21

Static Lung and Chest Wall Mechanics

LEARNING OBJECTIVES

Upon completion of this chapter, the student should be able to answer the following questions:

1. How is the alveolar pressure different from the pleural pressure?
2. How is the transpleural pressure gradient created?
3. What is the difference between a lung volume and a lung capacity? How is the vital capacity measured by spirometry? Why can't residual volume be measured by spirometry?
4. Why do changes in the static mechanical properties of the lung cause measurable changes lung volume measurements?
5. What is lung compliance?
6. What is pulmonary surfactant, and how does it help maintain lung compliance?

To achieve its primary function of gas exchange, air must be moved into and out of the lung. The mechanical properties of the lung and chest wall determine the ease or difficulty of this bulk air movement. Lung mechanics is the study of the mechanical properties of the lung and chest wall (including the **diaphragm**, **abdominal cavity**, and **anterior abdominal muscles)**. Lung mechanics is important for understanding normal lung function, and how disease disrupts this normal function. Most lung diseases affect the mechanical properties of the lungs, chest wall, or both. In addition, death from lung disease is almost always due to respiratory muscle fatigue, which results from an inability of the respiratory muscles to overcome the altered mechanical properties of the lungs, chest wall, or both. Lung mechanics includes static mechanics (the mechanical properties of a lung whose volume is not changing with time) and dynamic mechanics (properties of a lung whose volume is changing with time). Dynamic mechanics of the lung and chest wall are described in Chapter 22.

Pressures in the Respiratory System

In healthy people, the lungs and chest wall move together as a unit. Between these structures is the **pleural space,** which under normal conditions is best thought of as a potential space. Because the lungs and chest wall move together, changes in their respective volumes are equal during inspiration and exhalation. Volume changes in the lungs and chest wall are driven by changes in the surrounding pressure. In accordance with convention, pressures inside the lungs and chest wall are referenced in relation to atmospheric pressure, which is considered 0. Thus, a negative pressure in the pleural space is a pressure that is lower than atmospheric pressure. Also, in accordance with convention, pressures across surfaces such as the lungs or chest wall have been defined as the difference between the pressure inside and the pressure outside the surface. The pressure differences across the lung and across the chest wall are defined as the transmural (across a wall or surface) pressure. For the lung, this transmural pressure is called the **transpulmonary** (or translung) **pressure** (P_L), and it is defined as the pressure difference between the air spaces (alveolar pressure [P_A]) and the pressure surrounding the lung (pleural pressure [P_{pl}]):

Equation 21.1

$$P_L = P_A - P_{pl}$$

The **transmural pressure across the chest wall** (P_w) is the difference between pleural (inside) pressure (P_{pl}) and the pressure surrounding the chest wall (P_b), which is the atmospheric (barometric) pressure or pressure on the external body surface:

Equation 21.2

$$P_W = P_{p1} - P_b$$

The pressure across the respiratory system (P_{rs}) is the sum of the pressure across the lung and the pressure across the chest wall:

Equation 21.3

$$\begin{aligned} P_{rs} &= P_L + P_w \\ &= \left(P_A - P_{pl}\right) + \left(P_{pl} - P_b\right) \\ &= P_A - P_b \end{aligned}$$

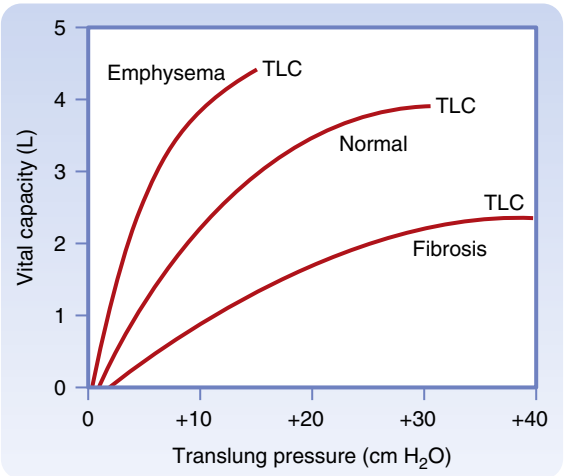
How a Pressure Gradient Is Created

Air flows into and out of the lungs from areas of higher pressure to areas of lower pressure. In the absence of a pressure gradient, there is no airflow. Thus, at the end of inspiration and at the end of exhalation, which are periods of time

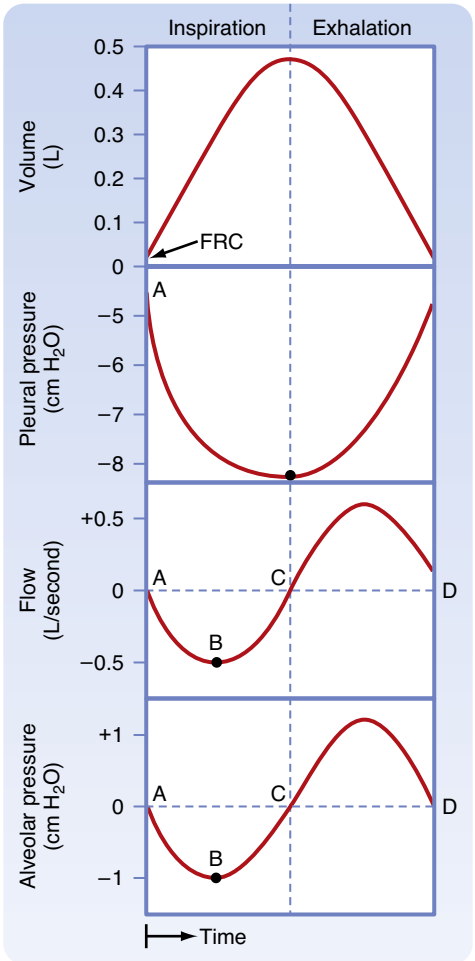
when there is no airflow, alveolar pressure (P_A) is the same as atmospheric pressure (P_b), and there is no pressure gradient ($P_b - P_A = 0$). Pleural pressure at these same times, however, is not 0. Before inspiration begins, the pleural pressure in normal individuals is approximately −3 to −5 cm H_2O. Therefore, the pressure in the pleural space is negative in relation to atmospheric pressure. This negative pressure is created by the inward elastic recoil pressure of the lung, and it acts to "pull the lung" away from the chest wall. The lung is not able, however, to pull away from the chest wall, inasmuch as the two function as a unit. Thus, the inward elastic recoil pressure of the lung is balanced by the outward recoil of the chest wall.

