The Mechanics of Breathing 6.1

Learning Objectives

- Describe the overall function of the respiratory system
- Identify the force that moves air into and out of the lungs
- List the conditioning effects of the nasal passageways
- Explain what is meant by "mucus escalator"
- Identify the muscle responsible for quiet inspiration
- Identify the cause of air movement during quiet expiration
- Identify on a drawing: trachea, visceral pleural, parietal pleura, pleural space
- Describe the location and function of the external and internal intercostal muscles
- Identify the components of elastic recoil of the lungs/chest system
- Write the Law of Laplace and explain its significance for lung expansion
- Describe the chemical nature of surfactant and list its functions
- Explain why intrapleural pressure is nearly always negative (subatmospheric)
- Explain why a pneumothorax collapses the lungs
- Identify the FRC on the relaxation volume–pressure curve

THE RESPIRATORY SYSTEM SUPPLIES O_2 AND REMOVES WASTE CO_2

As described in Chapters 2.9–2.11, all cells of the body derive their energy from the slow and controlled oxidation of foodstuffs. The overall oxidation of glucose is described by the chemical equation:

$$C_6H_{12}O_6 + 6O_2 \Rightarrow 6CO_2 + 6H_2O + \text{heat}$$

and the complete oxidation of a triglyceride such as tripalmitin is described by

$$C_{51}H_{98}O_6 + 72.5O_2 \Rightarrow 51CO_2 + 49H_2O + \text{heat}$$

Both of these oxidations have large negative changes in free energy, ΔG, shown here as heat energy, which can be harnessed to produce work. Collectively, these reactions make up **cellular respiration**. In the body, the oxidation reactions occur slowly and the released chemical energy is captured in the terminal phosphate bond of ATP. The energy captured in ATP is used to perform mechanical work, concentration work, synthetic work, and electrical work. As ATP is consumed, metabolic pathways regenerate it so that the cellular concentration of ATP remains relatively constant while ATP continually turns over. The maintenance of the constancy of the body's systems, homeostasis, depends on a continual throughput of energy, which is possible only by continually supplying O_2 and removing CO_2. This is the function of the respiratory system: to exchange CO_2 and O_2 with the atmosphere so that the circulatory system can supply cells with adequate amounts of O_2 and remove the waste CO_2.

FOUR CORE ASPECTS OF RESPIRATORY PHYSIOLOGY

The four main parts of respiratory physiology are:

1. **Pulmonary ventilation**: The process in which a volume of gas is added to or removed from the lungs.
2. **Gas exchange**: The process in the lung by which blood is recharged with O_2 and dumps its waste CO_2.
3. **Transport of O_2 and CO_2** between the tissues and the lungs.
4. **Regulation of ventilation:** The process by which bodily needs are translated into more rapid or slower ventilation.

We will discuss these four topics in order in this unit. We begin by discussing pulmonary ventilation.

AIR FLOWS THROUGH AN EXTENSIVE AIRWAY SYSTEM THAT *FILTERS, WARMS,* AND *HUMIDIFIES* THE AIR

Inspired air enters through the nose or mouth, or both, where it is **conditioned**: it is filtered, warmed, and humidified. Many hairs and sticky mucus trap large dust particles and thus filter the inspired air. Outcroppings of tissue in the nasal cavity called **turbinates** expose the air to a large surface area and mix the air within the nasal passages, humidifying and warming the air to 37°C.

After leaving the nasal passages, air travels through the throat, or pharynx, and then through the larynx or voice box. It then enters the **trachea**, which subsequently branches many times. The pharynx, larynx, and early generations of the airways leading to the lungs do not participate in gas exchange. The airways are lined with **goblet cells** that produce mucus and a **ciliated epithelium** that constantly moves mucus toward the mouth. The mucus

DOI: http://dx.doi.org/10.1016/B978-0-12-800883-6.00060-4

traps dirt and dust. The movement of the mucus is like a "mucus escalator" that constantly cleans the lungs. The mucus brought to the mouth is typically **expectorated** (spat out) or swallowed. Persons with **cystic fibrosis** produce thick mucus that cannot be easily removed. Part of their treatment is a vigorous thumping of the chest to clear out the lungs (see Clinical Applications: Cystic Fibrosis box).

The airways beyond the trachea constitute the **tracheobronchial tree**. Each branching of the airways produces the next generation, like a family tree. The first few generations conduct the air toward the gas exchanging regions, but they do not themselves exchange gases. The larger branches are the **bronchi** and **bronchioles**. These conductive airways become progressively smaller and more numerous as they branch, leading eventually to **terminal bronchioles**, **respiratory bronchioles**, and **alveolar ducts**, ending in dead-end sacs called **alveoli** (see Figure 6.1.1). The alveoli are small sacs, about 0.3 mm in diameter, where tiny distances separate the blood from the alveolar gases. The lungs contain some 300×10^6 alveoli. Thus the airways from nose to alveoli consist of a **conducting zone** of generations 0–16 and a **respiratory zone** in series with the conducting zone, with the respiratory zone consisting of generations 17–23.

