Lung Volumes and Airway Resistance 6.2

Learning Objectives

- Identify on a spirometer trace and be able to calculate TV, IRV, ERV, and RV
- Identify on a spirometer trace and be able to calculate IC, VC, FRC, and TLC
- Define the respiratory minute volume and pulmonary ventilation
- Describe the procedure followed in obtaining the forced vital capacity
- Indicate how a spirometer can measure airway resistance
- Distinguish between laminar and turbulent flows
- Describe how resistance varies as a function of flow in the airways
- Write the equation for the Reynolds number and be able to predict when flow is turbulent
- Define dynamic compression
- Explain how airway resistance is modified by tracheobronchiole smooth muscle
- Explain how pursed-lips breathing can increase airflow

SPIROMETERS MEASURE LUNG VOLUMES AND ALLOW IDENTIFICATION OF SEVERAL LUNG VOLUMES AND LUNG CAPACITIES

The volume of air that can be inhaled or exhaled can be estimated using **spirometry**. Several different kinds of spirometers exist. Here we describe a volume–displacement Collins respirometer in which a person breathes through a small tube that is connected to an air space located within a lightweight bell jar that is isolated from the ambient air by a layer of water. When air enters the lungs, it leaves the bell jar and reduces the volume of air in the jar by the same volume of air that is inhaled, and this can be measured continuously by linking movement of the bell jar to a recording pen. The setup is illustrated in Figure 6.2.1.

The spirometer aids in identifying several useful lung volumes and capacities. These are:

1. The **tidal volume, TV**, is the amount of air breathed in and out during normal, restful breathing. Its typical value, as shown in Figure 6.2.1, is about 500 mL = 0.5 L. The magnitude of the TV depends on the size of the individual and their metabolic state. The spirometer recording shown in Figure 6.2.1 is idealized: the TV usually varies from breath to breath.
2. The **inspiratory reserve volume, IRV**, is the additional volume of air that can be inspired at the end of a normal or tidal inspiration. The typical value for a young adult male of normal size is about 3000 mL.
3. The **expiratory reserve volume, ERV**, is the additional volume of air that can be expired after a normal or tidal expiration. A typical value is about 1100 mL for a young adult male.
4. The **residual volume, RV**, is the volume remaining in the lung after a maximum expiration. Even a maximum effort cannot void the lungs of all air. This volume of air cannot be measured by spirometry but it can be calculated by measuring the functional residual capacity by two other techniques: **gas dilution** and **body plethysmography**. The value of the RV is typically about 1200 mL.

LUNG CAPACITIES ARE COMBINATIONS OF TWO OR MORE LUNG VOLUMES

We have identified four lung volumes, three of which are easily measured by spirometry. We also identify four lung capacities. These are:

1. The **functional residual capacity, FRC**, is the volume of air remaining in the lungs after a normal or tidal expiration. It is the sum of two lung volumes: the RV and the ERV. A typical value for a young adult male is FRC = RV + ERV = 1.2 L + 1.1 L = 2.3 L. The FRC is that point during the respiratory cycle when the pressure across the entire respiratory system, P_{rs}, is zero. At this point, the recoil force of the lungs exactly balances the expansive force of the chest wall.
2. The **inspiratory capacity, IC**, is the volume of air that can be inspired after a normal or tidal expiration. The inspiratory capacity thus is the volume of air that can be inspired beginning at the FRC. According to Figure 6.2.1, the **IC** is the sum of the IRV and the TV. Thus, IC = IRV + TV = 3.0 L + 0.5 L = 3.5 L.
3. The **vital capacity, VC**, is the sum of all lung volumes above the RV: the ERV, the TV, and the

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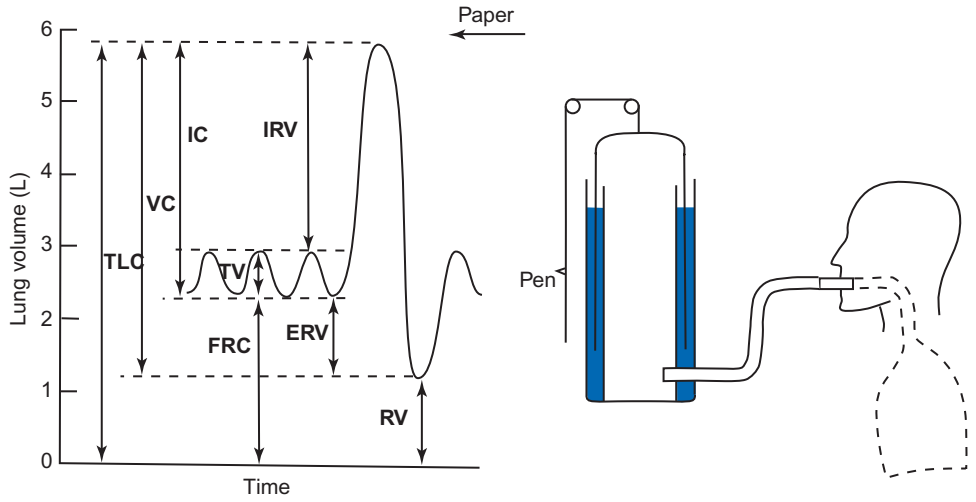

FIGURE 6.2.1 Typical setup for a volume–displacement spirometer. The person places a clip on the nose so that all air passes through the mouth. The person then breathes in air that is connected to a closed space in a light cylindrical bell jar that is sealed from the outside by a layer of water retained between two concentric cylinders. The movement of the bell jar is converted to the movement of a pen that writes on moving paper. The pen movement is inverted from the original bell jar. Inspiration results in downward movement of the bell jar and upward movement of the pen. The person is instructed to breathe normally for a few breaths, then to inspire as deeply as possible, and then expire as deeply as possible. The trace allows identification and measurement of several lung volumes and capacities, as described in the text.

