The field of pulmonary mechanics—the physics of the lungs, airways, and chest wall—deals with how the body moves air in and out of the lungs, producing a change in lung volume ($V_L$). When we examine these mechanical properties while no air is flowing, we are studying static properties. The situation becomes more complicated under dynamic conditions, when the lungs are changing volume and air is flowing either in or out.

### Static Properties of the Lung

#### The Balance Between the Outward Elastic Recoil of the Chest Wall and the Inward Elastic Recoil of the Lungs Generates a Subatmospheric Intrapleural Pressure

The interaction between the lungs and the thoracic cage determines $V_L$. The lungs have a tendency to collapse because of their elastic recoil, a static property represented by the inwardly directed arrows in Figure 27-1A. The chest wall also has an elastic recoil. However, this elastic recoil tends to pull the thoracic cage outward (Fig. 27-1B). The stage is thus set for an interaction between the lungs and the chest wall: at equilibrium, the inward elastic recoil of the lungs exactly balances the outward elastic recoil of the chest wall (Fig. 27-1C). This interaction between lungs and chest wall does not occur by direct attachment but through the intrapleural space between the visceral and parietal pleurae (see Chapter 26). This space is filled with a small amount of pleural fluid and is extremely thin (5 to 35 μm). Because the lungs and chest wall pull away from each other on opposite sides of the intrapleural space, the intrapleural pressure ($P_{IP}$) is less than barometric pressure ($P_b$); that is, the intrapleural space is a relative vacuum. Although the designation $P_{IP}$ implies that we are referring exclusively to the intrapleural space, this description is not entirely accurate. Indeed, in addition to the intrapleural space, $P_{IP}$ is probably similar to the pressure in several other regions of the chest cavity:

1. the virtual space between the chest wall or diaphragm and the parietal pleura;
2. the virtual space between the lung and the visceral pleura;
3. the interstitial space that surrounds all pulmonary airways;
4. around the heart and vessels;
5. around and—to the extent that smooth muscle tone can be neglected—inside the esophagus.

It is helpful to think of $P_{IP}$ as the intrathoracic pressure—the pressure everywhere in the thorax except in the lumens of blood vessels, lymphatics, or airways.

The vacuum is not uniform throughout the intrapleural space. When the subject is upright, the vacuum is greatest (i.e., $P_{IP}$ is least) near the apex of the lungs and progressively falls along the longitudinal axis to its lowest value near the bases of the lungs (Fig. 27-2). If a subject whose lungs are ∼30 cm tall has finished a quiet expiration, and if $P_b$ is 760 mm Hg, $P_{IP}$ is ∼753 mm Hg near the apices of the lungs and ∼758 mm Hg near the bases. The $P_{IP}$ gradient is about what one would expect, given the density of the lungs. Note that $P_{IP}$ is subatmospheric throughout the chest cavity. Because respiratory physiologists historically measured these small pressures with water manometers rather than with less sensitive mercury manometers, it has become customary to express $P_{IP}$ in cm H$_2$O relative to a $P_b$ of 0 cm H$_2$O. Thus, $P_{IP}$ is about −10 cm H$_2$O at the apex and −2.5 cm H$_2$O at the base of the lungs.

The reasons for the apex-to-base $P_{IP}$ gradient are gravity and posture. When an individual stands vertically on the surface of the earth, gravity pulls the lungs downward and away from the apex of the thoracic cage. This force creates a greater vacuum (i.e., a lower $P_{IP}$) at the apex. Gravity also pushes the bases of the lungs into the thoracic cavity, reducing the vacuum there. Standing on one’s head would invert these relationships. Lying on one’s side would create a $P_{IP}$ gradient along a frontal-horizontal axis (i.e., from side to side), although the $P_{IP}$ gradient would be much smaller because the side-to-side dimension of the thorax (and therefore the gradient created by the weight of the lungs) is less than the longitudinal dimension. In outer space, the $P_{IP}$ gradient would vanish. Thus, the local $P_{IP}$ depends on the position within the gravitational field.
For most of the remainder of this book, we ignore the $P_{IP}$ gradient and refer to an average $P_{IP}$ of about $-5 \text{ cm H}_2\text{O}$ after a quiet expiration (Fig. 27-2).

Contraction of the Diaphragm and Selected Intercostal Muscles Increases the Volume of the Thorax, Producing an Inspiration

We have seen that the opposing elastic recoils of the lungs and chest wall create a negative $P_{IP}$ that keeps the lungs expanded. Any change in the balance between these elastic recoils will cause $V_L$ to change as well. For example, imagine a healthy person with a functional residual capacity (FRC) of 3 L and a $P_{IP}$ of $-5 \text{ cm H}_2\text{O}$. If that person now develops pulmonary fibrosis, which increases the elastic recoil of the lungs, FRC would decrease because a $P_{IP}$ of $-5 \text{ cm H}_2\text{O}$ would no longer be adequate to keep the resting $V_L$ at 3 L. Moreover, as the lungs shrink, $P_{IP}$ would become more negative, causing chest volume to decrease as well. Under normal circumstances, the key elastic recoil is the one we control: the elastic recoil of the chest wall, which we change moment to moment by modulating the tension of the muscles of respiration.

The muscles of inspiration expand the chest, increasing the elastic recoil of the chest wall and making $P_{IP}$ more negative. Despite the $P_{IP}$ gradient from the apex to the base of the lungs when no air is flowing at FRC (Fig. 27-2), the $\Delta P_{IP}$ during inspiration is similar throughout the thoracic cavity. Responding to this enhanced intrathoracic vacuum, the lungs expand passively. The increase in $V_L$ is virtually the same as the increase in thoracic volume. The muscles that produce a quiet inspiration are called the primary muscles of inspiration and include the diaphragm and many intercostal muscles.

The most important component of the increase in chest volume is the rise in the chest cavity’s rostral-caudal diameter, a result of the action of the diaphragm. Stimulated by the phrenic nerves (derived from cervical roots C3 to C5), the diaphragm contracts and moves downward into the abdomen $\sim 1 \text{ cm}$ during quiet ventilation.

The external and internal intercostal muscles, innervated by segmental spinal nerves, span the space between adjacent ribs. The action of each such muscle depends partly on its orientation but especially—because of the shape of the rib cage—on its position along the rostral-caudal axis and around the dorsal-ventral circumference of the rib cage. Thus, not all external intercostals are inspiratory, and not all internal intercostals are expiratory. Inspiratory neurons preferentially stimulate the most rostral and dorsal external intercostals and the parasternal internal intercostals, both of which have inspiratory mechanical advantages. The contraction of these muscles has two consequences (Fig. 27-3A).

First, the rib cage and the tissues between the ribs stiffen and are therefore better able to withstand the increasingly negative $P_{IP}$. Second, thoracic volume increases as ribs 2 through 10 rotate upward and outward, increasing the transverse diameter (bucket-handle effect, Fig. 27-3B), and the upper ribs rotate the sternum upward and outward, increasing the anterior-posterior diameter (water pump-handle effect).

During a forced inspiration, the accessory (or secondary) muscles of inspiration also come into play:
1. **Scalenes.** These muscles lift the first two ribs.

2. **Sternocleidomastoids.** These muscles lift the sternum outward, contributing to the water pump–handle effect.

3. **Neck and back muscles.** These elevate the pectoral girdle (increasing the cross-sectional area of the thorax) and extend the back (increasing the rostral-caudal length).

4. **Upper respiratory tract muscles.** The actions of these muscles decrease airway resistance.

**Relaxation of the Muscles of Inspiration Produces a Quiet Expiration**

During a *quiet* inspiration, normal lungs store enough energy in their elastic recoil to fuel a quiet expiration, just as stretching of a rubber band stores enough energy to fuel the return to initial length. Thus, a quiet expiration is normally passive, accomplished simply by relaxation of the muscles of inspiration. Thus, there are no primary muscles of expiration.

Expiration is not always entirely passive. One example is a forced expiration in an individual with normal airway resistance. Another is even a quiet expiration of a person with a disease that increases airway resistance (e.g., asthma, chronic bronchitis, emphysema). In either case, the accessory muscles of expiration help make $P_{\text{IP}}$ more positive:

1. **Abdominal muscles** (internal and external oblique, rectoabdominal and transverse abdominal muscles). Contraction of these muscles (Fig. 27-3C) increases intra-abdominal pressure and forces the diaphragm upward into the chest cavity, decreasing the rostral-caudal diameter of the thorax and increasing $P_{\text{IP}}$.

2. **Intercostals.** The most ventral-caudal external intercostals, the most caudal internal intercostals, and an intercostal-like muscle called the triangularis sterni all have an expiratory mechanical advantage. Expiratory neurons selectively stimulate these muscles, reducing both the anterior-posterior and the transverse diameters of the thorax. These actions are particularly important for coughing.

3. **Neck and back muscles.** Lowering of the pectoral girdle reduces the cross-sectional area of the thorax, whereas flexion of the trunk reduces the rostral-caudal diameter.

During a forced inspiration, the accessory muscles of inspiration use their energy mainly to increase $V_L$ (rather than to overcome resistance to airflow); the lungs store this extra energy in their elastic recoil. During a forced expiration, the accessory muscles of expiration use their energy mainly to overcome the resistance to airflow, as discussed later.

