03 - 296 Disturbances of Respiratory Function

296 Disturbances of Respiratory Function

lung volumes, and a low DLCO should prompt further evaluation for pulmonary vascular disease. Arterial blood gas testing is often helpful in assessing respiratory disease. Hypoxemia, while usually apparent with pulse oximetry, can be further evaluated with the measurement of arterial PO2 and the cal culation of an alveolar gas and arterial blood oxygen tension difference ([A–a]DO2). Patients with diseases that cause ventilation-perfusion mismatch or shunt physiology have an increased (A–a)DO2 at rest. Arterial blood gas testing also allows the measurement of arterial PCO2. Hypercarbia can accompany disorders of ventilation, as seen in severe airway obstruction (e.g., COPD) or progressive restrictive physiology. Chest Imaging (See Chap. A12) Most patients with disease of the respiratory system undergo imaging of the chest as part of the initial evaluation. Clinicians should generally begin with ultrasound of the chest or a plain chest radiograph, preferably posterior-anterior and lateral films. Ultrasound is often readily available and can help rapidly diagnose pneumothorax, pleural effusion, and consolidation of lung parenchyma. Chest radiographs give additional detail and can reveal findings including opacities of the parenchyma, blunting of the costophrenic angles, mass lesions, and volume loss. Of note, many diseases of the respiratory system, particularly those of the airways and pulmonary vasculature, are associated with a normal chest radiograph. Computed tomography (CT) scan of the chest can also be useful to delineate parenchymal processes, pleural disease, masses or nodules, and large airways. If the test includes administration of intravenous contrast, the pulmonary vasculature can be assessed with particular utility for determination of pulmonary emboli. Intravenous contrast also allows lymph nodes to be examined in greater detail. When coupled with positron emission tomography (PET), lesions of the chest can be assessed for metabolic activity, helping differentiate between malignancy and scar. ■ ■FURTHER STUDIES Depending on the clinician’s suspicion, a variety of other studies may be done. Concern about large-airway lesions may warrant bronchos copy. This procedure may also be used to sample the alveolar space with bronchoalveolar lavage or to obtain nonsurgical lung biopsies. Blood testing may include assessment for hypercoagulable states in the setting of pulmonary vascular disease, serologic testing for infectious or rheumatologic disease, or assessment of inflammatory markers or leukocyte counts (e.g., eosinophils). Genetic testing is increasingly used for heritable lung diseases such as cystic fibrosis. Sputum evalu ation for malignant cells or microorganisms may be appropriate. An echocardiogram to assess right- and left-sided heart function is often obtained. Finally, at times, a surgical lung biopsy is needed to diagnose certain diseases of the respiratory system. All of these studies will be guided by the preceding history, physical examination, pulmonary function testing, and chest imaging. ■

■FURTHER READING Bohadana A et al: Fundamentals of lung auscultation. N Engl J Med 370:744, 2014. Chung KF et al: Cough hypersensitivity and chronic cough. Nat Rev Dis Primers 8:45, 2022. García-de-Acilu M et al: Use of thoracic ultrasound in acute respira tory distress syndrome. Ann Transl Med 11:320, 2023. Mojoli F et al: Lung ultrasound for critically ill patients. Am J Resp Crit Care Med 199:701, 2019. Parshall MB et al: An official American Thoracic Society state ment: Update on the mechanisms, assessment, and management of dyspnea. Am J Respir Crit Care Med 185:435, 2012. Pellegrino R et al: Interpretive strategies for lung function tests. Eur Respir J 26:948, 2005. Stanojevic S et al: ERS/ATS technical standard on interpretative strategies for routine lung function tests. Eur Respir J 60:2101499, 2022.