TABLE 6.2.1 Ratios of VC, RV, and TLC to the Cube of the Height in Meters

Age (years)	VC/h^3 (L m^{-3})	RV/h^3 (L m^{-3})	TLC/h^3 (L m^{-3})
18–19	0.990	0.24	1.23
20–29	1.025	0.275	1.30
30–34	1.020	0.30	1.30
35–39	1.010	0.31	1.32
40–44	1.000	0.32	1.32
45–49	0.990	0.33	1.32
50–54	0.970	0.35	1.32
55–59	0.950	0.37	1.32
60–64	0.930	0.39	1.32

The values were obtained from European men of different ages in the upright posture.
Data from E. Agostoni and J. Mead, Statics of the respiratory system, in W.O. Fenn and H. Rahn, eds., Handbook of Physiology, *1964.*

IRV, as shown in Figure 6.2.1. Its volume is given as VC = ERV + TV + IRV = 1.1 L + 0.5 L + 3.0 L = 4.6 L. The VC is the largest volume of air that can be expired from a maximal inspiration.

4. The **total lung capacity, TLC**, is the maximum volume of air that the respiratory system can hold. It is the sum of all four lung volumes. Thus TLC = VC + RV. Because this includes the RV, it cannot be determined using spirometry. Its value is given as TLC = IRV + TV + ERV + FV = 3.0 L + 0.5 L + 1.1 L + 1.2 L = 5.8 L. Again, this value is a "typical" value for a young adult male. Such a person is largely fictitious in that most people are not normal young adult males. Particular values should be interpreted by considering the age, sex, and body size of the particular person.

LUNG VOLUMES AND CAPACITIES VARY MAINLY WITH BODY SIZE

Generally speaking, larger people have larger lung volumes and capacities compared to their smaller counterparts. But what do we mean by "larger"? Suitable measures of size include height, weight, and surface area, and these are not independent. Taller people often weigh more and have a larger surface area—but not always. Extensive studies of European males in the 1950s showed a fairly constant relation between the cube of the height and VC, RV, and TLC. These results (see Table 6.2.1) also show that the relationship between lung volumes and height changes with age. The values for women are typically about 10% less than those for men of the same age and height.

PULMONARY VENTILATION IS THE PRODUCT OF RESPIRATORY RATE AND TIDAL VOLUME

The purpose of the respiratory system is to exchange gases between the blood and the inspired air in order to supply oxygen to metabolizing tissues and to remove waste CO_2 to the air. When the tissues metabolize more quickly, as during exercise, the exchange of gases must increase to match demand. This is not a static problem, but a dynamic one, and it is the rate of ventilation, rate of gas exchange, and rate of O_2 consumption and CO_2 production, that matter. The lung volumes and lung capacities are all measured in liters, whereas rates of ventilation, gas exchange, and consumption are expressed in L min^{-1}.

The pulmonary ventilation is the rate at which air moves out of the lungs. Suppose that 500 mL leaves the lungs with each tidal respiration at rest and that the resting respiratory rate (RR) is 12 breaths per minute. Then the pulmonary ventilation, $Q_V = TV \times RR = 0.5$ L $breath^{-1} \times 12$ breaths $min^{-1} = 6$ L min^{-1}. Because usually more O_2 is consumed than CO_2 is produced, the volume of dry air that enters the lung is a tiny bit larger than the volume of dry gas that is expired. The resting pulmonary ventilation is often called the **respiratory minute volume**.

DURING EXERCISE, PULMONARY VENTILATION INCREASES DUE TO INCREASED RR AND TV

Typically, exercise increases both the RR and the TV. The increased TV usually uses only part of the IRV and part of the ERV. During exercise the pulmonary ventilation can reach 80–100 L min^{-1} in healthy young adults. This is about a 15-fold increase from the resting respiratory minute volume.

THE MAXIMUM VOLUNTARY VENTILATION EXCEEDS PULMONARY VENTILATION DURING EXERCISE

The **maximum voluntary ventilation** refers to the maximum rate of pulmonary ventilation. This can be measured using a spirometer, but the period of maximal breathing is limited to 15 s because the individual can become alkalotic and he can fatigue. Figure 6.2.2 shows a spirometer trace of an individual moving as much air as possible. In this case, the TV during the maximum voluntary ventilation was 2.8 L (1.7 L of IRV + 0.5 L V + 0.6 L of ERV), and the RR was 15 breaths in the 15 s period, giving 60 breaths min^{-1}. This gives a maximum voluntary ventilation of 60 breaths $min^{-1} \times 2.8$ L $breath^{-1} = 168$ L min^{-1}. This is an impressive maximum voluntary ventilation which typically can be reached only in very fit young adults. Normal values depend on size, age, and sex. The maximal voluntary ventilation exceeds pulmonary ventilation during exercise because the person focuses only on moving as much air as possible for a very short time. It is not possible to continue such maximal ventilation for protracted times.

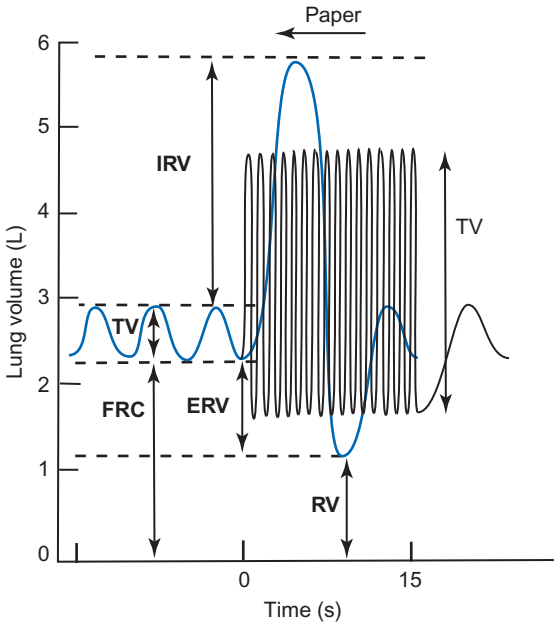

FIGURE 6.2.2 Spirometer trace of maximum voluntary ventilation. The blue trace represents maximum inspiration and expiration, as described in Figure 6.2.1. Superimposed on this is 15 s of maximum ventilation in which the person increases both the rate and depth of ventilation. In this case, some of the IRV and some of the ERV were used to increase the TV from the normal 0.5 to 2.8 L. The RR increased from about 12 to 60 min^{-1}.