**Increase of the Static Compliance Makes It Easier to Inflate the Lungs**

Imagine that a person suffers a puncture wound to the chest cavity, so that air enters the thorax from the atmosphere, raising $P_{\text{IP}}$ to the same level as $P_b$. This condition is called a pneumothorax (from the Greek pneuma [air]). With no vacuum to counter their elastic recoil, alveoli will collapse—a condition known as atelectasis. The upper part of Figure 27-4A illustrates an extreme hypothetical case in which pres-
Collapse and re-inflation of the lungs. In normal breathing, pressure-volume loop has much less hysteresis. In principle, we can measure \( P_A \) and \( P_{IP} \), so that transpulmonary pressure \( P_{TP} \) falls to 0, collapsing the lungs.

\[
P_{TP} = P_A - P_{IP}
\]

When the glottis is open under static conditions, the pressure that inflates the alveoli (i.e., \( P_{TP} \)) is simply the negative of \( P_{IP} \). We can re-expand the lungs to FRC by any combination of an increase in \( P_a \) and a decrease in \( P_{TP} \), as long as \( P_{TP} \) ends up at 5 cm H\(_2\)O (Fig. 27-4A, lower panels). Thus, it makes no difference whether we increase \( P_a \) from 0 to +5 cm H\(_2\)O with \( P_{IP} \) fixed at 0 (the principle behind positive-pressure ventilation in an intensive care unit) or whether we decrease \( P_{IP} \) from 0 to −5 cm H\(_2\)O with \( P_a \) fixed at 0 (the principle behind physiological ventilation). In both cases, \( V_l \) increases by the same amount.

A clinician would treat the pneumothorax by inserting a chest tube through the wound into the thoracic cavity and gradually pumping out the intrathoracic air. The clinician might also insert a tube through the mouth and into the upper trachea (to ensure a patent airway), use a mechanical ventilator (to ensure gas exchange), and sedate the patient (to prevent the patient from fighting the ventilator). Between the inspiratory cycles of the ventilator, the lungs are under static conditions and \( V_l \) depends only on \( P_{TP} \)—that is, the difference between \( P_a \) (which is set by the ventilator) and \( P_{IP} \). As we remove air from the thorax, \( P_{IP} \) becomes more negative and the alveoli re-expand. We can characterize the elastic (or static) properties of the lungs by plotting \( V_l \) versus \( P_{TP} \) as \( V_l \) increases (Fig. 27-4B, purple curve). How do we obtain the necessary data? In principle, we could determine \( V_l \) by using one of the methods discussed in Equation 26-4. We could read off \( P_a \) (needed to compute \( P_{TP} \)) directly from the ventilator. Finally, we could in principle measure \( P_{IP} \) by using a pressure transducer at the tip of the chest tube. Most important, we must take our readings between inspiratory cycles of the ventilator—under static conditions.
During the re-inflation, measured under static conditions, we can divide the effect on \( V_L \) into four stages, starting at the left end of the purple curve in Figure 27-4B:

**Stage 1:** Stable \( V_L \). In the lowest range of \( P_{tr} \) values, making \( P_{tr} \) more negative has little or no effect on \( V_L \). For example, decreasing \( P_{tr} \) from 0 to \(-1\) cm H\(_2\)O (i.e., increase \( P_{tr} \) from 0 to \(+1\) cm H\(_2\)O), we record no change in \( V_L \). Why? As discussed later, it is very difficult—because of the surrounding tissue created by the air-water interface—to open a previously closed airway that is completely collapsed. Until \( P_{tr} \) is large enough to overcome the collapsing effects of surface tension, a decrease in \( P_{tr} \) has no effect on \( V_L \).

**Stage 2:** Opening of airways. Decreasing \( P_{tr} \) beyond about \(-8\) cm H\(_2\)O produces \( V_L \) increases that are at first small, reflecting the opening of proximal airways with the greatest compliance. Further decreasing \( P_{tr} \) produces larger increases in \( V_L \), reflecting the expansion of already open airways as well as recruitment of others.

**Stage 3:** Linear expansion of open airways. After all the airways are already open, making \( P_{tr} \) increasingly more negative inflates all airways further, causing \( V_L \) to increase in a roughly linear fashion.

**Stage 4:** Limit of airway inflation. As \( V_L \) approaches TLC, decreases in \( P_{tr} \) produce ever smaller increases in \( V_L \), reflecting decreased airway and chest wall compliance and the limits of muscle strength.

What would happen if, having inflated the lungs to TLC, we allowed \( P_{tr} \) to increase to 0 cm H\(_2\)O once again? Obviously, the \( V_L \) would decrease. However, the lungs follow a different path during deflation (Fig. 27-4B, red curve), creating a \( P_{tr}-V_L \) loop. The difference between the inflation and the deflation paths—hysteresis—exists because a greater \( P_{tr} \) is required to open a previously closed airway, owing to a deficit of surfactant at the air-water interface, than to keep an open airway from closing, reflecting abundant surfactant. We will discuss surfactant in the next section. The horizontal dashed line in Figure 27-4B shows that inflating collapsed lungs to FRC requires a \( P_{tr} \) of \(-12\) cm H\(_2\)O (red point), whereas maintaining previously inflated lungs at FRC requires a \( P_{tr} \) slightly less negative than \(-5\) cm H\(_2\)O (blue point).

During normal ventilation, the lungs exhibit much less hysteresis, and the green \( P_{tr}-V_L \) loop in Figure 27-4B lies close to the red deflation limb of our original loop. The changes in \( V_L \) in Figure 27-4B reflect mainly changes in the volume of alveoli, with a small contribution from conducting airways.

We will now focus on just the red curve in Figure 27-4B, a portion of which is the middle curve in Figure 27-5. Here, \( P_{tr} \) is \(+5\) cm H\(_2\)O when \( V_L \) is at FRC. As the subject makes a normal inspiration with a tidal volume (\( V_t \)) of 500 mL, \( P_{tr} \) increases (i.e., \( P_{tr} \) decreases) by 2.5 cm H\(_2\)O. The ratio of \( \Delta V_L \) to \( \Delta P_{tr} \) (i.e., the slope of the \( P_{tr}-V_L \) curve) is the compliance and a measure of the distensibility of the lungs. In our example,

\[
C = \frac{\Delta V_L}{\Delta P_{tr}} = \frac{0.5L}{(7.5-5.0) cm H_2O} = 0.2 \frac{L}{cm H_2O} \quad (27-4)
\]

Because we made this measurement under conditions of zero airflow, \( C \) is the static compliance. Static compliance, like \( V_L \), is mainly a property of the alveoli. The elastance of the lungs, which is a measure of their elastic recoil, is the reciprocal of the compliance \((E = 1/C)\). Lungs with a high compliance have a low elastic recoil, and vice versa.

Figure 27-5 also shows representative \( P_{tr}-V_L \) relationships for lungs of patients with pulmonary fibrosis (bottom curve) and emphysema (top curve). In pulmonary fibrosis, the disease process causes deposition of fibrous tissue, so that the lung is stiff and difficult to inflate. Patients with restrictive lung disease, by definition, have a decreased \( C \) (i.e., a decreased slope of the \( V_L \) versus \( P_{tr} \) relationship in Fig. 27-5) at a given \( V_L \). The same \( \Delta P_{tr} \) that produces a 500-mL \( V_L \) increase in normal lungs produces a substantially smaller \( V_L \) increase in fibrotic lungs. In other words, static compliance (\( \Delta V_L/\Delta P_{tr} \)) is much less, or elastic recoil is much greater.

In emphysema, the situation is reversed. The disease process, a common consequence of cigarette smoking, destroys pulmonary tissue and makes the lungs floppy. An important part of the disease process is the destruction of the extracellular matrix, including elastin, by elastase released from macrophages. Normal mice that are exposed to cigarette smoke develop emphysema rapidly, whereas the disease does not develop in “smoker” mice lacking the macrophage elastase gene. The same increase in \( P_{tr} \) that produces a 500-mL \( V_L \) increase in normal lungs produces a substantially larger \( V_L \) increase in lungs with emphysema. In other words, static compliance is much greater (i.e., much less elastic recoil).

Because it requires work to inflate the lungs against their elastic recoil, one might think that a little emphysema might be a good thing. Although it is true that patients with emphysema exert less effort to inflate their lungs, the cigarette smoker pays a terrible price for this small advantage. The destruction of pulmonary architecture also makes emphysema-affected airways more prone to collapse during expiration, drastically increasing airway resistance.

Two additional points are worth noting. First, compliance (i.e., slope of \( P_{tr}-V_L \) curve) decreases as \( V_L \) increases...
restrictive Pulmonary Disease

Two major categories of pulmonary disease—restrictive and obstructive—can severely reduce total ventilation, that is, the amount of air entering and leaving the lungs per unit of time. Pulmonologists use the term restrictive lung disease in an inclusive sense to refer to any disorder that reduces functional residual capacity, vital capacity, or total lung capacity (see Fig. 26-8), thereby making the lungs difficult to inflate. Pure restrictive disease does not affect airway resistance. Restrictive disease can affect the lung parenchyma or three extrapulmonary structures.

Lung Parenchyma

Restrictive diseases of the lung parenchyma decrease the static compliance of the lung—mainly a property of the alveoli. To overcome increased elastic recoil, the patient must make extra effort to inhale. The patient compensates by making rapid but shallow inspirations. In newborns, an example is infant respiratory distress syndrome, caused by a deficiency in surfactant. Pulmonary edema is a buildup of fluid in the interstitial space between the alveolar and capillary walls and, eventually, the alveolar space. Interstitial inflammation of a variety of causes (e.g., infection, drugs, environmental exposure) can lead to the deposition of fibrous tissue and a group of diseases called diffuse interstitial pulmonary fibrosis.

Pleura

A buildup in the intrapleural space of either air (pneumothorax) or fluid (pleural effusion) can restrict the expansion of a vast number of alveoli.

Chest Wall

Rigidity of the chest wall makes it difficult to increase thoracic volume even if the neuromuscular system (see next) can generate normal forces. Ankylosing spondylitis is an inflammatory disorder of the axial skeleton that may reduce the bucket-handle rotation of the ribs during quiet inspirations and the flexion and extension of the trunk during forced inspirations and expirations. In kyphoscoliosis (angulation and rotation of the spine), deformation of the vertebrae and ribs may reduce ventilation. In both conditions, impairment of coughing predisposes to lung infections.

