumptions, such as concurrent flow, no axial diffusion, uniform O$_2$ uptake and several others, to enable this calculation but, in the final analysis, the Krogh model has proven