CHAPTER 8

PULMONARY STATICS IN DISEASE

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Although once at the cutting edge of clinical pulmonary physiology, the measurement of static pressure–volume (*P–V*) curves of the lung has now fallen somewhat into disfavor. The advent of computed tomography (CT) scanning has led to a decrease in interest in the use of the *P–V* curve as a clinical diagnostic tool or even as an adjunct to research. Nevertheless, the concepts underlying the measurement of static lung mechanics are essential for understanding and interpreting other pulmonary function tests and for clinically important measurements in the intensive care unit. Moreover, there are still niches where the *P–V* curve can make an important contribution to solving diagnostic problems. The *P–V* curve is above all an attempt to evaluate the elasticity of the lung. Although it is possible to consider both the dynamic and static lung elasticity, this chapter focuses on the static *P–V* curve, with the goal of reviewing its clinical applications and how its measurement has contributed to our understanding of disease pathophysiology.

MEASUREMENT OF THE *P–V* CURVE

The overall aim of *P–V* curve measurement is to infer the elastic properties of the lung from changes in transpulmonary pressure (ie, the difference between airway opening pressure and pleural pressure) and changes in lung volume. This requires some means of estimating pleural pressure changes. Although there have been reports of measuring pleural pressure directly,[1] the esophageal balloon technique, which is based on the notion that swings in esophageal pressure reflect those in the pleura, has long been the standard method for constructing *P–V* curves in humans. The details and pitfalls of the esophageal balloon technique are discussed elsewhere in this book (see Chapter 55, "Esophageal Pressure Measurement"). Although it is theoretically possible to measure the full scale of the *P–V* relationship from residual volume (RV) to total lung capacity (TLC) and back to RV, in clinical practice *P–V* curves are usually measured between functional residual capacity (FRC) and TLC. Moreover, there is evidence to suggest that deflation curves are more reproducible than inflation curves,[2] and most publications on clinical applications of *P–V* curves focus on the deflation curve from TLC to FRC. Therefore, in this chapter we largely restrict ourselves to discussions of the deflation *P–V* curve.

P–V CURVE INTERPRETATION

From a clinical standpoint, interpretation of the *P–V* curve requires a systematic analysis of its component parts, pressure and volume. The mechanical relationship between changes in pressure and volume may be plotted in several ways, but, traditionally, volume as a percentage of predicted TLC is plotted on the ordinate and transpulmonary pressure in cm H_2O or kPa on the abscissa (Figure 8-1). Plotting the TLC in terms of its predicted value has the immediate advantage that abnormalities in lung volume can be seen at a glance. Thus, restriction or hyperinflation can be diagnosed directly from the graph as displacements of the curve to lower or higher volumes, respectively. In contrast, there is no need to display the transpulmonary pressure in terms of predicted values as there is little variation in the *range* of pressures among healthy individuals or even across species. For example, the maximal transpulmonary pressure in a mouse is of the same magnitude as in a human,[3] although the scale of the lung volume is clearly much different.

INSPECTION

Much of the diagnostic information in a *P–V* curve can be gleaned from inspection. The TLC and FRC can be determined by looking at the volume range of the curve. Similarly, the position of the curve on the abscissa yields information about overall stiffness. The maximum transpulmonary pressure ($P_{L,max}$) achieved is a measure of the maximal elastic recoil pressure against which lung inflation takes place. As $P_{L,max}$ is increased in cases of parenchymal lung restriction, such, as pulmonary fibrosis, and decreased in emphysema, this index provides some information about overall lung elasticity. It is, however, dependent on muscle

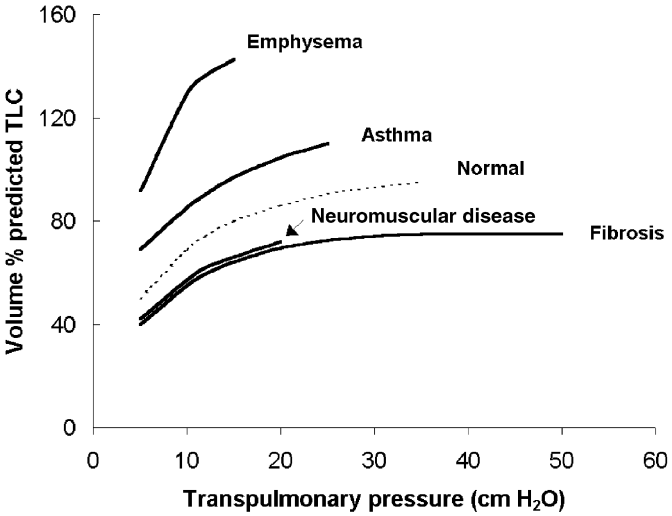

FIGURE 8-1 Examples of prototype *P–V* curves under different clinical conditions. Adapted from Hughes JMB, Pride NB, editors. Lung function tests: physiological principles and clinical applications. 1st ed. Philadelphia: WB Saunders; 1999. p. 49.

