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Respiratory System

7.1 Respiration Anatomy

Lungs • Conducting Airways • Alveoli • Pulmonary Circulation • Respiratory Muscles

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As functioning units, the lung and heart are usually considered a single complex organ, but because these organs contain essentially two compartments — one for blood and one for air — they are usually separated in terms of the tests conducted to evaluate heart or pulmonary function. This chapter focuses on some of the physiologic concepts responsible for normal function and specific measures of the lung’s ability to supply tissue cells with enough oxygen while removing excess carbon dioxide.

7.1 Respiration Anatomy

The respiratory system consists of the lungs, conducting airways, pulmonary vasculature, respiratory muscles, and surrounding tissues and structures (Fig. 7.1). Each plays an important role in influencing 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, leaving room for the heart. The right lung accounts for 55% of total gas volume and the left lung for 45%. Lung tissue is spongy because of the very small (200 to 300 \times 10^{-6} \text{ m}) gas-filled cavities called alveoli, which are the ultimate structures for gas exchange. There are 250 million to 350 million alveoli in the adult lung, with a total alveolar surface area of 50 to 100 m² depending on the degree of lung inflation [Johnson, 1991].

Conducting Airways

Air is transported from the atmosphere to the alveoli beginning with the oral and nasal cavities, through the pharynx (in the throat), past the glottal opening, and into the trachea or windpipe. Conduction of air begins at the larynx, or voice box, at the entrance to the trachea, which is a fibromuscular tube 10 to 12 cm in length and 1.4 to 2.0 cm in diameter [Kline, 1976]. 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. 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. Smooth muscle is present throughout the respiratory bronchiolus and alveolar ducts but is absent in the last alveolar duct, which terminates in one to several alveoli. 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 bronchioli, which further subdivide, and so on, until finally reaching the alveolar level. Table 7.1 provides a description and dimensions of the airways of adult humans. A model of the geometric arrangement of these air passages is presented in Fig. 7.2. It will be noted that 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.

Movement of gases in the respiratory airways occurs mainly by bulk flow (convection) throughout the region from the mouth to the nose to the fifteenth generation. Beyond the fifteenth generation, gas diffusion is relatively more important. 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 into 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 with animals with low levels of oxygen consumption.

Alveoli
Alveoli are the structures through which gases diffuse to and from the body. To ensure gas exchange occurs efficiently, alveolar walls are extremely thin. For example, the total tissue thickness between the inside of the alveolus to pulmonary capillary blood plasma is only about $0.4 \times 10^{-6}$ m. Consequently, the principal barrier to diffusion occurs at the plasma and red blood cell level, not at the alveolar membrane [Ruch and Patton, 1966].
### TABLE 7.1 Classification and Approximate Dimensions of Airways of Adult Human Lung (Inflated to about 3/4 of TLC)*

<table>
<thead>
<tr>
<th>Common Name</th>
<th>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 165 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 bronchial 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. Pulmonary capillaries are in the septae that form the alveoli.</td>
</tr>
<tr>
<td>Alveoli</td>
<td>24</td>
<td>300,000,000</td>
<td>0.2</td>
<td></td>
<td></td>
<td></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.

Source: Used with permission from Staub [1963] and Weibel [1963]; adapted by Comroe [1965].
Molecular diffusion within the alveolar volume is responsible for mixing of the enclosed gas. Due to small alveolar dimensions, complete mixing probably occurs in less than 10 ms, fast enough that alveolar mixing time does not limit gaseous diffusion to or from the blood [Astrand and Rodahl, 1970].

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. It is the present view that surfactant acts like a detergent, changing the stress-strain relationship of the alveolar wall and thereby stabilizing the lung [Johnson, 1991].

Pulmonary Circulation

There is no true pulmonary analogue to the systemic arterioles, since the pulmonary circulation occurs under relatively low pressure [West, 1977]. Pulmonary blood vessels, especially capillaries and venules, are very thin walled and flexible. Unlike systemic capillaries, pulmonary capillaries increase in diameter, and pulmonary capillaries within alveolar walls separate adjacent alveoli with increases in blood pressure or decreases in alveolar pressure. Flow, therefore, is significantly influenced by elastic deformation. Although pulmonary circulation is largely unaffected by neural and chemical control, it does respond promptly to hypoxia.