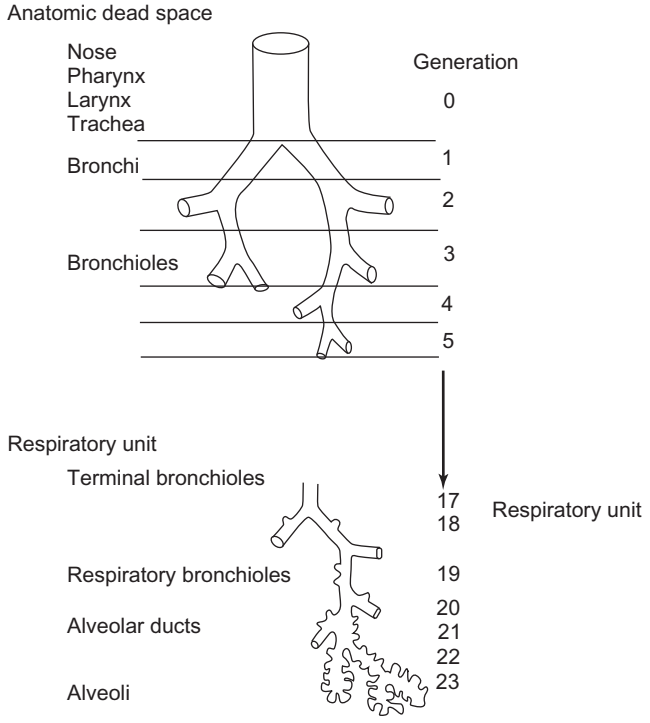

FIGURE 6.1.1 Highly schematic diagram of the extensive branching of the tracheobronchial tree to form the gas exchanging regions of the lung. Inspired air is conditioned in the anatomic dead space, so named because this region does not participate in gas exchange. The conditioning includes cleansing by nasal hairs and the mucus escalator, humidification, and warming. The airways branch successively to form bronchi, bronchioles, terminal bronchioles, respiratory bronchioles, alveolar ducts, and alveoli. They are on the order of 23 generations of branches, which generate 2^{24} airways. The last airways contain progressively more alveoli until the airways end in a blind sac covered with multiple alveoli. Gas exchange occurs in the respiratory unit from generations 17 to 23, consisting of terminal bronchioles, respiratory bronchioles, alveolar ducts, and alveoli.

Clinical Applications: Cystic Fibrosis

Cystic Fibrosis is a disease caused by mutations in the gene encoding for a protein called **CFTR**, which stands for **c**ystic **f**ibrosis **t**ransmembrane conductance **r**egulator. This protein belongs to a large superfamily of proteins called ABC transport proteins, which stands for **A**TP-**b**inding **c**assette transport proteins. CFTR consists of a single amino acid chain of 1480 amino acids that has five distinct functional regions. Two transmembrane domains are involved in forming a Cl^- channel, two domains bind nucleotides, and another regulatory domain is phosphorylated by protein kinase A, which is controlled by the second messenger, cAMP. The full function of CFTR is not yet known. It is a voltage-independent Cl^- channel, but it may also regulate the conductance of other apical channels. There are a variety of mutations of CFTR that produce symptoms. The most common mutation (about 70% of cases) is the deletion of phenylalanine at amino acid 508.

CFTR is present in the apical membrane of a variety of epithelial cells including those of the intestine, airways, secretory glands, and bile ducts. It appears to be necessary for the proper secretion of watery solutions by these epithelia. Insufficient watery secretion by tissues possessing defective CFTR results in insufficient dilution of the mucus secreted by the epithelium. The tissues become covered with sticky mucus that is difficult to remove. Persons afflicted with defective CFTR suffer from increased bacterial infections because of the failure of the mucus escalator.

In 1970, the median life expectancy of persons with defective CFTR was 8 years. Because of advances in treatment, the median life expectancy today is near 30 years. New treatments include an enzyme that breaks down the mucus to help get it moving and antibiotics. About 40,000 persons in the United States suffer from cystic fibrosis, and about 2500 new cases arrive every year.

GAS FLOWS IN RESPONSE TO PRESSURE DIFFERENCES

Gas is a fluid that obeys the same general principles of other fluids: it flows from a region of high pressure to a region of low pressure. In laminar flow through straight cylindrical pipes, in which the flow is streamlined, flow is described by Poiseuille's law:

$$[6.1.1] \qquad Q_V = \frac{\pi a^4}{8\eta}\frac{\Delta P}{\Delta x}$$

where $P/\Delta x$ is the pressure gradient, Q_V is the flow, a is the radius of a right cylindrical tube through which flow occurs, and η is the viscosity of the flowing medium. According to this equation, the flow of gas is directly proportional to the pressure difference. In a straight cylindrical pipe of radius a and length L, the equation becomes a hydraulic equivalent of Ohm's law:

$$[6.1.2] \qquad Q_V = \frac{\Delta P}{R}$$

where R is the equivalent resistance to gas flow through the airways. These equations are identical to those we use in cardiovascular physiology (see Unit 5).

CHANGES IN LUNG VOLUMES PRODUCE THE PRESSURE DIFFERENCES THAT DRIVE AIR MOVEMENT

The Ideal Gas Law describes the relation between pressure and volume in an ideal gas:

$$PV = nRT \quad [6.1.3]$$

where P is the pressure measured in atmospheres or mmHg or Pa ($=\text{N m}^{-2}$), or some other appropriate unit, V is the volume, n is the number of moles, R is the gas constant, and T is the temperature in kelvin. When P is in atmospheres and V is in L, $R = 0.082\ \text{L atm mol}^{-1}\ \text{K}^{-1}$. The inverse relation between pressure and volume is the basic principle responsible for pulmonary ventilation: increasing the volume of the thoracic cavity, with the enclosed lungs, decreases the pressure of the gas in the lungs and so air rushes in from the outside. Conversely, the reduction of the volume of the thoracic cavity increases the pressure of the gas in the lungs and so air moves from the lungs back out into the ambient air.

SKELETAL MUSCLES POWER INSPIRATION

THE DIAPHRAGM IS THE MAJOR MUSCLE DRIVING NORMAL INSPIRATION

Inspiration refers to taking air into the lungs. **Expiration** refers to the removal of air from the lungs. Alternative terms are **inhalation** and **exhalation**. Normal resting inspiration begins with contraction of the diaphragm, a dome-shaped muscle that separates the **thoracic cavity** containing the heart and lungs from the **abdominal cavity** containing the liver, stomach, and intestines. The **phrenic nerve** innervates the diaphragm. We must consciously control the diaphragm in order to eat or speak or swim or sing. Because breathing is essential to life, back-up systems exist so that breathing becomes automatic when we sleep or when we lose consciousness (see Chapter 6.6).

When the diaphragm contracts, it expands the thoracic cavity at the expense of the abdominal cavity. The increase in volume of the thoracic cavity decreases the intrathoracic pressure so that, if the **glottis** is open, air will flow from the atmosphere into the lungs (see Figure 6.1.2). The glottis consists of the two vocal folds in the larynx and the slit between them.