SPIROMETRY ALSO PROVIDES A CLINICALLY USEFUL MEASURE OF AIRWAY RESISTANCE

The major difference between the static behavior of the lungs and its dynamic behavior is the resistance that accompanies airflow and partially limits the ability to ventilate the lungs. A clinically useful measure of the ability to move air quickly is the **forced vital capacity (FVC)**. In this procedure, a person connected to a spirometer is instructed to breathe in as deeply as possible and then to expire as *completely* and *rapidly* as possible. A hypothetical spirometer tracing of this procedure is shown in Figure 6.2.3. The volume of air that can be expired this way is the FVC. The timescale is expanded to resolve the time course of the FVC, and the volumes expired at 1, 2, and 3 s are measured. These are referred to as FEV_1, FEV_2, and FEV_3 for forced **e**xpiratory **v**olume at 1, 2, and 3 s. The absolute values of FEV_1, FEV_2, and FEV_3 vary with FVC, and so these values are normalized by dividing by FVC.

The clinical presentation of the FVC is often turned around and presented as shown in Figure 6.2.4. This spirogram provides four test results: **FVC, FEV1, FEV1/VC, and FEF25–75**, also called the **maximal midexpiratory flow rate**. This is the averaged forced expiratory flow rate from 25% of FVC to 75% of FVC.

A more modern approach is the **flow–volume loop**, obtained from clinical spirometers (see Figure 6.2.5). The main results from this presentation of the data are the **FVC** and the **peak expiratory flow rate**, **PEFR**, the maximum flow during forceful expiration. For healthy

EXAMPLE 6.2.1 Lung Volumes and Airway Resistance

The lung capabilities in an older individual were measured by spirometry, and the following data were obtained:

TV = 0.4 L; IRV = 2.3 L; ERV = 1.2 L; FEV_1 = 2.0 L

Calculate the VC and FRC. Are these normal? Is the airway resistance normal?

The VC is calculated as VC = ERV + TV + ERV = 1.2 L + 0.4 L + 2.3 L = **3.9 L**. We cannot calculate the FRC because this requires knowledge of the RV, which we cannot obtain from spirometric data. You cannot determine whether this VC is normal or not without information about the size and age of the person.

We calculate an indicator of airway resistance as FEV_1/VC = 2.0 L/3.9 L = **0.51**. This number is definitely below the normal value of 0.80–0.90.

adult males, the PEFR is in the range of 9–11 L s^{-1}; for adult females, it is about 6–7 L s^{-1}.

AIRWAY RESISTANCE DEPENDS ON WHETHER AIRFLOW IS LAMINAR OR TURBULENT

STREAMLINE OR LAMINAR FLOW ENTAILS A RESISTANCE THAT IS INDEPENDENT OF FLOW

The relation between laminar flow and pressure in a right cylindrical tube was covered in Chapters 1.2 and 5.8. It is described by Poiseuille's law:

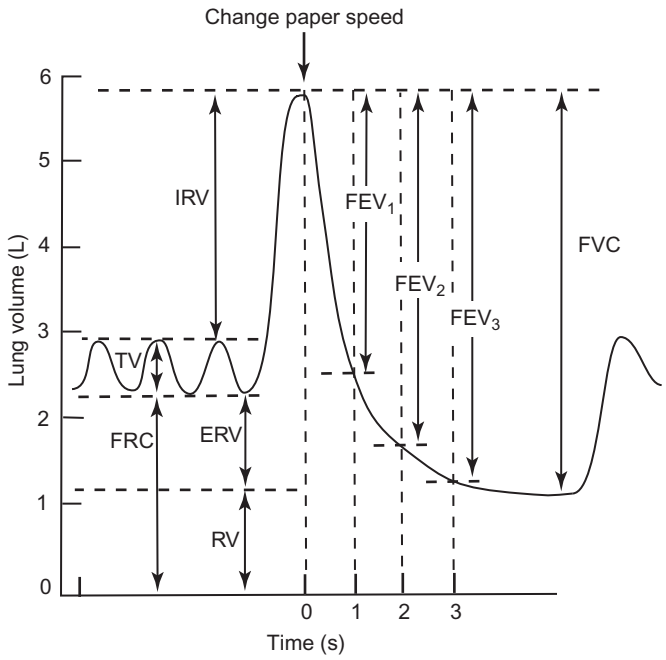

FIGURE 6.2.3 Spirometer tracing of a FVC. The person connected to the spirometer is instructed to breathe normally for a few breaths, then to inspire as deeply as possible, and then to expire as rapidly and completely as possible. Near the peak of inspiration, the chart speed is changed to resolve the time course of the FVC. The volumes expired at 1, 2, and 3 s are recorded as the forced expiratory volume (FEV_1, FEV_2, and FEV_3). The ratio of FEV_1, FEV_2, and FEV_3 to the FVC provides clues to the airway resistance. The FVC should be equal to the VC, but it is typically expired much faster than for the measurement of the VC. FEV_1/FVC is typically greater than 0.80; a value significantly lower than this indicates abnormally high airway resistance. FEV_2/FVC should exceed 0.90; FEV_3/FVC should exceed 0.95.

