4.1 ANATOMY

4.1.1 General
As shown in Fig. 4.1, the pulmonary system consists of two lungs; each lung is conical in shape, with an inferior border (or base) that is concave as it overlies the diaphragm and abdominal structures and a superior border (or apex) that is convex and extends above the first rib. The anterior, lateral, and posterior lung surfaces are adjacent to the rib cage, while the medial surface is adjacent to the mediastinum, which contains the heart, great vessels, and esophagus. All of the lung surface is covered by the visceral pleural membrane, while the inside of the chest wall, mediastinum, and diaphragm are covered by the parietal pleural membrane. The two pleural membranes are separated by a thin liquid film (~20 to 40 µm thick) called the pleural fluid which occupies the pleural space, Fig. 4.1. This fluid lubricates the sliding motion between the lung and chest wall, and its pressure distribution determines lung inflation and deflation. Because the air-filled lung is surrounded by the pleural liquid, it experiences a buoyancy force that contributes to the overall force including lung weight and fluid pressures.¹⁷

4.1.2 Airway Divisions
The right main bronchus branches from the end of the trachea to the right lung, while the left main bronchus branches to the left. This division of a “parent” airway into two “daughter” airways is called a bifurcation. Each level of branching is called a generation and is given an integer value $n$, according to the Weibel symmetric model³⁵ shown in Table 4.1. The trachea is designated as $n = 0$, the main bronchi, $n = 1$, etc. For a symmetrically bifurcating geometry, then, there would be $2^n$ airways at each generation level. Generations $0 \leq n \leq 16$ constitute the conducting zone (trachea to terminal
bronchiole) whose airways have no alveoli and, hence, do not participate in gas exchange with the pulmonary blood circulation. Each terminal bronchiole enters an acinus or respiratory zone unit for $17 \leq n \leq 23$; see Fig. 4.2. The respiratory bronchioles occupy generations $17 \leq n \leq 19$ and are tubes with partially alveolated surfaces. Generations $20 \leq n \leq 22$ are the alveolar ducts, tubes with totally alveolated surfaces. The alveoli are polyhedral in shape, but, viewed as nearly spherical caps, they each have a diameter of $\sim200 \, \mu m$ at $3/4$ inflation.

4.1.3 Pulmonary Circulation

The pulmonary circulation consists of mixed venous blood entering the pulmonary artery from the right ventricle of the heart. After passing through the pulmonary capillary bed, the blood returns to the left atrium via the pulmonary vein. Flow through portions of the capillary bed that are in ventilated alveolar regions of the lung will discharge $CO_2$ and absorb $O_2$. Flows that go to unventilated alveoli will not exchange gas and are called the shunt flow. Typical values of pulmonary arterial blood pressures are 20 mmHg systolic/12 mmHg diastolic, about one-sixth the systemic vascular pressures. Because the pulmonary system is a low-pressure system, the vessel walls are much thinner than their systemic counterparts. The pulmonary arterial and venous systems have accompanying divisions, forming a triad with each airway division. The pulmonary capillaries, with a vessel diameter of $\sim6 \, \mu m$, form a multivessel mesh surrounding each alveolus and are contained in the alveolar walls. The blood-gas barrier is composed of (starting from the gas side): the alveolar liquid lining, alveolar epithelial cell, basement membrane, and capillary endothelial cell. These combined layers sum to approximately 0.5 to 1.0 $\mu m$, in thickness. This is the distance gas must diffuse to enter or leave the blood under normal conditions.

The conducting airways are fed by a second blood supply, the bronchial circulation, which comes from the systemic circulation via the bronchial arteries. Blood returns via the bronchial veins, which empty partly to the systemic veins and partly to the pulmonary veins. The latter case is a circuit that bypasses the lungs entirely and makes the systemic cardiac output slightly larger than the pulmonary cardiac output or lung perfusion $Q$. 

---

**FIGURE 4.1** Sketch of the pulmonary system. **FIGURE 4.2** The respiratory zone of the airway network.
4.1.4 Lymphatics and Nerves

To maintain homeostasis, the continuous transudation of fluid and solutes from the pulmonary capillary bed into the surrounding interstitium and alveolar space is balanced by lymphatic drainage out of the lung. The lymphatic flow is directed toward the hilum from the pleural surfaces. From lymph nodes in the hilum, the lymph travels to the paratracheal nodes and then eventually into the venous system via the thoracic duct. The lung has nerve fibers from both the vagal nerves (parasympathetic) and the sympathetic nerves. The efferent fibers go to the bronchial musculature and the afferents come from the bronchi and alveoli.