THE EXTERNAL INTERCOSTAL MUSCLES EXPAND THE THORACIC CAGE BY ELEVATING AND EXTENDING THE STERNUM

The external intercostal muscles originate on the inferior surfaces of the proximal parts of the ribs and insert on the superior and distal parts of the next lower rib. These

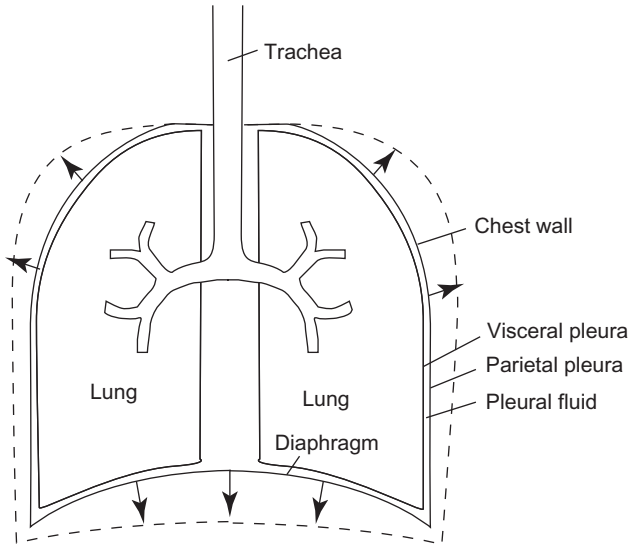

FIGURE 6.1.2 Expansion of the thoracic cavity during inspiration. The lungs are shown as "floating" within the thoracic cavity, being anchored by the bronchi. The surface of the lungs is covered by a membrane, the **visceral pleura**, which is continuous with the pleura lining the inside of the chest wall, the **parietal pleura**. The intrapleural space is very thin (about 10–20 μm) and filled with pleural fluid. Contraction of the diaphragm causes expansion of the lungs, which lowers the pressure of its enclosed air. The inspiration is aided by external intercostal muscles and accessory muscles connected to the bones of the rib cage which raise the rib cage and increase its posterior–anterior dimensions.

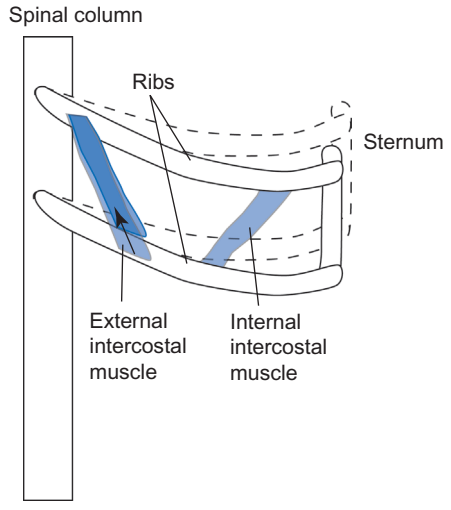

FIGURE 6.1.3 Schematic diagram of the action of the external intercostal muscles. The external intercostal muscles connect the ribs in such a way that the contraction of the muscles lifts the ribs and rib cage and expands the anterior–posterior dimensions of the rib cage. Contraction of the internal intercostals, which are oriented opposite of the external intercostals, produces the opposite effect: lowering of the ribs and reduction in the anterior–posterior dimension.

are innervated by intercostal nerves originating in thoracic segments of the spinal cord. Contraction of these muscles raises the rib cage upward and outward, thereby contributing to the expansion of the thoracic cavity and reduction of pressure within the lung, causing air to move from the air into the lungs (see Figure 6.1.3). Contraction of the internal intercostal muscles has the opposite effects and aids in expiration.

ACCESSORY MUSCLES AID IN FORCEFUL INSPIRATION

The sternocleidomastoid muscles connect the sternum to the mastoid process behind the ear. Contraction of this muscle helps lift the sternum along with the rest of the rib cage. The **scalene** muscles lift the first two ribs. These muscles generally contribute little to expansion of the rib cage during rest but are recruited at high levels of ventilation during strenuous exercise, for example.

RESTING EXPIRATION IS PASSIVE; ABDOMINAL MUSCLES AID IN FORCEFUL EXPIRATION

By expanding the lungs and chest wall, the muscles of inspiration store mechanical energy in the elastic lungs and chest wall system. When these inspiratory muscles relax, the lungs and chest wall recoil, producing a contraction of the thoracic cavity and subsequent rise in the intrathoracic pressure. This forces air out of the lungs, but the force is passive.

Contraction of the abdominal muscles compresses the contents of the abdominal cavity, thereby reducing the volume of the thoracic cavity, and pulls down on the rib cage. Both actions increase the flow of gas during expiration, allowing for more rapid pulmonary ventilation. These abdominal muscles include the rectus abdominus, transverse abdominus, external oblique, and internal oblique. The internal intercostal muscles are oriented opposite to the external intercostals: they lower the rib cage and decrease its anterior dimensions. These muscles assist expiration only during strenuous breathing.

THE PLEURA AND THE PLEURAL FLUID JOIN THE LUNGS TO THE CHEST WALL

According to Figure 6.1.2, there is no rigid structural connection between the lungs and the chest wall and the lungs mostly "float" in the thoracic cavity. So how can the lungs follow the chest wall as if they were attached? The tensile properties of the thin layer of pleural fluid effectively join the lungs to the chest wall. Consider two flat, horizontal glass plates separated by a thin layer of water, as shown in Figure 6.1.4. The layer of water allows the two plates to slip easily past each other, in the horizontal plane, but it is extremely difficult to separate the plates vertically because the water effectively binds them together. Application of a large force normal to the surface produces a large negative pressure within the fluid between the plates. This is analogous to the situation with the lung and the chest wall.

COMPLIANCE MEASURES THE EASE OF EXPANDING THE LUNGS

The compliance describes the ease of expansion of a volume. It is *defined* as

$$C = \frac{\Delta V}{\Delta P} \qquad [6.1.4]$$

where C is the compliance, ΔV is the change in volume, and ΔP is the change in pressure. A large compliance means that the volume is easily distended, because a large volume change results from a small pressure change. The compliance of the lungs can be obtained from the slope of the volume–pressure curve. Figure 6.1.5 shows the volume–pressure curves when excised lungs are filled first with air and then with saline. These results illustrate several key concepts:

1. Filling the lungs with air shows **hysteresis**—the curves are different for inflation and deflation.
2. The curves are nonlinear and so the compliance depends on the volume at which it is measured.
3. The compliance is greatly different for inflation with air and with saline. This shows that a large component of the compliance is the **surface tension** between the lungs and air.

