

SECTION 3 RESPIRATORY DISORDERS

CHAPTER

27

Introduction to Pulmonary Function Testing

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KEY CONCEPTS

- 1 Normal ventilation–perfusion ratio. The function of the lungs is to maintain P_{aO_2} and P_{aCO_2} within normal ranges. This goal is accomplished by matching 1 mL mixed venous blood with 1 mL fresh air ($\dot{V}/\dot{Q} = 1$). Normally, ventilation (\dot{V}) is less than perfusion (\dot{Q}), and \dot{V}/\dot{Q} ratio is 0.8.
- 2 The air in the lung is divided into four compartments: tidal volume—air exhaled during quiet breathing; inspiratory reserve volume—maximal air inhaled above tidal volume; expiratory reserve volume—maximum air exhaled below tidal volume; and residual volume—air remaining in the lung after maximal exhalation. The sum of all four components is the total lung capacity.
- 3 Obstructive lung disease is defined as an inability to get air out of the lung. It is identified on spirometry when FEV_1/FVC (force expiratory volume in the first second of expiration/forced vital capacity [total amount of air that can be exhaled during a forced exhalation]) is $<70\%$ to 75% .
- 4 Reversible airway obstruction is common in asthma and chronic obstructive pulmonary disease. An increase in FEV_1 of 12% (and >0.2 L in adults) after an inhaled β -agonist suggests an acute bronchodilator response.
- 5 Restrictive lung disease is defined as an inability to get air into the lung and is best defined as a reduction in total lung capacity. It is suspected when FVC is low and FEV_1/FVC is normal.
- 6 Restrictive lung disease can be produced by a number of defects, such as increased elastic recoil (interstitial lung disease), respiratory muscle weakness (myasthenia gravis), mechanical restrictions (pleural effusion or kyphoscoliosis), and poor effort.

The primary function of the respiratory system is to maintain normality of arterial blood gases, that is, arterial pressure of oxygen

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(P_{aO_2}) and arterial pressure of carbon dioxide (P_{aCO_2}). To achieve this goal, several processes must be accomplished, including alveolar ventilation, pulmonary perfusion, ventilation–perfusion matching, and gas transfer across the alveolar–capillary membrane. Alveolar ventilation is achieved by the cyclic process of air movement in and out of the lung. During inspiration, the inspiratory muscle contracts and generates negative pressure in the pleural space. This pressure gradient between the mouth and the alveoli draws fresh air (tidal volume) into the lung. Approximately one third of the inspired gas stays in the conducting airways (dead space), and two thirds reaches the alveoli.

- 1 The human lung contains a series of branching, progressively tapering airways that originate at the glottis and terminate in a matrix of thin-walled alveoli. Coursing through this matrix of alveoli is a rich network of capillaries that originates from the pulmonary arterioles and terminates in the pulmonary venules. The adequacy of respiration in each gas exchange unit depends on the opposition of a thin film of mixed venous blood with just the right amount of fresh alveolar gas. During “ideal” gas exchange, blood flow and ventilation are uniform; accordingly, there is no alveolar–arterial difference (or gradient) in the partial pressure of oxygen [$P(A-a)O_2$, sometimes called the $A-a$ gradient]. However, gas exchange is not perfect, even in the normal lung. Normally, alveolar ventilation is less than pulmonary blood flow, and the overall ventilation–perfusion ratio is 0.8 (not 1.0).

Normal expiration is a passive process, and when the inspiratory muscles end their contraction, the elastic recoil of the lung pulls the lung back to its original size and shape. This process makes the alveolar pressure positive relative to the pressure at the mouth, and air flows out of the lung. During inspiration, the respiratory muscles must overcome the elastic properties of the lung (elastic recoil) and the resistance to airflow by the airways. During expiration, the flow of air is determined primarily by the elastic recoil and airway resistance.

Different pulmonary function tests (PFTs) are used to evaluate the physiologic processes of the respiratory system. Physiologic abnormalities that can be measured by pulmonary function testing include obstruction to airflow, restriction of lung size, and decrease in transfer of gas across the alveolar–capillary membrane. Abnormal values on PFTs are outside the range of values obtained from a group of normal individuals matched according to age, height, sex, and race. A PFT is labeled abnormal when the results fall outside the range in which 95% of people the same age, height, and sex would be found (95% confidence interval). This definition is arbitrary and

may misclassify a small percentage of normal individuals as having lung dysfunction; it also may miss patients with mild pulmonary disease. Therefore, clinical correlation and serial pulmonary function testing may be necessary for optimal interpretation of PFTs.

Potential uses of pulmonary function testing include evaluation of patients with known or suspected lung disease; evaluation of symptoms such as chronic cough, dyspnea, or chest tightness; monitoring of the effects of exposure to dust, chemicals, or pulmonary toxic drugs; risk stratification prior to surgery; monitoring of the effectiveness of therapeutic interventions; and objective assessment of impairment or disability.¹

DEFINITIONS OF LUNG VOLUMES AND EXPIRATORY FLOWS

② The air within the lung at the end of a forced inspiration can be divided into four compartments or lung volumes (Fig. 27-1). The volume of air exhaled during normal quiet breathing is the *tidal volume* (VT). The maximal volume of air inhaled above tidal volume is the *inspiratory reserve volume* (IRV), and the maximal air exhaled below tidal volume is the *expiratory reserve volume* (ERV). The *residual volume* (RV) is the amount of air remaining in the lungs after a maximal exhalation.