4.2 MECHANICS OF BREATHING

4.2.1 Chest Wall

The rib cage and its muscles form the chest wall, which protects the vital thoracic organs while keeping the lungs inflated. During inspiration, the ribs swing on an axis defined by their articulation with the vertebrae, dashed lines in Fig. 4.3. The result is that upper ribs, such as rib 1, swing forward and up, like a pump handle, increasing the anterior-posterior diameter of the upper chest wall. However, lower ribs swing primarily laterally, like a bucket handle pinned at the spine and sternum. Their motion increases the lateral diameter of the thorax.

![Fig. 4.3 Rib motion during inspiration.](image-url)

4.2.2 Muscles of Inspiration and Expiration

The major muscles involved in inspiration and expiration include the diaphragm and the intercostal muscles. During inspiration, the diaphragm contracts, pulling the inferior lung surface (via the pleural...
4.4 MECHANICS OF THE HUMAN BODY

Fluid) downward, while the external intercostal muscles contract, lifting the ribs; see Fig. 4.4. Expiration is primarily a passive event; the elastic structures simply return to their original, less-stretched, state as the diaphragm and external intercostals relax. At a normal breathing rate of 15 breaths per minute (bpm), inspiration may occupy one-third of the 4-second breathing cycle, while passive expiration occupies the rest, an inspiratory to expiratory time ratio of 1:2. Forceful expiration is accomplished by contraction of the internal intercostal muscles and the abdominal wall muscles that squeeze the abdominal contents hard enough to push them upward. The normal inspiratory to expiratory time ratio can increase with forceful expiration, as may occur during exercise, or decrease with prolonged expiration, as one finds in obstructive airways disease like asthma or emphysema.

![FIGURE 4.4 Diaphragm and abdominal muscles during inspiration and expiration.](image)

4.3 VENTILATION

4.3.1 Lung Volumes

There is common terminology for different lung volume measurements, as shown in Fig. 4.5. The maximum volume is total lung capacity (TLC), which can be measured by dilution of a known amount of inspired helium gas whose insolubility in tissue and blood prevents it from leaving the air spaces. The minimum is residual volume (RV). Normal ventilation occurs within an intermediate range and has a local minimum called functional residual capacity (FRC). The volume swing from FRC to the end of inspiration is the tidal volume $V_T$. The vital capacity (VC) is defined by $VC = TLC - RV$. Within the lung there are also important volume concepts. The anatomic dead space $V_D$ is the summed volume of all conducting airways, measured by the Fowler method, while the physiologic dead space is that portion of the

![FIGURE 4.5 Lung volumes and definitions.](image)
lung that does not transfer CO₂ from the capillaries, measured by the Bohr method. While the methods used to determine these two values are different, normally they yield essentially the same result, approximately 150 cm³ in an adult male. In some disease states, however, the Bohr method may be affected by abnormalities of the ventilation-perfusion relationship. The alveolar volume \( V_A \), where gas exchange occurs, is the lung volume minus the dead space.

### 4.3.2 Air Flow and Resistance

A typical \( V_T \) of 500 cm³ at a rate of 15 bpm yields a total ventilation \( \dot{V} \) of (0.5 liters × 15 breaths/min) = 7.5 liters/min. Assuming that air flows in the conducting airways like a plug, for each 500 cm³ breath inspired the tail 150 cm³ fills the dead space while the front 350 cm³ expands the alveoli, where it mixes with the alveolar gas previously retained at FRC. This makes the alveolar ventilation \( \dot{V}_A = (0.5 - 0.15) \) liters × 15 bpm = 5.25 liters/min. The plug flow assumption is not correct, of course, but for resting ventilation it is a useful simplification. It fails, for example, in high-frequency ventilation, where the mechanical ventilator can operate at 15 Hz with \( V_T \leq 5 \) cm³; i.e., the tidal volumes can be smaller than the dead space. Adequate gas exchange occurs under these circumstances, because of the Taylor dispersion mechanism, which is a coupling of curvilinear, axial velocity profiles with radial diffusion applied to a reversing flow. The properties of airway branching, axial curvature, and flexibility can modify the mechanism considerably.