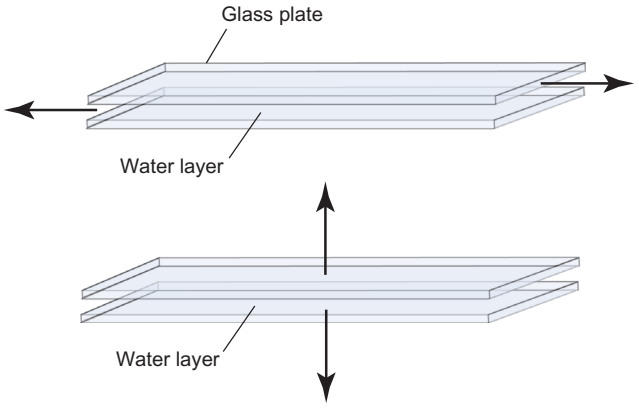

FIGURE 6.1.4 Lubricating and tensile effects of a thin water layer. A thin layer of water separates two flat glass plates. Application of a force in the plane of the glass causes the glass plates to slip past each other. The water layer reduces the friction between the glass plates and facilitates movement in the plane of the plates. Application of a force normal to the plane of the plates causes a slight expansion of the water layer and production of a large negative pressure within that layer. Separation of the plates in this direction requires much larger forces compared to movement of the plates along their planes.

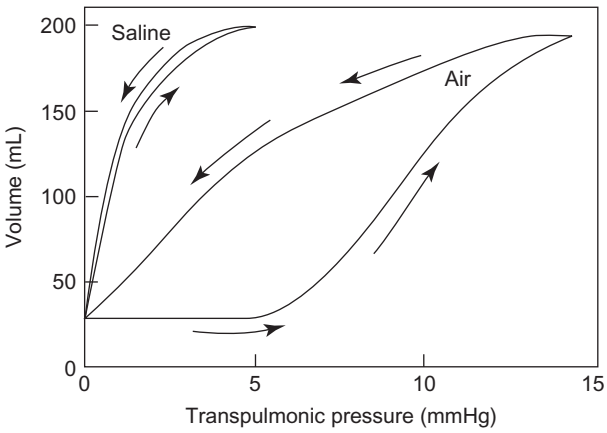

FIGURE 6.1.5 Compliance of the isolated lung. The isolated lung expands when positive pressure is applied to fluids entering the lung. The slope of the volume–pressure curve is the compliance at that volume. The compliance demonstrates hysteresis or markedly different behavior upon inflation or deflation. Also, the compliance is nonlinear: it requires more incremental pressure to begin inflation than to continue it. Lastly, the compliance is greatly increased when saline instead of air is used to inflate the lung.

THE COMPLIANCE AND RECOIL TENDENCY OF THE LUNG IS PRODUCED BY *ELASTIC FIBERS* AND BY *SURFACE TENSION*

As described above, it takes effort to expand the lungs but the lungs recoil on their own accord. The lung's elasticity is due to elastic fibers in the lung and airways and to the surface tension. The elastic fibers include **elastin** and **collagen** fibers in the extracellular space surrounding the alveoli, bronchioles, and pulmonary capillaries. They account for about one-third of the recoil tendency.

As discussed in Chapter 2.4, surface tension arises from the unequal forces applied to molecules at the interface between two phases; in this case the phases are air and the thin layer of fluid that lines the alveoli. Surface tension produces a force along a plane surface that is measured in units of force per unit length. It takes effort to expand the surface, and this effort is expressed as the increment in surface energy, as described in Eqn [2.4.1]:

$$[6.1.5] \qquad dG = \gamma dA$$

where dG is the increment in the surface free energy, γ is the **surface tension**, and dA is the increment in area.

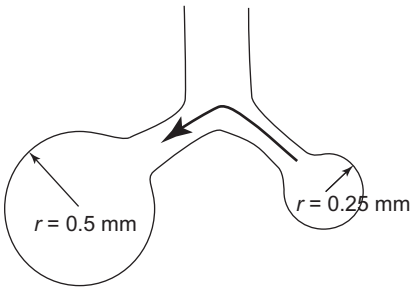

FIGURE 6.1.6 Schematic diagram of the predicted instability of alveoli. According to the Law of Laplace, the pressure within alveoli at mechanical equilibrium would be given by $P = 2\gamma/r$. If the surface tension is the same in both alveoli, but r is smaller on the right, then the pressure on the right will be larger and air will move from the smaller alveolus to the larger one. This does **not** happen, in fact, because the surface tension is highly dependent on r and because the alveoli are not independent, individual spheres. The alveoli are connected to other alveoli because they share walls and as one collapses it is supported or kept open by its neighbors.

In a sphere at equilibrium, the surface tension is related to the pressure and the size of the sphere according to the **Law of Laplace**:

$$[6.1.6] \qquad P = \frac{2\gamma}{r}$$

where P is the pressure within the sphere, γ is the surface tension, and r is the radius of the sphere. The Law of Laplace can be derived from energetic principles (see PS2.1) or mechanical principles (see Chapter 5.4). One way of looking at this is to say that the surface tension produces a pressure on the gas within an elastic sphere that opposes its expansion. Another way of looking at it is that the surface tension promotes the recoil of the sphere. About two-thirds of the recoil tendency of the lung originates in the aggregate surface tension in the millions of alveoli. When the lungs are filled with saline, there is no air–water interface and therefore there is no surface tension. Under these conditions, the compliance of the lungs increases (see Figure 6.1.5).

THE LAW OF LAPLACE PREDICTS ALVEOLAR INSTABILITY

In the lungs the alveoli approximate spheres, but instead of being closed they are open to the airways and are connected to each other through the gas within the lungs. According to the Law of Laplace, small alveoli would have larger pressures than the larger alveoli, and thus the smaller alveoli should collapse and the larger ones grow larger (see Figure 6.1.6).

PULMONARY SURFACTANT LOWERS THE SURFACE TENSION IN THE ALVEOLI

Alveolar type II cells secrete a lipoprotein material called **surfactant**, whose primary function is to **reduce the surface tension** in the alveoli. Surfactant is a lipoprotein that consists mainly of dipalmitoylphosphatidylcholine and some glycoprotein components. This material spreads out over the surface of the alveoli and reduces its surface tension by interaction of the hydrophilic parts of the surfactant molecule with the water layer next to the alveolar cells and by the interaction of

EXAMPLE 6.1.1 Pressure Within Alveoli of Different Sizes

Consider the two alveoli in Figure 6.1.6. Suppose that the surface tension was constant at 50 dyne cm^{-1} (1 dyne is 1 g cm s^{-2}, the unit of force in the CGS system, which is not part of the SI system of units). What is the pressure in each of the alveoli?