[6.2.1] $$Q_V = \frac{\pi a^4}{8\eta l}\Delta P$$

where Q_V is the flow, in volume per unit time, a is the radius, η is the viscosity of the flowing medium, l is the length of the cylinder, and ΔP is the pressure difference between the beginning and the end of the cylinder. This is the hydraulic analogy of Ohm's law:

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

where R is the **resistance** of the airway to flow. This equation can be rewritten as

[6.2.3] $$\Delta P = RQ_V$$

Equation [6.2.3] is presented this way to emphasize a different point: the pressure difference necessary to maintain a steady flow of Q_V is linearly related to Q_V, and the coefficient is the resistance. Here the resistance to flow

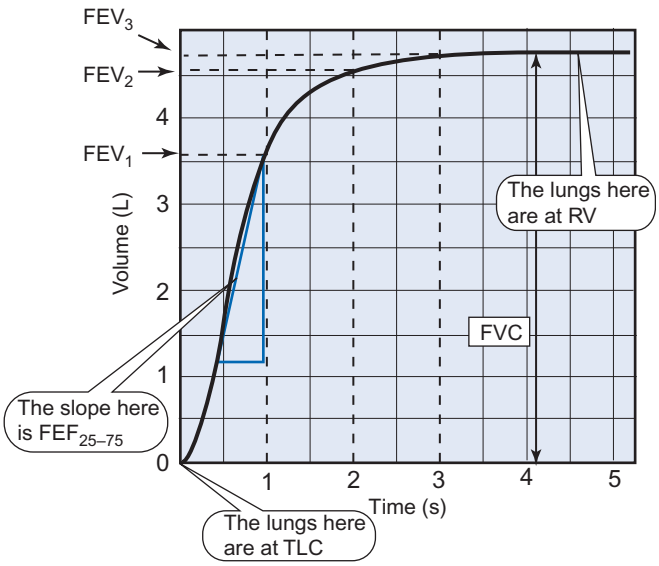

FIGURE 6.2.4 Clinical spirogram. The person in this case is instructed to inspire as deeply as possible, and then to exhale as rapidly and completely as possible. The expired volume is plotted as a function of time after beginning expiration, so the plot is the reverse of the positive-displacement spirometer. The clinically useful test results are the **FVC**, equal to the total volume of gas expired following maximal inspiration; **FEV_1**, the forced expiratory volume after 1 s; **FEV_1/FVC**; and the **maximal midexpiratory flow rate** or **FEF_{25-75}**, which is the slope of the volume–time curve between 25% of FVC and 75% of FVC.

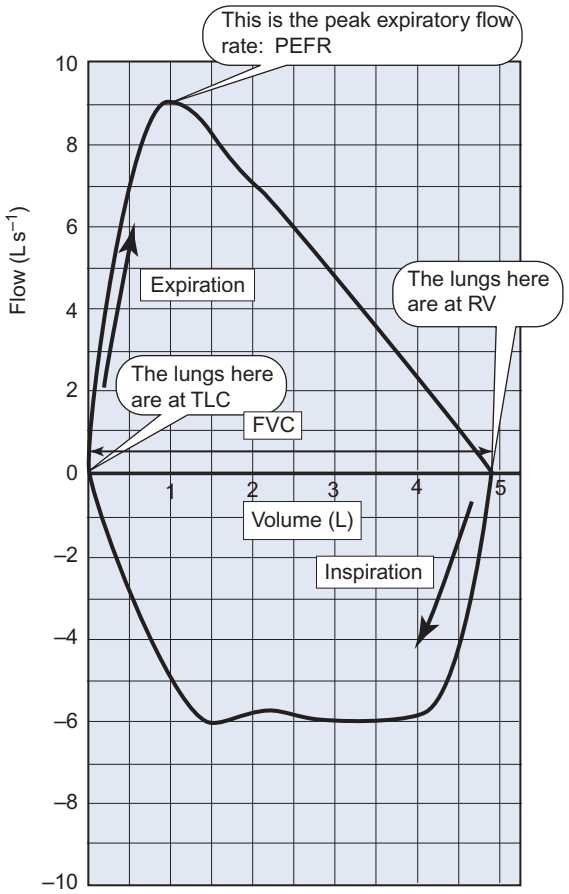

FIGURE 6.2.5 Flow–volume loop for the FVC. The person is instructed to inspire as deeply as possible and then to exhale as rapidly and completely as possible. The expiratory phase is shown above the abscissa, and volume refers to the volume of exhaled air. The zero volume begins with the lungs as full as possible; their volume at this time is the TLC. After exhaling as much as possible, the volume remaining in the lungs is the RV. The volume of air expired in the maneuver is the FVC. The maximum flow during expiration is the PEFR. The maximum flow rate during inspiration can be nearly as great as that during maximal expiration. In diseased lungs, maximum inspiratory flow can be greater than the maximal expiratory flow due to **dynamic compression** of the airways during expiration.

depends only on the viscosity of the air, the radius of the airway, and its length. It does not depend on the rate of airflow and we would expect that the plot of Q_V against ΔP would be linear with slope $= 1/R$. Equation [6.2.3] can be rearranged to emphasize a different point: **the resistance is defined as the ratio of $\Delta P/Q_V$.**

TURBULENT FLOW PRODUCES A NONLINEAR RELATION BETWEEN FLOW AND PRESSURE DIFFERENCE

Turbulent flow differs from laminar flow in that the pressure difference needed to sustain a constant turbulent flow is proportional to the square of the flow:

$$\Delta P = K_2 Q_V^2 \quad [6.2.4]$$

where K_2 is a coefficient for the equation but it is not the resistance because the relationship is not Ohmic. This equation describes the relation between ΔP and Q_V only over the range of turbulent Q_V.

