CHAPTER 4  
Respiratory Responses

Air which has thus served the purpose of animal respiration is no longer common air; it approaches to the nature of fixed air [air containing CO₂ and not O₂] in as much as it is capable of combining with lime-water and precipitating the lime from it, in the form of a calcareous earth; but it differs from fixed air.

—Antoine Lavoisier describing the work of Priestley

4.1 INTRODUCTION

Of all the bodily functions performed during exercise, respiration appears to be one of the most highly regulated and optimized. The amount of work performed by respiratory muscles to supply air for the exercising body can be considered to be a large part of the body's overhead. Respiratory work, which accounts for 1–2% of the total body oxygen expenditure during rest, may rise to as much as 10% or higher during exercise. This represents oxygen that is unavailable to the skeletal muscles for performing useful work. It appears reasonable, therefore, that neural mechanisms regulating respiration would aim to minimize the work of respiration. Simultaneous adjustments in airflow pattern, respiration rate, and respiratory mechanics appear to be directed toward minimizing oxygen expenditure of respiratory overhead.

Respiratory ventilation during rest is subject to a high degree of voluntary control. In exercise this does not appear to be true. Except for specialized sports such as swimming (where breathing must be synchronized to gulp air, not water) and weight lifting (where breath-holding is practiced to increase torso rigidity), respiration during exercise appears to be very highly deterministic; conscious control is difficult and usually not brought to bear. We thus find that models to predict respiratory responses usually match experimental findings very well. Even where external events such as stepping during running and pedaling during bicycling tend to synchronize breathing, many respiratory parameters can be predicted.

As in other chapters, mechanics and control are introduced before models are presented. The reader should note the similarity (and coupling; Whipp and Ward, 1982) between cardiovascular and respiratory mechanics and control. Both systems propel fluids, both have conducting passageways, and both represent support functions not directly involved in useful external work. Therefore, both are subject to some degree of optimization to reduce the burden of support during exercise.

4.2 RESPIRATORY MECHANICS

Respiratory mechanics, perhaps more than mechanics of other systems in this book, is an extremely complicated topic. The respiratory system, we all know, functions to bring air to the blood. It also functions to maintain thermal equilibrium and acid-base balance of the blood. Even while its primary function of air movement is occurring, there are gaseous fluid
mechanics, physical diffusion, gas-to-liquid mass transport, muscular movement, and neural integration to consider. Although it can be argued that many of the same processes occur in the cardiovascular system, for instance, it was convenient to ignore all but those that were in consonance with the theme of this book. These mechanisms are intrinsic to respiratory functioning, however, and it is not possible to ignore them. Therefore, a slightly less integrated approach has been taken for respiratory matters compared to cardiovascular and thermal studies.

Mechanical properties of the respiratory system are best understood by first reviewing respiratory anatomy. Following that, it will be clearer how various mechanical models are formulated to account for structural considerations.

4.2.1 Respiratory Anatomy

The respiratory system consists of the lungs, conducting airways, pulmonary vasculature, respiratory muscles, and surrounding tissues and structures (Figure 4.2.1). Each of these is discussed to show the ways in which it influences respiratory responses.

Lungs. There are two lungs in the human chest; the right lung is composed of three incomplete divisions called lobes and the left lung has two. The right lung accounts for 55% of total gas volume and the left lung accounts for 45%. Lung tissue is spongy because of the very small (200-300 x 10^{-6} m diameter in normal lungs at rest) gas-filled cavities called alveoli, which are the ultimate structures for gas exchange. There are 250 million to 350

![Figure 4.2.1 Schematic representation of the respiratory system.](image)

\(^1\)This conveniently leaves room in the chest for the heart.
<table>
<thead>
<tr>
<th>Common Name</th>
<th>Numerical Order of Generation</th>
<th>Number of Each</th>
<th>Diameter, mm</th>
<th>Length, mm</th>
<th>Total Cross-Sectional Area, cm²</th>
<th>Description and Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trachea</td>
<td>0</td>
<td>1</td>
<td>18</td>
<td>120</td>
<td>2.5</td>
<td>Main cartilaginous airway; partly in thorax.</td>
</tr>
<tr>
<td>Main bronchus</td>
<td>1</td>
<td>2</td>
<td>12</td>
<td>47.6</td>
<td>2.3</td>
<td>First branching of airway; one to each lung; in lung root; cartilage.</td>
</tr>
<tr>
<td>Lobar bronchus</td>
<td>2</td>
<td>4</td>
<td>8</td>
<td>19.0</td>
<td>2.1</td>
<td>Named for each lobe; cartilage.</td>
</tr>
<tr>
<td>Segmental bronchus</td>
<td>3</td>
<td>8</td>
<td>6</td>
<td>7.6</td>
<td>2.0</td>
<td>Named for radiographical and surgical anatomy; cartilage.</td>
</tr>
<tr>
<td>Subsegmental bronchus</td>
<td>4</td>
<td>16</td>
<td>4</td>
<td>12.7</td>
<td>2.4</td>
<td>Last generally named bronchi; may be referred to as medium-sized bronchi; cartilage.</td>
</tr>
<tr>
<td>Small bronchi</td>
<td>5-10</td>
<td>1,024</td>
<td>1.3</td>
<td>4.6</td>
<td>13.4</td>
<td>Not generally named; contain decreasing amounts of cartilage. Beyond this level airways enter the lobules as defined by a strong elastic lobular limiting membrane.</td>
</tr>
<tr>
<td>Bronchioles</td>
<td>11-13</td>
<td>8,192</td>
<td>0.8</td>
<td>2.7</td>
<td>44.5</td>
<td>Not named; contain no cartilage, mucus-secreting elements, or cilia. Tightly embedded in lung tissue.</td>
</tr>
<tr>
<td>Terminal bronchioles</td>
<td>14-15</td>
<td>32,768</td>
<td>0.7</td>
<td>2.0</td>
<td>113.0</td>
<td>Generally 2 or 3 orders so designated; morphology not significantly different from orders 11-13.</td>
</tr>
<tr>
<td>Respiratory bronchioles</td>
<td>16-18</td>
<td>262,144</td>
<td>0.5</td>
<td>1.2</td>
<td>534.0</td>
<td>Definite class; bronchiolar cuboidal epithelium present, but scattered alveoli are present giving these airways a gas exchange function. Order 16 often called first-order respiratory bronchiole; 17, second-order; 18, third-order.</td>
</tr>
<tr>
<td>Alveolar ducts</td>
<td>19-22</td>
<td>4,194,304</td>
<td>0.4</td>
<td>0.8</td>
<td>5,880.0</td>
<td>No bronchiolar epithelium; have no surface except connective tissue framework; open into alveoli.</td>
</tr>
<tr>
<td>Alveolar sacs</td>
<td>23</td>
<td>8,388,608</td>
<td>0.4</td>
<td>0.6</td>
<td>11,800.0</td>
<td>No reason to assign a special name; are really short alveolar ducts.</td>
</tr>
<tr>
<td>Aveoli</td>
<td>24</td>
<td>300,000,000</td>
<td>0.2</td>
<td></td>
<td></td>
<td>Pulmonary capillaries are in the septae that form the alveoli.</td>
</tr>
</tbody>
</table>


The number of airways in each generation is based on regular dichotomous branching.

Numbers refer to last generation in each group.
Conducting Airways. Air is transported from the atmosphere to the alveoli beginning with the oral and nasal cavities, and through the pharynx (in the throat) past the glottal opening, into the trachea, or windpipe. The larynx, or voice box, at the entrance to the trachea, is the most distal structure of the passages solely for conduction of air. The trachea is a fibromuscular tube 10–12 cm in length and 1.4–2.0 cm in diameter (Sackner, 1976a). At a location called the carina, the trachea terminates and divides into the left and right bronchi. Each bronchus has a discontinuous cartilaginous support in its wall (Astrand and Rodahl, 1970). Muscle fibers capable of controlling airway diameter are incorporated into the walls of the bronchi, as well as in those of air passages closer to the alveoli. The general tendency of airways closer to the alveoli is to be less rigid and more controllable by muscle fibers (Table 4.2.1). Smooth muscle is present throughout the respiratory bronchioles and alveolar ducts but is absent in the last alveolar duct, which terminates in one to several alveoli (Sackner, 1976a). The alveolar walls are shared by other alveoli and are composed of highly pliable and collapsible squamous epithelium cells.

The bronchi subdivide into subbronchi, which further subdivide into bronchioles, which further subdivide, and so on, until finally reaching the alveolar level. The Weibel model is commonly accepted as one geometrical arrangement of air passages (another more
Figure 4.2.3  Linear velocity of flow in airways plotted against the airway branch number. Bulk flow is more important than diffusion in gas transport until generation 15 is reached. At that point, diffusion in the airways becomes important in gas transfer to and from the alveoli. (Used with permission from Muir, 1966.)

A complicated asymmetrical model is described in Yeates and Aspin, 1978). In this model (Figure 4.2.2), each airway is considered to branch into two subairways. In the adult human there are considered to be 23 such branchings, or generations, beginning at the trachea and ending in the alveoli.

Dichotomous branching is considered to occur only through the first 16 generations, which is called the conductive zone because these airways serve to conduct air to and from the lungs. After the sixteenth generation branching proceeds irregularly dichotomously or trichotomously for three generations. A limited amount of respiratory gas exchange occurs in this transition zone. In the respiration zone, generations 20–23, most gas exchange occurs.

Movement of gases in the respiratory airways occurs mainly by bulk flow (convection) throughout the region from the mouth and nose to the fifteenth generation (Figure 4.2.3). Beyond the fifteenth generation, gas diffusion is relatively more important (Pedley et al., 1977; Sackner, 1976a). With the low gas velocities that occur in diffusion, dimensions of the space over which diffusion occurs (alveolar space) must be small for adequate oxygen delivery to the walls; smaller alveoli are more efficient in the transfer of gas than are larger ones. Thus animals with high levels of oxygen consumption are found to have smaller diameter alveoli compared to animals with low levels of oxygen consumption (Figure 4.2.4).

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2The airways also serve to temper air conditions by (usually) heating and humidifying the air and removing dust particles (see Chapter 5 for thermal effects). In cold weather, some of the moisture added to the air is recovered by condensation in the nostrils, thus leading to a runny nose.

3About 2% of the oxygen consumption at rest, and a slightly larger percentage of carbon dioxide lost, occurs in humans by diffusion through the skin (Hildebrandt and Young, 1966).

4Radial gaseous diffusion in the upper airways appears to be much more important in gas mixing and flow than axial gaseous diffusion (Pedley et al., 1977).

5When lung inflation doubles, as during exercise, the nearly spherical alveoli increase their diameters by only 1.3. Thus diffusion distances do not change greatly.
Alveoli. Alveoli are the structures through which gases diffuse to and from the body. One would expect, then, that alveolar walls would be extremely thin for gas exchange efficiency, and that is found to be the case. Total tissue thickness between the inside of the alveolus to pulmonary capillary blood plasma is only about $0.4 \times 10^{-6}$ m (Figure 4.2.5). From the relative dimensions, it is apparent that the principal barrier to diffusion is not the alveolar membrane but the plasma and red blood cell (Hildebrandt and Young, 1966).

Molecular diffusion within the alveolar volume is responsible for mixing of the enclosed gas. Due to the small alveolar dimensions, complete mixing probably occurs in less than 10 msec (Astrand and Rodahl, 1970), fast enough that alveolar mixing time does not limit gaseous diffusion to or from the blood.