The combinations or sums of two or more lung volumes are termed *capacities* (Fig. 27-1). *Vital capacity* (VC) is the maximal amount of air that can be exhaled after a maximal inspiration. It is equal to the sum of IRV, VT, and ERV. When measured on a forced expiration, it is called the *forced vital capacity* (FVC). When measured over an exhalation of at least 30 seconds, it is called the *slow vital capacity* (SVC). The VC is approximately 75% of the *total lung capacity* (TLC), and when the SVC is within the normal range, a significant restrictive disorder is unlikely. Normally, the values for SVC and FVC are very similar unless airway obstruction is present.

TLC is the volume of air in the lung after the maximal inspiration and is the sum of the four primary lung volumes (IRV, VT, ERV, and RV). Its measurement is difficult because the amount of air remaining in the chest after maximal exhalation (RV) must be measured by indirect methods. The definition of restrictive lung disease is based on a reduction in TLC (i.e., an inability to get air into the lung or restriction to air movement on inhalation).

The *functional residual capacity* (FRC) is the volume of air remaining in the lungs at the end of a quiet expiration. FRC is the normal resting position of the lung; it occurs when there is no contraction of either

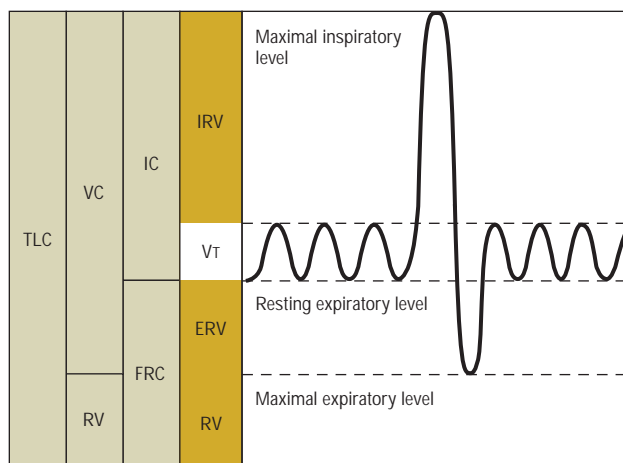


FIGURE 27-1. Lung volumes and capacities. (ERV, expiratory reserve volume; FRC, functional residual capacity; IC, inspiratory capacity; IRV, inspiratory reserve volume; RV, residual volume; TLC, total lung capacity; VC, vital capacity; VT, tidal volume.)

inspiratory or expiratory muscles and normally is 40% of TLC. *Inspiratory capacity* (IC) is the maximal volume of air that can be inhaled from the end of a quiet expiration and is the sum of VT and IRV.

FVC, which represents the total amount of air that can be exhaled, can be expressed as a series of timed volumes. The *forced expiratory volume in the first second of expiration* (FEV₁) is the volume of air exhaled during the first second of the FVC maneuver. Although FEV₁ is a volume, it conveys information on obstruction because it is measured over a known time interval. FEV₁ depends on the volume of air within the lung and the effort during exhalation; therefore, it can be diminished by a decrease in TLC or by a lack of effort. A more sensitive way to measure obstruction is to express FEV₁ as a ratio of FVC. This ratio is independent of the patient's size or TLC; therefore, FEV₁/FVC is a specific measure of airway obstruction with or without restriction. Normally, this ratio is ≥75%, and any value <70% to 75% suggests obstruction.

Because *flow* is defined as the change in volume with time, forced expiratory flow can be determined graphically by dividing the volume change by the time change. The *forced expiratory flow* (FEF) during 25% to 75% of FVC (FEF_{25%-75%}) represents the mean flow during the middle half of the FVC. FEF_{25%-75%}, formerly called the *maximal midexpiratory flow*, is reported frequently in the assessment of small airways. The 95% confidence limit is so wide that FEF_{25%-75%} has limited utility in the early diagnosis of small airways disease in an individual subject. The *peak expiratory flow* (PEF), also called *maximum forced expiratory flow* (FEF_{max}), is the maximum flow obtained during FVC. This measurement is used often in the outpatient management of asthma because it can be measured with inexpensive peak flowmeters.

All lung volumes and flows are compared to normal values obtained from healthy subjects. There are significant ethnic and racial variations in normal values, and all PFTs should report that race/ethnic adjustment factors have been used. The 2005 American Thoracic Society–European Respiratory Society (ATS–ERS) guidelines for interpretation of PFT results recommend that, for spirometry in the United States, the National Health and Nutrition Examination Survey (NHANES) III reference be used for subjects aged 8 to 80 years and the Wang equation used in subjects younger than 8 years.²

SPIROMETRY/FLOW–VOLUME LOOP

Spirometry is the most widely available and useful PFT. It takes only 15 to 20 minutes, carries no risks, and provides information about obstructive and restrictive disease. Spirometry allows for measurement of all lung volumes and capacities except RV, FRC, and TLC; it also allows assessment of FEV₁ and FEF_{25%-75%}. Spirometry measurements can be reported in two different formats—standard spirometry (Fig. 27-2) and the flow–volume loop (Fig. 27-3). In standard

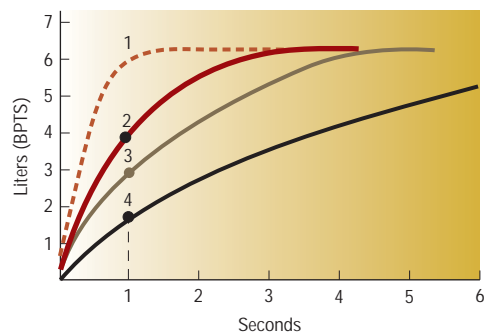


FIGURE 27-2. Standard spirometry. Curve 1 is for a normal subject with normal FEV₁; curve 2 is for a patient with mild airways obstruction; curve 3 is for a patient with moderate airways obstruction; curve 4 is for a patient with severe airways obstruction. (BPTS, body temperature saturated with water vapor.)