The ventilatory flow rate \( \dot{V} \) results from the pressure boundary conditions imposed at the trachea and alveoli. In lung physiology, the flow details are often neglected and simply lumped into a resistance to air flow defined as the ratio of the overall pressure drop \( \Delta P \) to the flow rate; i.e., \( \Delta P / \dot{V} = R_{es} \). A typical value is \( R_{es} = 0.2 \) cmH₂O-s/L for resting breathing conditions. The appeal of defining airway resistance this way is its analogy to electrical circuit theory and Ohm’s law, and other elements such as capacitance (see compliance, below) and inertance may be added. The frictional pressure drop \( \Delta P_f \) is always positive, but its value depends on the flow regime in each airway generation. For fully developed, laminar tube flow (Poiseuille flow) \( \Delta P_F = (128 \mu L/d^4)\dot{V} \), where \( \mu \) is the fluid (gas) viscosity, \( d \) is the tube diameter, and \( L \) is the axial distance. This formula is helpful in understanding some of the general trends for \( R \), like its strong dependence on airway diameter, which can decrease in asthma. Airways are aerodynamically short tubes under many respiratory situations, i.e., not long enough for Poiseuille flow to develop. Then the viscous pressure drop is governed by energy dissipation in a thin boundary layer region near the airway wall where the velocity profile is curvilinear. For this entrance flow, \( \Delta P_F \sim \dot{V}^{7/4} \), so resistance now is flow dependent. The local Reynolds number is given by \( Re = u_d/v \), where \( v = 0.15 \) cm²/s is the kinematic viscosity of air. For \( Re \gg 2300 \), (see Table 4.1), the flow is turbulent and \( \Delta P_F \) in those airways has an even stronger dependence on ventilation, \( \Delta P_F \sim \dot{V}^{1/2} \) smooth wall, \( \sim \dot{V}^{5/4} \) rough wall. Expressing these three cases for a single tube (airway) in terms of the friction coefficient, \( C_F = \Delta P_F/\dot{V}^{1/2} \). The comparison is shown in Eq. (4.2):

\[
C_F = \begin{cases} 64 \frac{L}{d} Re^{-1} & \text{Poiseuille flow} \\ 6 \left( \frac{L}{d} \right)^{1/2} Re^{-1/2} & \text{entrance flow} \\ 0.32 \frac{L}{d} Re^{-1/4} & \text{turbulent flow smooth wall} \\ \frac{4}{3} \frac{k}{d} & \text{turbulent flow rough wall} 
\end{cases} \tag{4.2}
\]
where \( k \) depends on the wall roughness; a typical value is \( k = 0.04 \). Experiments of inspiratory flow with a multigeneration cast of the central airways\(^3\) show that Poiseuille effects dominate for \( 350 \leq \text{Re}_n \leq 500 \), entrance effects for \( 500 \leq \text{Re}_n \leq 4000 \), and rough-walled turbulent effects for \( 4000 \leq \text{Re}_n \leq 30,000 \), approximately. \( C_f \) tends to be higher during expiration than inspiration.

As shown from measurements in airway models\(^9\) or theories using modifications of the friction coefficients,\(^2\) the vast majority of the pressure drop across the entire lung occurs within the large airways, say \( 0 \leq n \leq 8 \). Thus clinical evaluation of total airway resistance can miss diseases of the small airways whose diameters are less than 2 mm, the so-called silent zone of the network. Pressure drop measurements and models are also important for the design of ventilators and other respiratory assist or therapeutic devices that interface with lung mechanics.

### 4.3.3 Gas Transport

Transport of \( \text{O}_2 \), \( \text{CO}_2 \), anesthetics, toxins, or any other soluble gas occurs by convection, diffusion, and their interplay. The ability of one gas species to diffuse through another is quantified by the molecular diffusivity \( D \) for the gas pair. For \( \text{O}_2 \) diffusing through air, the value of \( D \) is \( D_{\text{O}_2-\text{air}} = 0.22 \text{ cm}^2/\text{s} \) (at atmospheric pressure and 37°C), whereas for \( \text{CO}_2 \) the value is less, \( D_{\text{CO}_2-\text{air}} = 0.17 \text{ cm}^2/\text{s} \).