Of particular importance to proper alveolar operation is a thin surface coating of surfactant. Without this material, large alveoli would tend to enlarge and small alveoli would collapse. From the law of Laplace (see Section 3.2.3) for spherical bubbles

$$p = \frac{2\tau \Delta r}{r}$$

where
- $p = \text{gas pressure inside the bubble, N/m}^2$
- $\tau = \text{surface tension, N/m}^2$
- $r = \text{bubble radius, m}$
- $\Delta r = \text{wall thickness, m}$

Large spherical bubbles ($r$ large) have small internal pressures. Smaller bubbles have larger internal pressures. Connect the two bubbles together and the contents of the smaller
bubble are driven into the larger one. If we generalize this instability to the lung, it is not hard to imagine the lung composed of one large, expanded alveolus and many small, collapsed alveoli. Surfactant, which acts like a detergent, changes the stress-strain relationship of the alveolar wall and stabilizes the lung (Notter and Finkelstein, 1984).6

**Pulmonary Circulation.** The pulmonary circulation is relatively low pressure (Fung and Sobin, 1977). Because of this, pulmonary blood vessels, especially capillaries and venules, are very thin walled and flexible. Unlike systemic capillaries, pulmonary capillaries increase in diameter with any increase in blood pressure or decrease in alveolar pressure. Flow, therefore, is significantly influenced by elastic deformation.

Pulmonary circulation is largely unaffected by neural and chemical control (Fung and Sobin, 1977). It responds promptly to hypoxia, however. And a key anatomical consideration is that pulmonary capillaries within alveolar walls are exposed to alveolar air on both sides, since alveolar walls separate adjacent alveoli.

There is no true pulmonary analog to the systemic arterioles (Fung and Sobin, 1977).

---

6Surfactant is always present on the surface of the alveoli of healthy individuals. Sighs or yawns may function by stretching closed alveoli and spreading surfactant across their surfaces so they will stay open. This contention is disputed by Provine et al. (1987). Lung surfactant is likely to be dipalmitoyl phosphatidyl choline, or DPPC (Mines, 1981).
TABLE 4.2.2 Pulmonary Capillary Transit Time

<table>
<thead>
<tr>
<th>Condition</th>
<th>Capillary Volume, m³ x 10⁻⁴ (cm³)</th>
<th>Cardiac Output, m³ x 10⁻⁴/sec (cm³/sec)</th>
<th>Transit Time, sec</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest, sitting</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Rest, supine</td>
<td>1.1</td>
<td>1.0</td>
<td>1.1</td>
</tr>
<tr>
<td>Exercise</td>
<td>2.0</td>
<td>4.0</td>
<td>0.5</td>
</tr>
</tbody>
</table>

That is, the pressure-reduction function performed by the systemic arterioles (see Section 3.2.2) is not matched by the pulmonary arterioles. Therefore, pulmonary vessels, including capillaries and venules, exhibit blood pressures that vary approximately 30–50% from systole to diastole (Fung and Sobin, 1977).

There is also a high-pressure systemic blood delivery system to the bronchi which is completely independent of the pulmonary low-pressure (~ 3330 N/m²) circulation in healthy individuals (Fung and Sobin, 1977). In diseased states, however, bronchial arteries are reported to enlarge when pulmonary blood flow is reduced, and some arteriovenous shunts become prominent (Fung and Sobin, 1977).

Total pulmonary blood volume is approximately 300–500 cm³ in normal adults (Sackner, 1976c) with about 60–100 cm³ in the pulmonary capillaries (Astrand and Rodahl, 1970). This value is quite variable, depending on such things as posture, position, disease, and chemical composition of the blood (Sackner, 1976c).

Pulmonary arterial blood is oxygen-poor and carbon dioxide-rich. It exchanges excess carbon dioxide for oxygen in the pulmonary capillaries, which are in close contact with alveolar walls.

At rest, the transit time for blood in the pulmonary capillaries,

\[ t = \frac{V_c}{V_c} \]

where \( t \) = blood transit time, sec

\( V_c \) = capillary blood volume, m³

\( V_c \) = total capillary blood flow

\( V_c \) = cardiac output, m³/sec

is somewhat less than 1 sec (Table 4.2.2).

Carbon dioxide diffusion is so rapid that carbon dioxide partial pressure in the blood is equilibrated to that in the alveolus by 100 msec after the blood enters the capillary and oxygen equilibrium is reached by 500 msec (Astrand and Rodahl, 1970).

At rest, pulmonary venous blood returns to the heart nearly 97% saturated with oxygen. During exercise blood transit time in the capillaries may be only 500 msec or even less (Astrand and Rodahl, 1970), and hemoglobin saturation (see Section 3.2.1) may be limited because blood transit time is not long enough.

**Respiratory Muscles.** The lungs fill because of a rhythmic expansion of the chest wall. The action is indirect in that no muscle acts directly on the lung.

The diaphragm is the muscular mass accounting for 75% of the expansion of the chest cavity (Ganong, 1963). The diaphragm is attached around the bottom of the thoracic cage, arches over the liver, and moves downward like a piston when it contracts (Ganong, 1963). The external intercostal muscles are positioned between the ribs and aid inspiration by moving the ribs up and forward. This, then, increases the volume of the thorax. Other muscles (Table 4.2.3) are important in the maintenance of thoracic shape during breathing.

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7This figure would be closer to 100% if pulmonary anastomoses and some nonventilated alveoli were not present.
TABLE 4.2.3 Active Respiratory Muscles

<table>
<thead>
<tr>
<th>Phase</th>
<th>Quiet Breathing</th>
<th>Moderate to Severe Exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inspiration</td>
<td>Diaphragm</td>
<td>Diaphragm</td>
</tr>
<tr>
<td></td>
<td>Internal intercostals of parasternal region</td>
<td>External intercostals</td>
</tr>
<tr>
<td></td>
<td>Scaleni</td>
<td>Scaleni</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sternomastoids</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vertebral extensors</td>
</tr>
<tr>
<td>Expiration</td>
<td>(Passive, except during early part of expiration, when some inspiratory contraction persists)</td>
<td>Transverse and oblique abdominals</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Internal intercostals</td>
</tr>
</tbody>
</table>

Source: Used with permission from Hildebrandt and Young, 1965.

Quiet expiration is usually considered to be entirely passive: pressure to force air from the lungs comes from elastic expansion of the lungs and chest wall. Actually, there is evidence (Hämäläinen and Viljanen, 1978a; Loring and Mead, 1982; McIlroy et al., 1963) that even quiet expiration is not entirely passive. Sometimes, too, inspiratory muscle activity continues through the early part of expiration. During moderate to severe exercise, the abdominal and internal intercostal muscles are very important in forcing air from the lungs much more quickly than would otherwise occur.

Inspiration requires intimate contact between lung tissues, pleural tissues (the pleura is the membrane surrounding the lungs), and chest wall and diaphragm. This contact is maintained by reduced intrathoracic pressure (which tends toward negative values during inspiration). Any accumulation of gas in the intrapleural space in the thorax, which would ruin tissue-to-tissue contact, is absorbed into the pulmonary circulation because pulmonary venous total gas pressure is subatmospheric (Astrand and Rodahl, 1970).

The diaphragm is the respiratory muscle of most importance in developing the muscle pressure required to move air in the lungs. Its shape is largely determined because it separates the air-filled, spongy, and easily deformed lung material from the largely liquid abdominal contents. Because of the difference in height of the liquid in the abdomen across the dome shape assumed by the diaphragm, there is a significant vertical hydrostatic pressure gradient in the abdomen and a consequent difference in transdiaphragmatic pressure over the surface of the diaphragm (Whitelaw et al., 1983). Diaphragm tension should be able to be determined from its shape by the law of Laplace (Equation 4.2.1).

As the lungs fill, they become stiffer. The diaphragm must be able to produce higher pressures in order to move air into filled lungs. Normally, this would run counter to the muscular length-tension (Section 5.2.5) relationship, which indicates higher muscular tensions for longer lengths. In any case, muscular efficiencies would be expected to change during the respiratory cycle and muscle pressures exerted on the lungs would be expected to vary with position.

4.2.2 Lung Volumes and Gas Exchange

Of primary importance to lung functioning is the movement and mixing of gases within the respiratory system. Depending on the anatomical level under consideration, gas movement is determined mainly by diffusion or convection. This discussion begins with determinants of convective gaseous processes, that is, the lung volumes which change from rest to exercise.

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8The terms exhalation and expiration, and the terms inhalation and inspiration, are used completely synonymously in this book. Both forms are derived from Latin roots meaning to breathe (-halare and -spirare).

9Producing negative work on the inspiratory muscles (see Section 5.2.5).
**Lung Volumes.** Without the thoracic musculature and rib cage, the barely inflated lungs would occupy a much smaller space than they occupy in situ. However, the thoracic cage holds them open. Conversely, the lungs exert an influence on the thorax, holding it smaller than should be the case without the lungs. Because the lungs and thorax are connected by tissue, the volume occupied by both together is between the extremes represented by relaxed lungs alone and thoracic cavity alone. The resting volume \( V_r \) is that volume occupied by the lungs with glottis\(^{10} \) open, muscles relaxed, and with no elastic tendency to become larger or smaller.

Functional residual capacity (FRC) is often taken to be the same as the resting volume. There is a small difference between resting volume and FRC because FRC is measured while the patient breathes, whereas resting volume is measured with no breathing.\(^{11} \) FRC is properly defined only at end-expiration at rest and not during exercise.

Tidal volume \( V_T \) is the amount of air exhaled\(^{12} \) at each breath. Tidal volume increases as the severity of exercise increases. Dividing \( V_T \) by respiratory period (the time between identical points of successive breaths) \( T \) gives the minute volume \( \dot{V}_E \), or the amount of air that would be exhaled per unit time if exhalation could be sustained. Sometimes \( \dot{V}_E \), is measured as accumulated exhaled air for one minute.

Lung volumes greater than resting volume are achieved during inspiration. Maximum inspiration is represented by inspiratory reserve volume (IRV). IRV is the maximum additional volume that can be accommodated by the lung at the end of inspiration.

Lung volumes less than resting volume do not normally occur at rest but do occur during exhalation while exercising (when exhalation is active). Maximum additional expiration, as measured from lung volume at the end of expiration, is called expiratory reserve volume (ERV).

A small amount of air remains in the lung at maximum expiratory effort. This is the residual volume (RV).

Vital capacity (VC) is the sum of ERV, IRV, and \( V_T \). Total lung capacity (TLC) equals VC plus RV. These volumes are illustrated in Figure 4.2.6.

Tidal volume ventilates both the active (alveolar) regions of the lung, composed of alveolar ventilation volume \( V_A \), and inactive regions, called dead volume \( V_D \), or dead space. Alveolar ventilation volume consists of air that diffuses to and from the pulmonary circulation. Respiratory dead volume is air that does not take part in gas exchange. Not all air that reaches the alveoli interacts with gases in the blood, and thus there is a portion of the total dead volume known as alveolar dead volume. The volume occupied by the respiratory system exclusive of the alveoli is normally called anatomic dead volume. The volume of gas not equilibrating with the blood is called physiological dead volume. Normally, anatomical and physiological dead volumes are nearly identical, but during certain diseases, when portions of the lung are unperfused by blood, they can differ significantly.

Dead volume is important because it represents wasted respiratory effort. During exhalation, the most oxygen-poor and carbon dioxide-rich air is the last to be expelled (so-called end-tidal air). Because of the accumulation of this air in the dead volume (Tatsis et al., 1984), this is the first air to be drawn back into the alveoli.\(^{13} \) Extra respiratory effort must be expended to overcome dead volume accumulation.

Alveolar volume increases during exercise because of increased alveolar inflation and

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\(^{10}\)The glottis is the opening between the vocal cords in the larynx. The epiglottis is the small flap of cartilaginous and membranous tissue that closes off the windpipe during swallowing.