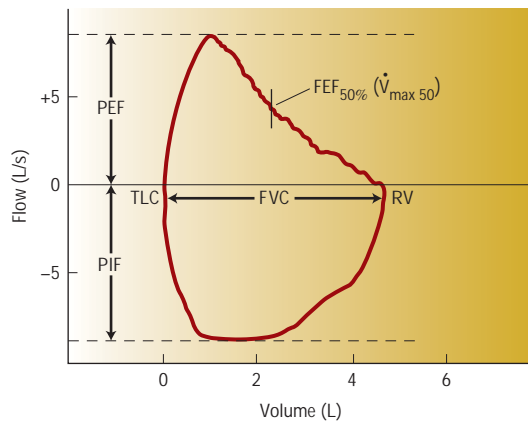


FIGURE 27-3. Normal flow–volume loop. Flows are measured on the vertical (y) axis, and lung volumes are measured on the horizontal (x) axis. Forced vital capacity (FVC) can be read from the tracing as the maximal horizontal deflection. Instantaneous flow (\dot{V}_{max}) at any point in FVC also can be measured directly. ($FEF_{50\%}$, forced expiratory flow at 50% of forced vital capacity; PEF, peak expiratory flow; PIF, peak inspiratory flow; RV, residual volume; TLC, total lung capacity.)

spirometry, the volumes are recorded on the vertical (y) axis and the time on the horizontal (x) axis. In flow–volume loops, volume is plotted on the horizontal (x) axis, and flow (derived from volume/time) is plotted on the vertical (y) axis. The shape of the flow–volume loop can be helpful in differentiating obstructive and restrictive defects and in diagnosing upper airway obstruction (Fig. 27-4). This curve gives a visual representation of obstruction because the expiratory descent becomes more concave with worsening obstruction.

LUNG VOLUMES

Spirometry measures three of the four basic lung volumes but cannot measure RV. RV must be measured to determine TLC. TLC should be measured anytime VC is reduced. In the setting of chronic obstructive pulmonary disease (COPD) and a low VC, measurement of TLC can help to determine the presence of a superimposed restrictive disorder. The four methods for measuring TLC are helium dilution, nitrogen washout, body plethysmography, and chest x-ray

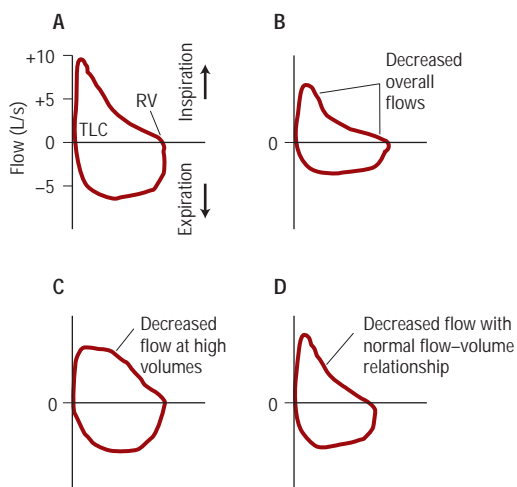


FIGURE 27-4. A. Flow–volume loop depicting mild obstruction characterized by decrease flow at low lung volumes. B. Moderate airflow obstruction characterized by a more concave curve. C. Variable intrathoracic obstruction in which peak flow is decreased at higher lung volumes with normalization of curve at lower lung volumes. D. Restrictive lung disease with a curve that is decreased in width but with a normal shape. (RV, residual volume; TLC, total lung capacity.)

measurement (planimetry). The first two methods are called *dilution techniques* and only measure lung volumes in communication with the upper airway. In patients with airway obstruction who have trapped air, dilution techniques will underestimate the actual volume of the lungs. Planimetry measures the circumference of the lungs on the posteroanterior view and lateral views of a chest x-ray film and estimates the total lung volume.

Body plethysmography, or body box, is the most accurate technique for lung volume determinations. It measures all the air in the lungs, including trapped air. The principle of the measurement of the body box is Boyle's gas law ($P_1V_1 = P_2V_2$): A volume of gas in a closed system varies inversely with the pressure applied to it. The changes in alveolar pressure are measured at the mouth, as well as pressure changes in the body box. The volume of the body box is known. Lung volumes can be determined measuring the changes in pressures caused by panting against a closed shutter.² Measurement of lung volumes provides useful information about elastic recoil of the lungs. If elastic recoil is increased (as in interstitial lung disease), lung volumes (TLC) are reduced. When elastic recoil is reduced (as in emphysema), lung volumes are increased.