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

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

Since 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 is computed as

\[ t = \frac{V_c}{\dot{V}_c} \]

where
- \( t \) = blood transmit time, s
- \( V_c \) = capillary blood volume, m³
- \( \dot{V}_c \) = total capillary blood flow = cardiac output, m³/s

and is somewhat less than 1 s, while during exercise it may be only 500 ms or even less.

**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, the muscular mass accounting for 75% of the expansion of the chest cavity, is attached around the bottom of the thoracic cage, arches over the liver, and moves downward like a piston when it contracts. 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 are important in the maintenance of thoracic shape during breathing. (For details, see Ruch and Patton [1966] and Johnson [1991]).

Quiet expiration is usually considered to be passive; i.e., pressure to force air from the lungs comes from elastic expansion of the lungs and chest wall. 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 is accomplished by reduced intrathoracic pressure (which tends toward negative values) during inspiration.

Viewing the lungs as an entire unit, one can consider the lungs to be elastic sacs within an air-tight barrel — the thorax — which is bounded by the ribs and the diaphragm. Any movement of these two boundaries alters the volume of the lungs. The normal breathing cycle in humans is accomplished by the active contraction of the inspiratory muscles, which enlarges the thorax. This enlargement lowers intrathoracic and interpleural pressure even further, pulls on the lungs, and enlarges the alveoli, alveolar ducts, and bronchioli, expanding the alveolar gas and decreasing its pressure below atmospheric. As a result, air at atmospheric pressure flows easily into the nose, mouth, and trachea.

**7.2 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 anatomic level under consideration, gas movement is determined mainly by diffusion or convection.

Without the thoracic musculature and rib cage, as mentioned above, 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 \( V_{RS} \), then, is that volume occupied by the lungs with glottis open and muscles relaxed.

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). Residual volume is the amount of gas remaining in the lungs at the end of maximal expiration.

Tidal volume $V_T$ is normally considered to be the volume of air entering the nose and mouth with each breath. Alveolar ventilation volume, the volume of fresh air that enters the alveoli during each breath, is always less than tidal volume. The extent of this difference in volume depends primarily on the anatomic dead space, the 150- to 160-ml internal volume of the conducting airway passages. The term dead is quite appropriate, since it represents wasted respiratory effort; i.e., no significant gas exchange occurs across the thick walls of the trachea, bronchi, and bronchiolus. Since normal tidal volume at rest is usually about 500 ml of air per breath, one can easily calculate that because of the presence of this dead space, about 340 to 350 ml of fresh air actually penetrates the alveoli and becomes involved in the gas exchange process. An additional 150 to 160 ml of stale air exhaled during the previous breath is also drawn into the alveoli.

The term volume is used for elemental differences of lung volume, whereas the term capacity is used for combination of lung volumes. Figure 7.3 illustrates the interrelationship between each of the following lung volumes and capacities:

1. **Total lung capacity** (TLC): The amount of gas contained in the lung at the end of maximal inspiration.
2. **Forced vital capacity** (FVC): The maximal volume of gas that can be forcefully expelled after maximal inspiration.
3. **Inspiratory capacity** (IC): The maximal volume of gas that can be inspired from the resting expiratory level.
4. **Functional residual capacity** (FRC): The volume of gas remaining after normal expiration. It will be noted that functional residual capacity (FRC) is the same as the resting volume. There is a small difference, however, between resting volume and FRC because FRC is measured while the patient breathes, whereas resting volume is measured with no breathing. FRC is properly defined only at end-expiration at rest and not during exercise.

![Lung capacities and lung volumes](image-url)
These volumes and specific capacities, represented in Fig. 7.3, have led to the development of specific
tests (that will be discussed below) to quantify the status of the pulmonary system. Typical values for
these volumes and capacities are provided in Table 7.2.

### 7.3 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 atrium by blood flow. This three-step process involves (1) alveolar
ventilation, (2) the process of diffusion, and (3) ventilatory perfusion, which involves pulmonary blood
flow. Obviously, an alveolus that is ventilated but not perfused cannot exchange gas. Similarly, a perfused
alveolus that is not properly ventilated cannot exchange gas. The most efficient gas exchange occurs when
ventilation and perfusion are matched.