THE REYNOLDS NUMBER INDICATES THE TENDENCY TO TURBULENT FLOW

Whether the flow of air is laminar or turbulent depends on several physical factors including the velocity of flow, the density of the air, the viscosity of the air, and the size and physical characteristics such as the smoothness or roughness of the wall of the tubes through which flow occurs. The Reynolds number incorporates some of these factors (see Chapter 5.8). The Reynolds number is a dimensionless ratio of the inertial forces to the viscous forces of the fluid. It is given as

$$Re = \frac{2a\langle V\rangle\rho}{\eta} \quad [6.2.5]$$

where Re is the Reynolds number, a is the radius of the airway, $\langle V\rangle$ is the average velocity of airflow, ρ is the density of air, and η is its viscosity. When $Re > 2500$, turbulent flow dominates; at lower values of Re, laminar flow is more likely. Equation [6.2.5] shows that Re is large when the airway radius is large and flow velocities are high. The density of air (at 1 atm) at 37°C is 1.13 g L^{-1} and its viscosity is 19.1×10^{-6} Pa s, where 1 Pa = 1 N m^{-2} = 10 dyne cm^{-2}. Q_V is the flow in units of volume time^{-1} and J_V, the flux, is the flow per unit area, in units of length time^{-1} (volume area^{-1} time^{-1}). J_V is the velocity of fluid flow. For streamline flow, J_V is not constant across the tube but varies from zero at the sides of the tube to a maximum in the center of the tube. We calculate the average velocity as

$$\langle V\rangle = \frac{Q_V}{A} \quad [6.2.6]$$

where A is the area through which the flow occurs. Insertion of $\langle V\rangle$ from Eqn [6.2.6] into Eqn [6.2.5] gives

$$Re = \frac{2aQ_V\rho}{A\eta} \quad [6.2.7]$$

Here A is the total cross-sectional area of airways of radius a. Thus $A = n\pi a^2$, where n is the number of airways of the same generation. Using this equation and the results shown in Figure 6.2.6 for the morphometry of the lungs, we can calculate the Reynolds number for each generation of airway. It is clear from Eqn [6.2.7] that the Reynolds number increases directly with Q_V and inversely with total cross-sectional area. The results show that for normal TV, $Re < 2000$ everywhere in the tracheobronchial tree, suggesting that turbulent flow most likely does not occur during resting respiration. At higher flows, turbulence becomes apparent in the upper airways mainly because the total cross-sectional area is small.

THE POISEUILLE EQUATION DERIVED FOR RIGHT CYLINDERS DOES NOT MODEL THE COMPLICATED AIRWAYS

A complicated system of tubes such as the tracheobronchial tree with its branches, irregular wall surfaces, and changes in caliber is not amenable to direct application of equations that have been derived to describe flow through right cylinders. Calculation of airway resistance,

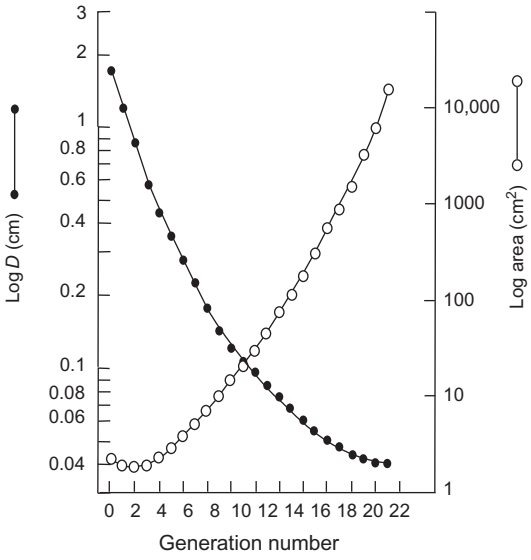

FIGURE 6.2.6 Morphometry of the lungs. The morphometry of human lungs was estimated from plastic casts for the larger airways and from histological sections for the smaller airways. The diameter of the airways is plotted against the generation number (*closed circles*). The generation number refers to the number of times the airways have branched. The diameter decreases nearly exponentially with the generation number during the first few generations and then decreases more slowly thereafter. Even though the airways are markedly smaller, there is a tremendous number of smaller airways, so that the total cross-sectional area increases markedly with generation number. Because the cross-sectional area increases, the velocity of airflow through the airways diminishes as the airways divide toward the alveoli. *Data from W.R. Weibel,* Morphometry of the Human Lung, *Springer, 1963.*

however, suggests that both laminar flow and turbulent flow occur within the airways.

AIRWAY RESISTANCE IS THE SLOPE BETWEEN ΔP AND Q_V

Equation [6.2.3] describing laminar flow predicts a linear relation between the pressure and the flow. On the other hand, Eqn [6.2.4], which describes turbulent flow predicts a parabolic relationship between ΔP and Q_V. Which describes the lungs? Figure 6.2.7 illustrates that the relationship between ΔP and Q_V is neither linear nor parabolic but is a sum of both processes.

TURBULENT AND LAMINAR FLOWS RESULT IN RESISTANCES THAT OCCUR IN SERIES AND ADD

The tracheobronchial tree consists of a series of airways that branch. The airways become progressively smaller, as shown in Figure 6.2.6, and at the same time the number of parallel airways becomes larger. Thus the airways consist of both series and parallel components. The collection of parallel airways at each generation can be lumped to form a single equivalent resistance, and these lumped resistances then are arranged in series and the equivalent resistances add. At some levels of the generations of airways, the flow is laminar and resistance is given by Eqn [6.2.3] as