\(^{11}\)At rest, exhalation is assumed to be passive, and the shape of the flow waveform is therefore exponential. It takes an infinite amount of time for all air above the resting volume to be expelled. The small amount of excess air that remains in the lungs upon initiation of inspiration, when added to resting volume, equals FRC.

\(^{12}\)Some people define tidal volume as the amount of air inhaled during each breath. The two volumes are not the same because of the different temperatures of the inhaled and exhaled air, and, to a lesser extent, due to water vapor addition and different gas composition of exhaled air. Inhaled volume is somewhat easier to measure because higher resting flow rates are usually incurred.

\(^{13}\)In a similar manner, when a hot-water faucet is turned on at home, the first water you get is cold water.
recruitment of additional alveolar areas. Apparent dead volume increases because of these
same reasons, and because of different patterns of gas mixing in the lungs. When flow
becomes turbulent, as it does in regions of the conducting air passages as flow rate increases,
mixing is enhanced. Alveolar gas being mixed with freshly inhaled air is oxygen-poor and
carbon dioxide-rich; thus dead volume increases. Gray et al. (1956) measured the dependence
of dead volume on tidal volume for five subjects and obtained this relationship:

\[ V_D = 1.8 \times 10^{-4} + 0.023 V_T \]  \hspace{1cm} (4.2.3)

where \( V_D \) = dead volume, m\(^3\)
\( V_T \) = tidal volume, m\(^3\)

It can be seen, then, that the ratio of dead volume to tidal volume \( V_D/V_T \) decreases during
exercise when tidal volume increases (Whipp, 1981).

Normal values\(^{14}\) of all lung volumes are listed in Table 4.2.4. Subordinate volumes are
indented. Lung volumes are normally given in units of liters or milliliters, but to be consistent
with other chapters, cubic meters are used as primary units. Tabled volumes should be
multiplied by 0.76 for healthy females because lung volumes are related to body size (see
Section 5.2.6). Cerny (1987) also suggests race-related differences.

Posture affects many of these volumes through the influence of gravity. In a supine
position, gravity pulls on the upper thoracic wall, depressing lung volumes. In the standing
position, the effect of gravity is to expand lung volumes.

\(^{14}\)Schorr-Lesnick et al. (1985) compared pulmonary function tests, including lung volumes, between singers, wind-instrument
players, and other string or percussion instrumentalists. Contrary to popular opinion, no significant differences were found
among these groups. Singers, however, generally smoked less and exercised more than the others, thus evidence of heightened
awareness of health.
### TABLE 4.2.4 Typical Lung Volumes for Normal, Healthy Males

<table>
<thead>
<tr>
<th>Lung Volume</th>
<th>Normal Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total lung capacity (TLC)</td>
<td>$6.0 \times 10^{-3}$ m³ (6,000 cm³)</td>
</tr>
<tr>
<td>Residual volume (RV)</td>
<td>$1.2 \times 10^{-3}$ m³ (1,200 cm³)</td>
</tr>
<tr>
<td>Vital capacity (VC)</td>
<td>$4.8 \times 10^{-3}$ m³ (4,800 cm³)</td>
</tr>
<tr>
<td>Inspiratory reserve volume (IRV)</td>
<td>$3.6 \times 10^{-3}$ m³ (3,600 cm³)</td>
</tr>
<tr>
<td>Expiratory reserve volume (ERV)</td>
<td>$1.2 \times 10^{-3}$ m³ (1,200 cm³)</td>
</tr>
<tr>
<td>Functional residual capacity (FRC)</td>
<td>$2.4 \times 10^{-3}$ m³ (2,400 cm³)</td>
</tr>
<tr>
<td>Anatomical dead volume ($V_d$)</td>
<td>$1.5 \times 10^{-4}$ m³ (150 cm³)</td>
</tr>
<tr>
<td>Upper airways volume</td>
<td>$8.0 \times 10^{-4}$ m³ (80 cm³)</td>
</tr>
<tr>
<td>Lower airways volume</td>
<td>$7.0 \times 10^{-4}$ m³ (70 cm³)</td>
</tr>
<tr>
<td>Physiological dead volume ($V_d$)</td>
<td>$1.8 \times 10^{-4}$ m³ (180 cm³)</td>
</tr>
<tr>
<td>Minute volume ($V_e$) at rest</td>
<td>$1.0 \times 10^{-4}$ m³/sec (6,000 cm³/min)</td>
</tr>
<tr>
<td>Respiratory period ($T$) at rest</td>
<td>4 sec</td>
</tr>
<tr>
<td>Tidal volume ($V_t$) at rest</td>
<td>$4.0 \times 10^{-4}$ m³ (400 cm³)</td>
</tr>
<tr>
<td>Alveolar ventilation volume ($V_a$) at rest</td>
<td>$2.5 \times 10^{-4}$ m³ (250 cm³)</td>
</tr>
<tr>
<td>Minute volume during heavy exercise</td>
<td>$1.7 \times 10^{-4}$ m³/sec (10,000 cm³/min)</td>
</tr>
<tr>
<td>Respiratory period during heavy exercise</td>
<td>1.2 sec</td>
</tr>
<tr>
<td>Tidal volume during heavy exercise</td>
<td>$2.0 \times 10^{-4}$ m³ (2,000 cm³)</td>
</tr>
<tr>
<td>Alveolar ventilation volume during exercise</td>
<td>$1.8 \times 10^{-4}$ m³ (1,820 cm³)</td>
</tr>
</tbody>
</table>

*Source: Adapted and used with permission from Forster et al., 1986.*

A reduction in lung tissue elasticity with age increases the relative proportion of residual volume by reducing the recoil pressure driving expiration. The ratio of RV/TLC is about 20% in young individuals but doubles in individuals 50-60 years of age (Astrand and Rodahl, 1970).

**Perfusion of the Lung.** For gas exchange to occur properly in the lung, air must be delivered to the alveoli via the conducting airways, gas must diffuse from the alveoli to the capillaries through extremely thin walls, and the same gas must be removed to the cardiac right atrium by blood flow. The first step in this three-step process is called ventilation, and we have already been introduced to alveolar ventilation volume. When the time for alveolar ventilation to happen is taken into account, alveolar ventilation rate results. The second step is the process of diffusion.

The third step involves pulmonary blood flow, and this is called ventilatory perfusion. Obviously, an alveolus which is ventilated but not perfused cannot exchange gas. Similarly, a perfused alveolus which is not properly ventilated cannot exchange gas. The most efficient gas exchange occurs when ventilation and perfusion are matched (Figure 4.2.7).

There is a wide range of ventilation-to-perfusion ratios that naturally occur in various regions of the lung (Petrini, 1986). Blood flow is greatly affected by posture because of the effects of gravity. In the upright position, there is a general reduction in the volume of blood in the thorax, allowing for larger lung volume. Gravity also influences the distribution of blood, such that the perfusion of equal lung volumes is about five times greater at the base compared to the top of the lung (Astrand and Rodahl, 1970). There is no corresponding distribution of ventilation, hence the ventilation-to-perfusion ratio is nearly five times smaller at the top of the lung (Table 4.2.5). A more uniform ventilation-to-perfusion ratio is found in the supine position and during exercise (Jones, 1984b).

Blood flow through the capillaries is not steady. Rather, blood flows in a halting manner and may even be stopped if intra-alveolar pressure exceeds intracapillary blood pressure during diastole. Mean blood flow is not affected by heart rate (Fung and Sobin, 1977), but the

---

15There is a much smaller blood circulation to the respiratory upper airways with the purpose of nourishing these airways. This bronchial circulation is derived from the heart left ventricle rather than the right, which supplies blood to perfuse the lung (Deffebach et al., 1987).
Figure 4.2.7 Schematic illustration of a lung alveolus ventilated by air and perfused by blood. Both flows are required for adequate gas exchange to occur. Only with high ventilation and high perfusion (middle condition) does the alveolus perform its intended function of adequate gas exchange.

### TABLE 4.2.5 Ventilation-to-Perfusion Ratios from the Top to Bottom of the Lung of a Normal Man in the Sitting Position

<table>
<thead>
<tr>
<th>Percent Lung Volume, %</th>
<th>Alveolar Ventilation Rate, cm³/sec</th>
<th>Perfusion Rate, cm³/sec</th>
<th>Ventilation-to-Perfusion Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Top</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>4.0</td>
<td>1.2</td>
<td>3.3</td>
</tr>
<tr>
<td>8</td>
<td>5.5</td>
<td>3.2</td>
<td>1.8</td>
</tr>
<tr>
<td>10</td>
<td>7.0</td>
<td>5.5</td>
<td>1.3</td>
</tr>
<tr>
<td>11</td>
<td>8.7</td>
<td>8.3</td>
<td>1.0</td>
</tr>
<tr>
<td>12</td>
<td>9.8</td>
<td>11.0</td>
<td>0.90</td>
</tr>
<tr>
<td>13</td>
<td>11.2</td>
<td>13.8</td>
<td>0.80</td>
</tr>
<tr>
<td>13</td>
<td>12.0</td>
<td>16.3</td>
<td>0.73</td>
</tr>
<tr>
<td>13</td>
<td>13.0</td>
<td>19.2</td>
<td>0.68</td>
</tr>
<tr>
<td><strong>Bottom</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>13.7</td>
<td>21.5</td>
<td>0.63</td>
</tr>
<tr>
<td>100</td>
<td>84.9</td>
<td>100.0</td>
<td></td>
</tr>
</tbody>
</table>

*Source: Used with permission from West, 1962.*
highly distensible pulmonary blood vessels admit more blood when blood pressure and cardiac output increase. During exercise, higher pulmonary blood pressures allow more blood to flow through the capillaries. Even mild exercise favors more uniform perfusion of the lungs (Astrand and Rodahl, 1970). Pulmonary artery systolic pressure increases from 2670 N/m\(^2\) (20 mm Hg) at rest to 4670 N/m\(^2\) (35 mm Hg) during moderate exercise to 6670 N/m\(^2\) (50 mm Hg) at maximal work (Astrand and Rodahl, 1970).

Perfusion therefore is not steady, but average perfusion is generally all that is needed for exercise studies. Even during heavy work some parts of the lungs may be unperfused during diastole (Astrand and Rodahl, 1970). However, as long as heart rate is many times the respiration rate, average perfusion can still be close to ideal.

There are local mechanisms which tend to restore overall ventilation-to-perfusion ratios to normal when local ratios are not ideal. Inadequate alveolar ventilation results in low oxygen concentration. This, in turn, causes alveolar vasoconstriction and reduced blood flow, shunting blood to better ventilated areas (Astrand and Rodahl, 1970). Oppositely, reduced blood flow produces low concentration of alveolar carbon dioxide, and this causes local bronchiolar constriction (Astrand and Rodahl, 1970). Gas flow is thus shunted to better perfused areas. These mechanisms are far from perfect, but they seem to be adequate for matching blood flow to ventilated areas of the lung.

Gas Partial Pressures. The primary purpose of the respiratory system is gas exchange. Yet we have already seen the complexity required to perform this function. Fresh air must be brought to the alveolar gas exchange surface by an extensive piping network in order to supply oxygen to the body. On the way, the oxygen concentration is diluted in the anatomical dead volume. When it reaches the alveolus, ventilation may not be matched well enough to perfusion to accomplish the necessary gas exchange. In the gas exchange process, gas must diffuse through the alveolar space, across tissue, through plasma into the red blood cell, where it finally chemically joins to hemoglobin. A similar process occurs for carbon dioxide elimination. In this section, we deal with many of the details of gas movement.