CARBON MONOXIDE DIFFUSING CAPACITY

The diffusing capacity of the lungs (DL) is a measurement of the ability of a gas to diffuse across the alveolar–capillary membrane. Carbon monoxide is the usual test gas because normally it is not present in the lungs and is much more soluble in blood than in lung tissue. When the diffusing capacity is determined with carbon monoxide, the test is called the *diffusing capacity of lung for carbon monoxide* (DLCO). Because DLCO is directly related to alveolar volume (V_A), it frequently is normalized to the value DL/V_A , which allows for its interpretation in the presence of abnormal lung volumes (e.g., after surgical lung resection).

The diffusing capacity will be reduced in all clinical situations where gas transfer from the alveoli to capillary blood is impaired.³ Common conditions that reduce DLCO include lung resection, emphysema (loss of functioning alveolar–capillary units), and interstitial lung disease (thickening of the alveolar–capillary membrane). Normal PFTs with reduced DLCO should suggest the possibility of pulmonary vascular disease (e.g., pulmonary embolus) but also can be seen with anemia, early interstitial lung disease, and mild *Pneumocystis carinii* pneumonia (PCP) infection in patients with acquired immune deficiency syndrome.

OBSTRUCTIVE LUNG DISEASE

3 Obstructive lung disease implies a reduced capacity to get air through the conducting airways and out of the lungs. This reduction in airflow may be caused by a decrease in the diameter of the airways (bronchospasm), a loss of their integrity (bronchomalacia), or a reduction in elastic recoil (emphysema) with a resulting decrease in driving pressure. The most common diseases associated with obstructive pulmonary functions are asthma, emphysema, and chronic bronchitis; however, bronchiectasis, infiltration of the bronchial wall by tumor or granuloma, aspiration of a foreign body, and bronchiolitis also cause obstructive PFTs. The standard test used to evaluate airway obstruction is the forced expiratory spirogram.

Standard spirometry and flow–volume loop measurements include many variables; however, according to ATS guidelines, the diagnosis of obstructive and restrictive ventilatory defects should be made using the basic measurements of spirometry.³ A reduction in FEV_1 (with normal FVC) establishes the diagnosis of obstruction. When both FEV_1 and FVC are reduced, FEV_1 cannot be used to assess airway obstruction because such patients may have either obstruction or restriction. In restrictive lung disease, the patient has

an inability to get air into the lung, which results in a reduction of all expiratory volumes (FEV_1 , FVC, and SVC). In obstructed patients, a better measurement is the ratio FEV_1/FVC . Patients with restrictive lung disease have reduced FEV_1 and use of reduced FVC, but FEV_1/FVC remains normal. Although a normal FEV_1/FVC ratio is $>70\%$ to 75% , the ratio is age dependent, and slightly lower values may be normal in older patients. Younger children have increased lung elastic recoil and may have higher ratios. Children with asthma often have $FEV_1/FVC >90\%$ despite obstructive lung disease. In children, the improvement in FEV_1 after an inhaled bronchodilator often is the only way to document mild-to-moderate obstructive lung disease. Caution should be used in interpreting obstruction when FEV_1/FVC is below normal, but FEV_1 and FVC both are within the normal range because this pattern can be seen with healthy, athletic subjects. In screening spirometry performed in office practice, FEV_6 (forced expiratory volume in 6 seconds) can be used in place of FVC. FEV_6 is a more reproducible number when obtained by less skilled personnel. The measurement of $FEF_{25\%-75\%}$ also is abnormal in patients with obstructive airways disease. In general, this test has so much variability that it adds little to the measurement of FEV_1 and FEV_1/FVC . $FEF_{25\%-75\%}$ has been of value in monitoring lung transplant patients for graft rejection,⁴ and a reduced value may be an early indicator of acute rejection.

Although there is no standardization for interpretation of severity of obstruction, most pulmonary laboratories state that $FEV_1/FVC <70\%$ of the predicted value is diagnostic for obstruction, and the degree of obstruction then is based on the percent predicted of FEV_1 . $FEV_1 <60\%$ of the predicted value is moderate obstruction, and $<40\%$ of the predicted value is severe obstruction. In patients with obstruction, a dose of a bronchodilator (e.g., albuterol or isoproterenol) by metered-dose inhaler is given during the initial examination. An increase in FEV_1 of $>12\%$ and >0.2 L suggests an acute bronchodilator response.³ Because bronchodilator responsiveness is variable over time, the lack of an acute bronchodilator response should not preclude a 6- to 8-week trial of bronchodilators and/or corticosteroids.

Although all patients with obstructive lung disease of any etiology will have reduced flow rates on forced exhalation, the pattern on PFTs may be helpful in differentiating among the various etiologies (Table 27-1). Asthma is characterized by variable obstruction that often improves or resolves with appropriate therapy. Because asthma is an inflammatory disorder of the airways (predominantly large airways), DLCO is normal. Most patients with acute asthma have a bronchodilator response $>15\%$ to 20% ; however, this response is also seen in 20% of patients with COPD. These patients are said to have asthmatic bronchitis. Chronic bronchitis may be limited to the airways, but the vast majority of patients with chronic bronchitis and airway obstruction have a mixture of bronchitis and emphysema and have a reduction in DLCO. Therefore, DLCO is the best PFT for separating asthma from COPD.

TABLE 27-1 Specific Patterns of Pulmonary Function in Patients with Chronic Obstructive Pulmonary Disease

	COPD		
	Asthma	Chronic Bronchitis	Emphysema
Decreased FEV_1	++++	++++	++++
Decreased FEV_1/FVC	++++	++++	++++
Increased airway resistance	++++	++++	+
Decreased DLCO	—	-/++ ^a	++++
Response to bronchodilators	++++	+ ^b	- ^b

DLCO, diffusing capacity of carbon monoxide; FEV_1 , forced expiratory volume in the first second of expiration; FVC, forced vital capacity.