With the onset of inspiration, the muscles of the diaphragm and chest wall contract, which causes a downward movement of the diaphragm and an outward and upward movement of the rib cage. As a result, pleural pressure decreases during inspiration. This negative pleural pressure is transmitted across the lung tissue and results in a decrease in alveolar pressure. As alveolar pressure decreases below 0 (i.e., from atmospheric pressure to below atmospheric pressure), air moves into the airways when the glottis is open. As air flows into the airways to the alveoli, the pressure gradient along the airways decreases, and flow stops when there is no longer a pressure gradient between the atmosphere and the alveoli. The decrease in pleural pressure at the start of inspiration secondary to inspiratory muscle contraction is greater than the transmitted fall in alveolar pressure, and, as a result, transpulmonary pressure at the start of inspiration is positive (see Eq. 21.1). Positive transpulmonary pressure is necessary to increase lung volume, and lung volume increases with increasing transpulmonary pressure (Fig. 21.1). Similarly, during inspiration, the chest wall expands to a larger volume. Because pleural pressure is negative in relation to atmospheric pressure during quiet breathing, the transmural pressure across the chest wall is negative (see Eq. 21.2).

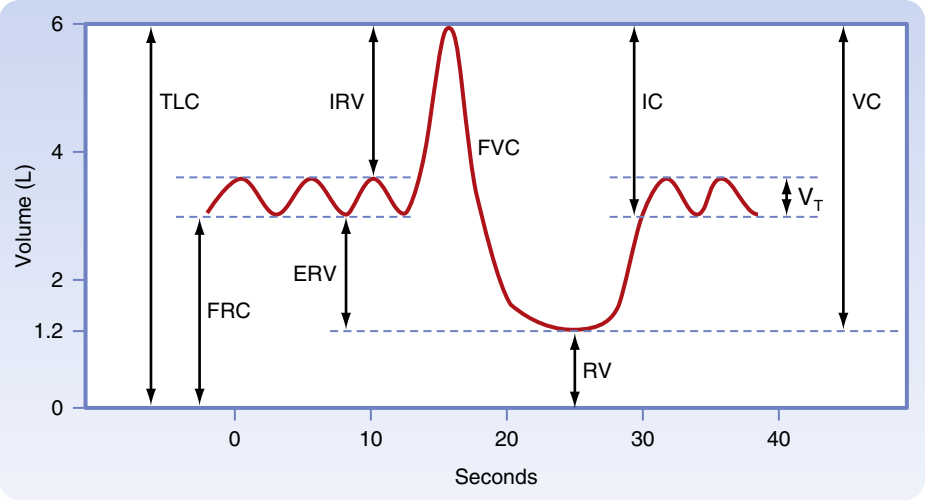
On exhalation, the diaphragm moves higher into the chest, pleural pressure increases (i.e., becomes less negative), alveolar pressure becomes positive, the glottis opens, and gas again flows from a higher (alveolar) pressure to a lower (atmospheric) pressure. In the alveoli, the driving force for exhalation is the sum of the elastic recoil of the lungs and pleural pressure (see Chapter 22). This relationship between changes in pressure, changes in airflow, and changes in volume during inspiration and exhalation is displayed in Fig. 21.2. During tidal volume breathing in normal individuals, the decrease in alveolar pressure at the start of inspiration is small (1–3 cm H_2O). It is much larger in individuals with airway obstruction because of the larger pressure drop that occurs across obstructed airways. Airflow stops in the absence of a pressure gradient, which occurs whenever alveolar pressure and atmospheric pressure are equal.



• **Fig. 21.1** Volume of the lung as a function of the transpulmonary pressure in health and disease. As the transpulmonary pressure increases, lung volume increases. Also shown are the changes in lung volume in the presence of emphysema and pulmonary fibrosis. Note that for the same change in transpulmonary pressure, in the presence of either of these types of diseases, the changes in lung volume are different. *TLC*, Total lung capacity (the total volume of gas in the lung).



• **Fig. 21.2** Changes in alveolar and pleural pressure during quiet breathing (tidal volume). Inspiration is represented to the *left* of the *vertical dotted line,* and exhalation is represented to the *right* of it. Positive (in relation to atmospheric) pressures are represented above the *horizontal dotted line,* and negative pressures are represented below it. See text for details. At points of no airflow (points *A* and *C*), alveolar pressure is 0. *FRC*, Functional residual capacity.