Neuromuscular System

The central nervous system may fail to stimulate the respiratory muscles adequately, or the muscles may fail to respond appropriately to stimulation. In polio, the virus occasionally attacks respiratory control centers in the brainstem. Amyotrophic lateral sclerosis (ALS or Lou Gehrig’s disease) leads to the destruction of premotor and motor neurons, including those to the muscles of respiration. (See Chapter 32.) Indeed, dyspnea on exertion is a common early symptom of ALS. Certain drug overdoses (e.g., barbiturate poisoning) may temporarily inhibit respiratory control centers in the brainstem. In the absence of supportive therapy (i.e., mechanical ventilation), the respiratory failure can be fatal. The pain that accompanies surgery or other injuries to the chest can also severely limit the ability to ventilate. Local paralysis of intercostal muscles allows the enhanced intrathoracic vacuum to suck in intercostal tissues during inspiration. This paradoxical movement reduces the efficiency of inspiration. Paradoxical movement may also occur with broken ribs, a condition known as flail chest.

Surface Tension at the Air-Water Interface of the Airways Accounts for Most of the Elastic Recoil of the Lungs

What is the basis of the elastic recoil that determines the static compliance of the lungs? The elasticity of pulmonary cells and the extracellular matrix (e.g., elastin and collagen), what we might think of as the “anatomical” component of elastic recoil, generally accounts for a small part. The basis of most of the recoil was suggested in 1929 by von Neergaard, who excised lungs from cats and inflated them by applying positive pressure to the trachea under two conditions. When he filled the lungs with air, the $P_{TP} - V_t$ curve looked similar to the one we have seen before (Fig. 27-6A, blue curve). However, when he degassed the airways and re-inflated them with saline, he found that (1) the $P_{TP} - V_t$ relationship (Fig. 27-6A, orange curve) exhibited far less hysteresis and (2) the static compliance was substantially greater (i.e., much less pressure was required to inflate the lungs). These changes occurred because the saline-filled lungs lacked the air-water interface that generated surface tension in the air-filled lungs. It is this surface tension that is responsible for a large fraction of the lung’s elastic recoil.

Surface tension is a measure of the force acting to pull a liquid’s surface molecules together at an air-liquid interface (Fig. 27-6B). Water molecules in the bulk liquid phase are equally attracted to surrounding water molecules in all directions, so that the net force acting on these “deep” water molecules is zero. However, water molecules at the surface are equally attracted to others in all directions but “up,” where no molecules are available to pull surface water molecules toward the air phase. Thus, a net force pulls surface molecules away from the air-water interface toward the bulk water phase.

We can think of the surface water molecules as beads connected by an elastic band. The force that pulls a water molecule down into the bulk also creates a tension between the molecules that remain at the surface, in a direction that is parallel to the surface. If we try to overcome this tension and stretch the air-water interface (Fig. 27-6C), thus increasing its area, we must apply force ($F$) to bring water molecules...
Figure 27-6  Effect of surface tension on the lung.
from the bulk liquid (a low-energy state) to the surface (a high-energy state). If the body of water on which we tug has a length of \( l \), then the surface tension \( T \) is

\[
T = \frac{F}{l}
\]  
(27-5)

For a simple air-water interface at 37°C, the surface tension is \( \sim 70 \text{ dynes/cm} \).

A drop of water falling through the air tends to form into a sphere because this shape has the smallest surface area and thus the lowest energy. Put differently, when the drop is spherical, it is impossible for any additional water molecules to leave the surface.

In the reverse scenario, a spherical air bubble surrounded by water (Fig. 27-6D), unbalanced forces acting on surface water molecules cause them to dive into the bulk, decreasing the surface area and creating tension in the plane of the air-water interface. This surface tension acts like a belt tightening around one’s waist. It tends to decrease the volume of compressible gas inside the bubble and increases its pressure. At equilibrium, the tendency of increased pressure to expand the gas bubble balances the tendency of surface tension to collapse it. Laplace’s equation describes this equilibrium:

\[
P = \frac{2T}{r}
\]  
(27-6)

\( P \) is the dependent variable; the surface tension \( T \) is a constant for a particular interface, and the bubble radius \( r \) is the independent variable. Therefore, the smaller the bubble’s radius, the greater the pressure needed to keep the bubble inflated. See Chapter 19 for a description of how Laplace’s treatment applies to blood vessels.

Our bubble-in-water analysis is important for the lung because a thin layer of water covers the inner surface of the alveolus. Just as surface tension at the air-water interface of our gas bubble causes the bubble to constrict, it also causes alveoli and other airways to constrict, contributing greatly to elastic recoil.

The analogy between air bubbles and alveoli breaks down somewhat because an alveolus only approximates a part of a sphere. A second complicating factor is that not all alveoli are the same size; some may have a diameter that is three or four times larger than that of others. Third, alveoli are interconnected.

Figure 27-6E shows what would happen if two imaginary air bubbles in water were connected by a tube with a valve that allows us to make or break the connection between the bubbles. For both, assume that the surface tension \( T \) is 70 dynes/cm. The valve is initially closed. The first bubble has a radius of 0.010 cm. The second is only half as wide. At equilibrium, the pressure required to keep the smaller bubble inflated is twice that necessary to keep the larger bubble inflated (see calculations in Fig. 27-6E). If we now open the valve between the two bubbles, air will flow from the smaller bubble to the larger bubble. To make matters worse for the smaller bubble, the smaller it becomes, the greater is the pressure needed to stabilize its shrinking radius. Because its pressure is less than required, air continues to flow out of the smaller bubble until it implodes completely.

In principle, the lung faces a similar problem. Smaller alveoli tend to collapse into larger ones. As we shall see, pulmonary surfactant minimizes this collapsing tendency by lowering surface tension. However, even without surfactant, the collapse of small alveoli could proceed only so far because each alveolus is tethered to adjacent alveoli, which help hold it open—the principle of interdependence.

Why would it matter if many smaller alveoli collapsed into a few larger alveoli? Such a collapse would reduce the total alveolar surface area available for diffusion of \( \text{O}_2 \) and \( \text{CO}_2 \) (see Chapter 29). Thus, from a teleological point of view, it is important for the lung to keep the alveoli as uniformly inflated as possible.

**Pulmonary Surfactant Is a Mixture of Lipids—Mainly Dipalmitoylphosphatidylcholine—and Apoproteins**

As noted earlier, surface tension accounts for most of the elastic recoil in normal lungs. However, if it were not for pulmonary surfactant, total elastic recoil would be even higher, and the lungs would be far more difficult to inflate. During quiet breathing, surfactant reduces surface tension to \( \sim 25 \text{ dynes/cm} \) or less, far below the value of 70 dynes/cm that exists at a pure air-water interface.

The term surfactant means a surface-active agent. Because surfactants have both a hydrophilic region (strongly attracted to water) and a hydrophobic region (strongly repelled by water), they localize to the surface of an air-water interface. An example of a synthetic surfactant is dishwashing detergent. As a younger student, you may have done a simple experiment in which you filled a small-diameter cup with water and carefully floated a thin sewing needle—lengthwise—on the surface. The needle, like an insect that walks on water, is supported by surface tension, which pulls in the plane of the air-water interface. When you add a drop of liquid detergent to the surface of the water, the needle instantly sinks. Why? The detergent greatly reduces the surface tension.

Detergent molecules orient themselves so that their hydrophilic heads point toward (and interact with) the most superficial water molecules, whereas the hydrophobic tails point toward the air (Fig. 27-7A). The hydrophilic surfactant heads pull strongly upward on the most superficial water molecules, greatly reducing the net force on these surface water molecules and minimizing their tendency to dive into the bulk water. What prevents surfactant at the air-surfactant interface from diving into the bulk water? The hydrophobic tails exert a counterforce, pulling the surfactant upward toward the air. The situation is not unlike that of a fishing line with a bobber at one end and a sinker at the other: as long as the bobber is sufficiently buoyant, it remains at the water’s surface. Thus, unlike surface water molecules, which are subjected to a large net force pushing them into the bulk, surfactant experiences a much smaller net force. The greater the surface density of surfactant molecules at the air-water interface (i.e., the smaller the surface occupied by water molecules), the smaller the surface tension.

**Pulmonary surfactant** is a complex mixture of lipids and proteins. Type II alveolar cells (see Chapter 26), cuboidal epithelial cells that coexist with the much thinner type I cells,
synthesize and secrete pulmonary surfactant. Clara cells in the respiratory bronchioles manufacture at least some components of pulmonary surfactant. Lipids make up ~90% of surfactant and are responsible for the surface-active properties. About half of the lipid is dipalmitoylphosphatidylcholine (DPPC; Fig. 27-7B), also known as dipalmitoyllecithin, which contains two fully saturated 16-carbon fatty acid chains (i.e., palmitates). The second most common lipids in pulmonary surfactant are phosphatidylglycerol (~11% of lipid) is overrepresented in surfactant.

**Table 27-1**  Surfactant Apoproteins

<table>
<thead>
<tr>
<th>Apoprotein</th>
<th>Solubility</th>
<th>Role</th>
</tr>
</thead>
<tbody>
<tr>
<td>SP-A</td>
<td>Water</td>
<td>Innate immunity Formation of tubular myelin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SP-B</td>
<td>Lipid</td>
<td>Speeds formation of monolayer Formation of tubular myelin</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SP-C</td>
<td>Lipid</td>
<td>Speeds formation of monolayer</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SP-D</td>
<td>Water</td>
<td>Innate immunity Metabolism of surfactant?</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Proteins account for the remaining ~10% of pulmonary surfactant. Plasma proteins (mainly albumin) and secretory IgA make up about half of the protein, and four apoproteins (SP-A, SP-B, SP-C, and SP-D) make up the rest. SP-A and SP-D are water soluble and have collagen-like domains (Table 27-1). Both contribute to “innate immunity” by acting as opsonins to coat bacteria and viruses, thereby promoting phagocytosis by macrophages resident in the alveoli. In addition, SP-A (Fig. 27-7C) may be important for exertion of feedback control that limits surfactant secretion. The two hydrophobic apoproteins, SP-B and SP-C, are intrinsic membrane proteins that greatly increase the rate at which surfactant enters the air-water interface and then spreads as a surface film. The hereditary absence of SP-B leads to respiratory distress that is fatal unless the newborn receives a lung transplant.