^aMost smokers with chronic bronchitis have reduced D_{LCO} .

^bTwenty percent of patients with chronic obstructive pulmonary disease (COPD) have a large (++++)
bronchodilator response.

After the diagnosis of obstructive airways disease is established, the course and response to therapy are best followed by serial spirometry. The multicenter Lung Health Study demonstrated an abnormally rapid decline (90 – 150 mL/y) in patients with COPD who continue to smoke.⁵ Smoking cessation often resulted in an increase in FEV_1 during the first year and a near-normal rate of decline (30 – 50 mL/y) in subsequent years.

AIRWAY HYPERREACTIVITY

4 *Airway hyperreactivity* or *hyperresponsiveness* is defined as an exaggerated bronchoconstrictor response to physical, chemical, or pharmacologic stimuli. Individuals with asthma, by definition, have hyperresponsive airways. The Lung Health Study Group observed nonspecific hyperresponsiveness in a significant number of patients with COPD. This group of patients with airway hyperreactivity appears to have a worse prognosis and an accelerated rate of decline in FEV_1 .⁶

Some patients with asthma (especially cough-variant asthma) present with no history of wheezing and normal PFTs. The diagnosis of asthma still can be established by demonstrating hyperresponsiveness to provocative agents. The two agents used most widely in clinical practice are methacholine and histamine. Other agents used for bronchial provocation include distilled water, cold air, and exercise. During a typical bronchoprovocation test, baseline FEV_1 is measured after inhalation of isotonic saline, then increasing doses of methacholine are given at set intervals. Hyperresponsiveness is defined as a decline in $FEV_1 \geq 20\%$ and reversibility of obstruction to bronchodilators. The result can best be expressed as the provocative concentration needed to cause a 20% fall in FEV_1 (PC_{20}). A test is considered positive if either methacholine or histamine demonstrates a PC_{20} for $FEV_1 \leq 8$ mg/mL or <60 to 80 cumulative breath units.⁷ This test is used most frequently to establish a diagnosis of asthma in patients with normal PFTs, but it also may be useful in following patients with occupational asthma, establishing the severity of asthma, and assessing the response to treatment.

UPPER AIRWAY OBSTRUCTION

Obstruction of airflow by abnormalities in the upper airway often goes undiagnosed or misdiagnosed because of improper interpretation of PFTs. Patients have obstructive physiology and often are misclassified as having asthma or COPD. The shape of the flow-volume loop, which includes inspiratory and expiratory flow-volume curves, and the ratio of forced expiratory and inspiratory flow at 50% of vital capacity ($FEF_{50\%}/FIF_{50\%}$) may be useful in the diagnosis of upper airway obstruction.⁸

The shape of the flow-volume curve differs depending on whether the obstruction is fixed or variable (Fig. 27-5). Fixed lesions, as in strictures from previous intubations or tracheostomy, cause a uniform caliber of airway during inspiration and expiration. With variable lesions, the airway caliber changes with changes in intrathoracic pressure. Variable lesions are subclassified into variable intrathoracic and variable extrathoracic. If the lesion is intrathoracic, as with tumors of the trachea, the negative pressure generated during inspiration opens the obstruction, whereas the positive pressure during expiration worsens the obstruction. If the lesion is a variable extrathoracic obstruction, as with vocal cord dysfunction, the negative pressure within the airways will pull the vocal cord toward the midline and potentiate the obstruction. In this case, there will be a plateau on the inspiratory limb of the flow-volume loop, and $FEF_{50\%}/FIF_{50\%}$ will be >1 . Typical flow-volume curves from upper airway obstruction are shown in Fig. 27-4.

Another test used to distinguish upper airway obstruction from COPD and asthma is $FEV_1/FEV_{0.5}$ (FEV at 0.5 second). This ratio

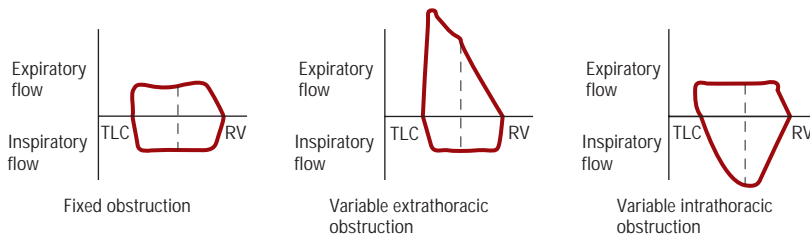


FIGURE 27-5. Maximum expiratory flow–volume curves from patients with fixed obstruction, variable extrathoracic obstruction, and variable intrathoracic obstruction. (RV, residual volume; TLC, total lung capacity.)

usually is >1.5 in patients with upper airway obstruction.⁹ This is so because $FEV_{0.5}$ is proportionately more reduced in upper airway obstruction because forced expiration measured at 0.5 second better reflects obstruction at high lung volumes. The abnormality seen on the flow–volume loop has been referred to as “straightening” of the curve during early expiration.

RESTRICTIVE LUNG DISEASE

5 *Restrictive lung disease* is defined as an inability to get air into the lungs and to maintain normal lung volumes. Restrictive lung disease reduces all the subdivisions of lung volumes (IRV, VT, ERV, and RV) without reducing airflow. Patients have normal airway resistance and $FEV_1/FVC >75\%$.