George R. Washko, William M. Oldham

Disturbances of

Respiratory Function The primary functions of the respiratory system—to oxygenate blood and eliminate carbon dioxide—require virtual contact between blood and fresh air, which facilitates diffusion of respiratory gases between blood and gas. This process occurs in the lung alveoli, where blood flowing through alveolar wall capillaries is separated from alveolar gas by an extremely thin membrane of flattened endothelial and epithelial cells, across which respiratory gases diffuse and equilibrate. Blood flow through the lung is unidirectional via a continuous vascular path along which venous blood absorbs oxygen from and loses CO_2 to inspired gas. The path for airflow, in contrast, reaches a dead end at the alveolar walls; thus, the alveolar space must be ventilated tidally, with inflow of fresh gas and outflow of alveolar gas alternating periodically at the respiratory rate (RR). To provide an enormous alveolar surface area (typically 70 m2) for blood-gas diffusion within the modest volume of a thoracic cavity (typically 7 L), nature has distributed both blood flow and ventilation among millions of tiny alveoli through multigen erational branching of both pulmonary arteries and bronchial airways. Ideally, for the lung to be most efficient in exchanging gas, the fresh gas ventilation of a given alveolus must be matched to its perfusion. How ever, as a consequence of variations in tube lengths and calibers along these pathways as well as the effects of gravity, tidal pressure fluctua tions, and anatomic constraints from the chest wall, the alveoli vary in their relative ventilations and perfusions even in health. Disturbances of Respiratory Function CHAPTER 296 For the respiratory system to succeed in oxygenating blood and eliminating CO_2, it must be able to ventilate the lung tidally and thus to freshen alveolar gas; it must provide for perfusion of the individual alveolus in a manner proportional to its ventilation; and it must allow adequate diffusion of respiratory gases between alveolar gas and capil lary blood. Furthermore, it must accommodate several-fold increases in the demand for oxygen uptake or CO_2 elimination imposed by meta bolic needs or acid-base derangement. Given these multiple require ments for normal operation, it is not surprising that many diseases disturb respiratory function. This chapter considers in some detail the physiologic determinants of lung ventilation and perfusion, elucidates how the matching distributions of these processes and rapid gas diffu sion allow normal gas exchange, and discusses how common diseases derange these normal functions, thereby impairing gas exchange—or at least increase the work required by the respiratory muscles or heart to maintain adequate respiratory function. ■ ■VENTILATION It is useful to conceptualize the respiratory system as three indepen dently functioning components: the lung, including its airways; the neuromuscular system; and the chest wall, which includes everything that is not lung or active neuromuscular system. Accordingly, the mass of the respiratory muscles is part of the

chest wall, while the force these muscles generate is part of the neuromuscular system; the abdomen (especially an obese abdomen) and the heart (especially an enlarged heart) are, for these purposes, part of the chest wall. Each of these three components has mechanical properties that relate to its enclosed volume (or—in the case of the neuromuscular system—the respiratory system volume at which it is operating) and to the rate of change of its volume (i.e., flow). The work of breathing required of the neuromuscular system is the sum of the work due to volume-related mechanical properties and the work from flow-related mechanical properties required to move air throughout the airways to create this volume change. Volume-Related Mechanical Properties—Statics Figure 296-1 shows the volume-related properties of each component of the respira tory system. The natural tendency of the lung is to collapse because

100% 100% 75% 75% Vital capacity 50% 50% Functional residual capacity 25% PART 7 Disorders of the Respiratory System Lung Chest wall 25% 0% Residual volume 0% –40 –30 –20 –10

Pressure (cm H2O) +40 +30 +20 +10 FIGURE 296-1 Pressure-volume curves of the isolated lung, isolated chest wall, combined respiratory system, inspiratory muscles, and expiratory muscles. FRC, functional residual capacity; RV, residual volume; TLC, total lung capacity. of both surface tension at the air-liquid interface between alveolar wall lining fluid and alveolar gas and elastic recoil of the lung tis sue itself. To stay inflated, the pressure within the alveolus must equal or exceed the pressure at the pleural surface. This difference in pressures (Palveolus – Ppleura) is expressed as the transpulmonary pressure. The elastic recoil of the lung is not constant, increasing with infla tion. At high lung volume, the lung becomes rather stiff, so that large changes in transpulmonary pressure are required for relatively small changes in lung volume. In contrast, the lung is compliant at lower volumes, including those at which tidal breathing normally occurs. At zero inflation pressure, even normal lungs retain some air in the alveoli. Because the small peripheral airways are tethered open by out ward radial pull from inflated lung parenchyma attached to adventitia, as the lung deflates during exhalation, those small airways are pulled open progressively less, and eventually close, trapping some gas in the alveoli. This effect can be exaggerated with age and especially with obstructive airway diseases, resulting in gas trapping at quite large lung volumes. Functional residual capacity (FRC) is the passive resting point of the respiratory system attained when the outward recoil of the chest wall is balanced exactly by the inward recoil of the lung. The elastic behavior of the passive chest wall (i.e., in the absence of neuromuscu lar activation), differs markedly from that of the lung. While the lungs become stiff at high volumes, the chest wall stiffens at low volumes due to squeezing together of ribs and intercostal muscles, diaphragm stretch, displacement of abdominal contents, and straining of liga ments and bony articulations. The normal lung and chest wall function in mechanical series, and the pressure required to displace the passive respiratory system (lungs plus chest wall) at any volume is simply the sum of the elastic recoil pressure of the lungs and the transmural pres sure across the chest wall. When plotted against respiratory system vol ume, this relationship assumes a sigmoid shape, exhibiting stiffness at high lung volumes (imparted by the lung), stiffness at low lung volumes (imparted by the chest wall or sometimes by airway closure), and com pliance in the middle range of lung volumes where normal tidal breath ing occurs. As these recoils are transmitted through the pleural fluid, the lung is pulled both outward and inward simultaneously at FRC, where the negative intrapleural pressure is exactly offset by the positive intrapulmonary pressure yielding an airway pressure of 0 mmHg. The normal passive respiratory system would equilibrate at the FRC and remain there were it not for the actions of the respiratory muscles. Gas