There is a wide range of ventilation-to-perfusion ratios that naturally occur in various regions of the
lung [Johnson, 1991]. Blood flow is somewhat 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 with 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 7.3). 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 intralveolar pressure exceeds intracapillary blood pressure during diastole. Mean blood
flow is not affected by heart rate [West, 1977], but the 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 pressures increases from
2670 N/m² (20 mmHg) at rest to 4670 N/m² (35 mmHg) during moderate exercise to 6670 N/m²
(50 mmHg) at maximal work [Astrand and Rodahl, 1970].

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### Table 7.2 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</td>
</tr>
<tr>
<td>Residual volume (RV)</td>
<td>$1.2 \times 10^3$ m³</td>
</tr>
<tr>
<td>Vital capacity (VC)</td>
<td>$4.8 \times 10^3$ m³</td>
</tr>
<tr>
<td>Inspiratory reserve volume (IRV)</td>
<td>$3.6 \times 10^3$ m³</td>
</tr>
<tr>
<td>Expiratory reserve volume (ERV)</td>
<td>$1.2 \times 10^3$ m³</td>
</tr>
<tr>
<td>Functional residual capacity (FRC)</td>
<td>$2.4 \times 10^3$ m³</td>
</tr>
<tr>
<td>Anatomic dead volume ($V_D$)</td>
<td>$1.5 \times 10^4$ m³</td>
</tr>
<tr>
<td>Upper airways volume</td>
<td>$8.0 \times 10^2$ m³</td>
</tr>
<tr>
<td>Lower airways volume</td>
<td>$7.0 \times 10^3$ m³</td>
</tr>
<tr>
<td>Physiologic dead volume ($V_{Dp}$)</td>
<td>$1.8 \times 10^4$ m³</td>
</tr>
<tr>
<td>Minute volume ($V_t$) at rest</td>
<td>$1.0 \times 10^4$ m³</td>
</tr>
<tr>
<td>Respiratory period ($T$) at rest</td>
<td>4 s</td>
</tr>
<tr>
<td>Tidal volume ($V_t$) at rest</td>
<td>$4.0 \times 10^4$ m³</td>
</tr>
<tr>
<td>Alveolar ventilation volume ($V_a$) at rest</td>
<td>$2.5 \times 10^4$ m³</td>
</tr>
<tr>
<td>Minute volume during heavy exercise</td>
<td>$1.7 \times 10^4$ m³</td>
</tr>
<tr>
<td>Respiratory period during heavy exercise</td>
<td>1.2 s</td>
</tr>
<tr>
<td>Tidal volume during heavy exercise</td>
<td>$2.0 \times 10^4$ m³</td>
</tr>
<tr>
<td>Alveolar ventilation volume during exercise</td>
<td>$1.8 \times 10^4$ m³</td>
</tr>
</tbody>
</table>

*Source: Adapted and used with permission from Forster et al [1986].*
The primary purpose of the respiratory system is gas exchange. In the gas-exchange process, gas must diffuse through the alveolar space, across tissue, and through plasma into the red blood cell, where it finally chemically joins to hemoglobin. A similar process occurs for carbon dioxide elimination.

As long as intermolecular interactions are small, most gases of physiologic significance can be considered to obey the ideal gas law:

\[ pV = nRT \]

where

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

The ideal gas law can be applied without error up to atmospheric pressure; it can be applied to a mixture of gases, such as air, or to its constituents, such as oxygen or 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.

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

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

where \( p_i \) = partial pressure of the \( i \)th constituent, \( \text{N/m}^2 \)

\( N \) = total number of constituents

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

### TABLE 7.3 Ventilation-to-Perfusion Ratios from the Top to Bottom of the Lung of Normal Man in the Sitting Position

<table>
<thead>
<tr>
<th>Percent Lung Volume, %</th>
<th>Alveolar Ventilation Rate, cm³/s</th>
<th>Perfusion Rate, cm³/s</th>
<th>Ventilation-to-Perfusion Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Top</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>Bottom</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].
so that

\[
\frac{PV}{nRT} = \frac{nR}{nRT}
\]

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:

\[
\frac{V_i}{V} = \frac{nR_i}{nR} = \frac{R_i}{R}
\]

Thus

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

where \( V/V \) is the volume fraction of a constituent in air and is therefore dimensionless. Table 7.4 provides individual gas constants, as well as volume fractions, of constituent gases of air.