• **Fig. 21.3** The various lung volumes and capacities. *ERV*, Expiratory reserve volume; *FRC*, functional residual capacity; *FVC*, forced vital capacity; *IC*, inspiratory capacity; *IRV*, inspiratory reserve volume; *RV*, residual volume; *TLC*, total lung capacity; *VC*, vital capacity; V_T, tidal volume.

Lung Volumes and Their Measurement

Lung volumes (Fig. 21.3) and the factors that determine these volumes are important components of lung mechanics. Various diseases can alter individual lung volumes and result in increased work of breathing (see Chapter 22). All lung volumes are subdivisions of **total lung capacity (TLC),** the total volume of air that is contained in the lung at the point of maximal inspiration. TLC is made up of four distinct lung volumes: Inspiratory Reserve Volume, Tidal Volume, Expiratory Reserve Volume, and Residual Volume. Tidal Volume [Vt] is the volume of air moved into and out of the lungs with each quiet breath. Inspiratory Reserve Volume (IRV) is the amount of air that can be inhaled after taking a normal tidal breath. This volume is considered to be in reserve, for use when ventilatory demand increases such as during exercise or illness. The Expiratory Reserve Volume (ERV) is the amount of air that can be exhaled after taking a normal tidal breath. Similar to the IRV, it is used during times of increased respiratory effort. Finally, the Residual Volume (RV) is the volume of air remaining ("trapped") in the lung following complete exhalation.

A lung capacity is defined as the sum of two or more of the previously defined lung volumes. The Vital Capacity (VC) is the sum of Vt, IRV, and ERV. It is the total volume of air that can be exhaled from the point of maximal inspiration to maximal exhalation. TLC is the sum of VC and RV.

Most lung volumes and capacities can be measured by a device called a **spirometer**. The patient breathes into this device and air movement is measured. With the patient breathing normally, tidal volume is determined. The patient then breathes in to the point of maximal inhalation (defining IRV) and then forcefully exhales until there is no more air to exhale. The volume of exhaled air is the VC. ERV can be calculated by subtracting the IRV and Vt from VC. RV cannot be directly measured by spirometry, and requires more sophisticated testing for measurement.

IN THE CLINIC

Pulmonary function tests are often used to diagnose abnormalities in lung function and to assess the progression of lung disease. They can distinguish the two major types of pulmonary pathophysiologic processes: obstructive lung diseases and restrictive lung diseases. For example, in normal individuals, the ratio of RV to TLC is less than 0.25. In a healthy individual, approximately 25% of the total volume of air remains in the lung ("is trapped") at the end of exhalation. In **obstructive pulmonary diseases,** the RV/TLC ratio may increase secondary to an increase in RV out of proportion to any increase in TLC. On chest imaging, the lungs may appear "hyperinflated" due to the increased volume of trapped air. In contrast, in **restrictive lung diseases** the thorax is unable to expand to the normal anticipated extent. As such, TLC decreases resulting in an increase in the RV/TLC ratio.

Lung Volumes and Capacities

RV and TLC can be measured in two ways: by helium dilution and by body plethysmography. Both methods are used clinically and provide valuable information about lung function and lung disease. The helium dilution technique is the older and simpler method, but it is often less accurate than body plethysmography, which requires sophisticated and expensive equipment.

In normal individuals, the functional residual capacity (FRC) measured by helium dilution and the FRC measured by plethysmography are the same (Table 21.1). This is not true in individuals with lung disease. The FRC measured by helium dilution is the volume of gas in the lung that communicates with the airways, whereas the FRC measured by plethysmography is the total volume of gas in the lungs at the end of a normal exhalation. If a significant amount of gas is trapped in the lungs (because of premature airway closure; see Chapter 22), the FRC determined by plethysmography is considerably higher than that determined by helium dilution.

TABLE 21.1 Sample Normal Values*

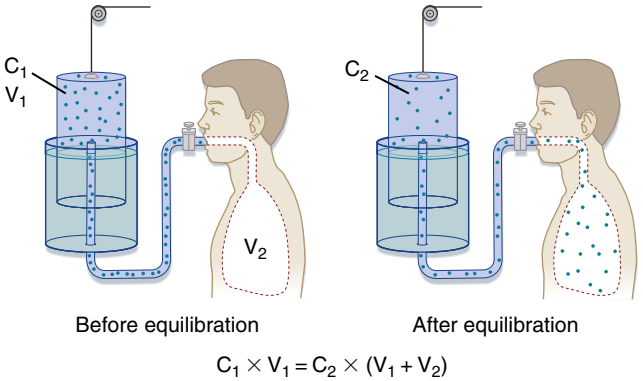
Lung Volumes

Functional residual capacity (FRC)	2.4 L
Total lung capacity (TLC)	6 L
Tidal volume (V_T)	0.5 L
Breathing frequency (f)	12/min

Static Mechanics

Pleural pressure (P_{pl}), mean	–5 cm H_2O
Chest wall compliance (C_w) at FRC	0.2 L/cm H_2O
Lung compliance (C_L) at FRC	0.2 L/cm H_2O

*Individual predicted normal values vary based upon height, weight, ethnic background, and biological sex.



• **Fig. 21.4** Measurement of lung volume by helium dilution. C_1, Known concentration of an inert gas; C_2, new (previously unknown) concentration of the gas; V_1, known volume of a box; V_2, lung volume (initially unknown).