flows from high to low pressure and the lung inflates when pres sure at the airway opening exceeds pressure in the alveoli. The lung deflates when pressure in the alveoli exceeds pressure at the airway

Total lung capacity Vital capacity Tidal volume Total lung capacity Expiratory reserve volume Functional residual capacity Residual volume FIGURE 296-2 Spirogram demonstrating a slow vital capacity maneuver and various lung volumes. opening. The inspiratory muscles act on the chest wall to expand the volume of the thorax, decreasing pleural pressure, lowering pressure in the alveoli below pressure at the airway opening. In contrast, the expira tory muscles raise the alveolar gas pressure above pressure at the airway opening, leading to an outflow of gas from the lung. The maximal pressures these sets of muscles can generate vary with the lung volume at which they operate. This variation is due to length-tension relationships in striated muscle sarcomeres and to changes in mechanical advantage as the angles of insertion change with lung volume (Fig. 296-1). Nonetheless, under normal conditions, the respiratory muscles are substantially “overpowered” for their roles and generate more than adequate force to drive the respiratory system to its stiffness extremes, as determined by the lung (total lung capacity [TLC]) or by chest wall or airway closure (residual volume [RV]); the airway closure always prevents the adult lung from emptying com pletely under normal circumstances. The excursion between full and minimal lung inflation is called vital capacity (VC; Fig. 296-2). The VC is easy to measure (see below), but it provides little information about the intrinsic properties of the respiratory system. As will become clear, it is much more useful for the clinician to consider TLC and RV individually. Flow-Related Mechanical Properties—Dynamics The pas sive chest wall and active neuromuscular system both exhibit mechani cal behaviors related to the rate of change of volume, but these behaviors become quantitatively important only at markedly supraphysiologic breathing frequencies (e.g., during high-frequency mechanical ventila tion), and thus will not be addressed here. In contrast, the dynamic airflow properties of the lung substantially affect its ability to ventilate and contribute importantly to the work of breathing, and these prop erties are often deranged by disease. Understanding dynamic airflow properties is, therefore, worthwhile. As with the flow of any fluid (gas or liquid) in any tube, maintenance of airflow within the pulmonary airways requires a pressure gradient that falls along the direction of flow, the magnitude of which is deter mined by the flow rate and the frictional resistance to flow. During quiet tidal breathing, the pressure gradients driving inspiratory or expiratory flow are small owing to the very low frictional resistance of normal pulmonary airways (Raw, normally <2 cmH2O/L/s). However, during rapid exhalation, another phenomenon reduces flow below that which would have been expected if frictional resistance were the only impediment to flow. This phenomenon is called dynamic airflow limitation, and it occurs because the bronchial airways through which air is exhaled are collapsible rather than rigid (Fig. 296-3). An important anatomic feature of the structure of the pulmonary airways is their tree-like branching pattern. While the individual airways in each successive generation, from most proximal (trachea) to most distal (respiratory bronchioles), are smaller than those of the par ent generation, their number increases exponentially such that the summed cross-sectional area of the airways becomes very large toward the lung periphery. Because flow (volume/time) is constant along the airway tree, the velocity of airflow (flow/summed cross-sectional area)