Although *restriction* could be defined as a reduction in vital capacity (VC or FVC) with normal FEV_1/FVC , poor effort also will reduce FVC with normal FEV_1/FVC . A reduction in TLC is the most accurate measurement of restrictive lung function. TLC can be measured by various techniques. The gas dilution methods (e.g., helium dilution and nitrogen washout) are unable to measure gas trapped in cysts or bullae and may underestimate the true lung volume. Therefore, TLC is best measured by plethysmography. Most restrictive lung disease is associated with impairment or destruction of the alveolar–capillary membrane; therefore, DLCO is reduced in most patients with restrictive lung disease. The reduction in DLCO may occur prior to a reduction in lung volumes and is used as a marker of early interstitial (restrictive) lung disease. DLCO may be abnormal even with a normal chest x-ray film, and thin-cut computed tomographic scans of the chest may be required to diagnose early interstitial lung disease.

TABLE 27-2 Causes of Restrictive Lung Disease

Interstitial lung diseases
Idiopathic pulmonary fibrosis
Sarcoidosis
Collagen vascular disease
Pneumoconiosis
Drug-induced lung disease
Pulmonary edema
Infiltrative lung diseases
Granulomatosis
Tumor
Pleural diseases
Pleural effusion
Fibrothorax
Pneumothorax
Chest wall diseases
Kyphoscoliosis
Ankylosing spondylitis
Neuromuscular disease
Miscellaneous causes
Obesity
Pregnancy
Ascites
Paralyzed diaphragm
Lung resection

Because peribronchiolar inflammation and fibrosis occur in patients with restrictive parenchymal lung disease, $FEF_{25\text{--}75\%}$ may be reduced and fail to respond to bronchodilators.

The severity of restrictive disease has not been standardized; however, many laboratories classify patients with reduced TLC as mild (TLC $\leq 80\%$), moderate (TLC $\leq 65\%$), or severe (TLC $\leq 50\%$). These definitions are completely arbitrary because a patient with obstructive lung disease may start with TLC 120% and subsequently develop a moderately severe restrictive lung disease while maintaining TLC within the normal range. On flow–volume loop, patients with restrictive disease have normal-shaped curves with a reduction in the height and width of the curve because peak expiratory flow rate and VC both depend on the amount of air within the lung prior to performance of expiratory maneuvers (Fig. 27–3).

6 Restrictive lung function can be produced by increased elastic recoil of the lung parenchyma (interstitial lung disease), respiratory muscle weakness, mechanical restrictions (chest wall deformities), and/or poor effort. Table 27–2 lists common causes of restrictive lung disease.

Restrictive lung function from parenchymal lung disease usually can be differentiated from processes causing mechanical restriction as a result of chest bellows malfunction (Table 27–3). Restrictive parenchymal diseases are associated with a reduction in alveolar volume and an increase in lung elastic recoil. All lung volumes, as well as DLCO, are reduced. RV/TLC (normal $\leq 30\%$) and measurements of maximal inspiratory pressure (normal = -75 cm H₂O in males, -50 cm H₂O in females) remain normal. In addition, patients exhibit mild resting hypoxemia that worsens with exercise. Monitoring gas exchange during exercise may be the most sensitive test for detecting progression of interstitial lung disease.¹⁰

Mechanical restriction caused by chest bellows malfunction may result from chest wall or skeletal deformity, loss of neuromuscular function, fibrosis of the pleural space, and abdominal overdistension causing upward displacement of the diaphragm, as well as decreased diaphragm movement. The most common pulmonary function pattern seen in these patients is a decrease in TLC and VC with only a slight decrease in RV. RV is maintained in these diseases because lung compliance remains normal. DLCO is normal or only minimally reduced, and DLCO/VA (corrected for alveolar volume) is normal. RV/TLC often is increased in patients with restrictive chest bellows disease.

TABLE 27-3 Patterns of Pulmonary Function

	Obstructive Lung Disease		Restrictive Lung Disease	
	Asthma	COPD	Parenchymal Disease	Chest Bellows Disease
FVC	NI or I	NI or I	D	D
FEV ₁	D	D	D	D
FEV ₁ /FVC	$<75\%$	$<75\%$	$\geq 75\%$	$\geq 75\%$
TLC	NI or I	NI or I	D	D
RV/TLC	NI or I	NI or I	NI	I
Airway resistance	I	I	NI	NI
DLCO	NI	D	D	NI

D, decreased; I, increased; NI, normal.

Patients with neuromuscular disease have reduced respiratory muscle function with a reduction in maximal inspiratory pressure.

PULMONARY GAS EXCHANGE

The essential function of the lungs is to maintain blood gas homeostasis. Arterial blood gas measurement plays an important role in the diagnosis and management of patients with pulmonary disease and should be ordered whenever hypoxemia, hypercapnia (CO_2 retention), and/or acid–base disorders are suspected clinically. Every time arterial blood gas determinations are ordered, the A–a gradient (difference between partial pressure of oxygen in the alveolus and partial pressure of oxygen in arterial blood) should be calculated. This is accomplished by computer on all automated blood gas machines, and a normal $P(A-a)\text{O}_2$ can be approximated for sea-level breathing room air by multiplying the age by 0.3. The presence of hypoxemia with a normal A–a gradient usually implies alveolar hypoventilation (e.g., sedative overdose). Most patients develop hypoxemia secondary to mismatching of ventilation and perfusion, and $P(A-a)\text{O}_2$ will be significantly elevated.