activity, and decreases in $P_{L,max}$ can reflect neuromuscular function or effort as well as decreased lung stiffness. The overall position and shape are very helpful diagnostically. Shifts to the left (lower P_L), particularly when accompanied by increased curvature and verticality, are strongly suggestive of emphysema (Figures 8-1 and 8-2A). Conversely, curves with high $P_{L,max}$ that are shifted downward and to the right are diagnostic of restriction due to increased parenchymal stiffness (Figures 8-1 and 8-2B). Normally shaped and positioned curves with decreased $P_{L,max}$ are suggestive of neuromuscular dysfunction.

P–V Indices

Although inspection may be useful for clinical purposes, it does not lend itself to comparisons among individuals, particularly in population studies. Furthermore, in some cases, the appearance of the *P–V* curve is ambiguous, with a shape that does not fully satisfy the criteria for emphysema, for example. To address this problem, a number of indices calculated from the *P–V* curve have been proposed as objective measures of lung elasticity. Each of these measures represents an attempt to deal with the characteristic nonlinearity of the *P–V* curve. Although many indices have been proposed for clinical and research use, this chapter focuses on the three most important: compliance, exponential analysis, and the use of transpulmonary pressures at multiple lung volumes.

Compliance Static compliance (C_{st}) is usually defined as the ratio of the change in volume to the change in pressure over a fixed volume range. Compliance is, in fact, the slope of the *P–V* curve when plotted with volume on the ordinate and transpulmonary pressure on the abscissa. This is referred to as a static compliance because the measurements of pressure and volume are made under conditions of zero flow. Measurements made during active breathing, with non-zero airflow, are referred to as *dynamic*. Dynamic compliance includes energy losses due to the viscoelastic properties of the lung, as well as those related to ventilatory inhomogeneity,[4] and are thus systematically different from static measurements.

Because of the nonlinear relationship between volume and pressure, compliance is not constant at all lung volumes. It is therefore necessary to calculate compliance over a limited portion of the *P–V* curve that is approximately linear. For practical reasons, the region near FRC is conventionally used as it provides a clinically relevant estimate