Luminal area _ Transmural pressure + FIGURE 296-3 Luminal area versus transmural pressure relationship. Transmural pressure represents the pressure difference across the airway wall from inside to outside. is much greater in the central airways than in the peripheral airways. During

exhalation, gas leaving the alveoli must, therefore, gain velocity as it proceeds toward the mouth. This acceleration reduces intralumi nal gas pressure and airway transmural pressure leading to a reduction in airway size. Referred to as the Bernoulli effect, this process may be best appreciated in the example of the airplane. As the flow of air accelerates over the curved surface of its wings, it provides lift to the plane (Fig. 296-3). If an individual attempts to exhale more forcefully, the local velocity increases further (increasing “lift”) and airway size grows smaller, resulting in no net increase in flow. Under these circum stances, flow has reached its maximum possible value, or its flow limit. Lungs normally exhibit such dynamic airflow limitation. This limi tation can be assessed by spirometry, in which an individual inhales fully to TLC and then forcibly exhales to RV. Maximal expiratory flow at any lung volume is determined by gas density, airway cross-section and distensibility, elastic recoil pressure of the lung, and frictional pres sure loss to the flow-limiting airway site. Under normal conditions, maximal expiratory flow falls with lung volume (Fig. 296-4), primarily because of the dependence of lung recoil pressure on lung volume (Fig. 296-1). In pulmonary fibrosis, lung recoil pressure is increased at any lung volume, and thus the maximal expiratory flow is elevated when considered in relation to lung volume. Conversely, in emphysema, lung recoil pressure is reduced; this reduction is a principal mechanism by A B C Expiratory Inspiratory Expiratory Inspiratory TLC Flow Flow Volume RV D Expiratory Inspiratory TLC Flow FIGURE 296-4 Flow-volume loops. A. Normal. B. Airflow obstruction. C. Fixed central airway obstruction (either above or below the thoracic inlet). D. Variable upper airway obstruction (above the thoracic inlet) E. Variable lower airway obstruction (below the thoracic inlet). RV, residual volume; TLC, total lung capacity.

which maximal expiratory flows fall. Diseases that narrow the airway lumen at any transmural pressure (e.g., asthma or chronic bronchitis) or that cause excessive airway collapsibility (e.g., tracheomalacia) also reduce maximal expiratory flow.

The Bernoulli effect also applies during inspiration, but the more negative pleural pressures during inspiration lower the pressure outside of the airways, thereby increasing transmural pressure and promoting airway expansion. Thus, inspiratory airflow limitation seldom occurs due to diffuse pulmonary airway disease. Conversely, extrathoracic airway narrowing (e.g., due to a tracheal adenoma or posttracheostomy stricture) can lead to inspiratory airflow limitation (Fig. 296-4). Disturbances of Respiratory Function CHAPTER 296 The Work of Breathing In health, the elastic (volume changerelated) and dynamic (flow-related) loads that must be overcome to ventilate the lungs at rest are small, and the work required of the respiratory muscles is minimal. However, the work of breathing can increase considerably due to a metabolic requirement for substantially increased ventilation, an abnormally increased mechanical load, or both. As discussed below, the rate of ventilation is primarily set by the need to eliminate carbon dioxide, and thus, ventilation increases dur ing exercise (sometimes by >20-fold) and during metabolic acidosis as a compensatory response. Naturally, the work rate required to over come the elasticity of the respiratory system increases with both the depth and the frequency of tidal breaths, while the work required to overcome the dynamic load increases with total ventilation. A modest increase of ventilation is most efficiently achieved by increasing tidal volume but not RR, which is the normal ventilatory response to lowerlevel exercise. At higher levels of exercise, deep breathing persists, but RR also increases. The work of breathing also increases when disease reduces the com pliance of the respiratory system or increases the resistance to airflow. The former occurs commonly in diseases of the lung parenchyma (interstitial processes or fibrosis, alveolar filling diseases such as

pul monary edema or pneumonia, or substantial lung resection), and the latter occurs in obstructive airway diseases such as asthma, chronic bronchitis, emphysema, and cystic fibrosis. Furthermore, severe air flow obstruction can functionally reduce the compliance of the respi ratory system by leading to dynamic hyperinflation. In this scenario, expiratory flows slowed by the obstructive airways disease may be Expiratory Inspiratory TLC TLC Flow RV Volume RV Volume E Expiratory Inspiratory TLC Flow RV RV

insufficient to allow complete exhalation during the expiratory phase of tidal breathing; as a result, the “functional residual capacity (FRC)” from which the next breath is inhaled is greater than the static FRC. With repetition of incomplete exhalations of each tidal breath, the operating FRC becomes dynamically elevated, sometimes to a level that approaches TLC. At these high lung volumes, the respiratory system is much less compliant than at normal breathing volumes, and thus, the elastic work of each tidal breath is also increased. The dynamic pulmo nary hyperinflation that accompanies severe airflow obstruction causes patients to sense difficulty in inhaling—even though the root cause of this pathophysiologic abnormality is expiratory airflow obstruction.