The lipid components of pulmonary surfactant enter type II cells from the bloodstream (Fig. 27-8A). Type II cells use the secretory pathway (see Chapter 2) to synthesize the four apoproteins, all of which undergo substantial post-translational modification. The final assembly of surfactant occurs in lamellar bodies, which are ~1 μm in diameter and consist of concentric layers of lipid and protein (Fig. 27-8B). Some of the material in these lamellar bodies represents newly synthesized components, and some of it represents recycled surfactant components retrieved from the alveolar surface. Each hour, the normal lung secretes into the alveolar space ~10% of the material present in the lamellar bodies.

The secretion of pulmonary surfactant occurs by constitutive exocytosis (see Chapter 2). Both synthesis and secretion are quite low until immediately before birth, when a surge in maternal glucocorticoid levels triggers these processes (see Chapter 57). Infants born prematurely may thus lack sufficient levels of surfactant and may develop infant respiratory distress syndrome (IRDS; see Chapter 57 for the box on this topic). In postnatal life, several stimuli enhance the surfactant secretion, including hyperinflation of the lungs (e.g., sighing and yawning), exercise, and pharmacological agents (e.g., β-adrenergic agonists, Ca²⁺ ionophores).

After its secretion into the thin layer of water that covers the alveolar epithelium, freed from the physical constraints of confinement to a lamellar body, pulmonary surfactant undergoes major structural changes. In this aqueous layer, surfactant takes on the form of a meshwork known as...
tubular myelin (Fig. 27-8B), which is rich in surfactant apoproteins. It is not clear whether surfactant normally passes through the tubular myelin state before forming a surface film at the air-water interface. However, tubular myelin is not required; SP-A knockout mice lack tubular myelin but have a normal surface film.

Two mechanisms remove components of pulmonary surfactant from the surface of alveoli. Alveolar macrophages degrade some of the surfactant. Type II cells take up the rest and either recycle or destroy it.

**Pulmonary Surfactant Reduces Surface Tension and Increases Compliance**

The pulmonary surfactant present at the alveolar air-water interface has three major effects.

First, because surfactant reduces surface tension, it increases compliance, making it far easier to inflate the lungs. If surfactant suddenly disappeared from the lungs, mimicking the situation in IRDS, total elastic recoil would increase (i.e., compliance would decrease) twofold or more, causing small airways to collapse partially. The situation would be similar to that described by the fibrosis curve in Figure 27-5. Because the compliance of the lungs is far lower than normal, an infant with IRDS—compared with a normal infant—must produce far larger changes in $P_{IP}$ (or $P_{EP}$) to achieve the same increase in $V_{I}$. Therefore, infants with low surfactant levels must expend tremendous effort to contract their inspiratory muscles and expand the lungs.

Second, by reducing surface tension, surfactant minimizes fluid accumulation in the alveolus. In the absence of surfactant, the large surface tension of the liquid layer between the air and the alveolar type I cell would cause the “air bubble” to collapse, drawing fluid into the alveolar space from the interstitium. The net effect would be to increase the thickness of the liquid layer, thereby impairing gas diffusion. With normal levels of surfactant, the surface tension of the water layer is low, and the tendency to draw fluid from the interstitium to the alveolar space is balanced by the negative interstitial hydrostatic pressure (i.e., $P_{IP}$), which favors fluid movement from the alveolar space into the interstitium.

Third, surfactant helps keep alveolar size relatively uniform during the respiratory cycle. Imagine that we start—after a quiet expiration—with two alveoli having the same radius (e.g., 100 μm) and the same surface density of surfactant (to yield a surface tension of 20 dynes/cm), as indicated by the inner dashed circles of the two alveoli in Figure 27-9. However, either the conducting airway leading to the lower alveolus has a higher resistance or the lower alveolus itself has more fibrous tissue. Either way, the lower alveolus inflates more slowly during inspiration and—at any time—has a smaller volume than the upper one. This size difference has two negative consequences. (1) The total surface area of the two alveoli is less than if they had inflated equally, impairing gas diffusion. (2) Because the final volume increase of the upper alveolus may be greater than that of the lower one, its ventilation may be greater. Such unevenness of ventilation impairs effective gas exchange (see Chapter 31).

Fortunately, surfactant helps alveoli dynamically adjust their rates of inflation and deflation, making ventilation more uniform among alveoli. During rapid inflation, the
alveolar surface expands more rapidly than additional surfactant can reach the surface from a surfactant pool beneath the surface. Thus, surfactant on the surface is thought to break up like a flow of ice on the sea, with open areas of pure water between clusters of surfactant. With more exposed water at the surface, surface tension increases. Surface tension may double during inspiration, compared with the resting value at FRC. This effect would be exaggerated in rapidly expanding alveoli, which would develop a higher surface tension more quickly than slowly expanding alveoli. This higher surface tension produces a greater elastic recoil that opposes further expansion. Thus, the dilution of surfactant tends to put more of a brake on rapidly expanding airways, slowing their expansion to more nearly match that of alveoli that tend to inflate more slowly.

The opposite appears to happen during expiration, when the surface area of rapidly contracting alveoli falls more rapidly than surfactant can dive back down into the subsurface pool. The compression of surfactant causes surface tension to fall precipitously. Surface tension during expiration may fall to half the resting value at FRC. The more rapidly an alveolus shrinks, the more quickly its surface tension falls, the lower is its elastic recoil, and the greater is its tendency to re-expand. This action puts a brake on rapidly contracting alveoli, slowing their rate of shrinkage to more closely match that of slowly contracting alveoli. These changes in surfactant contribute to the small amount of hysteresis in a \( P_a-V_f \) loop during quiet breathing (green loop in Fig. 27-4B).

**DYNAMIC PROPERTIES OF THE LUNG**

When air is flowing—that is, under dynamic conditions—one must not only exert the force necessary to maintain the lung and chest wall at a certain volume (i.e., static component of force) but also exert an extra force to overcome the inertia and resistance of the tissues and air molecules (i.e., dynamic component of force).

**Airflow Is Proportional to the Difference Between Alveolar and Atmospheric Pressure but Inversely Proportional to Airway Resistance**

The flow of air through tubes is governed by the same principles governing the flow of blood through blood vessels and the flow of electrical current through wires (see Equation 17-1). Airflow is proportional to driving pressure (\( \Delta P \)) but inversely proportional to total airway resistance (\( R_{AW} \)):

\[
\dot{V} = \frac{\Delta P}{R_{AW}} = \frac{P_A - P_B}{R_{AW}} \tag{27-7}
\]

\( \dot{V} \) (measured in liters per second) is airflow; the dot above the \( V \) indicates the time derivative of volume. For the lung, the driving pressure is the difference between alveolar pressure (\( P_a \)) and barometric pressure (\( P_b \)). Thus, for a fixed resistance, more airflow requires a greater \( \Delta P \) (i.e., more effort). Viewed differently, to achieve a desired airflow, a greater resistance requires a greater \( \Delta P \).

When airflow is laminar—that is, when air molecules move smoothly in the same direction—we can apply Poiseuille’s law, which states that the resistance (\( R \)) of a tube is proportional to the viscosity of the gas (\( \eta \)) and length of the tube (\( l \)) but inversely proportional to the fourth power of radius:

\[
R = \frac{8 \eta l}{\pi r^4} \tag{27-8}
\]

This equation is the same as Equation 17-11 for laminar blood flow. In general, changes in viscosity and length are not very important for the lung, although the resistance while breathing helium is greater than that for nitrogen, the major component of air, because helium has a greater viscosity. However, the key aspect of Equation 27-8 is that airflow is extraordinarily sensitive to changes in airway radius. The fourth-power dependence of \( R \) on radius means that a 10% decrease in radius causes a 52% increase in \( R \)—that is, a 34% decrease in airflow. Although Poiseuille’s law strictly applies only to laminar flow conditions, as discussed later, airflow is even more sensitive to changes in radius when airflow is not laminar.

In principle, it is possible to compute the total airway resistance of the tracheobronchial tree from anatomical measurements, applying Poiseuille’s law when the flow is laminar and analogous expressions for airways in which the flow is not laminar. In 1915, Rohrer used this approach, along with painstaking measurements of the lengths and diameters of the airways of an autopsy specimen, to calculate the \( R_{Aw} \) of the tracheobronchial tree. However, it is not practical to compute \( R_{Aw} \) values, especially if we are interested in physi-
mechanical or pathological changes in $R_{AW}$. Therefore, for both physiologists and physicians, it is important to measure $R_{AW}$ directly. Rearrangement of Equation 27-7 yields an expression for $R_{AW}$ that we can compute after measurement of the driving pressure and the airflow that it produces:

$$R_{AW} = \frac{\Delta P}{V} = \frac{P_A - P_B}{V} \left( \text{units: } \frac{\text{cm H}_2\text{O}}{\text{L/s}} \right) \quad (27-9)$$

We can measure airflow directly with a flowmeter (pneumotachometer) built into a tube through which the subject breathes. The driving pressure is more of a problem because of the difficulty in measuring $P_a$ during breathing. In 1956, DuBois and colleagues met this challenge by cleverly using Boyle’s law and a plethysmograph to measure the $P_a$ (Fig. 27-10). For example, if the peak $V$ during a quiet inspiration is ~0.5 L/s (by convention, a negative value denotes inflow) and $P_a$ at the same instant is ~1 cm H$_2$O (from the plethysmograph), then

$$R_{AW} = \frac{\Delta P}{V} = \frac{P_A - P_B}{V} = \frac{-1 \text{cm H}_2\text{O}}{0.5 \text{ L/s}} = 2 \text{ cm H}_2\text{O/L/s} \quad (27-10)$$

In normal individuals, $R_{AW}$ is ~1.5 cm H$_2$O/(L/s) but can range from 0.6 to 2.3. Resistance values are higher in patients with respiratory disease and can exceed 10 cm H$_2$O/(L/s) in extreme cases.