A characteristic time for diffusion to provide effective transport of a concentration front over a distance \( L \) is \( T_d = L^2/D \), where \( L \) can be the airway length \( L_n \). By contrast, a characteristic time for convective transport over the same distance is \( T_c = L/U \), where \( U = u_n \) is the average flow speed of the bulk gas mixture in an airway. The ratio of the two time scales tells us which mechanism, diffusion, or convection, may dominate (i.e., occur in the shortest time) in a given airway situation. This ratio is the Peclet number, \( \text{Pe} = T_d/T_c = UL/D \), where \( \text{Pe} \gg 1 \) indicates convection-dominated transport while \( \text{Pe} \ll 1 \) indicates diffusion-dominated transport. Table 4.1 shows how \( \text{Pe}_n \) for \( \text{O}_2 \) transport varies through the airway tree when \( \dot{V} = 500 \text{ cm}^3/\text{s} \). Convection dominates in the conducting airways, where negligible \( \text{O}_2 \) is lost, so the \( \text{O}_2 \) concentration in these airways on inspiration is essentially the ambient inspired level, normally \( P_{\text{Lo}} = 150 \text{ mmHg} \). At approximately generation 15, where \( \text{Pe} \) is close to unity and both convection and diffusion are important, the axial concentration gradient in \( \text{O}_2 \) develops over the next \( \sim 0.5 \text{ cm} \) in path length to reach the alveolar level (\( P_{\text{Aco}} = 100 \text{ mmHg} \)). \( \text{CO}_2 \) has the reverse gradient during inspiration from its alveolar level (\( P_{\text{Aco}} \) to the

### Table 4.1 Airway Geometry

<table>
<thead>
<tr>
<th>( n ) generation</th>
<th>Name</th>
<th>( 2^n ) number</th>
<th>( d_n ), diameter, cm</th>
<th>( L_n ), length, cm</th>
<th>( A_n ), total cross-sectional area, ( \text{cm}^2 )</th>
<th>( V_n ), volume of generation, ( \text{cm}^3 )</th>
<th>( X_n ), distance from carina, cm</th>
<th>( \text{Re}_n )</th>
<th>( \text{Pe}_n ) (( \text{O}_2 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Trachea</td>
<td>1.80</td>
<td>12.00</td>
<td>2.54</td>
<td>30.50</td>
<td>0</td>
<td>2,362</td>
<td>1,611</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Main bronchus</td>
<td>1.22</td>
<td>4.76</td>
<td>2.33</td>
<td>11.25</td>
<td>4.76</td>
<td>1,745</td>
<td>1,190</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Lobar bronchus</td>
<td>0.93</td>
<td>1.90</td>
<td>2.13</td>
<td>3.97</td>
<td>6.66</td>
<td>1,299</td>
<td>886</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Segmental bronchus</td>
<td>0.76</td>
<td>1.76</td>
<td>2.00</td>
<td>1.52</td>
<td>7.42</td>
<td>933</td>
<td>636</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Subsegmental bronchus</td>
<td>0.76</td>
<td>1.76</td>
<td>2.00</td>
<td>1.52</td>
<td>7.42</td>
<td>933</td>
<td>636</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Small bronchus</td>
<td>0.93</td>
<td>1.90</td>
<td>2.13</td>
<td>3.97</td>
<td>6.66</td>
<td>1,299</td>
<td>886</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Small bronchus</td>
<td>1.024</td>
<td>0.46</td>
<td>13.40</td>
<td>6.21</td>
<td>13.06</td>
<td>32</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Terminal bronchiole</td>
<td>0.93</td>
<td>1.90</td>
<td>2.13</td>
<td>3.97</td>
<td>6.66</td>
<td>1,299</td>
<td>886</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Respiratory bronchiole</td>
<td>0.93</td>
<td>1.90</td>
<td>2.13</td>
<td>3.97</td>
<td>6.66</td>
<td>1,299</td>
<td>886</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Alveolar duct</td>
<td>1,048,576</td>
<td>0.045</td>
<td>0.083</td>
<td>1,600.00</td>
<td>139.50</td>
<td>14.77</td>
<td>0.09</td>
<td>0.06</td>
</tr>
<tr>
<td>23</td>
<td>Alveolar sac</td>
<td>8,388,608</td>
<td>0.041</td>
<td>0.050</td>
<td>11,800.00</td>
<td>591.00</td>
<td>14.98</td>
<td>0.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>

\*\( \text{Re}_n \) and \( \text{Pe}_n \) for \( \text{O}_2 \) transport are evaluated for \( \dot{V} = 500 \text{ cm}^3/\text{s} \).