PART 7 Disorders of the Respiratory System Adequacy of Ventilation As noted above, the respiratory control system that sets the rate of ventilation responds to chemical signals, including arterial CO2 and oxygen tensions and blood pH, and to volitional needs, such as the need to inhale deeply before playing a long phrase on the trumpet. Disturbances in ventilation are discussed in Chap. 307. The focus of this chapter is on the relationship between ventilation of the lung and CO2 elimination. At the end of each tidal exhalation, the conducting airways are filled with alveolar gas that did not reach the mouth when expiratory flow stopped. During the ensuing inhalation, fresh gas immediately enters the airway tree at the mouth, but the gas first entering the alveoli at the start of inhalation is that same alveolar gas in the conducting airways that had just left the alveoli. Accordingly, fresh gas does not enter the alveoli until the volume of the conducting airways has been inspired. This volume is called the anatomic dead space (VD). Quiet breathing with tidal volumes smaller than the anatomic dead space introduces no fresh gas into the alveoli at all; only that part of the inspired tidal volume (VT) that is greater than the VD introduces fresh gas into the alveoli. The dead space can be further increased functionally if some of the inspired tidal volume is delivered to a part of the lung that receives no pulmonary blood flow and thus cannot contribute to gas exchange (e.g., the portion of the lung distal to a large pulmonary embolus). In this situation, exhaled minute ventilation ($\dot{V}_E = V_T \times RR$) includes a component of dead space ventilation ($\dot{V}_D = V_D \times RR$) and a component of fresh gas alveolar ventilation ($\dot{V}_A = [V_T - V_D] \times RR$). Carbon diox ide elimination from the alveoli is equal to VA times the difference in CO2 fraction between inspired air (essentially zero) and alveolar gas (typically ~5.6% after correction for humidification of inspired air, corresponding to 40 mmHg). In the steady state, the alveolar fraction of CO2 is equal to metabolic CO2 production divided by alveolar ventilation. Because, as discussed below, alveolar and arterial CO2 tensions are equal, and because the respiratory controller normally strives to maintain arterial Pco2 (Paco2) at ~40 mmHg, the adequacy of alveolar ventilation is reflected in Paco2. If the Paco2 falls much below 40 mmHg, alveolar hyperven tilation is present; if the Paco2 exceeds 40 mmHg, alveolar hypoventila tion is present. Ventilatory failure is characterized by extreme alveolar hypoventilation. In vivo, the production and clearance of CO2 can be assessed through sampling of the arterial and central venous blood. CO2 clearance can also be estimated noninvasively using capnography. Capnography enables visualization of respirophasic changes in CO2 concentration at the airway opening, which at end of a tidal breath (EtCO2)

provides an estimate of ventilation. As a consequence of oxygen uptake of alveolar gas into capillary blood, alveolar oxygen tension falls below that of inspired gas. The rate of oxygen uptake (determined by the body's metabolic oxygen con sumption) is related to the average rate of metabolic CO2 production, and their ratio—the "respiratory quotient" (R = V.co2/V.o2)—depends largely on the fuel being metabolized. For a typical American diet, R is usually around 0.85. Together, these phenomena allow the estimation of alveolar oxygen tension, according to the following relationship, known as the alveolar gas equation: Pao2 = Fio2 × (Pbar − Ph2o) − Paco2/R The alveolar gas equation also highlights the influences of inspired oxygen fraction Fio2 barometric pressure (Pbar), and vapor pressure of water (Ph2o = 47 mmHg at 37°C) in addition to alveolar ventilation