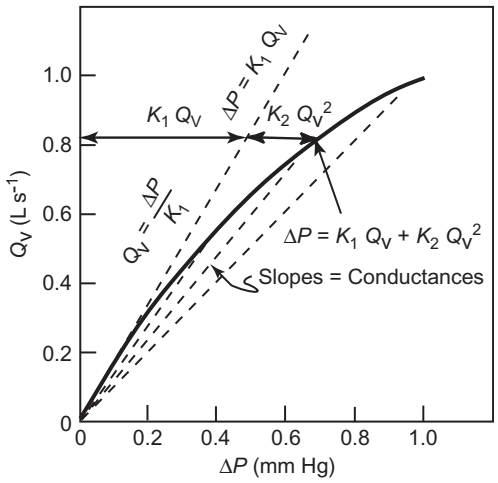

FIGURE 6.2.7 Relationship between flow and pressure difference in the lungs. The slope of the chord connecting the line with origin is the airway conductance and its inverse is the resistance (K_1). The resistance is not constant: it depends on the airflow. This is because as airflow increases, a greater fraction of the tracheobronchial tree exhibits turbulent flow with its higher resistance.

$$[6.2.8] \qquad R = \frac{\Delta P}{Q_V} = K_1$$

For those airways in which flow is turbulent, the resistance is given by Eqn [6.2.4] as

$$[6.2.9] \qquad R = \frac{\Delta P}{Q_V} = K_2 Q_V$$

Since the airways in which laminar flow occurs are in series with those in which turbulent flow occurs, we might expect the resistances to add. Thus we would expect

$$[6.2.10] \qquad R_{total} = \frac{\Delta P}{Q_V} = K_1 + K_2 Q_V$$
$$\Delta P = K_1 Q_V + K_2 Q_V^2$$

These equations form an adequate approximate description of overall airway resistance. As predicted from Eqn [6.2.10], the airway resistance, calculated as $\Delta P/Q_V$, is linearly related to Q_V with intercept K_1 and slope K_2. Thus the resistance is not constant but depends on the rate of flow.

AIRWAY RESISTANCE DEPENDS ON LUNG VOLUME

As the lungs expand, their recoil tendency increases and so they pull harder on the chest wall, resulting in a more negative intrapleural pressure. Lung tissue is also anchored to the airways, and so the expansion of the lungs also causes an expansion of the airways by pulling on them from the tissue side of the airways. The bronchial caliber is set in part by the radial traction of the surrounding lung tissue. The relationship is nearly hyperbolic, described by

$$[6.2.11] \qquad R_{total} = \frac{K}{V}$$

EXAMPLE 6.2.2 Calculate the Reynolds Number

The diameter of the trachea in one individual was 1.8 cm. The person's PEFR was measured to be 10 L s^{-1}. During normal resting respiration, the flow was about 0.3 L s^{-1}. Calculate the Reynolds number for the two circumstances.

The Reynolds number is $2a\langle V\rangle\rho/\eta$, where a is the radius, $\langle V\rangle$ is the average velocity ($=Q_V/A$), ρ is the density, and η is the viscosity. We use $\rho = 1.13$ g L^{-1} and $\eta = 19.1 \times 10^{-6}$ Pa s = 191×10^{-6} dyne cm^{-2} s. These conversions use the cgs system, which is often more convenient.

First, we calculate $\langle V\rangle = 10$ L $s^{-1}/\pi \times (0.9\text{ cm})^2 = 3.93$ L s^{-1} $cm^{-2} \times 1000$ cm^3 $L^{-1} = 3.93 \times 10^3$ cm s^{-1}.

During peak expiration, the Reynolds number is

$$1.8\text{ cm} \times 3.93 \times 10^3\text{ cm s}^{-1} \times 1.13\text{ g L}^{-1} \times 10^{-3}\text{ L cm}^{-3}/191 \times 10^{-6}\text{ g cm s}^{-2}\text{ cm}^{-2}\text{ s} = \mathbf{41{,}851}$$

This is clearly turbulent. At the lower flow, $\langle V\rangle = 0.3$ L $s^{-1} \times 1000$ cm^3 $L^{-1}/2.54$ $cm^2 = 118$ cm s^{-1}.

$$R_e = 1.8\text{ cm} \times 118\text{ cm s}^{-1} \times 1.13\text{ gL}^{-1} \times 10^{-3}\text{ L cm}^{-3}/191 \times 10^{-6}\text{ g cm s}^{-2}\text{ cm}^{-2}\text{ s} = \mathbf{1256}$$

which is not turbulent.

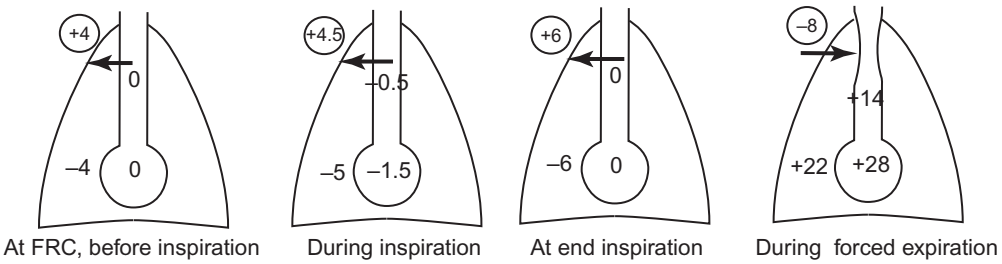

FIGURE 6.2.8 Schematic diagram of the pressures acting on the airways during various stages of breathing. Approximate intrapleural, alveolar, and airway pressures are given in mm Hg. The net pressure acting on the airways helps keep them open except in the case of a forceful expiration, in which the pressure within the airways becomes less than that in the intrapleural space. The pressure drops in the airways due to the resistance to flow at high volumes. The result is the dynamic compression of the airways and limitation of maximal expiration rates. *Modified from J.B. West,* Respiratory Physiology, *Williams and Wilkins, Baltimore, 1979.*

where V is the lung volume and K is some constant. The inverse of the resistance, R_{total}, is the **conductance**. According to Eqn [6.2.11], the airway conductance is linearly related to the lung volume.