Oxygen saturation as measured by pulse oximetry (SpO_2) is widely used in clinical practice for monitoring arterial saturation. A pulse oximeter is a small battery-operated device that is placed on the finger or the earlobe. The device emits and reads the reflected light from capillary blood, and estimates the saturation. Although SpO_2 is clinically very useful, SpO_2 is only an estimate of arterial saturation. Actual arterial oxygen saturation (SaO_2) can be $\pm 2\%$ to 4% of the oximetric reading. The error may be even greater with saturation $<88\%$. Pulse oximeters do not measure carboxyhemoglobin, and SpO_2 may be overestimated significantly in patients with smoke inhalation or in recent smokers. An initial validation of pulse oximetry with direct measurement of SaO_2 is recommended in any critically ill patient.

EXERCISE TESTING

Cardiopulmonary exercise testing allows for assessment of multiple organs involved in exercise and has benefits over assessment of either the cardiac system or pulmonary system alone. The major indications for exercise testing are dyspnea on exertion, evaluation of exercise-induced bronchospasm, and suspected arterial desaturation during exercise.^{11–14} Exercise testing also can be useful in the evaluation of ventilatory or cardiovascular limitations to work, assessment of general fitness or conditioning, evaluation of disability, establishment of safe levels for exercise, evaluation of drug therapy, determining the need and liter flow for supplemental oxygen therapy during exercise, assessment of the effects of a rehabilitation program, and preoperative assessment before lung resection.^{11–14}

Tests for general fitness include the 6-minute walking distance and the Harvard step test.^{11,13–15} For the 6-minute walking distance, the subject simply walks a predetermined route or circuit as fast as possible for 6 minutes. The subject is allowed to stop and rest, but the clock continues to run. The greater the distance covered, the better are the patient's general fitness and exercise tolerance. For the Harvard step test, the subject steps up and down on a 20-inch step at a set rate for 5 minutes. A 1-minute rest period is followed by measurement of the subject's recovery heart rate. The lower the recovery heart rate, the better is the subject's general fitness.

Exercise testing sometimes is performed to determine if exercise results in arterial oxygen desaturation ($\text{SaO}_2 <90\%$).^{12,13} The test may be useful for quantifying the level of exertion the patient can perform during the activities of daily living as well as determining appropriate levels of supplemental oxygen therapy. Typically, this test is done using a treadmill or cycle ergometer. A baseline measurement of arterial blood gas values or pulse oximetry is followed by up to 6

minutes of exercise, during which time the patient is monitored for oxygen desaturation using pulse oximetry. If significant desaturation occurs (saturation $\leq 88\%$ – 90%), the test is terminated. In the event of oxygen desaturation, the test can be repeated to determine the level of supplemental oxygen therapy needed to compensate for the desaturation that otherwise would occur.

When more formal exercise testing is needed for some of the indications previously listed (e.g., dyspnea evaluation, evaluation of ventilatory or cardiovascular limitations to work, evaluation of disability and preoperative assessment before lung resection), exercise tolerance tests or cardiopulmonary stress testing can be performed. Tests include measurement of oxygen consumption ($\dot{V}\text{O}_2$), carbon dioxide production ($\dot{V}\text{CO}_2$), minute volume ($\dot{V}\text{E}$), VT, respiratory rate, SpO_2 , heart rate, blood pressure, and recording or monitoring of the electrocardiogram. During exercise, $\dot{V}\text{O}_2$ increases with workload in a linear fashion until a maximum oxygen consumption level ($\dot{V}\text{O}_{2\text{max}}$) is reached. Consequently, $\dot{V}\text{O}_{2\text{max}}$ is a measure of an individual's muscular work capacity.^{11–13} Normal $\dot{V}\text{O}_{2\text{max}}$ is approximately 1,700 mL/min for a sedentary person and up to 5,800 mL/min for a trained athlete.¹³ This compares with a resting $\dot{V}\text{O}_2$ of approximately 250 mL/min. Ventilatory equivalents for oxygen, carbon dioxide, and O_2 pulse are often calculated. Ventilatory equivalent for oxygen is a measure of the efficiency of the ventilatory pump at various workloads^{11,13, 14} and is calculated as follows:

$$\text{Ventilatory equivalent for } \text{O}_2 = \dot{V}\text{E}/\dot{V}\text{O}_2.$$

A normal ventilatory equivalent for oxygen is 20 to 30.^{11,13}

TABLE 27-4 Indications and Contraindications for Exercise Testing

Indications

- Dyspnea upon exertion
- Exercise-induced bronchospasm
- Suspected arterial desaturation with exercise
- Evaluation of ventilatory limitations to exercise
- Evaluation of cardiac limitations to exercise
- Assessment of general fitness or conditioning
- Evaluation of cardiopulmonary disability
- Establishment of safe levels for exercise
- Evaluation of drug therapy
- Determining appropriate use of supplemental oxygen therapy
- Establishing an exercise prescription for a rehabilitation program
- Assessment of the effect of a rehabilitation program
- Evaluation of specific disease states or conditions (e.g., asthma, chronic obstructive pulmonary disease [COPD], interstitial lung disease, pulmonary vascular disorders, coronary artery disease, other vascular disorders, neuromuscular disorders, obesity, anxiety-induced hyperventilation)
- Assessment before resection
- Assessment before lung volume reduction surgery or lung transplantation