Source: Data from Weibel (1963) (Ref. 35).
ambient level of near zero. During expiration the alveolar levels of both gases are forced out through the airway tree.

Once in the alveoli, gas transport through the alveolar wall and endothelium into the blood (or vice versa) is diffusive transport, which is quantified by the concept of the lung’s diffusing capacity. As shown in Fig. 4.6, with wall thickness $h$, total alveolar membrane surface area $A_m$, and a gas concentration or partial pressure difference of $P_1$ (alveolar) - $P_2$ (blood serum), the mass flow rate across is

$$
\dot{V}_{gas} = A_m D_{gas-tiss}(P_1 - P_2)/h = D_L(P_1 - P_2).
$$

$D_{gas-tiss}$ is the diffusivity of the gas (O$_2$, CO$_2$) in tissue and is proportional to solubility/(molecular weight)$^{1/2}$, making $D_{CO2-tiss} \approx 20 \cdot D_{O2-tiss}$ since CO$_2$ has far greater solubility in tissue. The details of the area, thickness, and diffusivity are lumped into an overall coefficient called the diffusing capacity $D_L$. The diffusion equation can be simplified for transport of carbon monoxide, CO, which is so rapidly taken up by hemoglobin within the red blood cells that the serum $P_2$ value is essentially zero. Then we find, after rearranging, that the diffusing

$$
D_L = \frac{\dot{V}_{CO}}{P_{Aco}} \quad (4.3)
$$

capacity is given by and there are both single-breath and steady-state methods employed in pulmonary function testing to evaluate $D_L$ by breathing small concentrations of CO. Diseases that thicken the membrane wall, like pulmonary fibrosis, or reduce the available surface area, like emphysema, can cause abnormally low $D_L$ values.

### 4.4 ELASTICITY

#### 4.4.1 Pressure-Volume Relationship of Isolated Lung

The overall mechanical properties of the isolated lung are demonstrated by its pressure-volume ($P-V$) curve. Lung inflation involves both inflating open alveoli and recruiting those which are initially closed because of liquid plugs or local collapse. Deflation from TLC starts with a relatively homogenous population of inflated alveoli. This irreversible cycling process is partly responsible for the inflation and deflation limbs of the curve being different. Inflation requires higher pressures than deflation for any given volume; see the air-cycled (solid line) curve of Fig. 4.7 adapted from Ref. 26. Irreversible cycling of a system exhibits its hysteresis, and the hatched area within the loop created by the two limbs is called the hysteresis area. The magnitude of the area is the work per cycle required to cycle the lung. The overall slope of the curve, obtained by connecting the endpoints with a straight line, is the total compliance $C_{tot} = \Delta V/\Delta P$, which measures the total volume change obtained for the total pressure increase. Stiffer lungs have lower compliance, for example. Often one wants a local measure of compliance, which is the local slope of
the $V(P)$ curve, defined as the dynamic compliance $C_{\text{dyn}} = dV/dP$. Other useful parameters are the specific compliance $V^{\text{spec}} = dV/dP$, the elastance $1/C$, and the specific elastance $V^{\text{spec}} = dP/dV$.

Shown in Fig. 4.8 is the curve for a lung inflated and deflated with saline rather than air. Saline cycling was first noted by Von Neergaard$^{34}$ to reduce inflation pressures, as can be seen in the resulting curve that is shifted to the left, because of increased compliance, and has lost almost all of its hysteresis area. Because it removes the air-liquid interface that alveoli normally possess, saline cycling reveals that the surface tension forces exerted by this interface have very significant effects on the lung’s mechanical response. Saline cycling allows us to understand the elasticity and hysteresis properties of the lung tissue by removing the surface tension forces and their contributions to hysteresis and compliance.