Gas pressures and volumes can be measured for many different temperature and humidity conditions. Three of these are body temperature and pressure, saturated (BTPS); ambient temperature and pressure (ATP); and standard temperature and pressure, dry (STPD). To calculate constituent partial pressures at STPD, total pressure is taken as barometric pressure minus vapor pressure of water in the atmosphere:

\[
P_i = \left(\frac{V_i}{V}\right) \left(p - p_{H_2O}\right)
\]

where \( p \) = total pressure, kN/m²

\( p_{H_2O} \) = vapor pressure of water in atmosphere, kN/m²

and \( V/V \) as a ratio does not change in the conversion process.
Gas volume at STPD is converted from ambient condition volume as

\[ V_i = V_{\text{amb}} \left[ \frac{273}{273 + \Theta} \right] \left[ \frac{p - p_{H_2O}}{101.3} \right] \]

where

- \( V_i \) = volume of gas \( i \) corrected to STPD, m³
- \( V_{\text{amb}} \) = volume of gas \( i \) at ambient temperature and pressure, m³
- \( \Theta \) = ambient temperature, °C
- \( p \) = ambient total pressure, kN/m²
- \( p_{H_2O} \) = vapor pressure of water in the air, kN/m²

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

\[ V_i = V_{\text{amb}} \left[ \frac{310}{273 + \Theta} \right] \left[ \frac{p - p_{H_2O}}{p - 6.28} \right] \]

Table 7.5 provides gas partial pressure throughout the respiratory and circulatory systems.

### 7.5 Pulmonary Mechanics

The respiratory system exhibits properties of resistance, compliance, and inertance analogous to the electrical properties of resistance, capacitance, and inductance. Of these, inertance is generally considered to be of less importance than the other two properties.

Resistance is the ratio of pressure to flow:

\[ R = \frac{p}{V} \]

where

- \( R \) = resistance, N × s/m²
- \( P \) = pressure, N/m²
- \( V \) = volume flow rate, m³/s

Resistance can be found in the conducting airways, in the lung tissue, and in the tissues of the chest wall. Airways exhalation resistance is usually higher than airways inhalation resistance because the surrounding lung tissue pulls the smaller, more distensible airways open when the lung is being inflated. Thus airways inhalation resistance is somewhat dependent on lung volume, and airways exhalation resistance can be very lung volume–dependent [Johnson, 1991]. Respiratory tissue resistance varies with frequency, lung
volume, and volume history. Tissue resistance is relatively small at high frequencies but increases greatly at low frequencies, nearly proportional to $1/f$. Tissue resistance often exceeds airway resistance below 2 Hz. Lung tissue resistance also increases with decreasing volume amplitude [Stamenovic et al., 1990].

Compliance is the ratio of lung volume to lung pressure:

$$C = \frac{V}{p}$$

where $C =$ compliance, $m^3/N$,  
$V =$ lung volume/$m^3$  
$P =$ pressure, $N/m^2$

As the lung is stretched, it acts as an expanded balloon that tends to push air out and return to its normal size. The static pressure-volume relationship is nonlinear, exhibiting decreased static compliance at the extremes of lung volume [Johnson, 1991]. As with tissue resistance, dynamic tissue compliance does not remain constant during breathing. Dynamic compliance tends to increase with increasing volume and decrease with increasing frequency [Stamenovic et al., 1990].

Two separate approaches can be used to model lung tissue mechanics. The traditional approach places a linear viscoelastic system in parallel with a plastoelastic system. A linear viscoelastic system consists of ideal resistive and compliant elements and can exhibit the frequency-dependence of respiratory tissue. A plastoelastic system consists of dry-friction elements and compliant elements and can exhibit the volume dependence of respiratory tissue [Hildebrandt, 1970]. An alternate approach is to utilize a nonlinear viscoelastic system that can characterize both the frequency dependence and the volume dependence of respiratory tissue [Suki and Bates, 1991].

Lung tissue hysteresivity relates resistance and compliance:

$$wR = \frac{\eta}{C_{dyn}}$$

where $\omega =$ frequency, radians/s  
$R =$ resistance, $N \times s/m^2$  
$\eta =$ hysteresivity, unitless  
$C_{dyn} =$ dynamic compliance, $m^5/n$

Hysteresivity, analogous to the structural damping coefficient used in solid mechanics, is an empirical parameter arising from the assumption that resistance and compliance are related at the microstructural level. Hysteresivity is independent of frequency and volume. Typical values range from 0.1 to 0.3 [Fredberg and Stamenovic, 1989].