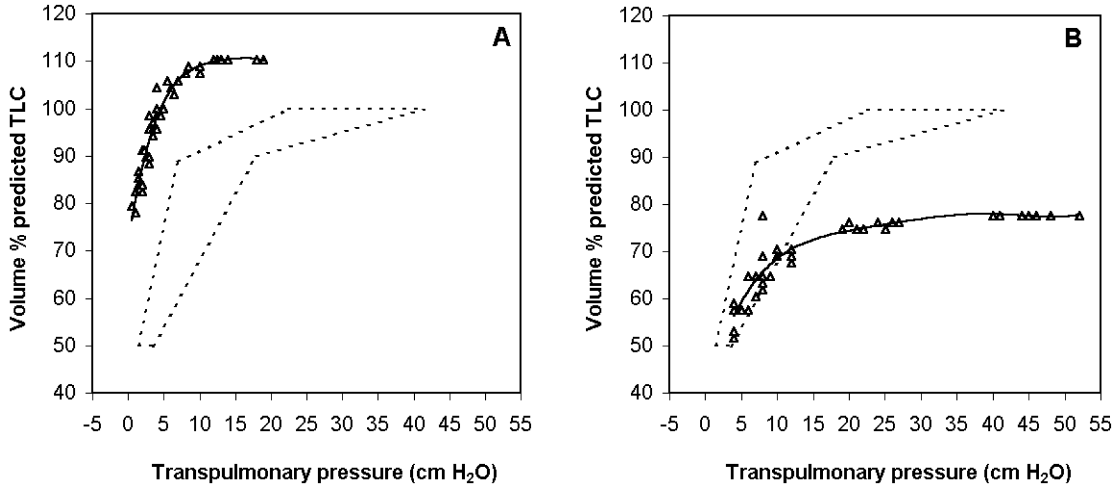

FIGURE 8-2 Examples of *P–V* curves in emphysema *A* and fibrosis *B* plotted as percentage predicted total lung capacity (TLC) versus transpulmonary pressure.[7] Single points represent individual measurements of pressure and volume. *Dashed lines* represent predicted normal range. The *P–V* indices for *A* were as follows: $C_{stat} = 0.973$ L/cm H_2O (247% predicted); $P_{L90} = 8$ cm H_2O (58.9% predicted); $P_{L,max} = 19$ cm H_2O (59.4% predicted); TLC = 7.5 L (110.3% predicted); $k = 0.2859$ (192.9% predicted). The *P–V* indices for *A* were as follows: $C_{stat} = 0.20$ L/cm H_2O (70% predicted); $P_L90 = 7$ cm H_2O (49.3% predicted); $P_{L,max} = 52$ cm H_2O (164.1% predicted); TLC = 5.3 L (76.1% predicted); $k = 0.1491$ (88.2% predicted).

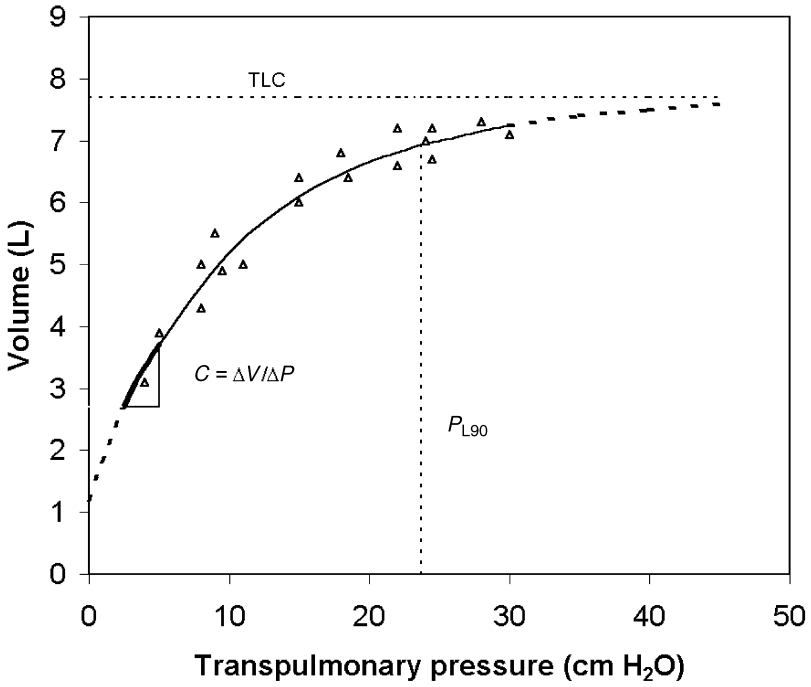

FIGURE 8-3 Demonstration of *P–V* indices. Volume is plotted on the ordinate and pressure on the abscissa. Each point represents one measurement of the *P–V* relationship. The *solid curve* is the result of fitting the equation $V = A - Be^{-kP}$, where V is lung volume and P is transpulmonary pressure. The *thick segment* represents the range over which compliance (C) is calculated as the slope of the *P–V* curve from FRC. The *vertical dashed line* represents the transpulmonary pressure at 90% of TLC (P_{L90}).

of lung stiffness in the tidal volume range (Figure 8-3). Most commonly, the ratio of the change in volume between FRC and FRC + 0.5 L, and the change in transpulmonary pressure over this volume range, is used:

$$C_{st} = \frac{\Delta V}{\Delta P}$$

C_{st} is reasonably useful, but because it scales proportionately to resting lung volume, it is subject to variation if FRC is not held constant. It is also difficult to compare individuals whose FRCs differ greatly. This is particularly important when comparing adults with children or when making comparisons across species. For this reason, it has been proposed to calculate a specific compliance (C_{sp}), in which the lung compliance is "corrected" by dividing by the resting lung volume (FRC).[5] The resulting value is somewhat more robust when comparisons across differently sized individuals are made and has been used to allow comparisons across species.

Exponential Analysis Another approach to dealing with the nonlinearity of the *P–V* curve has been to fit *P–V* data to nonlinear models and then describe the curve based on the parameters of this function. By far the most successful of these approaches is to fit *P–V* curve data to an exponential function, which reliably describes the *P–V* relationship between FRC and TLC, with the asymptote being close to TLC (see Figure 8-3). Since this is a nonlinear relationship, one needs to use either logarithmic transformation or an iterative fitting technique to do the calculations. Although several formulations for the exponential function have been proposed, the most widely used relationship, based on an approach first reported by Salazar and Knowles,[6] is shown here:

$$V = A - Be^{-kP}$$

In this equation, V is the lung volume, P is the transpulmonary pressure, and A describes the asymptote of the exponential which, in principle, should be slightly greater than the achieved TLC. The parameter B is the difference in volume between A and the intercept of the function with the ordinate. The parameter of greatest interest is k. Sometimes termed the shape constant, k is a dimensionless number that provides a measure of the curvilinearity of the curve. The more concave downward the curve, the greater the k value. Thus, in emphysematous patients, k is increased, whereas in fibrotic patients, it is low.