Pressure is given by the Law of Laplace, which is only an approximation to the situation here because of the fact that the alveoli are not spheres and there are other forces besides the surface tension involved. Nevertheless, we use it here as an approximation. The pressure on the left is given as $P = 2 \times 50$ dyne $cm^{-1}/0.5 \times 10^{-1}$ cm = **2000 dyne cm^{-2}**. The pressure on the right is $P = 2 \times 50$ dyne $cm^{-1}/0.25 \times 10^{-1}$ cm = **4000 dyne cm^{-2}**.

These values can be converted to Pa, atm, or mmHg using the conversion 1 dyne = 1 g cm $s^{-1} \times 10^{-3}$ kg $g^{-1} \times 10^{-2}$ m $cm^{-1} = 10^{-5}$ N; 1 dyne $cm^{-2} = 10^{-5}$ N $cm^{-2} \times (10^2$ cm $m^{-1})^2 = 10^{-1}$ N $m^{-2} = 10^{-1}$ Pa.

The pressure on the left is 2000 dyne $cm^{-2} \times 10^{-1}$ Pa (dyne $cm^{-2})^{-1}$ = **200 Pa** $\times$ 9.87 $\times 10^{-6}$ atm Pa^{-1} = **0.00197 atm** $\times$ 760 mmHg atm^{-1} = **1.5 mmHg**.

the hydrophobic parts of the surfactant with the air. Surfactant has multiple functions:

- Surfactant causes the hysteresis in the lung volume–pressure curve.
- Surfactant stabilizes alveolar size.
- Surfactant reduces the work of breathing.
- Surfactant keeps alveoli dry.

Surfactant can be extracted from the lung and spread out over water as a monolayer. The surface tension measured on the water film shows hysteresis, just like that of the isolated lung. Thus it is likely that surfactant is responsible for the hysteresis in the volume–pressure curves shown in Figure 6.1.5.

The ability of surfactant to lower the surface tension depends on its surface concentration. When an alveolus shrinks, the concentration of surfactant increases and the surface tension is reduced. The pressure inside the alveolus still obeys the Law of Laplace, but the surface tension in the Law of Laplace depends on the size of the alveolus. Higher concentration of surfactant lowers the alveolar pressure by lowering γ in Eqn [6.1.6] while shrinking of the alveolus raises the pressure by making r smaller. The final result is that the surfactant stabilizes alveolar size.

Surface tension contributes about two-thirds of the recoil tendency of the lungs. Inspiration requires work to expand the lungs against this recoil tendency. Because surfactant lowers that recoil tendency, surfactant reduces the work of breathing. Persons with insufficient surfactant indeed have difficulty breathing (see Clinical Applications: Respiratory Distress Syndrome).

The surface tension that tends to collapse alveoli (thus raising the pressure within the enclosed space) tends to draw the surface away from the interstitial fluid, thus *reducing* the pressure within the interstitial space. Low pressure in the interstitial space favors fluid filtration out of the pulmonary capillaries, according to the Starling–Landis equation (see Chapter 5.9). Excess surface tension thus leads to pulmonary edema, and the reduction of the surface tension by surfactant helps prevent edema.

THE LUNGS AND CHEST WALL INTERACT TO PRODUCE THE PRESSURES THAT DRIVE VENTILATION

STATIC PRESSURES ARE MEASURED WHEN AIRFLOW IS ZERO

The static lung volumes refer to the lung volumes when there is no flow of air through the airways. As mentioned earlier, both the lungs and chest wall are elastic structures whose volume depends on the pressure difference between the inside and outside, like a balloon. Because the muscles pull on the chest wall, part of the pressure is generated by the muscles. The balance of pressures in the static lung during no-flow conditions can be written as

$$[6.1.7] \qquad P_A - P_B = P_{muscles} + P_{lung} + P_{chest\ wall}$$

where P_B is the ambient, barometric pressure, P_A is the pressure within the alveoli, $P_{muscles}$ is the pressure due to muscular compression or expansion of the chest wall, P_{lung} is the pressure due to elastic properties of the lung, and $P_{chest\ wall}$ is the pressure due to the properties of the chest wall. These components can be separated in humans by having a person inhale or exhale to achieve a given volume, and then relaxing the muscles against a closed airway, while at the same time measuring $P_B - P_A$. Because the airway is closed, the airflow is zero; because the muscles are relaxed, $P_{muscles} = 0$ and Eqn [6.1.7] becomes

$$[6.1.8] \qquad P_A - P_B = P_{lung} + P_{chest\ wall} = P_{rs}$$

where P_{rs} is the pressure of the entire respiratory system consisting of lung and chest wall.

THE PRESSURE DROP ACROSS THE LUNG AND CHEST WALL CAN BE ESTIMATED USING P_{PL}

The contribution of the chest wall and the lung to the total pressure, P_{rs}, can be determined by recognizing that the **intrapleural space** divides the total pressures into two components, as shown in Figure 6.1.7. The difference between the alveolar pressure and the barometric pressure is P_{rs}.

THE RELAXATION VOLUME–PRESSURE CURVES SHOW THAT THE LUNGS AND CHEST WALL USUALLY PULL IN OPPOSITE DIRECTIONS, CAUSING A NEGATIVE INTRAPLEURAL PRESSURE

The relaxation volume–pressure curves for the lungs, chest wall, and total respiratory system can be obtained as described in Figure 6.1.7, by measuring P_A, P_B, and P_{pl}, and the results are shown in Figure 6.1.8. The chest acts like a spring; at low volumes (below point A in Figure 6.1.8) it recoils back to higher volumes, creating a