IN THE CLINIC

In the helium dilution technique, a known concentration (C_1) of an inert gas (such as helium) is added to a box of known volume (V_1). The box is then connected to a volume (V_2) that is unknown (the lung volume to be measured). After adequate time for distribution of the inert gas, the new concentration (C_2) of the inert gas is measured. The change in concentration of the inert gas is then used to determine the new volume in which the inert gas has been distributed (Fig. 21.4). Specifically,

$$C_1 \times V_1 = C_2 (V_1 + V_2)$$

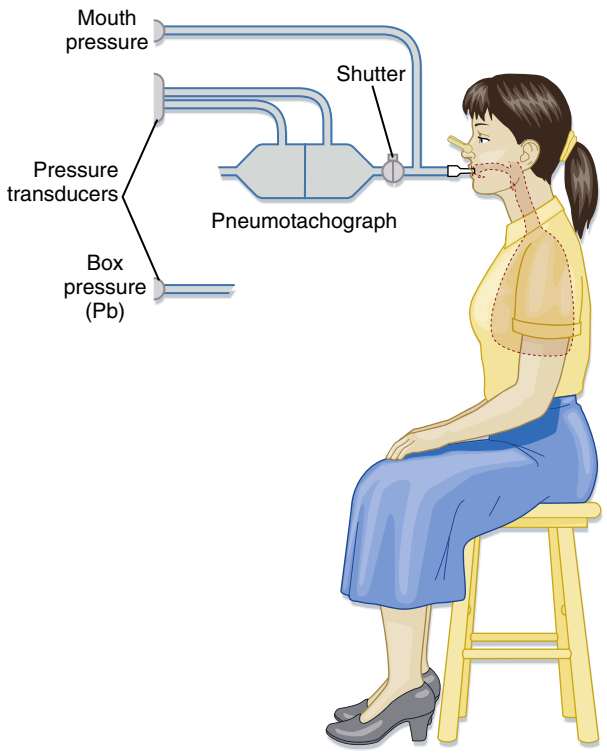
When measuring lung volume by body plethysmograph (body box), Boyle's gas law—that pressure multiplied by volume is constant (at a constant temperature)—is used to measure lung volumes. The patient sits in an airtight box (Fig. 21.5) and breathes through a mouthpiece that is connected to an airflow sensor (pneumotach). The patient then makes a panting respiratory effort against a closed mouthpiece. During the expiratory phase of the maneuver, the gas in the lung becomes compressed, lung volume decreases, and the pressure inside the box falls because the gas volume in the box increases. Once the volume of the box and the change in pressure of the box at the mouth are known, the change in volume (ΔV) of the lung can be calculated:

$$P_1 \times V = P_2 (V - \Delta V)$$

where P_1 and P_2 are mouth pressures and V is FRC. From the measurement of FRC, inspiratory capacity can be recorded as the volume of air inspired above FRC, and ERV can be determined as the volume of gas exhaled from FRC. These measurements can then be used to determine the other lung volumes.

Determinants of Lung Volume

What determines the volume of air in the lung at TLC or at RV? The answer lies in the properties of the lung parenchyma and in the interaction between the lungs and the chest wall. The lungs and chest wall always move together as a unit in healthy individuals. The lung contains elastic fibers that (1) stretch when stress is applied, which results in an increase in lung volume; and (2) recoil passively when this stress is released, which results in a decrease in lung volume. The elastic recoil of the lung parenchyma is very high. In the absence of external forces (such as the force generated by the chest wall), the lungs become almost airless (10% of TLC). Similarly, chest wall volume can increase when the respiratory muscles are stretched and decrease when respiratory muscle length is shortened. In the theoretical absence of the lung parenchyma, the resting volume of the chest wall increases and is approximately 60% of TLC.



• **Fig. 21.5** The body plethysmograph. Note that the box in which the patient sits is not depicted.

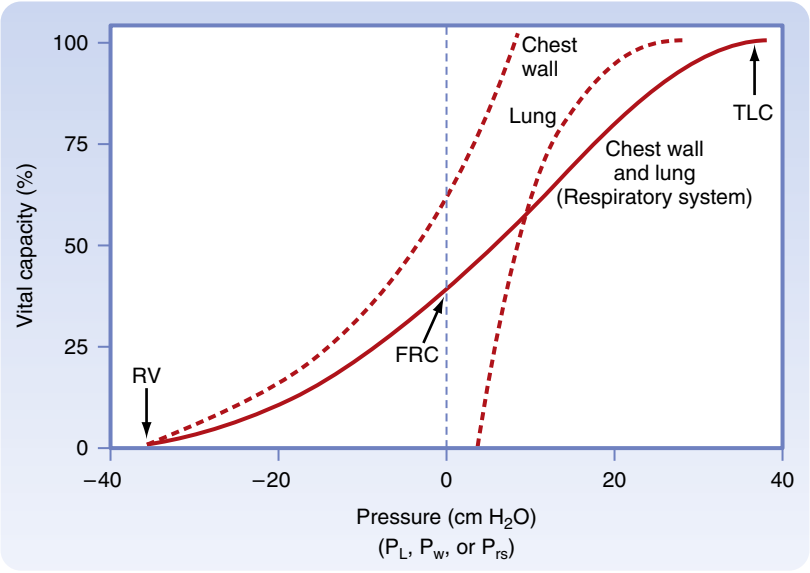
Lung volumes are determined by the balance between the lung's elastic properties and the properties of the muscles of the chest wall. The maximum volume of air contained within the lung and the chest wall (i.e., TLC) is controlled by the muscles of inspiration (see Chapter 20). With increasing lung volume, the chest wall muscles lengthen progressively. As these muscles lengthen, their ability to generate force decreases. TLC occurs when the inspiratory chest wall muscles are unable to generate the additional force needed to further distend the lung and chest wall. Similarly, the minimal volume of air in the lung (i.e., RV) is controlled by the expiratory muscle force. Decreasing lung volume results in shortening of the expiratory muscles, which, in turn, results in a decrease in muscle force. The decrease in lung volume is also associated with an increase in the outward recoil pressure of the chest wall. RV occurs when expiratory muscle force is insufficient to further reduce chest wall volume.