An important characteristic of k is that it is independent of lung volume. In principle, this means that similar values of k may be expected among individuals of differing size, making it an attractive candidate for a volume-independent measure of overall *P–V* curve shape. More importantly, since it describes the shape of the entire *P–V* curve, k is potentially very useful in population studies as an objective and quantitative measurement of the *P–V* relationship.

Multiple Transpulmonary Pressure Measurements Although indices such as C_{st} and k aim to encapsulate the

P–V curve in a single number, another approach to handling the nonlinear *P–V* curve has been to break it down into segments, describing it by a set of transpulmonary pressures at fixed proportions of the TLC. The *P–V* curve is thus described by the transpulmonary pressure at 90% of TLC ($P_{L,90}$), 80% of TLC ($P_{L,80}$), and so on down to $P_{L,40}$. Turner and colleagues[7] used this approach to report predicted values for normal *P–V* curves. Of these, $PL_{,90}$ appears to be the most robust, particularly as a marker of loss of elastic recoil, where it is more reproducible than measurements of $P_{L,max}$.[2]

CLINICAL APPLICATIONS

Emphysema and Chronic Obstructive Lung Disease

Although measurement of the static *P–V* curve has been applied clinically to a variety of lung diseases, the greatest interest has been in obstructive lung disease, particularly in cases of emphysema. It has long been known that emphysematous lungs exhibit diminished elastic recoil and that this decrease in stiffness is of great pathophysiologic importance. Although the advent of spirometry made it simple to detect airflow obstruction, confirmation of the diagnosis of emphysema was exceedingly difficult before CT scanning became available. Although bullae and widespread lung destruction can be detected on plain radiographs of the chest, emphysema has been considered a pathologic diagnosis that is confirmed only at autopsy or after surgery. This led to the hope that investigations of lung elasticity would be a helpful indicator of emphysema.

Before the invention of the esophageal balloon technique, measurement of the transpulmonary pressure was a key obstacle to the investigation of lung elasticity in emphysema. Christie was among the first to address this directly, by taking advantage of the practice of inducing therapeutic pneumothorax as a treatment for tuberculosis. In a classic publication, Christie[1] combined direct measurements of pleural pressure obtained through needles placed in the pleural space with spirometric measurements of lung volume to estimate pulmonary compliance in patients with emphysema. Christie laid the groundwork for future studies by demonstrating the feasibility of studying lung mechanics in vivo. Further advances in this area had to await the end of World War II, when electronic transducers and materials suitable for the construction of esophageal balloon catheter systems became available. By the early 1960s, the notion that emphysematous lung is significantly more compliant than normal lung, with a static *P–V* curve shifted leftward and upward (see Figure 8-2A), was well established in the literature.[8]

Attempts to relate compliance measurements to other features suggestive of emphysema have not been very successful. For example, Yip and colleagues[9] failed to find much evidence of correlation between increases in FRC and compliance in patients with stable chronic obstructive pulmonary disease (COPD). In contrast, the correlation between FRC and $P_{L,max}$ was much more significant, suggesting that data from the entire *P–V* curve are needed to adequately describe the changes in mechanics in emphysema, rather than limiting the measurements to the region near to FRC. This was consistent with a study by Silvers and colleagues,[10] who demonstrated the importance of loss of elastic recoil as a marker of emphysema even in cases of mild or minimal disease. The use of the shape factor *k* as a marker of mild or early emphysema has been evaluated in several studies. The results of studies in patients with emphysema did confirm increases in *k*,[11] but correlations with other markers of emphysema[2,12] or, later, with anatomic evidence of emphysema on CT scans was not as good as expected,[13] particularly in mild cases.