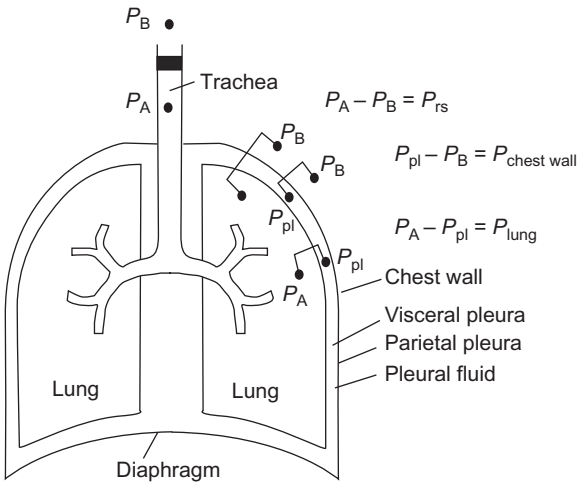

FIGURE 6.1.7 The intrapleural pressure is the pressure within the narrow space between the lung and the chest wall. Since the pressure drop across the entire respiratory system (P_{rs}) consists of the sum of the pressure drops across the lung and chest wall, each of the drops can be determined if the intrapleural pressure is known. The intrapleural pressure can be measured by insertion of a needle into the intrapleural space, but may be more easily approximated by the esophageal pressure. This pressure divides P_{rs} into a pressure drop across the chest wall and a pressure drop across the lung. The pressure drop across the chest wall is given as $P_{chest\ wall} = P_{pl} - P_B$, where P_{pl} is the pressure within the intrapleural space; the pressure drop across the lungs is $P_{lung} = P_A - P_{pl}$. The relaxation volume–pressure curves are obtained by relaxing the respiratory muscles when the airways are closed, as shown.

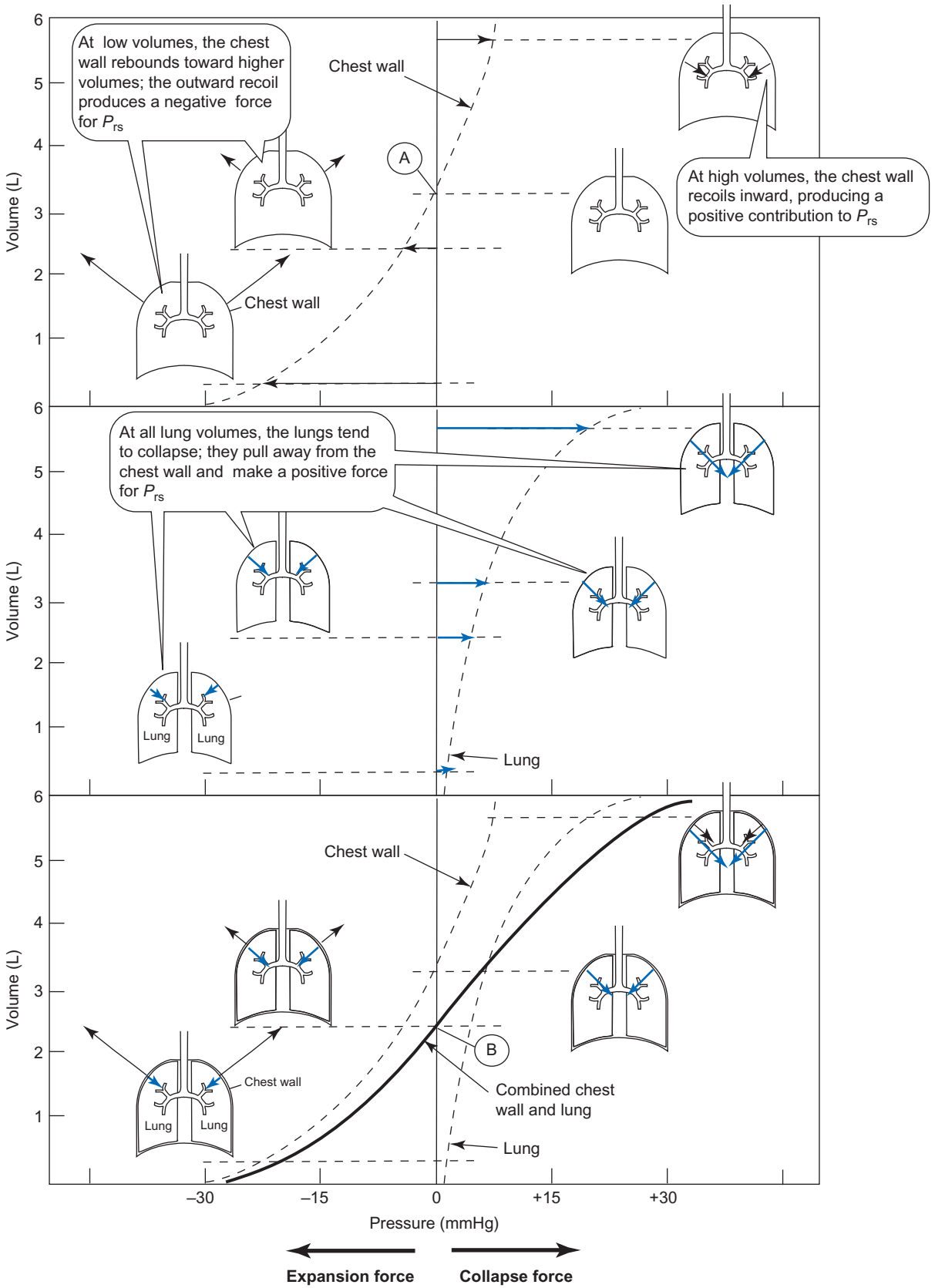

FIGURE 6.1.8 Relaxation volume–pressure curves for the chest wall, lungs, and combined respiratory system, so named because the muscles are relaxed when pressures are measured. At a single volume, the contribution to the total pressure is the sum of the pressures contributed by the chest wall and by the lungs (see Eqn [6.1.8]). Thus the pressures add as vectors along the dashed horizontal lines to form the combined chest and wall curve (solid line). Throughout most of the volume range, the chest wall tends to recoil toward a larger volume. At large volumes, the chest wall tends to recoil inward. Such large volumes can be accomplished by the action of respiratory muscles. The lungs always tend to collapse, and the tendency becomes larger with increasing volume. Except at high volumes, then, the lungs and the chest wall act in opposite directions: the lung tends to shrink whereas the chest wall tends to expand. *Modified from E. Agostoni and J. Mead, Statics of the respiratory system, in W.O. Fenn and H. Rahn, eds.,* Handbook of Physiology, *American Physiological Society, Washington, DC, 1964.*

negative pressure across the respiratory system. At high volumes it recoils back to lower volumes, creating a positive pressure across the respiratory system. Thus negative static pressures means there is a tendency to expand (which can be balanced only by negative pressures) and positive pressures means there is a tendency to collapse (which can be balanced only by positive pressures). Because these are static volumes, the negative pressure is necessary to stop expansion, and positive pressures are necessary to stop the collapse. These tendencies are illustrated by arrows in Figure 6.1.6, with an arrow to the left (negative pressure) showing a force for expansion and an arrow to the right showing a force for collapse. The lungs at all volumes tend to recoil toward a smaller volume, so they always contribute a positive pressure to the respiratory system. Because the lung is plastered to the chest wall by the pleural fluid, the combination creates either a negative or a positive pressure. The balance point is point B in the lower panel—here no muscle force is necessary to set the volume of the system.

