pulmonary hyperinflation, of which elevated TLC is the hallmark. FRC is more severely elevated due both to loss of lung elastic recoil and to dynamic hyperinflation—the same phenomenon as autoPEEP, 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. Residual volume is very severely elevated because of airway closure and because exhalation toward RV may take so long that RV cannot be reached before the patient must inhale again. Both FVC and FEV_1 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 R_{aw} is normal in "pure" emphysema. Loss of alveolar surface and capillaries in the alveolar walls reduces D_{LCO}; however, because poorly ventilated emphysematous acini are also poorly perfused (due to loss of their capillaries), arterial hypoxemia usually is not seen at rest until emphysema becomes very severe. However, during exercise, Pa_{O_2} may fall precipitously if extensive destruction of the pulmonary vasculature prevents a sufficient increase in cardiac output and mixed venous oxygen content falls substantially. Under these circumstances, any venous admixture through low $\dot{V}/\dot{Q}$ units has a particularly marked effect in lowering mixed arterial oxygen tension.

FUNCTIONAL MEASUREMENTS

Measurement of Ventilatory Function • ***LUNG VOLUMES*** Figure 306e-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 subject 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 respiratory 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 obstruction) may not receive much inspired inert gas and so do not contribute to its dilution. Therefore, inert gas dilution (especially in the single-breath method) often underestimates true lung volumes.

In the second approach, FRC is determined by measuring the compressibility of gas within the chest, which is proportional to the volume of gas being compressed. The patient sits in a body plethysmograph (a chamber usually made of transparent plastic to minimize claustrophobia) and, at the end of a normal tidal breath (i.e., when lung volume is at FRC), is instructed to pant against a closed shutter, thus periodically compressing air within the lung slightly. Pressure fluctuations at the mouth and volume fluctuations within the body box (equal but opposite to those in the chest) are determined, and from these measurements the thoracic gas volume is calculated by means of Boyle's law. Once FRC is obtained, TLC and RV are calculated by adding the value for inspiratory capacity and subtracting the value for expiratory reserve volume, respectively (both values having been obtained during spirometry) (Fig. 306e-2). The most important determinants of healthy individuals' lung volumes are height, age, and sex, but there is considerable additional normal variation beyond that accounted for by these parameters. In addition, race influences lung volumes; on average, TLC values are ~12% lower in African Americans and 6% lower in Asian Americans than in Caucasian Americans. In practice, a mean "normal" value is predicted by multivariate regression equations using height, age, and sex, and the patient's value is divided by the predicted value (often with "race correction" applied) to determine "percent predicted." For most measures of lung function, 85–115% of the predicted value can be normal; however, in health, the various lung volumes tend to scale together. For example, if one is "normal big" with a TLC 110% of the predicted value, then all other lung volumes and spirometry values will also approximate 110% of their respective predicted values. This pattern is particularly helpful in evaluating airflow, as discussed below.

AIR FLOW As noted above, spirometry plays a key role in lung volume determination. Even more often, spirometry is used to measure airflow, which reflects the dynamic properties of the lung. During an FVC maneuver, the patient inhales to TLC and then exhales rapidly and forcefully to RV; this method ensures that flow limitation has been achieved, so that the precise effort made has little influence on actual flow. The total amount of air exhaled is the FVC, and the amount of air exhaled in the first second is the FEV_1; the FEV_1 is a flow rate, revealing volume change per time. Like lung volumes, an individual's maximal expiratory flows should be compared with predicted values based on height, age, and sex. While the FEV_1/FVC ratio is typically reduced in airflow obstruction, this condition can also reduce FVC by raising RV, sometimes rendering the FEV_1/FVC ratio "artifactually normal" with the erroneous implication that airflow obstruction is absent. To circumvent this problem, it is useful to compare FEV_1 as a fraction of its predicted value with TLC as a fraction of its predicted value. In health, the results are usually similar. In contrast, even an FEV_1 value that is 95% of its predicted value may actually be relatively low if TLC is 110% of its respective predictied value. In this case, airflow obstruction may be present, despite the "normal" value for FEV_1.

The relationships among volume, flow, and time during spirometry are best displayed in two plots—the spirogram (volume vs. time) and the flow-volume loop (flow vs. volume) (Fig. 306e-4). In conditions that cause airflow obstruction, the site of obstruction is sometimes correlated with the shape of the flow-volume loop. In diseases that cause lower airway obstruction, such as asthma and emphysema, flows decrease more rapidly with declining lung volumes, leading to a characteristic scooping of the flow-volume loop. In contrast, fixed upper-airway obstruction typically leads to inspiratory and/or expiratory flow plateaus (Fig. 306e-4).

AIRWAYS RESISTANCE The total resistance of the pulmonary and upper airways is measured in the same body plethysmograph used to measure FRC. The patient is asked once again to pant, but this time against a closed and then opened shutter. Panting against the closed shutter reveals the thoracic gas volume as described above. When the shutter is opened, flow is directed to and from the body box, so that volume fluctuations in the box reveal the extent of thoracic gas compression, which in turn reveals the pressure fluctuations driving flow. Simultaneous measurement of flow allows the calculation of lung resistance (as flow divided by pressure). In health, R_{aw} is very low (<2 cmH_2O/L per second), and half of the detected resistance resides within the upper airway. In the lung, most resistance originates in the central airways. For this reason, airways resistance measurement tends to be insensitive to peripheral airflow obstruction.

RESPIRATORY MUSCLE STRENGTH To measure respiratory muscle strength, the patient is instructed to exhale or inhale with maximal effort against a closed shutter while pressure is monitored at the mouth. Pressures greater than ±60 cmH_2O at FRC are considered adequate and make it unlikely that respiratory muscle weakness accounts for any other resting ventilatory dysfunction that is identified.

Measurement of Gas Exchange • ***DIFFUSING CAPACITY (D_{LCO})*** This test uses a small (and safe) amount of carbon monoxide (CO) to measure gas exchange across the alveolar membrane during a 10-sec breath hold. CO in exhaled breath is analyzed to determine the quantity of CO crossing the alveolar membrane and combining with hemoglobin in red blood cells. This "single-breath diffusing capacity" (D_{Lco}) value increases with the surface area available for diffusion and the amount of hemoglobin within the capillaries, and it varies inversely with alveolar membrane thickness. Thus, D_{Lco} decreases in diseases that thicken or destroy alveolar membranes (e.g., pulmonary fibrosis, emphysema), curtail the pulmonary vasculature (e.g., pulmonary hypertension), or reduce alveolar capillary hemoglobin (e.g., anemia). Single-breath