The resistance that we measure in this way is the airway resistance, which represents ~80% of total pulmonary resistance. The remaining 20% represents tissue resistance—that is, the friction of pulmonary and thoracic tissues as they slide past one another as the lungs expand or contract.

In the Lung, Airflow Is Transitional in Most of the Tracheobronchial Tree

We have seen that laminar airflow is governed by a relationship that is similar to Ohm’s law. What happens when the airflow is not laminar? How can we predict whether the airflow is likely to be laminar? The flow of a fluid down a tube is laminar when particles passing any particular point always have the same speed and direction. Because of their viscosity, real fluids move fastest down the midline of the tube, and velocity falls to 0 as we approach the wall of the tube (Fig. 27-11A), as discussed for blood in Chapter 17. If the average velocity of the fluid flowing down the tube passes a critical value, flow becomes turbulent; local irregular currents, called vortices, develop randomly, and they greatly increase resistance to flow. Under ideal laboratory conditions, airflow generally is laminar when the dimensionless Reynolds number ($Re$) is less than 2000 (see Chapter 17):

$$Re = \frac{2r\bar{V}}{\eta} \quad (27-11)$$

$r$ is the radius of the tube, $\bar{V}$ is the velocity of the gas averaged over the cross section of the tube, $\rho$ is the density of the gas, and $\eta$ is its viscosity. When $Re$ exceeds ~3000, flow tends to be turbulent. Between $Re$ values of 2000 and 3000, flow is unstable and may switch between laminar and turbulent.

Reynolds developed Equation 27-11 to predict turbulence when fluids flow through tubes that are long, straight, smooth, and unbranched. Pulmonary airways, however, are short, curved, bumpy, and bifurcated. The branches are especially a problem because they set up small eddies (Fig. 27-11B). Although these eddies resolve farther along the airways, the air soon encounters yet other bifurcations, which establish new eddies. This sort of airflow is termed transitional. Because of the complex geometry of pulmonary airways, the critical $Re$ in the lungs is far lower than the ideal value of 2000. In fact, $Re$ must be less than ~1 for lung airflow to be laminar. Such low $Re$ values and thus laminar flow are present only in the small airways that are distal to terminal bronchioles (see Chapter 26).

Airflow is transitional throughout most of the tracheobronchial tree. Only in the trachea, where the airway radius is large and linear air velocities may be extremely high (e.g., exercise, coughing), is airflow truly turbulent (Fig. 27-11C).

The distinction among laminar, transitional, and turbulent airflow is important because these patterns influence how much energy one must invest to produce airflow. When flow is laminar (see Equation 27-7), airflow is proportional to $\Delta P$ and requires relatively little energy. When flow is transitional, one must apply more $\Delta P$ to produce the same airflow because producing vortices requires extra energy. Thus, the “effective resistance” increases. When flow is turbulent, airflow is proportional not to $\Delta P$ but to $\sqrt{\Delta P}$. Thus, we must apply an even greater $\Delta P$ to achieve a given flow (i.e., effective resistance is even greater).

The Smallest Airways Contribute Only Slightly to Total Airway Resistance in Healthy Lungs

As discussed earlier, airway resistance for healthy individuals is ~1.5 cm H$_2$O/(L/s). Because effective resistance can increase markedly with increases in airflow—owing to transitional and turbulent airflow—it is customary to measure resistances at a fixed, relatively low flow of ~0.5 L/s. The second column of Table 27-2 shows how $R_{AW}$ normally varies with location as air moves from lips to alveoli during a quiet inspiration. A striking feature is that the greatest aggregate resistance is in the pharynx-larynx and large airways (diameter > 2 mm, or before about generation 8). Of the $R_{AW}$ of 1.5 cm H$_2$O/(L/s) in this normal subject, 0.6 is in the upper air passages, 0.6 is in the large airways, and only 0.3 is in the small airways.

Because $R$ increases with the fourth power of airway radius (see Equation 27-8), it might seem counterintuitive that the small airways have the lowest aggregate resistance. However, although each small airway has a high individual resistance, so many are aligned in parallel that their aggregate resistance is very low. We see this same pattern of resistance in the vascular system, where capillaries make a smaller contribution than arterioles to aggregate resistance (see Chapter 19).

Table 27-2 also shows an example of a patient with moderately severe chronic obstructive pulmonary disease (COPD), a condition in which emphysema or chronic bronchitis increases $R_{AW}$ (see the box on obstructive pulmonary diseases). COPD is a common and debilitating consequence
The Respiratory System

**A SUBJECT AT REST**

- Plethysmograph
- Pneumotachometer (measures air flow, V)
- Box pressure ($P_{BOX}$)
- 1-liter calibrating syringe

**B SUBJECT BREATHING AGAINST A CLOSED SHUTTER**

1. Mouth pressure ($P_M$)
2. Because there is no airflow, mouth pressure ($P_M$) equals alveolar pressure ($P_A$). Thus, $\Delta P_M$ equals $\Delta P_A$.
3. As the subject inhales against a closed shutter...
4. ...the lungs increase, causing $P_A$ to decrease.
5. As the expanding lung encroaches on the air in the plethysmograph, $P_{BOX}$ increases by $\Delta P_{BOX}$.

**C SUBJECT BREATHING THROUGH AN OPEN SHUTTER**

1. Mouth pressure ($P_M$)
2. As the subject inhales against an open shutter...
3. ...air enters the lungs and the pneumotachometer records a negative $V$.
4. The positive $\Delta P_{BOX}$ allows us to calculate the negative $\Delta P_A$.

**Figure 27-10** Measurement of alveolar pressure ($P_A$) during airflow. This plethysmograph is similar to the one in Figure 26-9C, except that the spirometer is replaced by a sensitive device for measurement of the pressure inside the plethysmograph ($P_{BOX}$). The subject breathes plethysmograph air through a tube that has an electronically controlled shutter as well as meters for measurement of airflow and pressure at the mouth. In B, with the subject making an inspiratory effort against a closed shutter, pressure at the mouth equals $P_A$. We obtain the calibration ratio $\Delta P_A/\Delta P_{BOX}$ which allows us to convert future changes in the $P_{BOX}$ to changes in $P_A$. In C, the subject inspires through an open shutter. During the first moments of inspiration, the thorax expands before much air enters the lungs. Because alveoli expand without much of an increase in the number of gas molecules, $P_A$ must fall. Conversely, because the thorax encroaches on the plethysmograph air, which has hardly lost any gas molecules to the lungs, $P_{BOX}$ must rise. From the calibration ratio $\Delta P_A/\Delta P_{BOX}$, we calculate $\Delta P_A$ from $\Delta P_{BOX}$, during inspiration. $P_A$ at any point during the respiratory cycle is the sum of the known $P_b$ and the measured $\Delta P_A$. 
of cigarette smoking, far more common than the lung cancer that receives so much attention in the lay press. Notice where the disease strikes. Even though COPD increases total airway resistance to 5.0 cm H₂O/(L/s)—3.3-fold greater than in our normal subject—pharynx-larynx resistance does not change at all, and large-airway resistance increases only modestly. Almost all of the increment in $R_{AW}$ is due to a nearly 12-fold increase in the resistance of the smallest airways! According to Equation 27-8, we could produce a 12-fold increase in $R_{AW}$ by decreasing radius by about half.

Although small airways normally have a very low aggregate resistance, it is within these small airways that COPD has its greatest and earliest effects. Even a doubling of small-airway resistance from 0.3 to 0.6 cm H₂O/(L/s) in the early stages of COPD would produce such a small increment in $R_{AW}$ that it would be impossible to identify the COPD patient in a screening test based on resistance measurements. As discussed in Chapter 31, approaches that detect the nonuniformity of ventilation are more sensitive for detection of early airway disease. In addition to COPD, the other common cause of increased $R_{AW}$ is asthma (see the box on that topic).

**Obstructive Pulmonary Disease**

Two major categories of pulmonary disease can markedly reduce total ventilation: the restrictive pulmonary diseases (discussed in the box on diseases affecting ventilation); and the obstructive pulmonary diseases, in which the pathological process causes a decrease in airway resistance—primarily a property of the conducting airways (see Chapter 26).

The condition can be acute, as with the aspiration of a foreign body, the build up of mucus in an airway lumen, or the constriction of the airway lumen due to the contraction of smooth muscle in asthma (see the box on that topic).

**Chronic obstructive pulmonary disease (COPD)** is defined as an increase in airway resistance caused by chronic bronchitis (long-standing inflammation of the bronchi or bronchioles), emphysema (destruction of alveolar walls, producing a smaller number of large alveoli), or a combination of the two. In the United States, COPD is the fourth leading cause of death. The major risk factor is cigarette smoking, although the inherited absence of α₁-antitrypsin (see Table 18-1) also predisposes to COPD. Inflammation leads to the infiltration of the walls of conducting airways by macrophages, activated T lymphocytes, and neutrophils and the infiltration of alveolar walls by activated lymphocytes. The release of neutrophil elastase and other proteases overwhelms natural antiproteases, such as α₁-antitrypsin. Bronchitis increases airway resistance by narrowing the lumen. With its destruction of alveolar walls, emphysema increases the static compliance, which, by itself, would make it easier to inhale. However, the destruction of parenchyma also reduces the mechanical tethering of conducting airways, leading to an exaggerated collapse of these airways during expiration and thus an increase in airway resistance.