### 7.6 Respiratory Control

Control of respiration occurs in many different cerebral structures [Johnson, 1991] and regulates many things [Hornbein, 1981]. Respiration must be controlled to produce the respiratory rhythm, ensure adequate gas exchange, protect against inhalation of poisonous substances, assist in maintenance of body pH, remove irritations, and minimize energy cost. Respiratory control is more complex than cardiac control for at least three reasons:

1. Airways airflow occurs in both directions.
2. The respiratory system interfaces directly with the environment outside the body.
3. Parts of the respiratory system are used for other functions, such as swallowing and speaking.

As a result, respiratory muscular action must be exquisitely coordinated; it must be prepared to protect itself against environmental onslaught, and breathing must be temporarily suspended on demand.
All control systems require sensors, controllers, and effectors. **Figure 7.4** presents the general scheme for respiratory control. There are mechanoreceptors throughout the respiratory system. For example, nasal receptors are important in sneezing, apnea (cessation of breathing), bronchodilation, bronchoconstriction, and the secretion of mucus. Laryngeal receptors are important in coughing, apnea, swallowing, bronchoconstriction, airway mucus secretion, and laryngeal constriction. Tracheobronchial receptors are important in coughing, pulmonary hypertension, bronchoconstriction, laryngeal constriction, and mucus production. Other mechanoreceptors are important in the generation of the respiratory pattern and are involved with respiratory sensation.

Respiratory chemoreceptors exist peripherally in the aortic arch and carotid bodies and centrally in the ventral medulla oblongata of the brain. These receptors are sensitive to partial pressures of CO₂ and O₂ and to blood pH.

The respiratory controller is located in several places in the brain. Each location appears to have its own function. Unlike the heart, the basic respiratory rhythm is not generated within the lungs but rather in the brain and is transmitted to the respiratory muscles by the phrenic nerve.

Effector organs are mainly the respiratory muscles, as described previously. Other effectors are muscles located in the airways and tissues for mucus secretion. Control of respiration appears to be based on two criteria: (1) removal of excess CO₂ and (2) minimization of energy expenditure. It is not the lack of oxygen that stimulates respiration but increased CO₂ partial pressure that acts as a powerful respiratory stimulus. Because of the buffering action of blood bicarbonate, blood pH usually falls as more CO₂ is produced in the working muscles. Lower blood pH also stimulates respiration.

A number of respiratory adjustments are made to reduce energy expenditure during exercise: Respiration rate increases, the ratio of inhalation time to exhalation time decreases, respiratory flow waveshapes become more trapezoidal, and expiratory reserve volume decreases. Other adjustments to reduce energy expenditure have been theorized but not proven [Johnson, 1991].

### 7.7 The Pulmonary Function Laboratory

The purpose of a pulmonary function laboratory is to obtain clinically useful data from patients with respiratory dysfunction. The pulmonary function tests (PFTs) within this laboratory fulfill a variety of functions. They permit (1) quantification of a patient’s breathing deficiency, (2) diagnosis of different types of pulmonary diseases, (3) evaluation of a patient’s response to therapy, and (4) preoperative screening to determine whether the presence of lung disease increases the risk of surgery.
Although PFTs can provide important information about a patient’s condition, the limitations of these tests must be considered. First, they are nonspecific in that they cannot determine which portion of the lungs is diseased, only that the disease is present. Second, PFTs must be considered along with the medical history, physical examination, x-ray examination, and other diagnostic procedures to permit a complete evaluation. Finally, the major drawback to some PFTs is that they require full patient cooperation and for this reason cannot be conducted on critically ill patients. Consider some of the most widely used PFTs: spirometry, body plethysmography, and diffusing capacity.

**Spirometry**

The simplest PFT is the spirometry maneuver. In this test, the patient inhales to total lung capacity (TLC) and exhales forcefully to residual volume. The patient exhales into a displacement bell chamber that sits on a water seal. As the bell rises, a pen coupled to the bell chamber inscribes a tracing on a rotating drum. The spirometer offers very little resistance to breathing; therefore, the shape of the spirometry curve (Fig. 7.5) is purely a function of the patient’s lung compliance, chest compliance, and airway resistance. At high lung volumes, a rise in intrapleural pressure results in greater expiratory flows. However, at intermediate and low lung volumes, the expiratory flow is independent of effort after a certain intrapleural pressure is reached.