(which sets Paco2) in determining Pao2. An implication of the alveolar gas equation is that severe arterial hypoxemia rarely occurs as a pure consequence of alveolar hypoventilation at sea level while an individual is breathing air. The potential for alveolar hypoventilation to induce severe hypoxemia with otherwise normal lungs increases as Pbar falls with increasing altitude. ■ ■GAS EXCHANGE Diffusion For oxygen to be delivered to the peripheral tissues, it must pass from alveolar gas into alveolar capillary blood by diffus ing through alveolar membrane. The aggregate alveolar membrane is highly optimized for this process, with a very large surface area and minimal thickness. Diffusion through the alveolar membrane is so efficient in the human lung that in most circumstances hemoglobin of a red blood cell becomes fully oxygen saturated by the time the cell has traveled just one-third the length of the alveolar capillary. Thus, the uptake of alveolar oxygen is ordinarily limited by the amount of blood transiting the alveolar capillaries rather than by the rapidity with which oxygen can diffuse across the membrane; consequently, oxygen uptake from the lung is said to be "perfusion limited" rather than diffusion limited. CO2 also equilibrates rapidly across the alveolar membrane. Therefore, the oxygen and CO2 tensions in capillary blood leaving a normal alveolus are essentially equal to those in alveolar gas. Only in rare circumstances (e.g., at high altitude or in high-performance athletes exerting maximal effort) is oxygen uptake from normal lungs diffusion limited. Diffusion limitation can also occur in interstitial lung disease if substantially thickened alveolar walls remain perfused. Ventilation/Perfusion Heterogeneity As noted above, for gas exchange to be most efficient, ventilation (V.) to each individual alveo lus (among the millions of alveoli) should match perfusion (Q.) to its accompanying capillaries. Because of the differential effects of gravity on lung mechanics and blood flow throughout the lung and because of differences in airway and vascular architecture among various respiratory paths, there is minor ventilation/perfusion heterogeneity even in the normal lung; however, V./Q. heterogeneity can be particu larly marked in disease. Two extreme examples are (1) ventilation of unperfused lung distal to a pulmonary embolus, in which ventilation of the physiologic dead space is "wasted" in the sense that it does not contribute to gas exchange; and (2) perfusion of nonventilated lung (a "shunt"), which allows venous blood to pass through the lung unaltered. When mixed with fully oxygenated blood leaving other well-ventilated lung units, shunted venous blood disproportionately lowers the mixed arterial Pao2 as a result of the nonlinear oxygen content versus PO2 relationship of hemoglobin (Fig. 296-5). Furthermore, the resulting arterial hypoxemia is refractory to supplemental inspired oxygen. The reason is that (1) raising the inspired Fio2 has no effect on alveolar gas tensions in nonventilated alveoli and (2) while raising inspired Fio2 increases Paco2 in ventilated alveoli, the oxygen content of blood exit ing ventilated units increases only slightly, as hemoglobin will already have been nearly fully saturated. Furthermore, the solubility of oxygen in plasma is quite small, and in normobaric conditions, the dissolved

amount of oxygen in blood offers little additional physiologic benefit. A more common occurrence than the two extreme examples given above is a widening of the distribution of ventilation/perfusion ratios; such V./Q. heterogeneity is a common consequence of lung disease. In this circumstance, perfusion of relatively underventilated alveoli results in the incomplete oxygenation of exiting blood. When mixed with welloxygenated blood leaving higher V./Q. regions, this partially reoxygen ated blood disproportionately lowers arterial Pao2, although to a lesser extent than does a similar perfusion fraction of blood leaving regions of pure shunt. In addition, in contrast to shunt regions, inhalation of supplemental oxygen raises the Pao2 even in relatively underventilated low V./Q. regions, and so the arterial hypoxemia induced by V./Q. hetero geneity is typically responsive to oxygen therapy (Fig. 296-5). In sum, arterial hypoxemia can be caused by substantial reduction of inspired oxygen tension, severe alveolar hypoventilation, perfusion of relatively underventilated (low V./Q.) or completely unventilated

FIO2 = 0.21 FIO2 = 1 Shunt

mmHg

mmHg 40 mmHg (75%) 40 mmHg (75%) 40 mmHg (75%) 99 mmHg (100%) 55 mmHg (87.5%) . . FIO2 = 0.21 FIO2 = 1 V/Q Heterogeneity