4.4.2 Pressure-Volume Relationship of the Respiratory System

The $P-V$ curve for an isolated lung is only part of the total picture. The intact pulmonary system is contained within the chest cavity, which has its own $P-V$ characteristics. In Fig. 4.9 adapted from Ref. 22, the static $P-V$ curves for an isolated lung ($P_L$), a passive chest with no lung contents ($P_W$), and the total ($P_T = P_L + P_W$) are shown. When $P_T = 0$, the system is in equilibrium with the surrounding atmospheric pressure and the graph indicates that the lung is stretched from its near-zero volume at $P_L = 0$ while the chest cavity is compressed from its higher equilibrium volume at $P_W = 0$. Hence the elastic recoil of the chest wall is pulling outward while the lung tissue is pulling inward to balance the forces, which are in series.

4.4.3 Surface Tension Versus Surface Area

The internal surface of the lung is coated with a thin liquid film, which is in contact with the resident air. The surface tension arising at this air-liquid interface has significant effects on the overall lung mechanical response, as shown in Fig. 4.8, when it is removed. Alveolar Type II cells produce important surface-active substances called surfactants, which reduce the interfacial tension. A major component of lung surfactant is dipalmitoylphosphatidylcholine (DPPC). Lung surfactants reduce alveolar surface tension from the surfactant-free value for air-water, 70 dyn/cm, to 1 to 5 dyn/cm in the alveoli depending on the concentration and state of lung inflation. Figure 4.10 shows the relationship between surface tension and surface area for cycling of an air-liquid interface containing lung
surfactants. Note that there is a hysteresis area and average slope, or compliance, that characterize the loop and have significant effects on their counterparts in Fig. 4.7.

Insufficient surfactant levels can occur in premature neonates whose alveolar cells are not mature enough to produce sufficient quantities, a condition leading to respiratory distress syndrome, also called hyaline membrane disease.2 Instilling liquid mixtures, containing either natural or manmade surfactants, directly into Airways via the trachea has developed from early work in animal models9 into an important clinical tool called surfactant replacement therapy. The movement of these liquid boluses through the network relies on several mechanisms, including air-blown liquid plug flow dynamics, gravity, and surface tension and its gradients.4,10,18

4.5 VENTILATION, PERFUSION, AND LIMITS

The lung differs from many other organs in its combination of gas-phase and liquid-phase constituency. Because the densities of these two phases are so different, gravity plays an important role in determining regional lung behavior, both for gas ventilation and for blood perfusion. In an upright adult, the lower lung is compressed by the weight of the upper lung and this puts the lower lung’s alveoli on a more compliant portion of their regional \( P-V \) curve; see Fig. 4.7. Thus inhaled gas tends to be directed preferentially to the lower lung regions, and the regional alveolar ventilation \( \dot{V}_A \) decreases in a graded fashion moving upward in the gravity field.

Blood flow \( \dot{Q} \) is also preferentially directed toward the lower lung, but for different reasons. The blood pressure in pulmonary arteries, \( P_a \), and veins, \( P_v \), sees a hydrostatic pressure gradient in the upright lung. These vessels are imbedded within the lung’s structure, so they are surrounded by alveolar gas pressure, \( P_A \), which is essentially uniform in the gravity field since its density is negligible. Thus there is a region called Zone III in the upper lung where \( P_a < P_A \). This difference in pressures squeezes the capillaries essentially shut and there is relatively little pulmonary blood flow there. In the lower lung called Zone I, the hydrostatic effect is large enough to keep \( P_a > P_v > P_A \) and blood flow is proportional to the arterial-venous pressure difference, \( P_a - P_v \). In between these two zones is Zone II where \( P_a > P_A > P_v \). Here there will be some length of the vessel that is neither fully closed nor fully opened. It is partially collapsed into more of a flattened, oval shape. The physics of the flow, called the vascular waterfall39 or choked flow40 or flow limitation,48 dictates that \( \dot{Q} \) is no longer dependent on the downstream pressure, but is primarily determined by the pressure difference \( P_a - P_A \).