Measurements made from the spirometry curve can determine the degree of a patient’s ventilatory obstruction. Forced vital capacity (FVC), forced expiratory volumes (FEV), and forced expiratory flows (FEF) can be determined. The FEV indicates the volume that has been exhaled from TLC for a particular time interval. For example, FEV\(_{0.5}\) is the volume exhaled during the first half-second of expiration, and FEV\(_{1.0}\) is the volume exhaled during the first second of expiration; these are graphically represented in Fig. 7.5. Note that the more severe the ventilatory obstruction, the lower are the timed volumes (FEV\(_{0.5}\) and FEV\(_{1.0}\)). The FEF is a measure of the average flow (volume/time) over specified portions of the spirometry curve and is represented by the slope of a straight line drawn between volume levels. The average flow over the first quarter of the forced expiration is the FEF\(_{25-75\%}\), whereas the average flow over the middle 50% of the FVC is the FEF\(_{25-75\%}\). These values are obtained directly from the spirometry curves. The less steep curves of obstructed patients would result in lower values of FEF\(_{25-75\%}\) and FEF\(_{25-75\%}\) compared with normal values, which are predicted on the basis of the patient’s sex, age, and height.
Equations for normal values are available from statistical analysis of data obtained from a normal population. Test results are then interpreted as a percentage of normal.

Another way of presenting a spirometry curve is as a flow-volume curve. Figure 7.6 represents a typical flow-volume curve. The expiratory flow is plotted against the exhaled volume, indicating the maximum flow that may be reached at each degree of lung inflation. Since there is no time axis, a time must mark the FEV$_{0.5}$ and FEV$_{1.0}$ on the tracing. To obtain these flow-volume curves in the laboratory, the patient usually exhales through a pneumotach. The most widely used pneumotach measures a pressure drop across a flow-resistive element. The resistance to flow is constant over the measuring range of the device; therefore, the pressure drop is proportional to the flow through the tube. This signal, which is indicative of flow, is then integrated to determine the volume of gas that has passed through the tube.

Another type of pneumotach is the heated-element type. In this device, a small heated mass responds to airflow by cooling. As the element cools, a greater current is necessary to maintain a constant temperature. This current is proportional to the airflow through the tube. Again, to determine the volume that has passed through the tube, the flow signal is integrated.

The flow-volume loop in Fig. 7.7 is a dramatic representation displaying inspiratory and expiratory curves for both normal breathing and maximal breathing. The result is a graphic representation of the patient’s reserve capacity in relation to normal breathing. For example, the normal patient’s tidal breathing loop is small compared with the patient’s maximum breathing loop. During these times of stress, this tidal breathing loop can be increased to the boundaries of the outer ventilatory loop. This increase in ventilation provides the greater gas exchange needed during the stressful situation. Compare this condition with that of the patient with obstructive lung disease. Not only is the tidal breathing loop larger than normal, but the maximal breathing loop is smaller than normal. The result is a decreased ventilatory reserve, limiting the individual’s ability to move air in and out of the lungs. As the disease progresses, the outer loop becomes smaller, and the inner loop becomes larger.

The primary use of spirometry is in detection of obstructive lung disease that results from increased resistance to flow through the airways. This can occur in several ways:

1. Deterioration of the structure of the smaller airways that results in early airways closure.
2. Decreased airway diameters caused by bronchospasm or the presence of secretions increases the airway’s resistance to airflow.
3. Partial blockage of a large airway by a tumor decreases airway diameter and causes turbulent flow.
Spirometry has its limitations, however. It can measure only ventilated volumes. It cannot measure lung capacities that contain the residual volume. Measurements of TLC, FRC, and RV have diagnostic value in defining lung overdistension or restrictive pulmonary disease; the body plethysmograph can determine these absolute lung volumes.

**Body Plethysmography**

In a typical plethysmograph, the patient is put in an airtight enclosure and breathes through a pneumotach. The flow signal through the pneumotach is integrated and recorded as tidal breathing. At the end of a normal expiration (at FRC), an electronically operated shutter occludes the tube through which the patient is breathing. At this time the patient pants lightly against the occluded airway. Since there is no flow, pressure measured at the mouth must equal alveolar pressure. But movements of the chest that compress gas in the lung simultaneously rarify the air in the plethysmograph, and vice versa. The pressure change in the plethysmograph can be used to calculate the volume change in the plethysmograph, which is the same as the volume change in the chest. This leads directly to determination of FRC.