THE LOW INTRAPLEURAL PRESSURE IS CAUSED BY THE RECOIL TENDENCY OF THE LUNG

The recoil of the lung away from the chest wall causes a relatively lower pressure in the intrapleural space than in the alveolar space. As a consequence, the lung always experiences a positive pressure that keeps it inflated against its tendency to recoil. Although the net pressure on the lung is positive, the pressure is actually *caused* by the recoil tendency of the lung. That is, the lung recoils away from the chest wall until it develops a negative intrapleural pressure (positive $P_A - P_{pl}$) large enough to keep the lung inflated.

BREAKING THE SEAL ON THE INTRAPLEURAL SPACE COLLAPSES THE LUNGS

A puncture of the chest wall allows air to enter the intrapleural space and equilibrate its pressure with the ambient barometric pressure. In this case, the pressure inflating the lung becomes zero or negative and is not enough to counteract the natural recoil of the lung: the lungs collapse. This condition is called a **pneumothorax** (literally, air in the thorax), as illustrated in Figure 6.1.9.

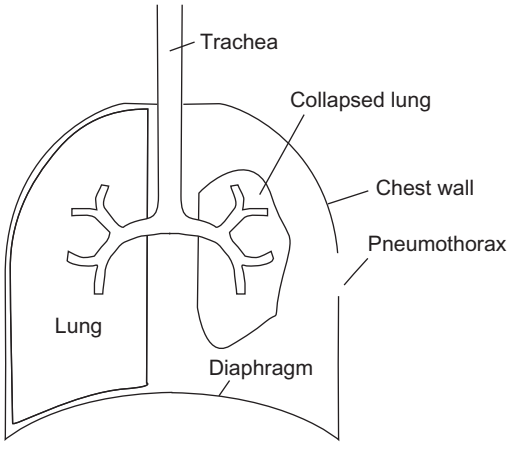

FIGURE 6.1.9 Schematic diagram of lung collapse upon the formation of a pneumothorax. Under normal conditions, a lung's recoil tendency produces a lower pressure within the intrapleural space. This lower pressure produces a net positive pressure that holds the lung against the chest wall. When air is introduced, the intrapleural pressure equilibrates with the ambient barometric pressure and the lung's natural recoil tendency causes it to collapse.

Clinical Applications: Respiratory Distress Syndrome

The first breath of air after being born poses its own set of problems. *In utero*, the baby can "inhale" amniotic fluid, which has a high degree of viscous resistance but has no air–water interface. In addition, the baby does not obtain gases from this fluid, as gas exchange is accomplished through the placental circulation. After birth, the baby must expand its lungs for the first time in the presence of the surface tension associated with air breathing. Accordingly, the concentration of surfactant in full-term infants is actually higher than that of adults, presumably to ease the transition from fluid to air breathing upon birth. Surfactant production by alveolar type II cells requires maturation of these cells, and this is not fully accomplished until about 36 weeks of gestation. Premature infants may lack sufficient surfactant, and the extra recoil tendency of the lungs produces difficulty in breathing. The condition is called **infant respiratory distress syndrome** or RDS. The condition is also called **hyaline membrane disease**, because the improper secretion of surfactant results in coagulation of cellular debris and plasma proteins in structures called hyaline membranes that line the alveoli.

RDS occurs in about 1% of newborns, but is most common in premature infants, affecting 75% of infants that are delivered after only 26 weeks of gestation. Affected infants take rapid and shallow breaths, have low oxygen tensions in the blood (hypoxemia), and are acidotic because they cannot get rid of excess CO_2 (see Chapter 6.5). These babies rapidly perish from the condition if they are left untreated. Treatment includes instillation of exogenous surfactant into the trachea, from which it spreads throughout the lungs during positive pressure artificial respiration. Most premature infants can be rescued from RDS by these means.

AIRWAY RESISTANCE PARTLY DETERMINES DYNAMIC PRESSURES

The relaxation volume–pressure curves shown in Figure 6.1.8 are obtained from the nonphysiological case when the muscles are relaxed and airflow is zero. This does not pertain during breathing, yet the curves help us to understand the origin of the forces. During dynamic breathing, air actually flows into or out of the lungs and respiratory muscles are active. In this case, the alveolar pressure and intrapleural pressure reflect not only the elastic properties of the lungs and chest wall but also the airway resistance.

The alveolar and intrapleural pressures during quiet breathing are shown in Figure 6.1.10. We begin at (1) in the figure, which corresponds to the situation at the end of normal expiration. At this point, the volume of