DYNAMIC COMPRESSION OF THE AIRWAYS DURING FORCEFUL EXPIRATION LIMITS AIRFLOW

The pressure difference between the intrapleural space and the airways is part of the balance of forces keeping them open. During forceful expirations, the pressure outside the airways is higher than it is inside. This transmural pressure difference diminishes the caliber of the airways, thereby increasing their resistance. Figure 6.2.8 illustrates the net pressures acting on the airways.

AIRWAY RESISTANCE IS MODIFIED BY SMOOTH MUSCLE CONTRACTION OF THE AIRWAYS

The airways are invested with a coat of smooth muscle that is innervated by parasympathetic fibers. Contraction of these smooth muscles causes **bronchoconstriction**, and relaxation causes **bronchodilation**. Parasympathetic excitation with its accompanying release of acetylcholine brings about bronchoconstriction. In addition, local factors can cause bronchoconstriction. The lungs sit at the interface between the body and the environment and provide a convenient route for the entry of all manner of foreign organisms and objects. As a result, the lung is provided with potent immune mechanisms and cells. Release of histamine from these cells upon presentation with an antigen contracts the smooth muscle and constricts the bronchioles. In severe cases, the bronchoconstriction can be fatal. This is the case in severe asthma attacks that claim the lives of approximately 2500 persons in the United States each year.

The smooth muscles of the airways possess β_2 receptors. Their stimulation increases cAMP in the cells and causes relaxation (see Chapter 3.8). Thus the rescue treatment for a person with bronchoconstriction is injection of epinephrine to relax the muscles and relieve the constriction. Sympathetic stimulation causes bronchodilation.

PURSED LIPS INCREASE AIRFLOW IN CASES OF INCREASED AIRWAY RESISTANCE

Persons with decreased lung recoil exhibit increased airway resistance because the lungs do not pull on the airways enough to keep them open. The effect is to increase the FRC because the balance between lung

Clinical Applications: COPD

COPD stands for **c**hronic **o**bstructive **p**ulmonary **d**isease. This is a set of different diseases that differ in their causes but have a common physiological effect: increased airway resistance. It includes **emphysema**, **chronic bronchitis**, and **bronchiectasis**. Although asthma is also a chronic obstructive condition, it is not considered to be a COPD because the term is reserved for irreversible conditions. Unlike emphysema, chronic bronchitis, and bronchiectasis, the airway obstruction in asthma is usually reversible. The increased airway resistance can be due to the loss of elastic recoil due to changes in the lung tissue, as seen in **emphysema**, or to airway inflammation as seen in **chronic bronchitis**.

Emphysema claimed 106,000 lives in the United States in 1998, making it the fourth leading cause of death nationwide. It entails abnormal enlargement of the air spaces distal to the terminal bronchioles with destruction of the tissue without fibrosis. Smoking tobacco is the primary cause of COPD, accounting for 80–90% of the risk of developing COPD. However, only 15% of smokers actually develop the disease. The mechanism by which cigarette smoke causes lung tissue destruction is controversial. For over 30 years, the favored explanation was that cigarette smoking caused an imbalance in the ratio of elastase/antielastase. Smoking causes neutrophils to collect in the lungs and these neutrophils contain elastase, an enzyme that degrades elastin, an important component of the extracellular matrix that allows the lungs to recoil. A serum protein called α_1-antitrypsin is made in the liver but is found mainly in the lungs. It inactivates neutrophil elastase. Persons with inherited deficits in α_1-antitrypsin who smoke have a much higher incidence of COPD. This theory has come into question because some persons with deficiency of α_1-antitrypsin who smoke do not develop the disease. Other causative elements include free radicals produced by neutrophils that are activated by cigarette smoke. The free radicals are postulated to oxidize a methionine residue of α_1-antitrypsin, thereby inactivating its inhibitory effects on elastase.

Whatever its cause, destruction of the elastin and collagen fibers of the lung results in the destruction of the alveoli. The air spaces become larger and the surface area of gas exchange becomes much smaller. The reduced recoil tendency no longer holds open the bronchioles and so these tend to collapse, producing the increased airway resistance that characterizes COPD.

Bronchiectasis results in dilated bronchi that easily collapse, causing the obstruction, due to the destruction of their muscle layers and supportive elastic tissue. It is characterized by persistent cough and production of large volumes of yellow or green sputum. Although multiple conditions lead to it, it usually is associated with bacterial infections. Persons with acquired immunodeficiency syndrome (AIDS) are susceptible to opportunistic infections, and AIDS is a leading cause of bronchiectasis. Tuberculosis is another leading cause of acquired bronchiectasis. Congenital causes include cystic fibrosis (which accounts for half of the cases of bronchiectasis in children and young adults) and primary ciliary dyskinesia, in which the cilia in the respiratory epithelium are defective, and the mucus escalator fails. This leads to respiratory infections and predisposes to bronchiectasis. Treatment includes surgery to remove localized bronchiectasis, controlling infections and removing obstruction and bronchial secretions.

Clinical Applications: Positive Pressure Breathing

In normal breathing, the pressures within the alveoli immediately prior to inspiration (at the end of a tidal expiration) and after inspiration (at the end of tidal inspiration) are equal to the atmospheric pressure. Fibrosis decreases the FRC because it is more difficult to expand the lungs, and movement of air is reduced because the work of breathing is greater, even though the pressure differences exceed normal values. This can be helped by increasing the pressure of the incoming air, artificially expanding the lung with air pressure instead of muscle action. This enables the system to operate at higher volumes and restores volume exchange. This is accomplished by ventilators.

Common mechanical ventilators use positive pressure to force air into the lungs, causing inflation of the lungs. The ventilator can be set to introduce a known tidal volume and then stop pushing more air, and allow the natural recoil of the respiratory system to produce expiration. Although expiration is passive, the ventilatory can be altered to allow expiration only when the expiratory pressure within the lungs exceeds a small positive value, the **PEEP** (positive end-expiratory pressure). The purpose of the PEEP is analogous to the actions of pursed-lips breathing: it keeps the airways open. The mechanical ventilator in this case allows the respiratory system to operate at a higher volume, leading to better gas exchange.