![Figure 27-11](image)

**Table 27-2 Airway Resistance**

<table>
<thead>
<tr>
<th>Locus</th>
<th>Normal</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharynx-larynx</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Airways &gt; 2 mm diameter</td>
<td>0.6</td>
<td>0.9</td>
</tr>
<tr>
<td>Airways &lt; 2 mm diameter</td>
<td>0.3</td>
<td>3.5</td>
</tr>
<tr>
<td>Total airway resistance</td>
<td>1.5</td>
<td>5.0</td>
</tr>
</tbody>
</table>

*Units of resistance, cm H₂O/(L/s).
Asthma

Asthma, a common condition, occurs in 5% to 10% of the American population. Asthma is primarily an inflammatory disorder; the familiar bronchospasm is secondary to the underlying inflammation. One hypothesis is that asthma represents the inappropriate activation of immune responses designed to combat parasites in the airways. When a susceptible person inhales a trigger (e.g., pollen), inflammatory cells rush into the airways, releasing a multitude of cytokines, leukotrienes, and other humoral substances (e.g., histamine) that induce bronchospasm. The patient suffering an acute asthma attack is usually easy to recognize. The classic presentation includes shortness of breath, wheezing, and coughing. Triggers include allergens, heat or cold, a host of occupational irritants, and exercise. The patient can often identify the specific trigger. Spirometry can confirm the diagnosis; the most characteristic feature is a decreased FEV₁. Many asthmatics use peak flowmeters at home because the severity of symptoms does not always correlate with objective measurements of the disease’s severity.

The type of treatment depends on the frequency and severity of the attacks. Patients with infrequent attacks that are not particularly severe can often be treated with an inhaled β₂-adrenergic agonist, only when needed. These medications, easily delivered by a metered-dose inhaler that can be carried around in one’s pocket or purse, act on β₂-adrenergic receptors to oppose bronchoconstriction. A patient who requires such an agent more than one or two times a week should receive an inhaled corticosteroid on a regular basis to suppress inflammation. Inhaled corticosteroids generally lack the side effects of oral corticosteroids, but oral corticosteroids may be required in a patient with sustained and severe asthma. Many patients rely on regular dosing of long-acting β₂-agonist inhalers and inhaled corticosteroids to keep their asthma under control. Theophylline (a phosphodiesterase inhibitor that raises cAMP, see Chapter 3), once a mainstay of asthma therapy, is now used far less commonly. Inhaled anticholinergic agents are more useful with COPD patients than with asthmatics but can be beneficial in some patients who cannot tolerate the side effects of β₂-adrenergic agonists (notably tachycardia). Smooth muscle relaxants (e.g., cromakalim-related drugs; see Chapter 7) and other anti-inflammatory agents (e.g., leukotriene inhibitors) also play a role in asthma therapy.

Vagal Tone, Histamine, and Reduced Lung Volume All Increase Airway Resistance

Several factors can modulate $R_{AW}$, including the autonomic nervous system (ANS), humoral factors, and changes in the volume of the lungs themselves. The vagus nerve, part of the parasympathetic division of the ANS, releases acetylcholine, which acts on an $M_3$ muscarinic receptor on bronchial smooth muscle (see Chapter 14). The result is bronchoconstriction and therefore an increase in $R_{AW}$. The muscarinic antagonist atropine blocks this action. Irritants such as cigarette smoke cause a reflex bronchoconstriction (see Chapter 32) in which the vagus nerve is the efferent limb.

Opposing the action of the vagus nerve is the sympathetic division of the ANS, which releases norepinephrine and dilates the bronchi and bronchioles but reduces glandular secretions. However, these effects are weak because norepinephrine is a poor agonist of the β₂-adrenergic receptors that mediate this effect through cyclic adenosine monophosphate (cAMP; see Chapter 14).

Humoral factors include epinephrine, released by the adrenal medulla. Circulating epinephrine is a far better β₂ agonist than is norepinephrine and therefore a more potent bronchodilator. Histamine constricts bronchioles and alveolar ducts and thus increases $R_{AW}$. Far more potent is the bronchoconstrictor effect of the leukotrienes LTC₄ and LTD₄.

One of the most powerful determinants of $R_{AW}$ is $V_L$. $R_{AW}$ is extremely high at residual volume (RV) but decreases steeply as $V_L$ increases (Fig. 27-12A). One reason for this effect is obvious: all pulmonary airways—including the conducting airways, which account for virtually all of $R_{AW}$—expand at high $V_L$, and resistance falls steeply as radius increases (see Equation 27-8). A second reason is the principle of interdependence—alveoli tend to hold open their neighbors by exerting radial traction or mechanical tethering (Fig. 27-12B). This principle is especially important for conducting airways, which have thicker walls than alveoli and thus a lower compliance. At high $V_L$, alveoli dilate more than the adjacent bronchioles, pulling the bronchioles farther open by mechanical tethering. Patients with obstructive lung disease, by definition, have an increased $R_{AW}$ at a given $V_L$ (Fig. 27-12A). However, because these patients tend to have a higher than normal FRC, they breathe at a higher $V_L$, where airway resistance is—for them—relatively low.

Intrapleural Pressure Has a Static Component ($-P_{IP}$) That Determines Lung Volume and a Dynamic Component ($P_A$) That Determines Airflow

In Equation 27-2, we defined transpulmonary pressure as the difference between alveolar and intrapleural pressure ($P_{TP} = P_A - P_{IP}$). What is the physiological significance of these three pressures, and how do we control them?

$P_P$ is the parameter that the brain—through the muscles of respiration—directly controls. Rearranging the definition of $P_{TP}$ in Equation 27-2:

$$P_P = (-P_{IP}) + P_A$$ (27-12)
Table 27-3  Static Versus Dynamic Properties of the Lungs

<table>
<thead>
<tr>
<th>Property</th>
<th>Static</th>
<th>Dynamic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anatomical correlate</td>
<td>Alveoli</td>
<td>Conducting airways</td>
</tr>
<tr>
<td>Key &quot;constant&quot;</td>
<td>Static compliance, C</td>
<td>Airway resistance, $R_{aw}$</td>
</tr>
<tr>
<td>Key pressure</td>
<td>$P_{TP}$ ($P_{TP} = P_a - P_I$)</td>
<td>$P_a$</td>
</tr>
<tr>
<td>Key parameter</td>
<td>$V_L$ ($C = \Delta V_L/\Delta P_{TP}$)</td>
<td>$\dot{V}$ ($\dot{V} = P_a/R_{aw}$)</td>
</tr>
<tr>
<td>Pathological change</td>
<td>Restrictive disease (e.g., fibrosis), caused by ↓$C$</td>
<td>Obstructive disease (e.g., COPD), caused by ↑$R_{aw}$</td>
</tr>
</tbody>
</table>

Thus, $P_{IP}$ has two components, $-P_{TP}$ and $P_a$, as summarized in Figure 27-13 and Table 27-3. As we will see in the next section, $P_{TP}$ and $P_a$ literally flow from $P_{IP}$.

**Transpulmonary Pressure**  $P_{TP}$ is a static parameter. It does not cause airflow. Rather, along with static compliance, $P_{TP}$ determines $V_L$. The curve in the lower left part of Figure 27-13—like the middle plot of Figure 27-5—describes how $V_L$ depends on $P_{TP}$. That is, this curve describes the $P_{TP}$ required to overcome the elastic (i.e., static) forces that oppose lung expansion but makes no statement about $\dot{V}$. We have already seen that the slope of this curve is static compliance, a property mainly of the alveoli, and that a decrease in $C$ can produce restrictive lung disease. Note that $P_{TP}$ not only determines $V_L$ under static conditions, when there is no airflow, but also under dynamic conditions (i.e., during inspiration and expiration). However, the brain does not directly control $P_{TP}$.

**Alveolar Pressure**  $P_a$ is a dynamic parameter. It does not determine $V_L$ directly. Instead, along with airway resistance, $P_a$ determines airflow. The curve in the lower right part of Figure 27-13 describes how $\dot{V}$ depends on $P_a$. That is, this curve describes the $P_a$ required to overcome inertial and
resistive (i.e., dynamic) forces that oppose airflow but makes no statement about \( V_t \). The slope of this plot is airway conductance, the reciprocal of \( R_{AW} \), which is mainly a property of the conducting airways. A decrease in \( R_{AW} \) can produce obstructive lung disease. When \( P_a \) is 0, \( V \) must be 0, regardless of whether \( V_t \) is at RV or TLC or anywhere in between. If the \( P_a \) is positive and the glottis is open, air flows from alveoli to atmosphere, regardless of \( V_t \). If \( P_a \) is negative, air flows in the opposite direction. As is the case with \( P_{TP} \), the brain does not directly control \( P_a \).

**During Inspiration, a Sustained Negative Shift in \( P_{TP} \) Causes \( P_a \) to BecomeTransiently More Negative**

During a quiet respiratory cycle—an inspiration of 500 mL, followed by an expiration—the body first generates negative and then positive values of \( P_a \). The four large gray panels of Figure 27-14 show an idealized time course of five key parameters. The uppermost panel is a record of \( V_t \). The next panel is a pair of plots, \( -P_{TP} \) and \( P_{TP} \). The third shows the record of \( P_a \). The bottom panel shows a simultaneous record of \( V \).

On the right side of Figure 27-14 are the static \( P_{TP}-V_t \) curve and the dynamic \( P_a-V \)-relationship (both copied from Fig. 27-13). On the left side is a series of four cartoons that represent snapshots of the key pressures (i.e., \( P_{TP} \), \( P_{TP} \), and \( P_a \)) at four points during the respiratory cycle:

- **a.** Before inspiration begins. The lungs are under static conditions at a volume of FRC.
- **b.** Halfway through inspiration. The lungs are under dynamic conditions at a volume of FRC + 250 mL.
- **c.** At the completion of inspiration. The lungs are once again under static conditions but at a volume of FRC + 500 mL.
- **d.** Halfway through expiration. The lungs are under dynamic conditions at a volume of FRC + 250 mL.
- **e.** At the end of expiration/ready for the next inspiration. The lungs are once again under static conditions at a volume of FRC.