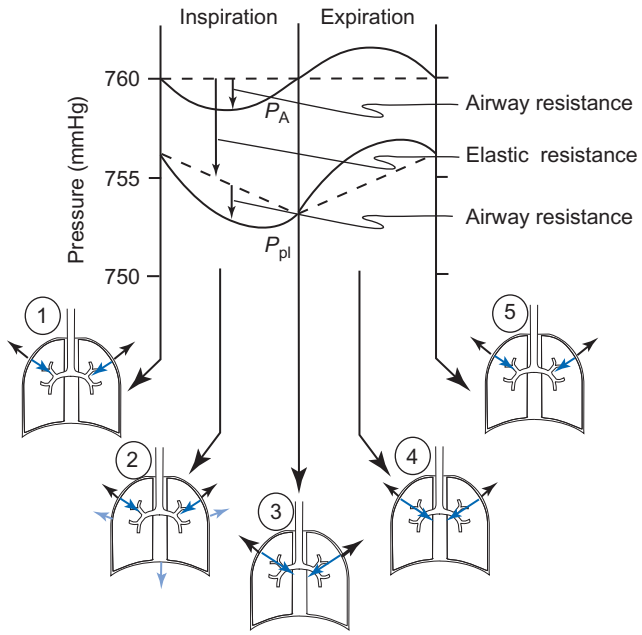

FIGURE 6.1.10 Alveolar and intrapleural pressures during dynamic breathing. If there were no airway resistance, the pressures would be nearly the same in the lungs as outside (the dashed lines). The alveolar pressure becomes lower when the inspiratory muscles pull the chest wall away from the lungs, making the intrapleural pressure lower, causing the lung to expand (because P_{lung} is more positive; see Figure 6.1.8) and alveolar pressure to drop. The expansion of the chest wall in normal breathing occurs when the chest wall forces are near zero, so that normal expansion occurs near the volume at which chest wall forces switch from expansion to recoil. At this larger volume, the expansion force of the chest wall is reduced so that removal of the inspiratory muscle forces causes the combined chest wall and lung system to recoil. In this case the intrapleural pressure is higher, because the muscles pulling on the chest wall are now relaxed. This in turn raises the alveolar pressure and air leaves the lung.

air in the lungs is called the **functional residual capacity** or **FRC**. Here the inspiratory and expiratory muscles are relaxed and alveolar pressure, P_A, is equal to the ambient barometric pressure, P_B. Thus the pressure across the entire respiratory system, P_{rs}, is zero according to Eqn [6.1.8]. This occurs when the recoil force of the lungs exactly balances the expansion force of the chest wall. At this point, the intrapleural pressure is lower than P_A or P_B. The lung and chest wall are pulling in opposite directions. This corresponds to point B in the lower panel of Figure 6.1.8.

At the beginning of a normal inspiration, the inspiratory muscles begin to pull the chest wall away from the lungs (light blue arrows at (2) in Figure 6.1.10), causing the intrapleural pressure to become lower. This causes the lungs to expand and alveolar pressure to drop, driving air into the lungs. If there were no airway resistance, then gas movement would be nearly instantaneous and the pressure differences driving air movement would be tiny. The airway resistance requires greater pressure drops to drive airflow. Normal inspiration of some 500 mL is enough to reduce the expansion tendencies of the chest wall to zero (point A in the top panel of Figure 6.1.8) and possibly large enough to enter the region of the curve where the chest wall contributes to overall respiratory system recoil. The intrapleural pressure falls even more than is necessary only to compensate for airway resistance. This additional fall overcomes elastic resistance.

At the beginning of expiration ((3) in Figure 6.1.10), the inspiratory muscles relax. This removes one of the expansion forces, and so at this point the recoil forces of the lungs dominate the balance of forces. The lungs recoil and intrapleural and alveolar pressures rise. Because the lungs are always tending to pull away from the chest wall, the intrapleural pressure remains subatmospheric throughout normal inspiration and expiration. The increased alveolar pressure overcomes airway resistance. The pressure increase in the intrapleural pressure overcomes both the airway resistance and the elastic resistance.

SUMMARY

The purpose of the respiratory system is to provide O_2 for metabolism and to remove waste CO_2. To do this, the respiratory system brings in new air and expires air that is depleted of O_2 and enriched in CO_2. Movement of air responds to pressure differences: inspiration is brought about by lowering the pressure in the lung by expanding the thoracic cavity. Expiration is brought about by increasing the pressure in the lungs. Inspiration is active. Contraction of the diaphragm expands the thoracic cavity against the recoil tendency of the lungs. In forceful breathing, the external intercostals may aid inspiration. Expiration is usually passive but may be aided by the abdominal muscles and internal intercostal muscles. The recoil tendency of the lungs arises from elastic fibers and surface tension in the millions of alveoli, little sacs of lung tissue that closely appose blood capillaries for the exchange of gases. The surface tension is reduced by surfactant, a lipoprotein produced by alveolar type II cells. This helps reduce the recoil tendency of the lung, which in turn reduces the work of breathing. Surfactant also helps keep alveoli the same size because it reduces the surface tension when alveolar size decreases. Surfactant also keeps the alveoli dry (by reducing negative pressure within the interstitial spaces) and causes hysteresis in the pressure–volume curves of the lungs.

Air passes along mucus membranes that line the nasal cavity, where it is conditioned by removal of dust particles, humidification, and warming. Air then passes through the tracheobronchial tree, which consists of progressively smaller and more numerous airways that lead eventually to the alveoli. The lung is suspended within the thoracic cavity. It is covered by a membrane, the visceral pleura, which is continuous with the parietal pleura that lines the chest wall. The pleural fluid is a thin layer of fluid that allows the lung to slide along the chest wall while remaining attached through the tension in the fluid. The intrapleural pressure is typically subatmospheric, caused by the recoil tendency of the lungs and the tendency of the chest wall to expand. Because the intrapleural pressure is less than alveolar pressure, the pressure across the lung itself is positive, keeping it expanded. During inspiration, the chest wall moves outward, making the intrapleural pressure more negative and thereby expanding the lung. This reduces the pressure

within the lung, causing air to move from the atmosphere into the lung. The reverse occurs during expiration.

REVIEW QUESTIONS

1. What functions of the tracheobronchial tree disappear during mouth breathing?
2. At the end of a normal expiration, the glottis is open but no air moves into or out of the lung. What is the alveolar pressure at this time with respect to barometric pressure? Find this point on the relaxation volume–pressure curve (see Figure 6.1.8)
3. Explain why surfactant (a) lowers surface tension, (b) reduces the work of breathing, (c) helps stabilize alveoli size, and (d) prevents low interstitial fluid pressures.
4. The relaxation volume–pressure curve shows that large lung volumes must be supported by large positive pressure (solid line in Figure 6.1.8). In dynamic breathing, alveolar pressure during inspiration is never positive! How do the lungs get to that position?
5. At rest, the pulmonary ventilation is about $6\ \mathrm{L\ min^{-1}}$. During exercise, it can increase markedly, depending on the size of the person and their physical fitness, to highs near $120\ \mathrm{L\ min^{-1}}$. What happens to alveolar pressure, P_A, during inspiration and expiration during exercise, with respect to its value at rest?