Negative-pressure ventilators, such as the iron lung used in the Polio epidemics in the United States during the 1950s, apply negative pressure to the thorax, thereby causing expansion of the lungs. Expiration is accomplished by positive pressure to the thorax.

Persons with obstructive sleep apnea typically have issues with intermittent closure of the airway due to physical obstruction. Commonly, extra tissue in obese persons applies weight to the airways, requiring abnormally high transmural pressures to keep them open. This obstruction occurs while laying down to sleep and produces periods of no breathing—apnea—better known as **sleep apnea**. Other anatomic structures may also obstruct the airways, also causing sleep apnea. Inflating the respiratory system at all points of the breathing cycle physically ensures that such structures no longer obstruct the airways. This requires continuous positive airway pressure (CPAP) that aids breathing by opening airways internally by inflation. CPAP machines are becoming more common and more portable. By wearing a tight-fitting mask while sleeping, patients with sleep apnea can use CPAP to remove or reduce airway obstructions, leading to the reduction of episodes of sleep apnea and reducing snoring is those so afflicted. About 12 million Americans have been diagnosed with sleep apnea but there are likely many more because persons so affected are often asymptomatic.

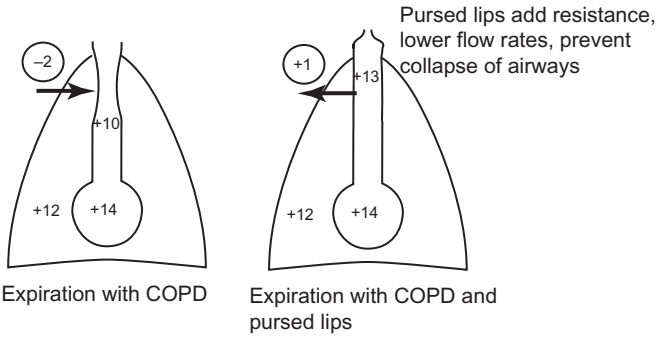

FIGURE 6.2.9 Pursed-lip breathing. For persons with obstructive airway disease, elastic tissue in the lungs is reduced, lowering the pull on the airways and causing them to collapse more easily. Forced expiration, by applying a positive intrapleural pressure rather than the negative one typically produced by lung recoil, causes the airways to collapse. Paradoxically, the airways can be kept open by pursing the lips and transferring the resistance to the lips rather than the airways.

recoil and chest expansion occurs at a higher lung volume. The patient has a difficult time getting air out of the lungs because of the reduced recoil force of the lungs. One way to increase airflow, somewhat counterintuitively, is to increase outflow resistance at the lips. That is, to breathe through pursed lips. This produces an increased resistance at the outflow point of the air, which increases its pressure in the airways, helping to keep the airways open. The patient is instructed to breathe slowly through pursed lips. Effectively, more of the resistance to airflow is transferred from the airways to the lips. This is shown diagrammatically in Figure 6.2.9.

SUMMARY

Spirometry can be used to measure three lung volumes and two capacities: the TV, IRV, ERV, IC and VC. The RV cannot be measured by spirometry and therefore the FRC and TLC also cannot be determined by spirometry. Combinations of these four volumes define the four lung capacities: the inspiratory capacity (IC = IRV + TV), vital capacity (VC = IRV + TV + ERV), the functional residual capacity (FRC = ERV + RV), and the total lung capacity (TLC = IRV + TV + ERV + RV). The lung volumes and capacities vary with body size, age, and sex.

Pulmonary ventilation is the product of the TV and RR. The maximum voluntary ventilation can also be measured using a spirometer. It usually exceeds the maximum ventilation during exercise. Spirometers also can provide a measure of airway resistance from the fraction of the FVC that can be expired in 1, 2, and 3 s.

At low flow rates, laminar or streamline airflow is described by an ohmic relationship between flow and the net pressure difference (ΔP) that drives flow. At high flow rates, the relationship between flow and ΔP is not linear. The presence of turbulence in the airways depends on the velocity of airflow, the diameter of the airways, and the density and viscosity of the air. The velocity of the air and diameter of the airways vary considerably, whereas density and viscosity of the air are nearly constant. Turbulence is likely when the Reynolds number exceeds 2500. The Reynolds number is calculated from

$$Re = \frac{2a\langle V\rangle\rho}{\eta}$$

The diameter of the airways decreases nearly exponentially with generation number, whereas the total cross-sectional area of the airways increases because the number of airways increases with generation number. Because the total cross-sectional area increases so much, the average velocity of airflow decreases with generation number. Thus the airways can be approximated by laminar flow and turbulent flow in series. At low pulmonary ventilation, there is little turbulent flow. At high flow rates, dynamic compression of the airways limits expiratory airflow. Airway resistance is also modified by smooth muscle contraction of smooth muscle surrounding the bronchioles. Parasympathetic stimulation constricts the bronchioles, whereas sympathetic stimulation dilates them.

REVIEW QUESTIONS

1. Draw a spirometer trace and label TV, IRV, ERV, RV, IC, FRC, VC, and TLC. Indicate which cannot be measured by spirometry alone.
2. Describe the procedure for measuring the FVC and indicate what results from the procedure indicate airway resistance.
3. Describe how you could determine pulmonary ventilation and maximum voluntary ventilation.
4. Write the equation for the Reynolds number. Do you think the transition between laminar flow and turbulent flow should be a narrow range of values for the Reynolds number or a fairly broad range?
5. Would you expect turbulent flow in the larger airways or in the smaller ones? Why?
6. What endogenous materials alter airway resistance, and how do they do it?