The \( V_t \) record in the top gray panel of Figure 27-14 shows that \( V_t \) rises more or less exponentially during inspiration and similarly falls during expiration.

Knowing the time course of \( V_t \), we obtained the \( P_{TP} \) values in the second gray panel by reading them off the static \( P_{TP}-V_t \) diagram to the right and plotted them as \( -P_{TP} \) (for consistency with Equation 27-12). As \( V_t \) increases during inspiration, \( P_{TP} \) increases (i.e., \( -P_{TP} \) becomes more negative). The opposite is true during expiration. Remember that \( P_{TP} \) (along with static compliance) determines \( V_t \) at any time.

The \( P_a \) record in the second gray panel shows that \( P_a \) is the same as \( -P_{TP} \) whenever the lungs are under static conditions (points \( a \), \( c \), and \( a \)). During inspiration, \( P_a \) rapidly becomes more negative than \( -P_{TP} \) but then merges with \( -P_{TP} \) by the end of inspiration. The difference between \( P_a \) and \( -P_{TP} \) is \( P_a \), which must be negative to produce airflow into the lungs. During expiration, \( P_{TP} \) is more positive than \( -P_{TP} \).

The \( P_a \) record in the third gray panel shows that alveolar pressure is zero under static conditions (points \( a \), \( c \), and \( a \)). During inspiration, \( P_a \) rapidly becomes negative but then relaxes to 0 by the end of inspiration. The opposite is true during expiration. The \( P_a \) values in this plot represent the differences between the \( P_{TP} \) and \( -P_{TP} \) plots in the preceding panel.

We computed \( \dot{V} \) (bottom gray panel) from the relationship in Equation 27-7: \( \dot{V} = (P_a - P_b)/R_{AW} \). Remember that \( P_a \) (along with \( R_{AW} \)) determines \( V \) at any time. Here, we assume that \( R_{AW} \) is fixed during the respiratory cycle at 1 cm H\(_2\)O/(L/s). Thus, the \( \dot{V} \) record has the same time course as \( P_a \).

The key message in Figure 27-14 is that during inspiration, the negative shift in \( P_{TP} \) has two effects. The body invests some of the energy represented by \( \Delta P_{TP} \) into transiently making \( P_a \) more negative (dynamic component). The result is that air flows into the lungs and \( V_t \) increases; but this investment in \( P_a \) is only transient. Throughout inspiration, the body invests an increasingly greater fraction of its energy in making \( P_{TP} \) more positive (static component). The result is that the body maintains the new, higher \( V_t \). By the end of inspiration, the body invests all of the energy represented by \( \Delta P_{TP} \) in maintaining \( V_t \) and none in further expansion. The situation is not unlike that faced by Julius Caesar as he, with finite resources, conquered Gaul. At first, he invested all of his resources in expanding his territory at the expense of the feisty Belgians; but as the conquered territory grew, he was forced to invest an increasingly greater fraction of his resources in maintaining the newly conquered territory. In the end, he necessarily invested all of his resources in maintaining his territory and was unable to expand further.

**Dynamic Compliance Falls as Respiratory Frequency Rises**

In the preceding section, we examined pressure, volume, and flow changes during an idealized respiratory cycle of 5 seconds, which corresponds to a respiratory frequency of 12/minute. The top curve in Figure 27-15A shows a normal \( V_t \) time course during an inspiration. As for any exponential process, the time constant (\( \tau \)) is the interval required for \( \Delta V_t \) to be \( \approx63\% \) complete. For healthy lungs, \( \tau \) is \( \approx0.2 \) second. Thus, for inspiration, the increase in \( V_t \) is 63% complete after 0.2 second, 86% complete after 0.4 second, 95% complete after 0.6 second, and so on. We will make the simplifying assumption that the time available for inspiration is half this time or 2.5 seconds, which represents more than 12 time constants! Thus, if the \( V_t \) after infinite time were 500 mL, the \( \Delta V_t \) measured 2.5 seconds after initiation of inspiration would also be \( \approx500 \) mL (Fig. 27-15A, green point). In Figure 27-15B, we replot this value as the green point at a frequency of 12/minute on the top curve (i.e., normal lungs).

For a respiratory frequency of 24/minute, 1.25 seconds is available for inspiration. At the end of this time, the \( \Delta V_t \) is \( \approx499 \) mL (Fig. 27-15B, blue point on the top curve).

If we further increase the respiratory frequency to 48/minute, only 0.625 second is available for inspiration. At the end of this period, only slightly more than 3 time constants, the \( \Delta V_t \) is \( \approx478 \) mL (Fig. 27-15B, red point on top curve).
Figure 27-14  The respiratory cycle. $P_B$, $P_{IP}$, $P_{TP}$, and $P_A$ are all in cm H$_2$O. The colored points (labeled $a$, $b$, $c$, and $d$) in each of the central panels correspond to the illustrations (on the left) with the same colored background. The two panels on the right are taken from Figure 27-13. $V_L$, lung volume; $V$, airflow.
**Effect of Respiratory Frequency on Tidal Volume**

When respiratory frequency increases, the time available for inspiration decreases. Thus, a fifth factor that modulates respiratory frequency is the time available for inspiration (Fig. 27-15C).

This pathological pattern is typical of asthma; $R_{aw}$ is elevated, but $C_{static}$ is relatively normal. In emphysema, both $R_{aw}$ and $C_{static}$ are elevated (Fig. 27-5, upper curve). Thus, a plot of $C_{dynamic}$ versus frequency would show that $C_{dynamic}$ is initially greater than $C_{static}$ at low respiratory frequencies, but it falls below $C_{static}$ as frequency increases. What do these frequency-dependent decreases in $C_{dynamic}$ mean for a patient? The greater the respiratory frequency, the less time is available for inspiration or expiration, and the smaller the $V_t$ (Fig. 27-15C).

This analysis greatly oversimplifies what happens in the lungs of real people. Although we have treated the lungs as if there were one value for $R_{aw}$ and one for $C_{static}$, each conducting airway has its own airway resistance and each alveolar unit has its own static compliance, and these values vary with parameters such as $V_t$, posture, and hormonal status. As a result, some alveolar units have greater time constants than others. Airway disease may make some of these time constants substantially higher. As respiratory frequency increases, alveoli with relatively high time constants will have less time to undergo volume changes. As a result, these “slow” airways—compared with the “faster” airways—will make progressively smaller contributions to the overall ventilation of the lungs. At sufficiently high frequencies, very slow airways may drop out of the picture entirely.

**Transmural Pressure Differences Cause Airways to Dilate During Inspiration and to Compress During Expiration**

We have noted three factors that modulate airway caliber: (1) the ANS, (2) humoral substances, and (3) $V_t$ (Fig. 27-12). A fourth factor that modulates $R_{aw}$ is flow of air...
through the conducting airway itself. Airflow alters the pressure difference across the walls of an airway, and this change in transmural pressure ($P_{TM}$) can cause the airway to dilate or to collapse. Figure 27-16A-C depicts the pressures along a single hypothetical airway, extending from the level of the alveoli to the lips, under three conditions: during inspiration (Fig. 27-16A), at rest (Fig. 27-16B), and during expiration (Fig. 27-16C). In all three cases, the lung is at the same volume, FRC; the only difference is whether air is flowing into the lung, not flowing at all, or flowing out of the lung. Because $V_t$ is at FRC, $P_{TM}$ (the $P_{TM}$ for the alveoli) is 5 cm H$_2$O in all three cases.

Static Conditions First consider what happens under static conditions (Fig. 27-16B). In the absence of airflow, the pressures inside all airways must be 0. Considering first the alveoli, $P_{TM}$ is 5 cm H$_2$O and the $P_a$ is 0, and thus $P_{IP}$ is −5 cm H$_2$O. We will ignore the effects of gravity on $P_{IP}$ and thus assume that $P_{IP}$ is uniform throughout the chest cavity. The $P_{IP}$ of −5 cm H$_2$O acts not only on alveoli but on all conducting airways within the thoracic cavity. For these, $P_{TM}$ at any point is the difference between the pressure inside the airway ($P_{AW}$) and $P_{IP}$ (see Equation 27-1):

$$P_{TM} = P_{AW} - P_{IP} = 0 - (−5\text{ cm H}_2\text{O}) = +5\text{ cm H}_2\text{O} \quad (27-14)$$

In other words, a transmural pressure of +5 cm H$_2$O acts on all thoracic airways (but not the trachea in the neck, for example), tending to expand them to the extent that their compliance permits.

Inspiration Now consider what happens during a vigorous inspiration (Fig. 27-16A). We first exhale to a $V_t$ below FRC and then vigorously inhale, so that the $P_a$ is −15 cm H$_2$O at the instant that $V_t$ passes through FRC. Because the lung is at FRC, $P_{TM}$ is +5 cm H$_2$O. The $P_{IP}$ needed to produce a $P_a$ of −15 cm H$_2$O is

$$P_{IP} = (−P_{TM}) + P_a = −5\text{ cm H}_2\text{O} + (−15\text{ cm H}_2\text{O}) = −20\text{ cm H}_2\text{O} \quad (27-15)$$

This “inspiring” $P_{IP}$ of −20 cm H$_2$O is just enough to produce the desired airflow and also to maintain the alveoli at precisely the same volume that they had under static conditions. But how does this exceptionally negative $P_{IP}$ affect airways upstream from the alveoli? $P_{AW}$ gradually decays from −15 cm H$_2$O in the alveoli to 0 at the lips. The farther we move from the alveoli, the less negative is $P_{AW}$, and thus the greater is $P_{TM}$.