mmHg

mmHg 40 mmHg (75%) 40 mmHg (75%) 45 mmHg (79%) 99 mmHg (100%) 58 mmHg (89.5%) FIGURE 296-5 Influence of air versus oxygen breathing on mixed arterial oxygenation in shunt and ventilation/perfusion heterogeneity. Partial pressure of oxygen (mmHg) and oxygen saturations are shown for mixed venous blood, for end capillary blood (normal vs affected alveoli), and for mixed arterial blood. Fio2 fraction of inspired oxygen; V . . /Q , ventilation/perfusion. (shunt) lung regions, and, in very unusual circumstances, limitation of gas diffusion. ■ ■PATHOPHYSIOLOGY Although many diseases injure the respiratory system, this system responds to injury in relatively few ways. For this reason, the pattern of physiologic abnormalities may or may not provide sufficient informa tion by which to discriminate among conditions. Figure 296-6 lists abnormalities in pulmonary function testing that are typically found in a number of common respiratory disorders and highlights the simultaneous occurrence of multiple physiologic abnormalities. The coexistence of some of these respiratory disorders results in more complex superposition of these abnormalities. Methods to measure respiratory system function clinically are described later in this chapter. Ventilatory Restriction due to Increased Elastic Recoil— Example: Idiopathic Pulmonary Fibrosis Idiopathic pulmo nary fibrosis raises lung recoil at all lung volumes, thereby lowering TLC, FRC, and RV as well as forced vital capacity (FVC). Maximal expiratory flows are also reduced from normal values but are elevated when considered in relation to lung volumes. Increased flow occurs both because the increased lung recoil drives greater maximal flow at any lung volume and because airway diameters are relatively increased due to greater radially outward traction exerted on bronchi by the stiff lung parenchyma. For the same reason, airway resistance is also nor mal. Destruction of the pulmonary capillaries by the fibrotic process results in a marked reduction in diffusing capacity (see below). Oxy genation is often severely reduced by persistent perfusion of alveolar

mmHg

mmHg 40 mmHg (75%) Disturbances of Respiratory Function CHAPTER 296 40 mmHg (75%) 40 mmHg (75%) 650 mmHg (100%) 56 mmHg (88%)

mmHg

mmHg 40 mmHg (75%) 40 mmHg (75%) 200 mmHg (100%) 650 mmHg (100%) 350 mmHg (100%) units that are relatively underventilated due to fibrosis of nearby (and mechanically linked) lung due to those alveolar units already being stretched to their maximum volume with little further increase in vol ume with inspiration. The flow-volume loop (see below) looks like a miniature version of a normal loop but is shifted toward lower absolute lung volumes and displays maximal expiratory flows that are increased for any given volume over the normal tracing. Ventilatory Restriction due to Chest Wall Abnormality— Example: Moderate Obesity As the size of the average American continues to increase, this pattern may become the most common of pulmonary function abnormalities. In moderate obesity, the outward recoil of the chest wall is blunted by the weight of chest wall adipose tissue and the space occupied by intraabdominal fat. In this situation, preserved inward recoil of the lung overbalances the reduced outward recoil of the chest wall, and FRC falls. Because respiratory muscle strength and lung recoil remain normal, TLC is typically unchanged (although it may fall in massive obesity) and RV is normal (but may be reduced in massive obesity). Mild hypoxemia may be present due to perfusion of alveolar units that are poorly ventilated because of airway closure in dependent portions of the lung during breathing near the reduced FRC. Flows remain normal, as does the diffusion capacity of the lung for carbon monoxide (DlCO) unless obstructive sleep apnea (which often accompanies obesity) and associated chronic intermittent hypoxemia have induced pulmonary arterial hypertension, in which case DlCO may be low. Ventilatory Restriction due to Reduced Muscle Strength— Example: Myasthenia Gravis In this circumstance, FRC remains

Restriction due to Restriction due to increased lung elastic recoil (pulmonary fibrosis) chest wall abnormality (moderate obesity) TLC 60% 95% FRC 60% 65% RV 60% 100% FVC 60% 92% PART 7 Disorders of the Respiratory System FEV1 75% 92% 1.0 1.0 Raw 60% 95% DLCO Flow Flow Volume Volume FIGURE 296-6 Common abnormalities of pulmonary function (see text). Pulmonary function values are expressed as a percentage of normal predicted values, except for Raw, which is expressed as cmH2O/L/s (normal, <2 cmH2O/L/s). The figures at the bottom of each column show the typical configuration of flow-volume loops in each condition, including the flow-volume relationship during tidal breathing. b.d., bronchodilator; DlCO diffusion capacity of lung for carbon monoxide; FEV1, forced expiratory volume in 1 s; FRC, functional residual capacity; FVC, forced vital capacity; Raw, airways resistance; RV, residual volume; TLC, total lung capacity. normal, as both lung recoil and passive chest wall recoil are normal. How ever, TLC is low and RV is elevated because respiratory muscle strength is insufficient to push the passive respiratory system fully toward either volume extreme. Caught between the low TLC and the elevated RV, FVC and forced expiratory volume in 1 s (FEV1) are reduced as “innocent bystanders.” As airway size and lung vasculature are unaffected, both Raw and DlCO are normal. Oxygenation is normal unless weakness becomes so severe that the patient has insufficient strength to reopen collapsed alveoli during sighs, with resulting atelectasis. Airflow Obstruction due to Decreased Airway Diameter— Example: Acute Asthma During an episode of acute asthma, luminal narrowing due to smooth