As long as intermolecular interactions are small,\(^a\) most gases of physiological significance can be considered to obey the ideal gas law:

\[ pV = nRT \]  
\[ (4.2.4) \]

where
- \( p \) = pressure, N/m\(^2\)
- \( V \) = volume of gas, m\(^3\)
- \( n \) = number of moles, mol
- \( R \) = gas constant, N·m/(mol· K)
- \( T \) = absolute temperature, K

Errors involved in applying the ideal gas law are negligible up to atmospheric pressure (101.3 kN/m\(^2\)). Equation 4.2.4 may even be applied to vapors, although errors up to 5% may be incurred with saturated vapors (Baumeister, 1967). The ideal gas law can be applied to a mixture of gases, such as air, or to its constituents, such as oxygen and nitrogen. All individual gases in a mixture are considered to fill the total volume and have the same temperature but reduced pressures. The pressure exerted by each individual gas is called the partial pressure of the gas and is denoted by a composition subscript on the pressure symbol \( p \) (see Section 3.2.1).

Dalton’s law states that the total pressure is the sum of the partial pressures of the constituents of a mixture:

\[ p = \sum_{i=1}^{N} p_i \]  
\[ (4.2.5) \]

\(^a\)These interactions can be considered to be significant at temperatures close to the boiling point of the gas and at pressures close to the pressure (at a particular temperature) at which the gas liquefies.
TABLE 4.2.6 Molecular Masses, Gas Constants, and Volume Fractions for Air and Constituents

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Molecular Mass, kg/mol</th>
<th>Gas Constant, N·m/(mol·K)</th>
<th>Volume Fraction In Air, m³/m³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>29.0</td>
<td>286.7</td>
<td>1.0000</td>
</tr>
<tr>
<td>Ammonia</td>
<td>17.0</td>
<td>489.1</td>
<td>0.0000</td>
</tr>
<tr>
<td>Argon</td>
<td>39.9</td>
<td>208.4</td>
<td>0.0093</td>
</tr>
<tr>
<td>Carbon dioxide</td>
<td>44.0</td>
<td>189.0</td>
<td>0.0003</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>28.0</td>
<td>296.9</td>
<td>0.0000</td>
</tr>
<tr>
<td>Helium</td>
<td>4.0</td>
<td>2078.6</td>
<td>0.0000</td>
</tr>
<tr>
<td>Hydrogen</td>
<td>2.0</td>
<td>4157.2</td>
<td>0.0000</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>28.0</td>
<td>296.9</td>
<td>0.7808</td>
</tr>
<tr>
<td>Oxygen</td>
<td>32.0</td>
<td>259.8</td>
<td>0.2095</td>
</tr>
</tbody>
</table>

Note: Universal gas constant is 8314.34 N·m/kg·mol·K).

where \( p_i = \) partial pressure of the \( i \)th constituent, N/m²
\( N = \) total number of constituents

Dividing the ideal gas law for a constituent by that for the mixture gives

\[
\frac{p_i V}{pV} = \frac{n_i R_i T}{nRT}
\]

so that

\[
\frac{p_i}{p} = \frac{n_i R_i}{nR}
\]

which states that the partial pressure of a gas may be found if the total pressure, mole fraction, and ratio of gas constants are known. For most respiratory calculations, \( p \) will be considered to be the pressure of 1 atmosphere, 101 kN/m². Avogadro’s principle states that different gases at the same temperature and pressure contain equal numbers of molecules:

\[
\frac{V_1}{V_2} = \frac{nR_1}{nR_2} = \frac{R_1}{R_2}
\]

Thus

\[
\frac{p_i}{p} = \frac{V_i}{V}
\]

where \( V_i/V \) = volume fraction of a constituent in air, dimensionless

In Table 4.2.6 are found individual gas constants, as well as volume fractions, of constituent gases of air. From the ideal gas law\(^1\) we can also see that

\[
R = \sum_{i=1}^{N} \frac{n_i}{n} R_i
\]

Water vapor is added to the inhaled air. Water vapor pressure is a function of only temperature insofar as the vapor is in equilibrium with liquid water (see Table 5.2.12). At the

\(^1\)If the volume in the ideal gas law is expressed as the volume of one molecular mass of the gas, then \( R \) is constant for all gases at 8314.34 N·m/(kg mol·K). If the volume is expressed as total volume including any mass of gas, then \( R \) will be 8314.34 divided by molecular mass of that gas.
body temperature of 37°C, water vapor pressure is 6279 N/m² (47 mm Hg). Since total pressure\(^{18}\) is assumed to be 101.3 kN/m², dry gas accounts for a pressure of 101.3 – 6.3 = 95.0 kN/m².

Since temperature, pressure, and composition of respired gas change during breathing and with position, it does not seem unusual that conventions were established to express gas properties (especially compositions and partial pressures) uniformly. There are two of these: (1) body temperature (37°C), standard pressure (101.3 kN/m²), saturated (\(p_{H2O} = 6.28\) kN/m²), or BTPS, and (2) standard temperature (0°C), standard pressure (101.3 kN/m²), dry (\(p_{H2O} = 0\)), or STPD. Of the two, STPD is the more often used.

To calculate constituent partial pressures at STPD, total pressure is taken as barometric pressure minus vapor pressure of water in the atmosphere:

\[
p_i = (V_i/V)(p - p_{H2O})
\]

(4.2.11)

where \(p = \) total pressure, kN/m²
\(p_{H2O} = \) vapor pressure of water in atmosphere, kN/m²
and \(V_i/V\) as a ratio does not change in the conversion process. (The process of water addition to the air reduces partial pressures of the other constituents.

Gas volume at STPD is converted from ambient condition volume as

\[
V_i = V_{amb} \left( \frac{273}{273 + \theta} \right) \left( \frac{p - p_{H2O}}{101.3} \right)
\]

(4.2.12)

where \(V_i = \) volume of gas \(i\) corrected to STPD, m³
\(V_{amb} = \) volume of gas \(i\) at ambient temperature and pressure, m³
\(\theta = \) ambient temperature, °C
\(p = \) ambient total pressure, kN/m²
\(p_{H2O} = \) vapor pressure of water in the air, kN/m²

Oxygen consumption of the body is conventionally reported under STPD conditions. STPD conditions will be assumed in later analyses unless otherwise stated.

Partial pressures and gas volumes may be expressed in BTPS conditions. In this case, gas partial pressures are usually known from other measurements. Gas volumes are converted from ambient conditions by

\[
V_i = V_{amb} \left( \frac{310}{273 + \theta} \right) \left( \frac{p - p_{H2O}}{p - 6.28} \right)
\]

(4.2.13)

**TABLE 4.2.7 Gas Partial Pressures (kN/m²) Throughout the Respiratory and Circulatory Systems**

<table>
<thead>
<tr>
<th>Gas</th>
<th>Inspired Air(^a)</th>
<th>Alveolar Air</th>
<th>Expired Air</th>
<th>Mixed Venous Blood</th>
<th>Arterial Blood</th>
<th>Muscle Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₂O</td>
<td>---</td>
<td>6.3</td>
<td>6.3</td>
<td>6.3</td>
<td>6.3</td>
<td>6.3</td>
</tr>
<tr>
<td>CO₂</td>
<td>0.04</td>
<td>5.3</td>
<td>4.2</td>
<td>6.1</td>
<td>5.3</td>
<td>6.7</td>
</tr>
<tr>
<td>O₂</td>
<td>21.2</td>
<td>14.0</td>
<td>15.5</td>
<td>5.3</td>
<td>13.3</td>
<td>4.0</td>
</tr>
<tr>
<td>N₂(^b)</td>
<td>80.1</td>
<td>75.7</td>
<td>75.3</td>
<td>76.4</td>
<td>76.4</td>
<td>76.4</td>
</tr>
<tr>
<td>Total</td>
<td>101.3</td>
<td>101.3</td>
<td>101.3</td>
<td>94.1</td>
<td>101.3</td>
<td>93.4</td>
</tr>
</tbody>
</table>

*Source:* Used with permission from Astrand and Rodahl 1970.

\(^a\)Inspired air considered dry for convenience.

\(^b\)Includes all other inert components.

\(^{18}\)Actually, total pressure will vary slightly with position in the respiratory system and during inhalation, exhalation, or pause.
Figure 4.2.8 Variations in oxygen and carbon dioxide partial pressures in tracheal air and alveolar air during one single breath at rest. Alveolar air changes very little. (Adapted and used with permission from Astrand and Rodahl, 1970. Modified from Holmgren and Astrand, 1966.)

Minute volume $V_{\text{E}}$ is conventionally measured at BTPS conditions, whereas rates of carbon dioxide production $V_{\text{CO}_2}$ and oxygen use $V_{\text{O}_2}$ are measured at STPD (Whipp, 1981). Ratios of $V_{\text{E}}/V_{\text{CO}_2}$ and $V_{\text{E}}/V_{\text{O}_2}$ are sometimes calculated without conversion to a consistent set of conditions. To make this conversion,

$$V_{\text{STPD}} = V_{\text{BTPS}} \left( \frac{273}{310} \right) \left( \frac{101.3 - 6.28}{101.3} \right) = 0.826V_{\text{BTPS}}$$  \hspace{1cm} (4.2.14)

Constituent partial pressures vary throughout the respiratory system and circulatory system. Table 4.2.7 shows some of this variation. Notice that nitrogen is considered to be inert, and in the nitrogen components are included all other inert gases.

Alveolar gas composition remains fairly constant despite large changes in composition of tracheal air (Figure 4.2.8). If this did not occur, there would be a large fluctuation in gaseous composition of blood and a serious impact on tissues sensitive to changes in blood composition (Morehouse and Miller, 1967). Partial pressures of carbon dioxide and oxygen nearly remain at 5.3 kN/m² (40 mm Hg) and 13.3 kN/m² (100 mm Hg) throughout inhalation and exhalation. These values translate into the volume fractions listed in Table 4.2.8. During exercise, the value of oxygen fraction in alveolar air decreases by nearly 2% and carbon dioxide increases by nearly 2%.

<table>
<thead>
<tr>
<th>TABLE 4.2.8 Percent Composition of Dry Inspired, Expired, and Alveolar Air in Resting Men at Sea Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gas</strong></td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>$\text{N}_2$</td>
</tr>
<tr>
<td>$\text{O}_2$</td>
</tr>
<tr>
<td>$\text{CO}_2$</td>
</tr>
</tbody>
</table>

*Source: Used with permission from Riley, 1965.*
**Respiratory Exchange Ratio.** Respiratory exchange ratio $R$ is defined as the rate of carbon dioxide expired ($V_{CO_2}$) to oxygen used ($V_{O_2}$):

$$R = \frac{V_{CO_2}}{V_{O_2}} \quad (4.2.15)$$

In the steady state, the respiratory exchange ratio is equal to the respiratory quotient (RQ), with RQ being defined as the rate of carbon dioxide produced divided by the rate of oxygen utilized. The difference, then, between $R$ and RQ is the difference between CO$_2$ exhaled and CO$_2$ produced. These are different during extremely heavy exercise.

RQ is measured to obtain the caloric value of oxygen consumption (see Section 5.2.5) and varies with the type of food being metabolized. For instance, carbohydrate contains multiples of carbon, hydrogen, and oxygen atoms in the ratio of 1:2:1 and is metabolized in a manner similar to glucose:

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O \quad (4.2.16)$$

Six volumes of oxygen are used to produce 6 volumes of CO$_2$. Thus the RQ of carbohydrate is 1.00.