FRC, or the volume of the lung at the end of a normal exhalation, is determined by the balance between the elastic recoil pressure generated by the lung parenchyma to become smaller (inward recoil) and the pressure generated by the chest wall to become larger (outward recoil). When the chest wall muscles are weak, FRC decreases (lung elastic recoil > chest wall muscle force). In the presence of airway obstruction, FRC increases because of premature airway closure, which traps air in the lung (see Chapter 22).

Pressure-Volume Relationships

A number of important observations can be made from an examination of the pressure-volume curves of the lung, chest wall, and respiratory system (Fig. 21.6). At the resting volume of the lung (FRC), the elastic recoil of the lung acts to decrease lung volume, but this inward recoil is offset by the outward recoil of the chest wall, which acts to increase lung volume. At FRC, these forces are equal and opposite, and the muscles are relaxed. As a result, the transmural pressure across the respiratory system (P_{rs}) at FRC is 0. At TLC, both lung pressure and chest wall pressure are positive, and both require positive transmural distending pressure. The resting volume of the chest wall, in the absence of the lungs, is the volume at which the transmural pressure for the chest wall is 0, and it is approximately 60% of TLC. At volumes greater than 60% of TLC, the chest wall recoils inward and positive transmural pressure is needed, whereas at volumes below 60% of TLC, the chest wall tends to recoil outward.

The lungs alone are smallest when transpulmonary pressure is 0. The lungs, however, are not totally devoid of air when transpulmonary pressure is 0 because of the surface tension–lowering properties of surfactant (see the section "Surfactant"). The transmural pressure for a healthy lung alone flattens at pressures higher than 20 cm H_2O because the elastic limits of the lung have been reached. Thus, further increases in transmural pressure produce little change in volume, and compliance (see the section "Lung Compliance") is low. Further distention is limited by the connective tissue (collagen, elastin) of the lung. If further pressure is applied, the alveoli near the lung surface can rupture, and air can escape into the pleural space. This is called a **pneumothorax.** Pneumothorax can be spontaneous (due to alveolar rupture), traumatic (due to penetrating chest wall injury), or following certain invasive thoracic procedures. In a pneumothorax, the lungs and chest wall no longer function as a single unit. The lungs recoil until transpulmonary pressure is 0; the chest wall then increases in size until trans chest wall pressure is 0.



• **Fig. 21.6** Relaxation pressure-volume curve of the lung, chest wall, and respiratory system. The curve for the respiratory system is the sum of the individual curves. The curve for the lung is the same as the one for the normal lung in Fig. 21.1. *FRC*, Functional residual capacity; P_L, transpulmonary (or translung) pressure; P_{rs}, the pressure across the respiratory system; P_w, the transmural pressure across the chest wall; *RV*, residual volume; *TLC*, total lung capacity.

The relationship between transpulmonary pressure and pleural, alveolar, and elastic recoil pressures is depicted in Fig. 21.7. Alveolar pressure is the sum of the pleural pressure and elastic recoil pressure (P_{el}) of the lung:

Equation 21.4

$$P_A = P_{pl} + P_{el}$$

Because transpulmonary pressure (P_L) = $P_A - P_{pl}$,

Equation 21.5

$$P_L = (P_{el} + P_{pl}) - P_{pl}$$
$$P_L = P_{el}$$

In general, P_L is the pressure distending the lung, whereas P_{el} is the pressure that tends to collapse the lung. Lung elastic recoil increases as the lung inflates.

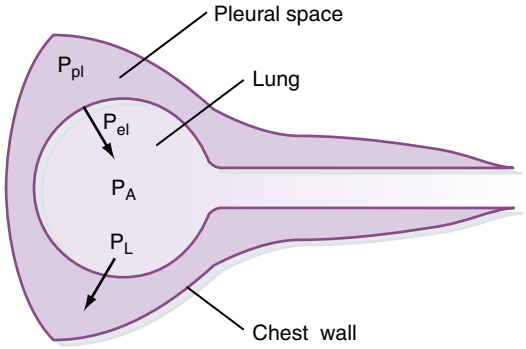
Lung Compliance

Lung compliance (C_L) is a measure of the elastic properties of the lung. It reflects how easily the lung is distended. Lung compliance is defined as the change in lung volume resulting from a 1-cm H_2O change in the distending pressure of the lung. The units of compliance are in milliliters (or liters) per centimeter of water. When lung compliance is high, the lung is readily distended. When lung compliance is low ("stiff" lung), the lung is not easily distended. The compliance of the lung (C_L) is expressed as