Contraindications

- $\text{PaO}_2 <40$ mm Hg on room air
- $\text{PaCO}_2 >70$ mm Hg
- $\text{FEV}_1 <30\%$ of predicted
- Recent (within 4 weeks) myocardial infarction
- Unstable angina pectoris
- Second- or third-degree heart block
- Rapid ventricular/atrial arrhythmias
- Orthopedic impairment
- Severe aortic stenosis
- Congestive heart failure
- Uncontrolled hypertension
- Limiting neurologic disorders
- Dissecting/ventricular aneurysms
- Severe pulmonary hypertension
- Thrombophlebitis or intracardiac thrombi
- Recent systemic or pulmonary embolus
- Acute pericarditis

TABLE 27-5 Typical Findings during Maximum Exercise with Poor Conditioning, Pulmonary Limitations to Exercise, and Cardiac Limitations to Exercise

Test Parameter	Poor Conditioning	Pulmonary Limitation	Cardiac Limitation
$\dot{V}O_{2\max}$	↓	↓	↓
SpO ₂	N	↓	N
O ₂ pulse	N or ↓	N or ↓	↓
Anaerobic threshold	↓ or N	↓ or N	↓
Ventilatory reserve ^a (MVV – VEmax)	N	↓	N or ↑

^aVentilatory reserve = Maximum voluntary ventilation (MVV) – Minute volume during maximum exercise (VEmax).

N, normal.

Adapted from Madama VE. *Pulmonary Function Testing and Cardiopulmonary Stress Testing*. Albany, NY: Delmar, 1993.

O₂ pulse is an estimate of oxygen consumption per cardiac cycle and can be decreased with cardiac problems. O₂ pulse can be calculated as follows:

$$O_2 \text{ pulse} = (\dot{V}O_2 [\text{in L/min}] \times 1,000) / \text{Heart rate.}$$

A normal O₂ pulse is 2.5 to 4.0 mL per beat at rest and increases to 10 to 15 mL per beat during strenuous exercise.^{11,13}

The anaerobic threshold is the point during strenuous exercise at which anaerobic metabolism and lactic acid production begin.^{11,13–14} $\dot{V}CO_{2\max}$ increases with exercise at about the same rate as $\dot{V}O_2$ until the subject's anaerobic threshold is reached. From that point on, $\dot{V}CO_2$ increases faster than $\dot{V}O_2$, and this change can be used to estimate the anaerobic threshold. A breath-by-breath plot of the ventilatory equivalents for O₂ and CO₂ also can be used to determine the anaerobic threshold. Anaerobic threshold is a measure of fitness in normal subjects, and aerobic training can delay the anaerobic threshold.^{11,13}

For exercise tolerance testing, the patient typically is subjected to either a constant workload (steady-state tests) or an increasing workload (progressive multistage tests) using a cycle ergometer or treadmill.^{11,13} With progressive multistage tests, the patient exercises to exhaustion or the occurrence of an adverse reaction, at which point the test is stopped. Safety during exercise testing is of major importance, and rigorous guidelines for termination of the test should be followed. Both types of tests can be used to determine $\dot{V}O_{2\max}$. A limit to exercise, as indicated by a decrease in $\dot{V}O_{2\max}$, can result from (1) poor conditioning, (2) pulmonary limitation, (3) cardiac limitation, or (4) poor effort. In the case of poor conditioning, SpO₂ and O₂ pulse will be normal. With a pulmonary limitation to exercise, SpO₂ will be reduced, and O₂ pulse will be normal. With a cardiac limitation to exercise, SpO₂ will be normal, and O₂ pulse will be reduced. Table 27-4 summarizes the indications and contraindications for exercise testing. Table 27-5 summarizes the findings during maximum exercise associated with poor conditioning, pulmonary limitations to exercise, and cardiac limitations to exercise.

ABBREVIATIONS

COPD: chronic obstructive pulmonary disease

DL: diffusing capacity of lung

DLCO: diffusing capacity of lung for carbon monoxide

ERV: expiratory reserve volume

FEF: forced expiratory flow

FEF_{25%–75%}: forced expiratory flow during 25% to 75% of forced vital capacity

FEF_{50%}: forced expiratory flow at 50% of forced vital capacity

FEFmax: maximum forced expiratory flow

FEV_{0.5}: forced expiratory volume at 0.5 second

FEV₁: forced expiratory volume in first second of expiration

FEV₆: forced expiratory volume in 6 seconds

FIF_{50%}: forced inspiratory flow at 50% of forced vital capacity

FRC: functional residual capacity

FVC: forced vital capacity

IC: inspiratory capacity

IRV: inspiratory reserve volume

P₁V₁ = P₂V₂: Boyle's gas law

P(A–a)O₂: alveolar–arterial difference in partial pressure of oxygen

PaCO₂: arterial partial pressure of carbon dioxide

PaO₂: arterial partial pressure of oxygen

PC₂₀: provocative concentration needed to cause a 20% fall in FEV₁

PCP: *Pneumocystis carinii* pneumonia

PFT: pulmonary function test

PO₂: partial pressure of oxygen

RV: residual volume

SaO₂: arterial oxygen saturation

SpO₂: oxygen saturation as measured by pulse oximetry

SVC: slow vital capacity

TLC: total lung capacity

VA: alveolar volume

VC: vital capacity

VT: tidal volume

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