Fats contain less oxygen than carbohydrates and therefore require more oxygen to produce the same amount of carbon dioxide compared to carbohydrates. For instance, tripalmitin is oxidized (Ganong, 1963) by

$$2C_{51}H_{98}O_6 + 145O_2 \rightarrow 102CO_2 + 98H_2O \quad (4.2.17)$$

and, like other fats, has an RQ of 0.70.

Protein composition varies greatly, and so does protein RQ. However, an average RQ for protein is 0.82. RQ has been measured for other important substances (Table 4.2.9).

Protein is not used as a fuel by working muscles when the supply of carbohydrate and fat is adequate (Astrand and Rodahl, 1970). Nitrogen excretion in the urine, a by-product of protein metabolism, does not rise significantly following muscular work.

For subjects on normal diets exercising aerobically, 50-60% of the energy required is obtained from fats (Astrand and Rodahl, 1970). In prolonged aerobic work, fat supplies up to 70% of the energy. Fats are very concentrated energy sources$^{19}$ because they do not contain

<table>
<thead>
<tr>
<th>TABLE 4.2.9 Respiration Quotients of Metabolizable Substances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance</td>
</tr>
<tr>
<td>Carbohydrate</td>
</tr>
<tr>
<td>Fat</td>
</tr>
<tr>
<td>Protein</td>
</tr>
<tr>
<td>Glycerol</td>
</tr>
<tr>
<td>β-Hydroxybutyric acid</td>
</tr>
<tr>
<td>Acetoacetic acid</td>
</tr>
<tr>
<td>Pyruvic acid</td>
</tr>
<tr>
<td>Ethyl alcohol</td>
</tr>
</tbody>
</table>

Source: Adapted from Ganong, 1963.

$^{19}$Fat energy density is about 39.7 N·m/kg (9 kcal/g). Adipose tissue, which is not all fat, contains 25–29 N·m/kg (6–7 kcal/g). Carbohydrate, on the other hand, has an energy density of 17.2 N·m/kg (4 kcal/g), and stored carbohydrate (glycogen) contains about 4 N·m/kg (1 kcal/g) because of stored water of hydration (Astrand and Rodahl, 1970).
much oxygen and energy is released by oxidizing both hydrogen and carbon in fat molecules (unlike carbohydrates, which release energy, in effect, by carbon oxidation alone).

Carbohydrates are quick energy sources used predominantly at rest and at the beginning of exercise (see Section 1.3.2). Blood glucose and muscle glycogen\(^{20}\) are the primary carbohydrate sources.

Resting RQ and RQ at the beginning of exercise are normally about 0.8 (Morehouse and Miller, 1967),\(^{21}\) indicating that about two-thirds of the required energy is obtained from fat and one-third from carbohydrate. During strenuous exercise the RQ rises toward 1.00, indicating that more of the energy is derived from carbohydrate. Hard work for a protracted time utilizes more fat, and RQ approaches 0.7. Differing muscles and other organs probably exhibit different RQs because of different metabolism states,\(^{22}\) and the overall RQ measured at the mouth is the weighted sum of these.

Total RQ depends on the individual substances metabolized:

\[
RQ = \sum X_i RQ_i
\]  
(4.2.18)

where \(RQ\) = total RQ, dimensionless  
\(X_i\) = fraction of substance \(i\) metabolized, dimensionless  
\(RQ_i\) = RQ of substance \(i\), dimensionless and

\[
\sum X_i = 1
\]  
(4.2.19)

Respiratory exchange ratio \(R\) differs from respiratory quotient RQ because less information concerning fuel for metabolism can be inferred from \(R\) than from RQ. During secretion of gastric juice, for instance, the stomach has a negative respiratory exchange ratio because it uses more CO\(_2\) from the arterial blood than it puts into the venous blood (Ganong, 1963). During anaerobic exercise, when there is not sufficient oxygen to completely metabolize the metabolic substrates, lactic acid is formed and pours into the blood from the working muscles. This excess acid drops the pH of the blood and shifts the balance of Equation 3.2.3 toward a higher amount of CO\(_2\) available for respiratory exchange. Therefore, there is a higher amount of carbon dioxide emitted from the lungs for the same amount of oxygen used. Apparent \(R\) thus increases, many times exceeding 1.0.\(^{23}\) This value is not due to the substances being oxidized: rather it is due to the manner in which they are being utilized (see Section 1.3.5).

While the respiratory exchange ratio exceeds 1.0, products of metabolism are being formed which will require oxygen to reform the original metabolites or to form carbon dioxide and water (see Section 1.3.3). This required oxygen, called the oxygen debt (Figure 1.3.2), is obtained at the cessation of exercise if the oxygen debt is large enough and widespread throughout the muscles, or it can be obtained in other parts of the body if nonaerobic metabolism is extremely localized.

At the cessation of heavy exercise, the repayment of the oxygen debt requires a large amount of oxygen to be supplied while carbon dioxide stores in the body are being rebuilt. During this time, \(R\) may drop as low as 0.50. Once the oxygen debt is repaid, the respiratory exchange ratio returns eventually to resting levels and again becomes indicative of the type of

---

\(^{20}\)Glycogen is the stored form of glucose, which, unlike glucose, is not able to pass directly from the cell. Glycogen is formed from glucose by phosphorylation and polymerization in a process called glycogenesis (Ganong, 1963).

\(^{21}\)Actually, this is nonprotein RQ, or RQ adjusted for metabolized protein. Since metabolized protein is usually much less than fat or carbohydrate, and the amount of protein metabolized does not greatly change during work, nonprotein RQ is often approximated by measured RQ.

\(^{22}\)For example, the RQ of the brain is regularly 0.97-0.99 (Ganong, 1963).

\(^{23}\)There have been efforts by many workers to correlate \(R > 1.0\) with the onset of anaerobic metabolism. These correlations have not always been successful, however, due to lack of agreement on a precise definition of the onset of anaerobic metabolism.
fuel being utilized.

The caloric equivalent of oxygen consumption is frequently needed for indirect calorimetry. The caloric equivalent of oxygen is often taken to be 20.18 N·m/cm³ (4.82 kcal/L). However, the exact caloric equivalent depends on the fuel being burned and cannot reliably be obtained whenever an oxygen debt is being incurred or repaid.

To determine more closely the caloric equivalent of oxygen consumption, a steady-state measurement of RQ must be obtained. This RQ measurement can be converted into nonprotein RQ by determining the urinary nitrogen excretion (Ganong, 1963). Each gram of urinary nitrogen is equivalent to 6.25 g of protein. Metabolizing each gram of protein consumes 940 cm³ O2 and produces 750 cm³ CO₂ (Brown and Brengelmann, 1966). These amounts of oxygen and carbon dioxide are subtracted from measured totals²⁴ and the results can be divided to give nonprotein RQ. Assuming, then, that carbohydrate and fat are the only other metabolized substances, it is possible to calculate the caloric equivalent of oxygen, based on RQ:

\[
X_{\text{CHO}} = \frac{(RQ - 0.7)}{0.3} \quad (4.2.20)
\]

where \(X_{\text{CHO}}\) = carbohydrate fraction of metabolites, dimensionless

RQ = total, or overall respiration quotient, dimensionless

Since each 1000 cm³ of oxygen consumed corresponds to 1.23 g carbohydrate and 0.50 g fat (Ganong, 1963), and the caloric equivalent of carbohydrate has been given as 17.2 N·m/kg and that of fat is 39.7 N·m/kg, then

\[
U_{O_2} = \frac{(17.2)(1.23)X_{\text{CHO}} + (1 - X_{\text{CHO}})(39.7)(0.50)}{1000}
\]

\[
= \frac{1.34X_{\text{CHO}} + 19.8}{1000} \quad (4.2.21)
\]

where \(U_{O_2}\) = caloric equivalent of oxygen, N·m/cm³

**Lung Diffusion.** Movement of gases occurs by two basic mechanisms in the respiratory system: (1) convection transport, or bulk flow of gas, which we have seen predominates to the fifteenth airway generation and (2) diffusion, which predominates thereafter. Diffusion of gases occurs by the well-known Fick’s second equation (Geankoplis, 1978):

\[
\frac{\partial c_i}{\partial t} = -D_{ij} \frac{\partial^2 c_i}{\partial x^2} \quad (4.2.22)
\]

where \(c_i\) = concentration of constituent \(i\), mol/m³

\(t\) = time, sec

\(D_{ij}\) = diffusion constant²⁵ of constituent \(i\) through medium \(j\), m²/sec

\(x\) = linear distance, m

From Equation 4.2.4,

\[
c_i = \frac{R_i}{V} \frac{p_j}{R_i T} \quad (4.2.23)
\]

where \(i\) denotes a particular gas constituent. Therefore, the diffusion equation (4.2.22)

²⁴Or protein RQ can be ignored for all practical purposes.
²⁵Diffusion constants are also called diffusion coefficients and mass diffusivities.
becomes
\[
\frac{\partial p_i}{\partial t} = - D_{ij} \frac{\partial^2 p_i}{\partial x^2}
\]
(4.2.24)

and has the advantage that gas partial pressures, rather than concentrations are used.

In the steady state, which is often assumed for simplicity, \( \frac{\partial p_i}{\partial t} = 0 \), and upon integrating Equation 4.2.24 we obtain

\[
J_{Ri} = - D_{ij} \frac{dp_i}{dx}
\]
(4.2.25)

where \( J_i \) = molar flux of constituent \( i \) in the \( x \) direction, mol/(m²·sec)

Diffusion constant values, experimentally obtained by steady-state means, depend on the constituent gas \( i \) and the composition of the medium through which the gas is diffusing. Representative values of diffusion constants are given in Table 4.2.10.

Diffusion coefficients for nontabled values can be calculated (Emmert and Pigford, 1963) from

\[
D_{ij} = \frac{10.13 \left( \frac{1}{M_i} + \frac{1}{M_j} \right)^{1/2} - 24.92 \left( \frac{1}{M_i} + \frac{1}{M_j} \right) \cdot r^{1.75}}{10^{-24} \rho r_j^2 I_D}
\]
(4.2.26)

where
\[
D_{ij} = \text{gas diffusivity of constituent } i \text{ through medium } j, \text{ m}^2/\text{sec}
\]
\( M_i \) = molecular weight of gas \( i \), dimensionless
\( \rho \) = absolute pressure, N/m²
\( r_{ij} \) = collision diameter, m
\( I_D \) = collision integral for diffusion, dimensionless
\( T \) = absolute temperature, °K

and
\[
r_{ij} = 0.5 \left[ r_i + r_j \right]
\]
(4.2.27)

| Table 4.2.10 Diffusion Constants of Gases and Vapors in Air at 25°C and 105 N/m² Pressure |
|---------------------------------|-----------------|
| Substance                        | Diffusion Constant, cm²/sec |
| Ammonia                          | 0.28             |
| Carbon dioxide                   | 0.164            |
| Hydrogen                         | 0.410            |
| Oxygen                           | 0.206            |
| Water                            | 0.256            |
| Ethyl ether                      | 0.093            |
| Methanol                         | 0.159            |
| Ethyl alcohol                    | 0.119            |
| Formic acid                      | 0.133            |
| Acetic acid                      | 0.159            |
| Aniline                          | 0.073            |
| Benzene                          | 0.088            |
| Toluene                          | 0.084            |
where \( r_i \) and \( r_j \) = collision diameters of the individual gases, m

Individual values of \( r_i \) for selected gases are found in Table 4.2.11.