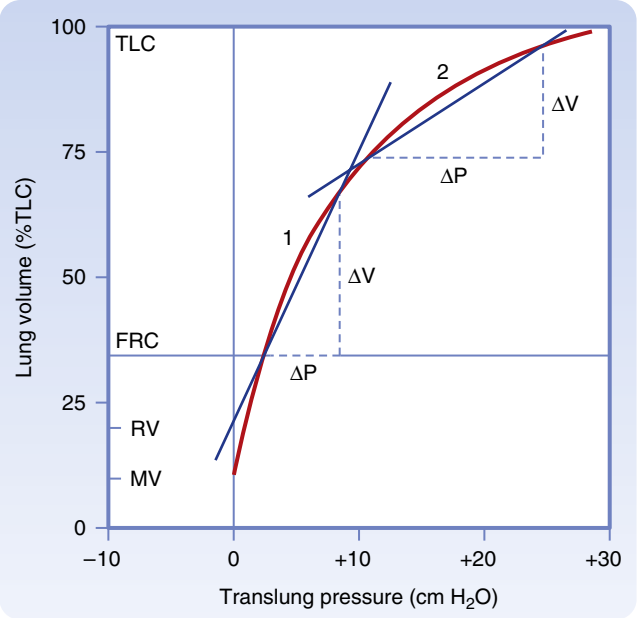
Equation 21.6

$$C_L = \Delta V/\Delta P$$

where ΔV is the change in volume and ΔP is the change in pressure. Graphically, lung compliance is the slope of the line between any two points on the deflation limb of the pressure-volume loop (Fig. 21.8). The compliance of a normal human lung is approximately 0.2 L/cm H_2O, but it varies with lung volume. Note that the lung is less distensible at high lung volumes. For this reason, compliance is corrected for the lung volume at which it is measured (specific compliance; Fig. 21.9). Compliance is not often measured for clinical purposes because it requires placement of an esophageal balloon. The esophageal balloon, which is connected to a pressure transducer, is used as a surrogate marker for pleural pressure, which is very difficult to measure directly. The change in pleural pressure (P_{pl}) is measured as a function of the change in lung volume; that is, $C_L = \Delta V/\Delta P_{pl}$ or $\Delta P_{pl} = \Delta C_L$.



• **Fig. 21.7** Relationship between transpulmonary pressure *(P_L)* and the pleural *(P_{pl})*, alveolar *(P_A)*, and elastic recoil *(P_{el})* pressures of the lung. Alveolar pressure is the sum of pleural pressure and elastic recoil pressure. Transpulmonary pressure is the difference between alveolar pressure and pleural pressure.

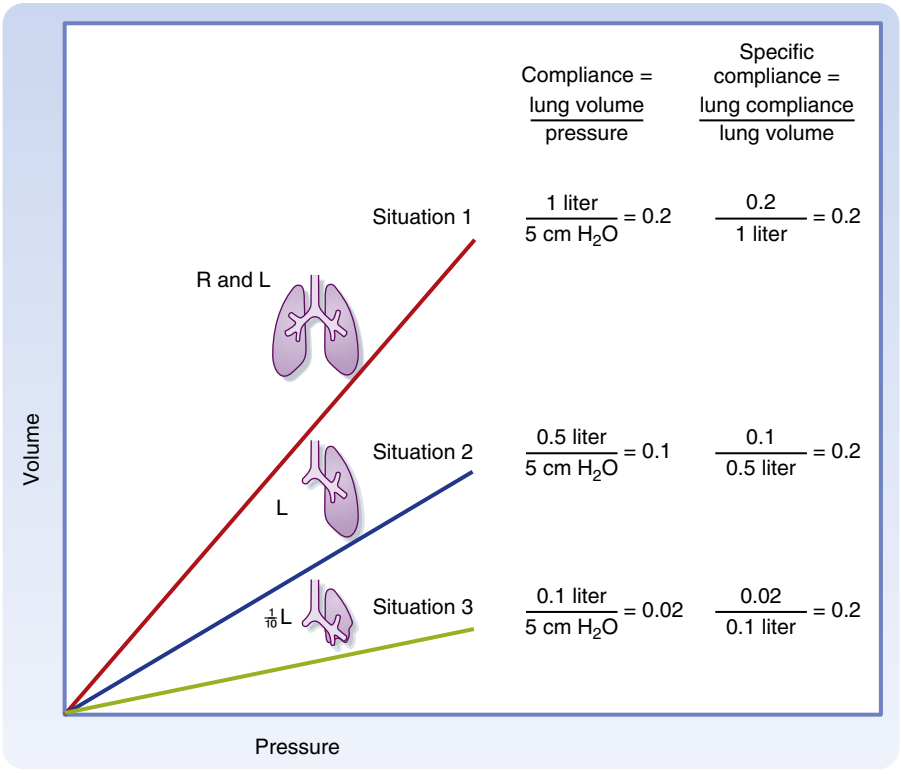


• **Fig. 21.8** Deflation pressure-volume curve. The patient inhales to total lung capacity, and transpulmonary pressure is measured with the use of an esophageal balloon (which measures pleural pressure). The patient then exhales slowly, and pressure is measured at points of no airflow, when the respiratory muscles are relaxed. The pressure-volume curve of the lung is not the same in inspiration (not shown) and exhalation. This difference is called **hysteresis,** and it is caused by the action of surfactant. In accordance with convention, the deflation pressure-volume curve is used for measurements. Compliance at any point along this curve is the change in volume per change in pressure. The curve demonstrates that lung compliance varies with lung volume. A line can be drawn between two different volumes on the curve, and the slope of this line represents the change in volume *(ΔV)* for a change in pressure *(ΔP)*. Compare the compliance at line 1 versus line 2. The slope of line 2 is less steep than the slope of line 1, and so the compliance is less at this higher lung volume than it is at the lower lung volume. In accordance with convention, lung compliance is the change in pressure from functional residual capacity (FRC) to FRC +1 L. *MV*, Minimal volume; *RV*, residual volume; *TLC*, total lung capacity.