**Figure 27-16** Dilation and collapse of airways with airflow. In all four panels, $V_t$ is FRC. $P_{TM}$ is the transmural pressure across conducting airways. Airway pressure ($P_{AW}$) and values in pale blue balloons represent pressures inside conducting airways (all in cm H$_2$O). Graphs at bottom show $P_{AW}$ profiles along airways (blue curve) from alveoli to mouth. $P_a$ is constant throughout the thorax (green curve). The upward arrows tend to expand the airways, whereas the downward arrows tend to squeeze them.
As an illustration, consider a point about halfway up the airway’s resistance profile, where $P_{AW}$ is $-8$ cm H$_2$O:

$$P_{TM} = P_{AW} - P_T$$

$$= -8\text{ cm H}_2\text{O} - (-20\text{ cm H}_2\text{O})$$  \hspace{1cm} (27-16)

$$= +12\text{ cm H}_2\text{O}$$

Thus, the transmural pressure opposing the elastic recoil at this point has increased from +5 cm H$_2$O at rest (Fig. 27-16B) to +12 cm H$_2$O during this vigorous inspiration (Fig. 27-16A). Because $P_{TM}$ has increased, the airway will dilate. The tendency to dilate increases as we move from the alveoli to larger airways. As shown in the graph in the lower part of Figure 27-16A, $P_{AW}$ (and thus $P_{TM}$, as indicated by the upward arrows) gradually increases. Note that the very positive $P_{TM}$ values that develop in the larger airways determine only the **tendency** to dilate. The extent to which an airway actually dilates also depends on its compliance. The amount of cartilage supporting the airways gradually increases from none for 11th-generation airways to a substantial amount for the mainstem bronchi. Because the increasing amount of cartilage in the larger airways decreases their compliance, they have an increasing ability to resist changes in caliber produced by a given change in $P_{TM}$.

**Expiration**  As might be expected, conducting airways tend to collapse during expiration (Fig. 27-16C). We first inhale to a $V_l$ above FRC and then exhale vigorously, so that $P_a$ is +15 cm H$_2$O at the instant that $V_l$ passes through FRC. Because the lung is at FRC, $P_{AW}$ is +5 cm H$_2$O. The $P_{IP}$ needed to produce a $P_a$ of +15 cm H$_2$O is

$$P_{IP} = (-P_{TP}) + P_a$$

$$= -5\text{ cm H}_2\text{O} + (+15\text{ cm H}_2\text{O})$$  \hspace{1cm} (27-17)

$$= +10\text{ cm H}_2\text{O}$$

This $P_{IP}$ of +10 cm H$_2$O is 5 less than the $P_a$ and thus maintains the alveoli at the same volume that prevailed under static conditions and during inspiration. What is the effect of this very positive $P_{IP}$ on the upstream airways? $P_{AW}$ must decrease gradually from +15 cm H$_2$O in the alveoli to 0 at the lips. The farther we move from the alveolus, the lower the $P_{AW}$ and thus the lower the $P_{TM}$. At a point about halfway up the airway’s resistance profile, where $P_{AW}$ is +8 cm H$_2$O:

$$P_{TM} = P_{AW} - P_T$$

$$= +8\text{ cm H}_2\text{O} - (+10\text{ cm H}_2\text{O})$$  \hspace{1cm} (27-18)

$$= -2\text{ cm H}_2\text{O}$$

Thus, at this point during a vigorous expiration, the transmural pressure opposing elastic recoil has fallen sharply from +5 cm H$_2$O at rest (which tends to mildly inflate the airway) to −2 cm H$_2$O during expiration (which actually tends to squeeze the airway). As we move from the alveoli to larger airways, $P_{AW}$ gradually decreases. That is, $P_{TM}$ gradually shifts from an ever-decreasing inflating force (positive values) to an ever-increasing squeezing force (negative values), as indicated by the change in the orientation of the arrows in the lower panel of Figure 27-16C. Fortunately, these larger airways—with the greatest collapsing tendency—have the most cartilage and thus some resistance to the natural collapsing tendency that develops during expiration. In addition, mechanical tethering helps all conducting airways surrounded by alveoli to resist collapse. Nevertheless, $R_{AW}$ is greater during expiration than it is during inspiration.

The problem of airway compression during expiration is exaggerated in patients with **emphysema**, a condition in which the alveolar walls break down. This process results in fewer and larger air spaces with fewer points of attachment and less mutual buttressing of air spaces. Although the affected alveoli have an increased compliance and thus a larger diameter at the end of an inspiration, they are flimsy and exert less mechanical tethering on the conducting airways they surround. Thus, patients with emphysema have great difficulty exhaling because their conducting airways are less able to resist the tendency to collapse. However, these patients make their expirations easier in three ways. We could predict them all from our knowledge of dynamic respiratory mechanics:

1. **They exhale slowly.** A low $V$ during expiration translates to a less positive $P_{IP}$ and thus a less positive $P_{TP}$, minimizing the tendency to collapse.
2. **They breathe at a higher $V_l$.** A high $V_l$ maximizes the mechanical tethering that opposes airway collapse during expiration and thus minimizes $R_{AW}$ (Fig. 27-12A).
3. **They exhale through pursed lips.** This maneuver—known as puffing—creates an artificial, high resistance at the lips. Because the greatest pressure drop occurs at the location of the greatest resistance, puffing causes a greater share of the $P_{AW}$ drop to occur across the lips rather than along collapsible, cartilage-free airways. Thus, puffing maintains relatively high $P_{AW}$ values farther along the tracheobronchial tree (Fig. 27-16D) and reduces collapsing tendencies throughout. The greatest collapsing tendencies are reserved for the largest airways that have the most cartilage (see Chapter 26). Of course, the patient pays a price for puffing: $V$ and thus the ventilation of the alveoli is low.

**Because of Airway Collapse, Expiratory Flow Rates Become Independent of Effort at Low Lung Volumes**

Cartilage and mechanical tethering oppose the tendency of conducting airways to collapse during expiration. Because tethering increases as $V_l$ increases, we expect airways to better resist collapse when $V_l$ is high. To see if this is true, we will examine how expiratory airflow varies with effort (i.e., alveolar pressure) at different $V_l$.

Imagine that we make a maximal inspiration and then hold our breath with glottis open (Fig. 27-17A). Thus, $P_a$ is 0. In addition, $P_{TP}$ is +30 cm H$_2$O to maintain TLC. From Equation $27-12$, $P_{IP} = (-P_{TP}) + P_a = -30$ cm H$_2$O. Now, starting from TLC, we make a maximal expiratory effort. Figure 27-17B summarizes the pressures in the alveoli and thorax at the instant we begin exhaling but before $V_l$ has had...
time to change. $P_{IP}$ is still $+30$ cm H$_2$O, but $P_a$ is now $+40$ cm H$_2$O (to produce a maximal expiration) and $P_{IP}$ is therefore $+10$ cm H$_2$O. As $V_t$ decreases during the course of the expiration, we will monitor $V$, $V_t$, and $P_a$.

The top curve in Figure 27-17C shows how $V$ changes as a function of $V_t$ when, starting from TLC, we make a maximal expiratory effort. Notice that $V$ rises to its maximal value at a $V_t$ that is somewhat less than TLC and then gradually falls to 0 as $V_t$ approaches RV. The data in this top curve, obtained with maximal expiratory effort (i.e., at maximal $P_a$), will help us determine how expiratory flow varies with effort. To get the rest of the necessary data, we repeat our experiment by again inhaling to TLC and then exhaling to RV. However, with each trial, we exhale with less effort (i.e., at smaller $P_a$)—efforts labeled as high, medium, and low in Figure 27-17C.

If we draw a vertical line upward from a $V_t$ of 5 L in Figure 27-17C, we see that at this very high $V_t$, $V$ gets larger and larger as the effort increases from low to medium to high to maximal. Because these efforts correspond to increasing $P_a$ values, we can plot these four $V$ data points (all obtained at a $V_t$ of 5 L) versus $P_a$ in the top curve of Figure 27-17D. Because $V$ increases continuously with the $P_a$, flow is effort dependent at a $V_t$ of 5 L. If the airways were made of steel, this plot of $V$ versus $P_a$ would be a straight line. Because the actual plot bends downward at higher values of $P_a$ (i.e., greater efforts), $R_{AW}$ must have increased with effort (i.e., the airways collapsed somewhat).

Returning to Figure 27-17C, we see that an important characteristic of these data is that the $V$ versus $V_t$ curve for maximal expiratory effort defines an envelope that none of the other three curves could penetrate. Thus, at a $V_t$ of 4 L, $V$ is $\sim 7$ L/s, regardless of whether the expiratory effort is high or maximal (i.e., the two points overlap one another on the graph). At a $V_t$ of 3 L, the four curves have practically merged, so that $V$ is $\sim 3.5$ L/s regardless of effort. Thus, at lung volumes that are below 3 L, it does not matter how much effort we make; the expiratory flow can never exceed a certain value defined by the envelope.

Shifting back to Figure 27-17D, we see that for the lower two $V$ versus $P_a$ plots, $V$ increases with $P_a$—up to a point. Further increases in effort (i.e., $P_a$) are to no avail because they produce a proportional increase in $R_{AW}$—expiration-induced airway collapse. Thus, the more positive values of $P_a$ not only produce more positive values of $P_a$ but also increase $R_{AW}$ so that $P_a/R_{AW}$ and thus $V$ remain constant.

At low lung volumes, flow becomes effort independent because the reduced mechanical tethering cannot oppose the tendency toward airway collapse that always exists during expiration. Moreover, at progressively lower $V_t$, flow becomes effort independent earlier. In other words, particularly at low lung volumes, it simply does not pay to try any harder.

**REFERENCES**

**Books and Reviews**


**Journal Articles**