Also needed in Equation 4.2.26 are values for \( J_0 \). These are obtained from Table 4.2.12 using individual force constant \((\epsilon_i/k)\) data from Table 4.2.11. \( \epsilon_i \) is the energy of molecular interaction (N·m) and \( k \) is the Boltzmann constant \((1.38 \times 10^{-11} \text{ N·m/}^\circ\text{K})\). Combined force constants are determined from

\[
\frac{\epsilon_{ij}}{k} = \left( \frac{\epsilon_i}{k} \right) \left( \frac{\epsilon_j}{k} \right)^{1/2}
\]

(4.2.28)

Emmert and Pigford (1963) estimate the accuracy of this method of calculation of gas diffusion constants to average within 4% of the true values with a maximum deviation of 16%.

Normally, one would be mainly interested in the diffusion constants of various gases through air, and these are probably the proper values of diffusion constants to use in the upper respiratory system. In the alveoli, however, gas composition, as we have seen (Table 4.2.7), is dissimilar from ambient air. Modified diffusion constants can be calculated from Equation 4.2.26, or a somewhat simpler method proposed by Fuller et al. (1966) can be used.

The approach used by Fuller et al. (1966) begins with the Stefan–Maxwell molecular hard sphere model and additive LeBas atomic volumes. With the form of the equations thus established, they used a nonlinear least squares analysis to empirically determine coefficient values from diffusion coefficients obtained from the literature. Their equation is

\[
D_{ij} = \frac{0.0103 T^{1.75} (1/M_i + 1/M_j)^{1/2}}{p V_i^{1/3} + V_j^{1/3} V_{ij}^{1/2}}
\]

(4.2.29)

where \( D_{ij} \) = diffusion coefficient, m²/sec
\( T \) = absolute temperature, K
\( M_i \) = molecular weight, dimensionless
\( p \) = absolute pressure, N/m²
\( V_i \) = atomic diffusion volume, m³

Values of atomic diffusion volumes are found in Table 4.2.13. Errors in numerical values of
### TABLE 4.2.12 Values of Collision Integral

<table>
<thead>
<tr>
<th>$kT/\varepsilon_{ij}$</th>
<th>$I_0$</th>
<th>$kT/\varepsilon_{ij}$</th>
<th>$I_0$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3</td>
<td>1.331</td>
<td>3.6</td>
<td>0.4529</td>
</tr>
<tr>
<td>0.4</td>
<td>1.159</td>
<td>3.8</td>
<td>0.4471</td>
</tr>
<tr>
<td>0.5</td>
<td>1.033</td>
<td>4.0</td>
<td>0.4418</td>
</tr>
<tr>
<td>0.6</td>
<td>0.9383</td>
<td>4.2</td>
<td>0.4370</td>
</tr>
<tr>
<td>0.7</td>
<td>0.8644</td>
<td>4.4</td>
<td>0.4326</td>
</tr>
<tr>
<td>0.8</td>
<td>0.8058</td>
<td>4.6</td>
<td>0.4284</td>
</tr>
<tr>
<td>0.9</td>
<td>0.7585</td>
<td>4.8</td>
<td>0.4246</td>
</tr>
<tr>
<td>1.0</td>
<td>0.7197</td>
<td>5</td>
<td>0.4211</td>
</tr>
<tr>
<td>1.1</td>
<td>0.6873</td>
<td>6</td>
<td>0.4062</td>
</tr>
<tr>
<td>1.2</td>
<td>0.6601</td>
<td>7</td>
<td>0.3948</td>
</tr>
<tr>
<td>1.3</td>
<td>0.6367</td>
<td>8</td>
<td>0.3856</td>
</tr>
<tr>
<td>1.4</td>
<td>0.6166</td>
<td>9</td>
<td>0.3778</td>
</tr>
<tr>
<td>1.5</td>
<td>0.5991</td>
<td>10</td>
<td>0.3712</td>
</tr>
<tr>
<td>1.6</td>
<td>0.5837</td>
<td>20</td>
<td>0.3320</td>
</tr>
<tr>
<td>1.7</td>
<td>0.5701</td>
<td>30</td>
<td>0.3116</td>
</tr>
<tr>
<td>1.8</td>
<td>0.5580</td>
<td>40</td>
<td>0.2980</td>
</tr>
<tr>
<td>1.9</td>
<td>0.5471</td>
<td>50</td>
<td>0.2878</td>
</tr>
<tr>
<td>2.0</td>
<td>0.5373</td>
<td>60</td>
<td>0.2798</td>
</tr>
<tr>
<td>2.2</td>
<td>0.5203</td>
<td>70</td>
<td>0.2732</td>
</tr>
<tr>
<td>2.4</td>
<td>0.5061</td>
<td>80</td>
<td>0.2676</td>
</tr>
<tr>
<td>2.6</td>
<td>0.4939</td>
<td>90</td>
<td>0.2628</td>
</tr>
<tr>
<td>2.8</td>
<td>0.4836</td>
<td>100</td>
<td>0.2585</td>
</tr>
<tr>
<td>3.0</td>
<td>0.4745</td>
<td>200</td>
<td>0.2322</td>
</tr>
<tr>
<td>3.2</td>
<td>0.4664</td>
<td>300</td>
<td>0.2180</td>
</tr>
<tr>
<td>3.4</td>
<td>0.4593</td>
<td>400</td>
<td>0.2085</td>
</tr>
</tbody>
</table>

*Source: Used with permission from Emmert and Piggford, 1963.*

### TABLE 4.2.13 Diffusion Volumes for Simple Molecules

<table>
<thead>
<tr>
<th>Gas</th>
<th>Volume, m³ x 10⁻⁶</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>20.1</td>
</tr>
<tr>
<td>Ammonia</td>
<td>14.9</td>
</tr>
<tr>
<td>Argon</td>
<td>16.1</td>
</tr>
<tr>
<td>Carbon dioxide</td>
<td>26.9</td>
</tr>
<tr>
<td>Carbon monoxide</td>
<td>18.9</td>
</tr>
<tr>
<td>Helium</td>
<td>2.88</td>
</tr>
<tr>
<td>Hydrogen</td>
<td>7.07</td>
</tr>
<tr>
<td>Krypton</td>
<td>22.8</td>
</tr>
<tr>
<td>Neon</td>
<td>5.59</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>17.9</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>35.9</td>
</tr>
<tr>
<td>Oxygen</td>
<td>16.6</td>
</tr>
<tr>
<td>Water vapor</td>
<td>12.7</td>
</tr>
</tbody>
</table>

*Source: Adapted and used with permission from Fuller et al., 1966.*
TABLE 4.2.14 Calculated Gas Diffusivities for Ambient Air at 298° K (25° C) and for Alveolar Air at 310°K (37° C) at 1 Atm Pressure (101.3 kNm²)

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Ambient Air</th>
<th>Alveolar Air</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mole Fraction</td>
<td>Diffusivity, cm²/sec</td>
</tr>
<tr>
<td>Water vapor</td>
<td>0.000</td>
<td>0.247</td>
</tr>
<tr>
<td>Carbon dioxide</td>
<td>0.000</td>
<td>0.154</td>
</tr>
<tr>
<td>Oxygen</td>
<td>0.209</td>
<td>0.194</td>
</tr>
<tr>
<td>Nitrogen</td>
<td>0.791</td>
<td>0.196</td>
</tr>
</tbody>
</table>

Diffusion coefficients are expected to be slightly greater using Equation 4.2.29 compared to Equation 4.2.26.

Diffusion which occurs within a binary system of gases with equimolar counterdiffusion

\[ J_i = -J_j \tag{4.2.30} \]

results in

\[ D_i = D_j \tag{4.2.31} \]

Diffusion within ambient air is usually managed by considering air to be a uniform and constant medium, a binary constituent. Alveolar air is not constant or uniform, and it cannot be considered to be binary. For multicomponent diffusion, Emmert and Pigford (1963) give

\[ D_i = \frac{1-X_i}{\sum_{j=1}^{N} (X_j / D_{ij})} \tag{4.2.32} \]

where \( D_i \) = diffusion coefficient of constituent \( i \) in the multicomponent system, m²/sec

\( X_i \) = mole fraction of constituent \( i \), dimensionless

Gas diffusion coefficients should be calculated for binary diffusion using Equation 4.2.29 and converted to multicomponent diffusion coefficients for alveolar air using Equation 4.2.32. Values of alveolar gas diffusivities calculated in this way appear in Table 4.2.14 and it can be seen that alveolar gas diffusivity values differ from ambient gas diffusivity values by about 15%.

During exercise, and at other times when the respiratory exchange ratio differs significantly from 1.0, the alveolar gas can no longer be considered to be a stagnant medium. There results a net movement of mass with a mean velocity \( \dot{V}_m \). This case is not strictly diffusion in that a convective flow is also present.

**Gas Mixing in the Airways.** In any thorough consideration of gas delivery to the lungs, account must be made for the effects of combined convection (bulk movement) and diffusion (molecular movement) within the conducting airways. Although this subject can be very involved because of the complicated geometry of the air passages, it is nonetheless especially important in high-frequency ventilation.\(^{26}\) There may also be an effect of non–steady-state gas mixing at the very high respiration rates achieved during heavy exercise.

\(^{26}\)It has been found clinically that normal blood gas compositions can be maintained inpatients with respiratory obstruction by assisted ventilation at high frequency (typically 5–15 cps) and low tidal volume (typically one-third of normal dead volume).
This subject has been very thoroughly presented by Pedley et al. (1977) and by Ultman (1981), and it will not be completely developed here. A few pertinent details will, however, be presented.

Flow in the conducting airways removes excess carbon dioxide during exhalation and supplies fresh oxygen during inhalation. In each case, there is a divergence between the gas composition of the flowing gas and that of the gas which is being displaced. Gas movement by convection is present for sure. Likewise, the difference in gas concentration between the displacing gas and the contacting displaced gas provides the opportunity for molecular diffusion.

Mathematical specification of axial gas transport in a conduit is given (Ultman, 1981) by

$$\dot{V}_i = F_i \dot{V} - (D_{ij} + D_{ij}) A \frac{dF_i}{dx}$$

(4.2.33)

where

- $\dot{V}_i$ = volume rate of flow of constituent $i$, m$^3$/sec
- $\dot{V}$ = volume rate of flow of entire plug of gas, m$^3$/sec
- $D_{ij}$ = diffusion coefficient, m$^2$/sec
- $D_{ij}$ = longitudinal dispersion coefficient, m$^2$/sec
- $F_i$ = average volume fraction of constituent $i$, m$^3$/m$^3$
- $A$ = total cross-sectional area of tube, m$^2$
- $x$ = distance along tube, m

The ratio of material delivery by axial convection to that by radial diffusion is known as the Péclet number ($Pe$). The rate of supply by convective flow is given by

$$\dot{V} = \nu A c_i$$

(4.2.34)

where

- $\dot{V}$ = volume rate of flow, m$^3$/sec
- $\nu$ = average flow velocity, m/sec
- $A$ = cross-sectional area, m$^2$
- $c_i$ = concentration, kg/kg

Steady-state material diffusion is given by

$$\dot{V} = D_{ij} A \frac{dc_i}{dx} = D_{ij} A \frac{c_i}{l}$$

(4.2.35)

where $(c/l) = \text{mean concentration gradient, m}^{-1}$

The Péclet number is thus given by

$$Pe = \frac{\nu l}{D_{ij}}$$

(4.2.36)

Péclet numbers within the respiratory system vary from 10,000 at the mouth to 0.01 at the alveolar ducts.