Figure 4.11a shows this interesting type of flexible tube
configuration and flow limitation phenomena where \( P_a = P_u, \) \( P_a = P_{ext}, \) \( P_x = P_y, \) and \( \dot{Q} = F. \) As downstream pressure \( P_d \) is decreased and upstream pressure \( P_u \) is kept fixed, the flow increases until the internal pressure of the tube drops somewhat below the external pressure \( P_{ext}. \) Then the tube partially collapses, decreasing in cross-sectional area according to its pressure-area or “tube law” relationship \( A(P), \) shown in Fig. 4.11b. As \( P_d \) is further decreased, the tube reduces its cross-sectional area while the average velocity of the flow increases. However, their product, the volumetric flow rate \( F, \) does not increase as shown in Fig. 4.11c. A simplified understanding of this behavior may be seen from the conservation of momentum equation for the flow, a Bernoulli equation, where the average fluid velocity \( U \) is defined as the ratio of flow to cross-sectional area, \( U = F/A, \) all of the terms pressure dependent.

\[
P_{res} = P + \frac{1}{2\rho} \left( \frac{F(P)}{A(P)} \right)^2
\]

where \( P_{res} \) = pressure in a far upstream reservoir where fluid velocity is negligibly small
\( \rho \) = fluid density

\( P_{res} \) is the alveolar air pressure, for example, when applied to limitation of air flow discussed below. Taking the derivative of Eq. (4.4) with respect to \( P \) and setting the criterion for flow limitation as \( dF/dP = 0 \) gives

\[
U_c = \left( \frac{A}{\rho} \frac{dP}{dA} \right)^{1/2} = \left( \frac{E}{\rho} \right)^{1/2}
\]

where \( E \) is the specific elastance of the tube. The quantity \( (E/\rho)^{1/2} \) is the “wave speed” of small pressure disturbances in a fluid-filled flexible tube, and flow limitation occurs when the local fluid speed equals the local wave speed. At that point, pressure information can no longer propagate upstream, since waves carrying the new pressure information are all swept downstream.

The overall effect of nonuniform ventilation and perfusion is that both decrease as one progresses vertically upward in the upright lung. But perfusion decreases more rapidly so that the dimensionless ratio of ventilation to perfusion, \( \dot{V}_A/\dot{Q} \), decreases upward, and can vary from approximately 0.5 at the lung’s bottom to 3 or more at the lung’s top.36 Extremes of this ratio are ventilated regions with no blood flow, called dead space, where \( \dot{V}_A/\dot{Q} \to \infty \), and perfused regions with no ventilation, called shunt, where \( \dot{V}_A/\dot{Q} \to 0. \)

The steady-state gas concentrations within an alveolus reflect the balance of inflow to outflow, as shown in the control volumes (dashed lines) of Fig. 4.12. For CO\(_2\) in the alveolar space, net inflow by perfusion must equal the net outflow by ventilation, \( \dot{Q}(C_{CO2} - C_{CO2}) = \dot{V}_A(C_{ACO2} - C_{ACO2}) \) where \( C \) indicates concentration. In the tissue compartment, the CO\(_2\) production rate from cellular metabolism, \( \dot{V}_{CO2} \), is balanced by net inflow versus outflow in the tissues; i.e., \( \dot{V}_{CO2} = \dot{Q}(C_{CO2} - C_{CO2}) \). Noting that \( C_{ACO2} = 0 \) and combining the two equations, while converting concentrations to partial pressures, leads to the alveolar ventilation equation

\[
\dot{V}_A = \frac{8.63}{P_{ACO2}} \dot{V}_{CO2}
\]

where the constant 8.63 comes from the units conversion. The inverse relationship between alveolar
ventilation and alveolar CO\textsubscript{2} is well known clinically. Hyperventilation drops alveolar, and hence arterial, CO\textsubscript{2} levels whereas hypoventilation raises them. Using a similar approach for oxygen consumption \(\dot{V}_{O_2}\) and using the results of the CO\textsubscript{2} balance yields the ventilation-perfusion equation

\[
\frac{\dot{V}_A}{\dot{Q}} = \frac{8.63R(C_{ao_2} - C_{vo_2})}{P_{ACO_2}}
\]

Equation 4.7 uses the definition of the respiratory exchange ratio, \(R = \dot{V}_{CO_2}/\dot{V}_{O_2}\), which usually has a value of \(R = 0.8\) for \(\dot{V}_A/\dot{Q} = 1\). It also replaces the end capillary concentration with the systemic arterial value, \(C_{ao_2} = C_{co_2}\), assuming equilibration. From Eq. 4.7, the extreme limits of \(\dot{V}_A/\dot{Q}\), mentioned earlier, may be recognized. Intermediate solutions are more complicated, however, since there are nonlinear relationships between gas partial pressure and gas content or concentration in the blood. Equation 4.7 also demonstrates that higher \(\dot{V}_A/\dot{Q}\), as occurs in the upper lung, is consistent with a higher end capillary and alveolar oxygen level. It is often thought that tuberculosis favors the upper lung for this reason.