Surface Tension and Surfactant

Surface Tension

In addition to the elastic properties of the lungs, another major determinant of lung compliance is surfactant and its effect on surface tension. **Surface tension** is caused by attractive forces between water molecules at the air-liquid interface. This tends to minimize surface area by collapsing alveoli resulting in decreased lung compliance. As a result, inflating the lungs becomes more difficult and requires more energy



• **Fig. 21.9** Relationship between compliance and lung volume. Imagine lungs in which a 5-cm H_2O change in pressure results in a 1-L change in volume (situation 1). If one lung is removed (situation 2), the compliance decreases, but when corrected for volume of the lung, there is no change (specific compliance). Even when the remaining lung is reduced by 90% (situation 3), the specific compliance is unchanged.

IN THE CLINIC

The compliance of the lungs is affected by several respiratory disorders. In emphysema, an obstructive lung disease associated with destruction of the alveolar septa, the lung is more compliant due to loss of elastic recoil; that is, for every 1 cm H_2O increase in pressure, the increase in volume is greater than that in a normal lung (see Fig. 21.1). In contrast, in pulmonary fibrosis, a restrictive lung disease associated with increased collagen fiber deposition in the interstitial space, the lung is less compliant; that is, for every 1 cm H_2O change in pressure, the change in volume is less. These changes in compliance are of clinical significance because a lung with low compliance (a "stiff lung") requires larger changes in pleural pressure to effect changes in lung volumes. As a result, the metabolic work of breathing is increased for every breath that the individual takes.

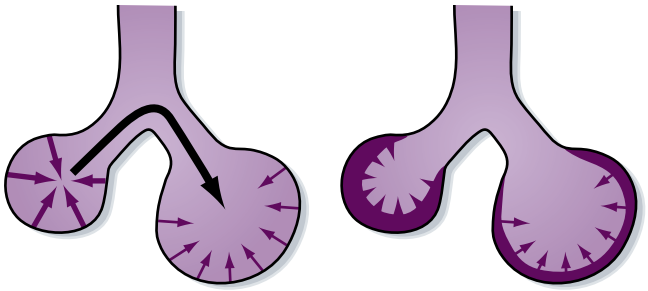
expenditure by the muscles of respiration. The effect of surface tension on lung inflation can be illustrated experimentally by a comparison of the volume-pressure curves of a saline-filled lung (with no air-liquid interface) and of an air-filled lung. Higher pressure is necessary to fully inflate the lung with air than with saline because of the higher surface tension forces in air-filled lungs than in saline-filled lungs. Surface tension is a measure of the attractive force of the surface molecules per unit length of material to which they are attached. The units of surface tension are those of a force applied per unit length. For a sphere (such as an alveolus), the relationship between the pressure within the sphere (P_s) and the tension in the wall is described by the law of Laplace:

Equation 21.7

$$P_s = 2T/r$$

where T is the wall tension (in dynes per centimeter) and r is the radius of the sphere.

The alveoli are lined with a predominantly lipid-based substance called **surfactant.** Pulmonary surfactant serves several physiological roles including (1) reducing the work of breathing by decreasing surface tension forces; (2) preventing collapse and sticking of alveoli on exhalation; and (3) stabilizing alveoli, especially those that tend to deflate at low surface tension. In the absence of surfactant, the surface tension at the air-liquid interface would remain constant, and the transalveolar pressure needed to keep it at that volume would be higher when alveolar volumes are lower (Fig. 21.10*A*). Therefore, higher transalveolar pressure would be necessary to produce a given increase in alveolar volume at lower lung volumes than at higher lung volumes. Surfactant stabilizes the inflation of alveoli because it allows the surface tension to increase as the alveoli become larger (see Fig. 21.10*B*). As a result, the transalveolar pressure necessary to keep an alveolus inflated increases as lung volume and transpulmonary pressure increases, and it decreases as lung volume decreases. In the presence of surfactant, surface tension is increased at high lung volume and decreased at



• **Fig. 21.10** Surface forces in a sphere attempt to reduce the area of the surface and generate pressure within the sphere. By Laplace's law, the pressure generated is inversely proportional to the radius of the sphere. **A,** In the absence of surfactant, surface forces in the smaller sphere generate higher pressure *(heavier purple arrows)* than do those in the larger sphere *(lighter purple arrows).* As a result, air moves from the small sphere (higher pressure) to the larger sphere (lower pressure; *black arrow*). This causes the small sphere to collapse and the large sphere to become overdistended. **B,** Surfactant *(shaded layer)* lowers surface tension and lowers it more in the smaller sphere than in the larger sphere. The net results are that the pressures in the small and larger spheres are similar, and the volumes of the spheres are stabilized.

low lung volume. The result is that the lungs can maintain alveoli at many different volumes. Otherwise, the gas in small alveoli would empty into large alveoli.