At the same time, alveolar pressure can be correlated to plethysmographic pressure. Therefore, when the shutter is again opened and flow rate is measured, airway resistance can be obtained as the ratio of alveolar pressure (obtainable from plethysmographic pressure) to flow rate [Carr and Brown, 1993]. Airway resistance is usually measured during panting, at a nominal lung volume of FRC and flow rate of ±1 liter/s.

Airway resistance during inspiration is increased in patients with asthma, bronchitis, and upper respiratory tract infections. Expiratory resistance is elevated in patients with emphysema, since the causes of increased expiratory airway resistance are decreased driving pressures and the airway collapse. Airway resistance also may be used to determine the response of obstructed patients to bronchodilator medications.

**Diffusing Capacity**

So far the mechanical components of airflow through the lungs have been discussed. Another important parameter is the diffusing capacity of the lung, the rate at which oxygen or carbon dioxide travel from the alveoli to the blood (or vice versa for carbon dioxide) in the pulmonary capillaries. Diffusion of gas across a barrier is directly related to the surface area of the barrier and inversely related to the thickness. Also, diffusion is directly proportional to the solubility of the gas in the barrier material and inversely related to the molecular weight of the gas.
Lung diffusing capacity (DL) is usually determined for carbon monoxide but can be related to oxygen diffusion. The popular method of measuring carbon monoxide diffusion utilizes a rebreathing technique in which the patient rebreathes rapidly in and out of a bag for approximately 30 s. Figure 7.8 illustrates the test apparatus. The patient begins breathing from a bag containing a known volume of gas consisting of 0.3% to 0.5 carbon monoxide made with heavy oxygen, 0.3% to 0.5% acetylene, 5% helium, 21% oxygen, and a balance of nitrogen. As the patient rebreathes the gas mixture in the bag, a modified mass spectrometer continuously analyzes it during both inspiration and expiration. During this rebreathing procedure, the carbon monoxide disappears from the patient-bag system; the rate at which this occurs is a function of the lung diffusing capacity.

The helium is inert and insoluble in lung tissue and blood and equilibrates quickly in unobstructed patients, indicating the dilution level of the test gas. Acetylene, on the other hand, is soluble in blood and is used to determine the blood flow through the pulmonary capillaries. Carbon monoxide is bound very tightly to hemoglobin and is used to obtain diffusing capacity at a constant pressure gradient across the alveolar-capillary membrane.

Decreased lung diffusing capacity can occur from the thickening of the alveolar membrane or the capillary membrane as well as the presence of interstitial fluid from edema. All these abnormalities increase the barrier thickness and cause a decrease in diffusing capacity. In addition, a characteristic of specific lung diseases is impaired lung diffusing capacity. For example, fibrotic lung tissue exhibits a decreased permeability to gas transfer, whereas pulmonary emphysema results in the loss of diffusion surface area.

**Defining Terms**

**Alveoli:** Respiratory airway terminals where most gas exchange with the pulmonary circulation takes place.

**Diffusion:** The process whereby a material moves from a region of higher concentration to a region of lower concentration.

**BTPS:** Body temperature (37°C) and standard pressure (1 atm), saturated (6.28 kN/m²).
Chemoreceptors: Neural receptors sensitive to chemicals such as gas partial pressures.

Dead space: The portion of the respiratory system that does not take part in gas exchange with the blood.

Expiration: The breathing process whereby air is expelled from the mouth and nose. Also called exhalation.

Functional residual capacity: The lung volume at rest without breathing.

Inspiration: The breathing process whereby air is taken into the mouth and nose. Also called inhalation.

Mass spectrometer: A device that identifies relative concentrations of gases by means of mass-to-charge ratios of gas ions.

Mechanoreceptors: Neural receptors sensitive to mechanical inputs such as stretch, pressure, irritants, etc.

Partial pressure: The pressure that a gas would exert if it were the only constituent.

Perfusion: Blood flow to the lungs.

Plethysmography: Any measuring technique that depends on a volume change.

Pleura: The membrane surrounding the lung.

Pneumotach: A measuring device for airflow.

Pulmonary circulation: Blood flow from the right cardiac ventricle that perfuses the lung and is in intimate contact with alveolar membranes for effective gas exchange.

STPD: Standard temperature (0°C) and pressure (1 atm), dry (moisture removed).

Ventilation: Airflow to the lungs.

References

Additional References