The \(\dot{V}_A/\dot{Q}\) variation leads to pulmonary venous blood having a mix of contributions from different lung regions. Consequently, there is a difference between the lung-average alveolar \(P_{ACO_2}\) and the average or systemic arterial \(P_{aO_2}\), sometimes called the \(A-a\) gradient of O\textsubscript{2}. An average \(P_{aO_2}\) can be derived from the alveolar gas equation,

\[
P_{AO_2} = P_{IO_2} - \frac{P_{ACO_2}}{R} + f
\]

which derives from the mass balance for O\textsubscript{2} in Fig. 4.12. Here \(P_{IO_2}\) is the inspired value and \(f\) is a small correction normally ignored. Clinically, an arterial sample yields \(P_{aCO_2}\), which can be substituted for \(P_{ACO_2}\) in Eq. 4.8. The \(A-a\) gradient becomes abnormally large in several lung diseases that cause increased mismatching of ventilation and perfusion.

### 4.6 AIRWAY FLOW, DYNAMICS, AND STABILITY

#### 4.6.1 Forced Expiration and Flow Limitation

A common test of lung function consists of measuring flow rate by a spirometer apparatus. When the flow signal is integrated with time, the lung volume is found. Important information is contained in the volume versus time curves. The amount of volume forcefully exhaled with maximum effort in 1 second, FEV1, divided by the maximal volume exhaled or forced vital capacity, FVC, is a dimensionless ratio used to separate restrictive and obstructive lung disease from normal lungs. FEV1/FVC is normally 80 percent or higher, but in obstructed lungs (asthma, emphysema) the patient cannot exhale very much volume in 1 second, so FEV1/FVC drops to diagnostically low levels, say 40 percent. The restricted lung (fibrosis) has smaller than normal FVC, though the FEV1/FVC ratio may fall in the normal range because of the geometric scaling as a smaller lung.

Flow and volume are often plotted against one another as in Fig. 4.13. The flow-volume curves shown are for increasing levels of effort during expiration. The
maximal effort curve sets a portion common to all of the curves, the effort-independent region. Expiratory flow limitation is another example of the choked flow phenomenon discussed earlier in the context of blood flow. Similar flow versus driving pressure curves shown in Fig. 4.11 can be extracted from Fig. 4.13 by choosing flows at the same lung volume and measuring the pressure drop at that instant, forming the isovolume pressure-flow curve. Since airway properties and $E$ vary along the network, the most susceptible place for choked flow seems to be the proximal airways. For example, we expect gas speeds prior to choke to be largest at generation $n = 3$ where the total cross-sectional area of the network is minimal; see Table 4.1. So criticality is likely near that generation. An interesting feature during choked flow in airways is the production of flutter oscillations, which are heard as wheezing breath sounds, so prevalent in asthma and emphysema patients whose maximal flow rates are significantly reduced, in part because $E$ and $U_c$ are reduced.

### 4.6.2 Airway Closure and Reopening

Most of the dynamics during expiration, so far, have been concerned with the larger airways. Toward the very end of expiration, smaller airways can close off as a result of plug formation from the liquid lining, a capillary instability, or from the capillary forces pulling shut the collapsible airway, or from some combination of these mechanisms. Surfactants in the airways help to keep them open by both static and dynamic means. The lung volume at which airway closure occurs is called the closing volume, and in young healthy adults it is ~10 percent of VC as measured from a nitrogen washout test. It increases with aging and with some small airway diseases. Reopening of closed airways was mentioned earlier as affecting the shape of the $P$-$V$ curve in early inspiration as the airways are recruited. When the liquid plugs break and the airway snaps open, a crackle sound, or cascade of sounds from multiple airways, can be generated and heard with a stethoscope. Diseases that lead to increased intra-airway liquid, such as congestive heart failure, are followed clinically by the extent of lung crackles, as are certain fibrotic conditions that affect airway walls and alveolar tissues.

### REFERENCES


**BIBLIOGRAPHY**