In laminar flow through a straight tube, the profile of velocities of gas particles flowing along the tube will appear to be parabolic (see Section 4.2.3). That is, the velocity of particles in the center of the tube will be twice the average velocity and the velocity at the wall will be zero. Thus molecules of a gas in higher concentration in the displacing gas mixture will travel downstream faster in the center of the tube than at the wall. Consequently, the resulting concentration difference between tube midline and tube wall enhances radial diffusion of this constituent gas (Ben Jebria, 1984). Taylor (1953) showed that this mechanism can be described as longitudinal dispersion with an equivalent virtual diffusion coefficient:

$$D_{ij} = D_{ij} + \frac{(\nu d)^2}{192 D_{ij}}$$

(4.2.37)

---

27This mechanism of enhanced diffusion by laminar convective transport is called Taylor dispersion.
where \( v \) = mean axial velocity, m/sec
\( d \) = tube diameter, m
The value for the number in the denominator, here shown as 192, varies with velocity profile (Ultman, 1981). For even moderate velocities and diameters, \( D_i >> D_{ij} \)28 And, interestingly, the lower the molecular diffusivity \( D_i \) of any gas, the higher will be the dispersion coefficient \( D_i \).

In turbulent flow, the velocity profile is much flatter. The equivalent dispersion coefficient is smaller (Ben Jebria, 1984):

\[
D_i = D_j + 0.73vd
\] (4.2.38)

With this cursory discussion, gas mixing in the airways due to simultaneous convection and diffusion can begin to be understood.

**Diffusion Capacity.** As if alveolar diffusion alone were not complicated enough, there is diffusion across the alveolar membrane into the capillary plasma, diffusion through the plasma, diffusion into the red blood cell, and chemical binding of both oxygen and carbon dioxide to account for. Furthermore, nonnormal lungs29 may not have a uniform distribution of inspired gas, thus having a nonuniform alveolar gas concentration (Sackner, 1976d). For these reasons it is often convenient to consider only the overall diffusing capacity of the lung. Certainly, it is much easier to make this measurement than to measure individual alveoli diffusion parameters.

Lung diffusing capacity30 is defined (Astrand and Rodahl, 1970) as

\[
D_L = \frac{\text{gas flow}}{\text{mean driving pressure}}
\] (4.2.39)

where \( D_L \) = lung diffusing capacity, m\(^5\)/N·sec
Mean driving pressure is the difference between average alveolar pressure and mean capillary partial pressure.

Lung diffusing capacity for oxygen is of primary interest. However, mean capillary oxygen partial pressure is difficult to ascertain. It would be better to choose a gas which is held by the pulmonary capillaries at a constant partial pressure, or which disappears entirely. Carbon monoxide has 210 times the affinity for hemoglobin as does oxygen (Sackner, 1976d) and, for all purposes, is completely removed from the plasma by circulating red blood cells. Carbon monoxide, in low concentration, has thus become the standard challenge gas for determination of lung diffusing capacity:

\[
D_{LCO} = \frac{\dot{V}_{CO}}{P_{A CO}}
\] (4.2.40)

where \( D_{LCO} \) = lung diffusing capacity for CO, m\(^5\)/N·sec
\( \dot{V}_{CO} \) = CO rate of absorption in the lung, m\(^3\)/sec
\( P_{A CO} \) = mean alveolar partial pressure for CO, N/m\(^2\)

Steady-state lung diffusion capacity for oxygen is obtained from steady-state lung diffusion capacity for carbon monoxide by multiplying the latter by 1.23 (Astrand and Rodahl, 1970).

28For \( (d/l)(Pe) > 180 \), the \( D_i < 0.05D_{ij} \), and for \( (d/l)(Pe) < 20 \), the \( D_i < 0.05D_{ij} \) where \( l \) = tube length, m (Ultman, 1981).

29These lungs are characterized by compartments with unequal time constants (flow resistance multiplied by compliance). Regions with small time constant fill faster and empty faster. Compartments can have long time constants (usually caused by high resistance) for one phase of breathing and short time constants for the other. For example, chronic obstructive pulmonary disease (COPD) and emphysema have particularly long time constants for emptying and are called obstructive pulmonary diseases; asthma, which is a restrictive pulmonary disease, is characterized by long filling and emptying time constants.

30Diffusing capacity is analogous to electrical conductance. For this reason, some authors call it "transfer factor," or "transfer coefficient."
Diffusion capacity values obtained at rest are not the same as diffusion capacity values obtained during exercise. Diffusion capacity is influenced by alveolar surface area (70–90 m²), thickness of the membrane separating air from blood, and pulmonary capillary blood volume, or hemoglobin content (Astrand and Rodahl, 1970). Figure 4.2.9 shows the large increase (three times) in diffusion capacity which occurs during exercise. Most of the increase is attributable to an increase in the number of capillaries open during work (Astrand and Rodahl, 1970). For a similar reason, diffusion rates for women are lower than those for men because alveolar surface area varies with body weight (Astrand and Rodahl, 1970).

Figure 4.2.5 illustrates the diffusion pathway taken by oxygen from the alveolar space to the interior of the red blood cell. Oxygen must diffuse across the alveolar capillary membranes and into the plasma, across the red cell membrane and through the red cell interior, finally to be bound to hemoglobin. Hill et al. (1977) used the kinetics of the reactions of oxygen and carbon dioxide at various stages in this process to formulate a model of oxygen and carbon dioxide exchanges during exercise.

Carbon dioxide diffusion rates are about 20 times those for oxygen (Astrand and Rodahl, 1970). Contributing to this ratio is the fact that CO₂ molecules are larger than O₂ molecules, thus slowing diffusion, but CO₂ diffuses about 25 times more rapidly than O₂ in aqueous liquids (Astrand and Rodahl, 1970). Reaction rates of Equation 3.2.3, the equilibrium reaction between bicarbonate and carbon dioxide in the blood, are so slow, however, that all the CO₂ which must be removed from the blood would not be available to diffuse into the lungs if it were not for carbonic anhydrase, which catalyzes the reaction and allows it to proceed much more rapidly. Without carbonic anhydrase, the blood would have to remain in the capillaries for almost 4 min for the CO₂ to be given off (Astrand and Rodahl, 1970).

Diffusion capacity for carbon dioxide has been found to be an insensitive predictor of abnormal gas exchange during exercise (Sue et al., 1987). Therefore, other measures, such as arterial blood gases, must be used to determine exercise gas exchange.

**Blood Gases.** As the physiological interface between air and blood, the respiratory system must be studied from both aspects. We have already dealt with blood gas partial pressure in this

![Figure 4.2.9](image)
chapter, as well as with blood gas dynamics in Chapter 3. Some details must still be introduced to complete the necessary background for study of respiratory contribution to blood gas exchange.

Carbon dioxide and oxygen are the most important gases for consideration. Other gases, such as nitrogen, do not normally play a large role in respiratory gas exchange. In a general sense, blood gas levels leaving the lung remain reasonably constant: blood $pCO_2$ is 5333 N/m² (40 mm Hg) and blood $pO_2$ is 13.3 kN/m² (100 mm Hg). Carbon dioxide partial pressure in mixed (pulmonary) venous blood and alveolar air is highly variable, but it begins at about 2000 N/m² at rest, decreases to about 1500 N/m² during light exercise, and increases again in severe exercise (Morehouse and Miller, 1967).

The relationships between alveolar partial pressures and respiratory blood partial pressures of oxygen and carbon dioxide are seen in Figure 4.2.10. Carbon dioxide partial pressure in the blood closely tracks carbon dioxide partial pressure in the alveolar space, and, for many practical purposes, can be considered to be the same.

There is a slight variation in arterial partial pressures of carbon dioxide and oxygen throughout the breathing cycle. Respiratory-related variations of about 900 N/m² (7 mm Hg) in $pO_2$ have been found in anesthetized dogs, lambs, and cats (Biscoe and Willshaw, 1981). For resting dogs, alveolar variation of $pO_2$, has been calculated to be 1300 N/m² (10 mm Hg) and for resting humans it has been calculated as 400 N/m² (3 mm Hg).

A variation in arterial $pCO_2$ has been measured indirectly as 270 N/m² (2 mm Hg) in anesthetized cats (Biscoe and Willshaw, 1981). Alveolar $pCO_2$ changes by about 270 N/m² (2 mm Hg) in resting man, but exercise is expected to increase the excursion.

The extent of variation depends greatly on mixing occurring in the heart. The higher the number of heartbeats per breath, the less mixing occurs and the greater is the partial pressure variation. Similarly, greater end-systolic volumes attenuate the variation more than lesser volumes (Biscoe and Willshaw, 1981).

Two factors contribute to the difference between alveolar and arterial oxygen partial pressures. The first of these is shunting of venous blood around the effective alveolar volume. 

---

**Figure 4.2.10** Alveolar and respiratory blood gas partial pressures during exercise. Carbon dioxide values track closely over the entire range of work rates used (about 0–150 N·m/sec external work), but oxygen does not.
to be mixed consequently with arterial blood from the effective alveolar volume. Although this has a large effect on oxygen partial pressure of the resulting blood mixture, it has but a small effect on carbon dioxide partial pressure because the CO₂ dissociation curve for blood is very steep (Figure 4.2.11), indicating a small partial pressure change per unit change in concentration (also see Figure 3.2.4). The second factor contributing to oxygen partial pressure difference between alveoli and blood is the diffusion rate of oxygen across the alveolar membrane, which is much slower for oxygen than for carbon dioxide.

More importantly, oxygen saturation of mixed (pulmonary) venous blood is nearly 100% during rest and exercise up to that requiring oxygen uptake of 67 x 10⁻⁶ m³/sec: (4 L/min) (Morehouse and Miller, 1967). This comes about because pulmonary vessels closed during rest open during exercise, with the effect that the volume of blood through the lungs increases without a corresponding increase of velocity of blood through the lungs. Blood transit time through the lungs therefore remains nearly constant. The resulting improvement in distribution of ventilation to perfusion results in a decrease in oxygen partial pressure difference across the capillary and alveolar membranes. During very heavy exercise, the increased acidity and temperature of the blood (see Figures 3.2.2 and 3.2.3) reduce the ability of hemoglobin to absorb oxygen, resulting in lower blood saturation (Morehouse and Miller, 1967).

The amount of oxygen in the blood (which comes, originally, from respiration) can be obtained from (see Section 3.2.1)

\[
c_{O_2} = 1340 S c_H + 0.023 \times 10^{-5} P_{O_2} \quad (4.2.41)
\]

where \(c_{O_2}\) = oxygen concentration of the blood, m³ O₂/m³ blood
\(S\) = hemoglobin saturation, fractional
\(c_H\) = hemoglobin concentration, kg hemoglobin/m³ blood

---

**Figure 4.2.11** Physiologic CO₂ dissociation curve. The change from systemic arterial to venous concentrations of carbon dioxide is accompanied by a very small change in carbon dioxide partial pressure. (Adapted and used with permission from Riley, 1965.)
The first term on the right-hand side of Equation 4.2.41 reflects the concentration of oxygen carried by hemoglobin, and the second term represents dissolved oxygen (see Section 3.2.1). Average men have about 160 kg hemoglobin per cubic meter of blood (Ganong, 1963), and hemoglobin saturation can be calculated from Equations 3.2.5 and 3.2.6 or from a similar procedure given by West and Wagner (1977). The amount of oxygen absorbed by the pulmonary blood is

\[ \dot{V}_{O_2} = (\Delta c_{O_2})(CO) \]  

(4.2.42)

where
- \( \dot{V}_{O_2} \) = oxygen uptake, m\(^3\)/sec
- \( CO \) = cardiac output, m\(^3\)/sec
- \( \Delta c_{O_2} \) = oxygen concentration difference between pulmonary arterial and pulmonary venous blood, m\(^3\) O\(_2\)/m\(^3\) blood

See Table 3.2.8 for representative values of cardiac output.