muscle constriction as well as inflammation and thickening within the small- and medium-sized bronchi raise frictional resistance and reduce airflow. “Scooping” of the flow-volume loop is caused by reduction of airflow, especially at lower lung volumes. Often, airflow obstruction can be improved through the administration of short-acting β2-adrenergic or muscarinic agonists acutely, or by treatment with longer-acting β2-adrenergic or muscarinic agonists, inhaled corticosteroids, and new systemically administered biologic immunotherapies chronically. TLC usually remains normal (although elevated TLC is sometimes seen in long-standing asthma), but FRC may be dynamically elevated. RV is often increased due to exaggerated airway closure at low lung volumes, and this elevation of RV reduces FVC. Because central airways are narrowed, airway resistance (Raw) is usually elevated. Mild arterial hypoxemia is often present due to perfusion of relatively underventilated alveoli distal to obstructed airways (and is responsive to oxygen supplementation), but DlCO is normal or mildly elevated. Airflow Obstruction due to Decreased Elastic Recoil— Example: Severe Emphysema Loss of lung elastic recoil in severe emphysema results in pulmonary hyperinflation, of which elevated TLC is the hallmark. FRC is more severely elevated due to both loss of lung elastic recoil and dynamic hyperinflation—the same phenomenon as auto-PEEP (auto–positive end-expiratory pressure), which is the positive end-expiratory alveolar pressure that occurs when a new breath is initiated before the lung volume is allowed to return to FRC. RV is very severely elevated because of airway closure and because exhalation toward RV may take so long that RV cannot be

Restriction due to respiratory muscle weakness (myasthenia gravis) Obstruction due to airway narrowing (acute asthma) Obstruction due to decreased elastic recoil (severe emphysema) 75% 100% 130% 100% 104% 220% 120% 120% 310% 60% 90% 60% 35% pre-b.d. 75% post-b.d. 35% pre-b.d. 38% post-b.d. 60% 2.5 1.5 1.0 120% 40% 80% Flow Flow Flow Volume Volume Volume reached before the patient must inhale again. Both FVC and FEV1 are markedly decreased, the former because of the severe elevation of RV and the latter because loss of lung elastic recoil reduces the pressure driving maximal expiratory flow and also reduces tethering open of small intrapulmonary airways. The flow-volume loop demonstrates marked scooping, with an initial transient spike of flow attributable largely to expulsion of air from collapsing central airways at the onset of forced exhalation. Otherwise, the central airways remain relatively unaffected, so Raw is normal in “pure” emphysema. Loss of alveolar surface and capillaries in the alveolar walls reduces DlCO; however, because poorly ventilated emphysematous acini are also poorly per fused (due to loss of their capillaries), arterial hypoxemia usually is not seen at rest until emphysema becomes very severe. However, during exercise, Pao2 may fall precipitously if extensive destruction of the pul monary vasculature prevents a sufficient increase in cardiac output and mixed venous oxygen content falls substantially. Under these circum stances, any venous admixture through low V./Q. units has a particularly marked effect in lowering mixed arterial oxygen tension. ■ ■FUNCTIONAL MEASUREMENTS Measurement of Ventilatory Function • LUNG VOLUMES

Figure 296-2 demonstrates a spirometry tracing in which the volume of air entering or exiting the lung is plotted over time. In a slow vital capacity maneuver, the patient inhales from FRC, fully inflating the lungs to TLC, and then exhales slowly to RV; VC, the difference between TLC and RV, represents the maximal excursion of the respira tory system. Spirometry discloses relative volume changes during these maneuvers but cannot reveal the absolute volumes at which they occur. To determine absolute lung volumes, two approaches are commonly used: inert gas dilution and body plethysmography. In the former, a known amount of a nonabsorbable inert gas (usually helium or neon) is inhaled in a single large breath or is rebreathed from a closed circuit; the inert gas is

diluted by the gas resident in the lung at the time of inhalation, and its final concentration reveals the volume of resident gas contributing to the dilution. A drawback of this method is that regions of the lung that ventilate poorly (e.g., due to airflow obstruc tion) may not receive much inspired inert gas and so do not contribute to its dilution. Therefore, inert gas dilution (especially in the singlebreath method) often underestimates true lung volumes.

Revision #1
Created 2026-01-06 16:34:04 UTC by Omar Ayman
Updated 2026-01-06 16:34:04 UTC by Omar Ayman