Surfactant

Pulmonary surfactant is synthesized by alveolar type II cells, stored in the cell in lamellar bodies, and secreted into the alveolar space in a precursor form (tubular myelin), from where it spreads throughout the entire alveolar surface and attains its ability to decrease surface tension. Surfactant is 85% to 90% lipids, predominantly phospholipids, and 10% to 15% proteins (Table 21.2). The major phospholipid is **phosphatidylcholine**, approximately 75% of which is present as **dipalmitoyl phosphatidylcholine** (DPPC). DPPC decreases surface tension and is the major surface-active component in surfactant. The second-most abundant phospholipid is **phosphatidylglycerol,** which accounts for 1% to 10% of total surfactant. These lipids are important in formation of the monolayer on the alveolar-air interface, and phosphatidylglycerol is important in the spreading of surfactant over a large surface area. Surfactant protein A, which is the protein most studied, is expressed in alveolar type II cells. Surfactant protein A is involved in the regulation of surfactant turnover, in immunoregulation within the lungs, and in the formation of tubular myelin.

Surfactant is secreted into the airway through exocytosis of the lamellar body by constitutive and regulated mechanisms. Numerous agents, including β-adrenergic agonists, activators of protein kinase C, leukotrienes, and purinergic agonists, stimulate the exocytosis of surfactant. The major routes of clearance of pulmonary surfactant within the lung are reuptake by type II cells, absorption into the lymphatic vessels, and clearance by alveolar macrophages. Surfactant is quickly inactivated by pathologic processes that introduce proteinaceous materials into the pleural space. These processes include infection, pulmonary edema fluid, and plasma proteins leaked into the airspaces. As a result of surfactant inactivation, alveolar surface tension increases, lung compliance decreases, and work of breathing increases.

In addition to surfactant, another mechanism, interdependence, contributes to stability of the alveoli. Alveoli, except for those on the pleural surface, are surrounded by other alveoli. The tendency of one alveolus to collapse is opposed by the traction exerted by the surrounding alveoli. Thus, collapse of a single alveolus causes stretching and distortion of

TABLE 21.2 Composition and Function of Surfactant Components

Component	% Composition	Function
Phospholipids	80–85	
Phosphatidylcholine	70–80	Decrease surface tension
Phosphatidylglycerol	1–10	Spreading ability
Phosphatidylethanolamine	1–2	Unclear
Phosphatidylserine	1–2	Unclear
Phosphatidylinositol	1–2	Unclear
Neutral Lipids	5–10	
Cholesterol	3–5	Stabilization
Cholesterol esters	1–3	Stabilization
Free Fatty Acids	1–3	
Proteins	2–5	
Surfactant protein A	2–4	Turnover, immune regulation, tubular myelin formation
Surfactant protein B	2–4	Decrease surface tension, spreading ability, lipid layering
Surfactant protein C	2–4	Decrease surface tension, spreading ability
Surfactant protein D	1–2	Unknown

the surrounding alveoli, which in turn are connected to other alveoli. Small openings **(pores of Kohn)** in the alveolar walls connect adjacent alveoli, whereas the **canals of Lambert** connect the terminal airways to adjacent alveoli. The pores of Kohn and the canals of Lambert provide collateral ventilation and prevent alveolar collapse **(atelectasis).**

IN THE CLINIC

In 1959, Avery and Mead discovered that in premature infants who died of hyaline membrane disease (HMD), the lungs were deficient in surfactant. HMD, also known as infant **respiratory distress syndrome,** is characterized by progressive atelectasis (deaeration) of lung units, respiratory failure, and (if severe) death. It is a major cause of morbidity and mortality in the neonatal period. The major surfactant deficiency in premature infants is lack of phosphatidylglycerol. In general, as the level of phosphatidylglycerol increases in amniotic fluid, the infant mortality rate decreases. Research in this field has culminated in successful attempts to treat HMD in premature infants with surfactant replacement therapy. Today, surfactant replacement therapy is standard care for premature infants. Additionally, steroids such as betamethasone are administered maternally prior to delivery to hasten fetal lung maturation. The steroid crosses the placenta and enters the fetal lung. There, it binds to a sterol regulatory domain in type II pneumocytes located upstream of the surfactant DNA sequence, leading to increased surfactant RNA transcription and increased surfactant protein production.

Key Points

1. Gas flows from areas of higher pressure to areas of lower pressure. Positive transpulmonary pressure is needed to increase lung volume. The pressure across the respiratory system is 0 at points of no airflow (end inspiration and end exhalation). At functional residual capacity (FRC), the pressure difference across the respiratory system is 0, and lung elastic recoil pressure, which operates to decrease lung volume, and the pressure generated by the chest wall to become larger are equal and opposite.
2. Pressure gradients in the respiratory system are created by the active contraction and subsequent relaxation of the muscles of respiration.
3. Lung volumes are determined by the balance between the lung's elastic recoil properties and the properties of the muscles and connective tissue of the chest wall.
4. Total lung capacity (TLC) is the total volume of air that can be exhaled after a maximal inspiration (vital capacity [VC]) plus the volume of air remaining in the lung after a maximal exhalation (residual volume [RV]).
5. Lung compliance is a measure of the elastic properties of the lung, defined as change in volume in response to change in pressure. Elastic recoil is decreased in patients with emphysema, and this decrease is associated with an increase in lung compliance. In contrast, diseases such as pulmonary fibrosis are associated with decreased lung compliance due to increased elastic recoil.
6. The surface tension-reducing and antisticking properties of surfactant increase lung compliance, decrease the work of breathing, and help stabilize alveoli of different size.