West and Wagner (1977) presented a procedure to calculate the amount of carbon dioxide taking part in respiration. They began with a procedure similar in theory to Equation 4.2.41:

\[ \text{total blood CO}_2 = \text{plasma CO}_2 + \text{red blood cell CO}_2 \]  

(4.2.43)

Based on the Henderson–Hasselbalch equation (see Equation 3.2.4) plasma CO\(_2\) or dissolved CO\(_2\) is calculated from

\[ \text{plasma CO}_2 = \alpha_{CO_2} p\text{CO}_2 (l+10^{(pH-pK)}) \]  

(4.2.44)

where
- \( \alpha_{CO_2} \) = solubility of CO\(_2\) in plasma, mol/(N·m)
- \( pH \) = negative logarithm of hydrogen ion concentration, dimensionless
- \( pK \) = negative logarithm of reaction constant, dimensionless

Values of \( pK \) and \( \alpha_{CO_2} \) may be taken as constant values of 6.10 and 0.236 (mol·m)/kN, but West and Wagner (1977) gave expressions for these as functions of temperature and pH:

\[ pK = 6.086 + 0.042(7.4 - pH) + (38 - \theta)[0.0047 + 0.0014(7.4 - pH)] \]  

(4.2.45)

where \( \theta \) = temperature, °C

and

\[ \alpha_{CO_2} = 0.230 + 0.0043(37 - \theta) + 0.0002(37 - \theta)^2 \]  

(4.2.46)

Since the fractions of red blood cells and plasma in the blood are related by hematocrit, carbon dioxide concentration is

\[ c_{CO_2} = 222[(Ht)(\text{red cell CO}_2) + (1 - Ht)(\text{plasma CO}_2)] \]  

(4.2.47)

where \( c_{CO_2} \) = total CO\(_2\) concentration in the blood, m\(^3\) CO\(_2\)/m\(^3\) blood
- \( Ht \) = hematocrit, fractional

West and Wagner (1977) calculated red blood cellular carbon dioxide as proportional to plasma carbon dioxide and oxygen saturation of hemoglobin. Thus total CO\(_2\) concentration becomes

\[ c_{CO_2} = (\text{plasma CO}_2) [222][(Ht)(B - 1) + 1] \]  

(4.2.48)

and

\[ B = B_1 + (B_2 - B_1)(1 - S) \]  

(4.2.49a)
\[ B_1 = 0.590 + 0.2913(7.4 - \text{pH}) - 0.08447(7.4 - \text{pH})^2 \]  
(4.2.49b)

\[ B_2 = 0.644 + 0.227(7.4 - \text{pH}) - 0.0938(7.4 - \text{pH})^2 \]  
(4.2.49c)

where \( S \) = fractional hemoglobin saturation, dimensionless

Fractional hematocrit is usually about 0.47 for mean and about 0.42 for women and children (Astrand and Rodahl, 1970).

Similar to oxygen, the amount of carbon dioxide taking part in respiratory exchange is

\[ \dot{V}_{\text{CO}_2} = (\Delta c_{\text{CO}_2})(\text{CO}) \]  
(4.2.50)

where \( \dot{V}_{\text{CO}_2} \) = carbon dioxide evolution, m\(^3\)/sec

\[ \Delta c_{\text{CO}_2} = \text{change in carbon dioxide concentration between pulmonary arterial and pulmonary venous blood}, \ m^3 \text{CO}_2/m^3 \]

\( \text{CO} \) = cardiac output, m\(^3\)/sec

**Pulmonary Gas Exchange.** The problem of pulmonary gas exchange is that experimental procedures limit the sites where data may be obtained. As we have seen, complex mechanisms and adjustments in the respiratory system are quite normal, but usual respiratory gas measurements can be made only at the mouth and sometimes in the systemic circulation. From these measurements must be inferred information concerning metabolic state, alveolar efficacy, pulmonary perfusion, respiratory dead volume, and a host of other interesting and clinically important processes possessed by the individual from whom the data were obtained.

Fortunately, there are mathematical means to deduce much useful pulmonary gas exchange information. The ideas in this section are relatively simple, and the algebra is not overwhelming. The problem, however, is in nomenclature; with so many subscripts and superscripts it is easy to become confused. It is hoped that the clear and straightforward presentation here will prevent that. Symbols generally follow those used by Riley (1965).

We begin with a simple steady-state mass balance, first on oxygen:

\[ \dot{O}_2 \text{ used} = \dot{O}_2 \text{ intake} - \dot{O}_2 \text{ exhausted} \]  
(4.2.51)

\[ \dot{V}_{\text{O}_2} = \dot{V}_i F_{\text{O}_2} - \dot{V}_e F_{\text{O}_2} \]  
(4.2.52)

where \( \dot{V}_{\text{O}_2} \) = oxygen uptake, m\(^3\)/sec

\( \dot{V}_i \) = inhaled flow rate, m\(^3\)/sec

\( \dot{V}_e \) = exhaled flow rate, m\(^3\)/sec

\( F_{\text{O}_2} \) = fractional concentration\(^{33}\) of oxygen in inhaled gas, m\(^3\)/m\(^3\)

\( F_{\text{O}_2} \) = fractional concentration of oxygen in exhaled dry gas, m\(^3\)/m\(^3\)

And next on carbon dioxide

\[ \dot{V}_{\text{CO}_2} = \dot{V}_e F_{\text{CO}_2} - \dot{V}_i F_{\text{CO}_2} \]  
(4.2.53)

where \( \dot{V}_{\text{CO}_2} \) = carbon dioxide efflux, m\(^3\)/sec

\( F_{\text{CO}_2} \) = fractional concentration of carbon dioxide in exhaled dry gas, m\(^3\)/m\(^3\)

\( F_{\text{CO}_2} \) = fractional concentration of carbon dioxide in inhaled dry gas, m\(^3\)/m\(^3\)

\( F_{\text{CO}_2} \) is usually assumed to be zero for atmospheric air breathing. There are cases, especially those where masks are worn, where \( F_{\text{CO}_2} \) cannot be assumed to be zero (Johnson, 1976). Notice, also, that all gases are assumed to be at STPD conditions (see Equation 4.2.14).

\(^{33}\)Fractional concentration is given as volume of gas A per unit volume of mixture of gases A and B. From Equation 4.2.9 we could have given fractional concentration in terms of partial pressures.
Since there is a difference between inspired and expired volumes, a mass balance on nitrogen, which is assumed to have no net exchange across the lungs, is performed to account for volume differences:

\[ \dot{V}_{N_2} = \dot{V_i} F_{eN_2} - \dot{V_e} F_{iN_2} \]

\[ \dot{V_i} = \dot{V_e} \left( F_{eN_2} / F_{iN_2} \right) \]

where \( \dot{V}_{N_2} \) = nitrogen uptake, m³/sec

\( F_{eN_2} \) = fractional concentration of nitrogen in exhaled dry gas, m³/m³

\( F_{iN_2} \) = fractional concentration of nitrogen in inhaled dry gas, m³/m³

Many relationships have been developed between these variables to aid pulmonary function testing. Since measurement technique is not the object of this book, most of these relationships are ignored here. The reader is referred to Riley (1965) for further details. One useful relationship is considered, however: the determination of respiratory dead volume \( V_D \).

During a single expiration the first air to leave the mouth is from the respiratory dead volume—the air closest to the mouth. This air has not exchanged gases with the blood and is virtually the same composition as inspired air (with the addition of water vapor, of course). Air that reaches the mouth after the dead volume air has been exhaled is considered to be from the alveolar space (see Figure 4.2.12). It is this air which is in equilibrium with the blood. Because carbon dioxide is continually evolving, the CO₂ content of alveolar air continually increases (Turney, 1983) with the rate of increase related to rate of CO₂ evolution (Newstead et al., 1980). Normally, pulmonary technicians have considered the so-called end-tidal CO₂ concentration to be representative of alveolar air. Because of the increasing CO₂ concentration, end-tidal air may not be as meaningful as previously supposed.

Considering the expired air to be composed of dead volume air and alveolar air:

\[ V_e = V_{de} + V_{ae} \]

Figure 4.2.12 A typical tracing of carbon dioxide concentration with time during an exhaled breath. The first air to be removed is dead volume air and the last is alveolar air. Carbon dioxide concentration of alveolar air increases with time because carbon dioxide from the blood is constantly being delivered to the alveoli.
where $V_e = \text{exhaled volume, m}^3$

$V_{Ae} = \text{exhaled volume from alveolar space, m}^3$

$V_{De} = \text{exhaled volume from dead space, m}^3$

total exhaled CO$_2$ comes from alveolar CO$_2$ and dead volume CO$_2$:

$$V_e F_{eCO_2} = V_{Ae} F_{AeCO_2} + V_{De} F_{DeCO_2} \tag{4.2.57}$$

where $F_{eCO_2} = \text{average mixed volume fractional concentration of CO}_2 \text{ from exhaled air, m}^3/\text{m}^3$

$F_{AeCO_2} = \text{fractional concentration CO}_2 \text{ from alveolar space, m}^3/\text{m}^3$

$F_{DeCO_2} = \text{fractional concentration CO}_2 \text{ from dead volume, m}^3/\text{m}^3$

Because no gas exchange occurs in the dead volume,

$$F_{DeCO_2} = F_{iCO_2} \tag{4.2.58}$$

and $F_{iCO_2}$ is usually assumed to be zero. Thus

$$V_{De} = \left[ \frac{F_{AeCO_2} - F_{eCO_2}}{F_{AeCO_2} - F_{iCO_2}} \right] V_e \tag{4.2.59}$$

This is called the Bohr equation. $F_{AeCO_2}$ is usually taken to be the maximum CO$_2$ concentration during the exhalation, and $F_{eCO_2}$ is the CO$_2$ concentration of the well-mixed total exhaled breath.

Pulmonary gas relationships will be developed for three effective pulmonary compartments (Riley, 1966): (1) effective, (2) ventilated but unperfused, and (3) perfused but unventilated. The effective compartment is considered to be the part of the lung where gas exchange occurs between alveoli and capillaries. Its volume is the alveolar volume $V_e$. Both second and third compartments are ineffective for gas exchange and comprise the respiratory dead volume. Compartment two corresponds to the anatomic dead volume and compartment three represents the alveolar dead volume.

Three similar compartments can be considered from the blood side of the alveolar membranes. In the respiratory circulation, however, we do not talk of blood dead volume, but rather of blood shunting. The effect of blood shunting is to mix unaerated mixed venous blood with aerated arterial blood.

A carbon dioxide balance of the effective volume, or alveolar volume, gives

$$\dot{V}_{CO_2} = \dot{V}_{Ae} F_{AeCO_2} - \dot{V}_{Ai} F_{AeCO_2} \tag{4.2.60}$$

where $\dot{V}_{Ae} = \text{alveolar ventilation rate during exhalation, m}^3/\text{sec}$

$\dot{V}_{Ai} = \text{alveolar ventilation rate during inhalation, m}^3/\text{sec}$

If $F_{AeCO_2} = 0$, then

$$\dot{V}_{CO_2} = \frac{\dot{V}_{Ae} p_{AeCO_2}}{P_B - p_{H_2O}} \tag{4.2.61}$$

where $p_{AeCO_2} = \text{mean CO}_2 \text{ partial pressure of effective alveolar space, N/m}^2$

$P_B = \text{total barometric pressure} = 101 \text{ kN/m}^2$

$p_{H_2O} = \text{partial pressure of water vapor at the temperature of the respiratory system} = 6280 \text{ N/m}^2$

and, as discussed previously, alveolar and arterial CO$_2$ partial pressures can be considered to be the same values:

$$p_{AeCO_2} = p_{aCO_2} \tag{4.2.62}$$

where $p_{aCO_2} = \text{arterial CO}_2 \text{ partial pressure, N/m}^2$