The lack of sensitivity of *P–V* curves in practice has not been completely explained. Several confounding factors certainly contribute. There is a natural loss of elasticity with age, independent of emphysema, so that in older subjects losses of recoil may be out of proportion to the degree of anatomic emphysema actually detected. Another problem relates to the heterogeneous nature of emphysema in most cases. Whereas the *P–V* curve represents the overall elastic behavior of the entire lung, emphysema typically causes regional destruction of the lungs. Measurement of average esophageal pressure changes and total lung volume may not be an effective way to investigate the behavior of the upper lobes that have been damaged by centrilobular emphysema. Under these conditions, the mechanical behavior of the most affected areas, where the ventilation is minimal and which make a negligible contribution to the vital capacity (VC), cannot be detected from the *P–V* curve. As Greaves and Colebatch pointed out,[11] the *P–V* curve and especially the *k* factor are most likely to reflect the less diseased parts of the lung, whereas anatomic measures of emphysema map the most damaged areas. This view is supported by classic physiologic–radiologic correlations carried out by Macklem and colleagues,[14] who used tantalum bronchograms to demonstrate the importance of the preserved areas of emphysematous lungs in determining their mechanical properties. In their studies, it was the nonemphysematous part of the lung that determined the compliance of the lung rather than the bullae. Furthermore, somewhat counterintuitively, the bullae exhibited low compliance, rather than the high compliance usually associated with emphysema.

Chest Wall For many years, it was believed that emphysema could lead, in at least some cases, to a decrease in chest wall compliance that, in some instances, would be sufficient to decrease overall respiratory system compliance. Although this has been found in several studies,[15,16] these investigations suffered from technical problems related to the difficulty in achieving full relaxation of the inspiratory muscles during the maneuver in often intensely dyspneic patients. Nevertheless, any decrease in chest wall compliance would have the dual effect of increasing the work of breathing and acting as a limiting factor in lung hyperinflation. In a careful study, Sharp and colleagues[17] demonstrated that the measured decrease in chest wall compliance in COPD patients is artifactual. They eliminated any inspiratory muscle activity with the use of neuromuscular

blockade, so that the purely passive static behavior of the chest wall could be measured. With fully relaxed musculature, they were able to inflate the lungs to volumes never reached in normal subjects, well above the normal TLC. They concluded that the thoracic wall compliance does not change significantly in emphysematous patients across the entire range of volumes that they explored. Thus, chest wall mechanics do not limit pulmonary hyperinflation in COPD patients.

Imaging The development of modern imaging techniques such as CT has revolutionized the study of emphysema pathophysiology. It has become possible to make anatomic assessments in living subjects and correlate them with measures of lung elasticity and other pulmonary function tests. High-resolution computed tomography (HRCT) can detect emphysema with high sensitivity and lends itself to the development of numerical algorithms for the quantification of disease extent and the relative importance of airway and parenchymal disease. Several approaches to this have been taken, ranging from subjective, visual scores of emphysema extent to objective scores based on the percentage of lung area occupied by pixels with low attenuation values. Indices based on the latter have been shown to be quite reproducible, providing a useful quantitative measure of emphysema. The results of studies in which imaging has been compared with pathologic assessments of emphysema have shown excellent correlations.

A few attempts have been made to relate HRCT evaluation and indices of lung elasticity, but they have yielded discrepant results. The results of some studies have demonstrated a poor correlation between the decrease in lung elastic recoil and emphysema score,[18] whereas those of others have shown a more significant correlation.[19] A major problem in interpreting the results of these studies is the lack of consistency of the indices used for both mechanics and imaging. For example, in some studies, $P_{L,max}$ was compared to a qualitative visual CT score,[18] whereas in others, k,[19] $P_{L,90}$,[19] and the natural logarithm of k have been used.[19] These difficulties have been compounded by variations in the patient populations.[13]

Most recently, Baldi and colleagues[13] carried out a detailed study in which all the main indices of lung mechanics (k factor, ln k, $P_{L,max}$, $P_{L,90}$) were compared to mean CT number and a quantitative CT emphysema score in 24 COPD patients with moderate-to-severe airflow obstruction. Only a weak correlation was found between loss of elastic recoil and the extent of emphysema, failing to reach statistical significance, although when indices of mechanics were plotted against the mean CT number, a measure of average tissue density, a significant correlation was found. These results parallel the studies on anatomic emphysema quantitation cited above, underscoring the inability of the *P–V* curve to reveal the most damaged areas of the lung. Instead, changes in the *P–V* curve seem to reflect what is going on in the relatively preserved, nonemphysematous parenchyma. Taken together, these findings tend to confirm that the *P–V* curve is not a useful measure of extent or severity of disease in emphysema.

Early Disease As the *P–V* curve seems to be highly influenced by those parts of the lung that are not yet greatly affected by anatomic emphysema, it is not unreasonable to hypothesize that measurement of *P–V* curves might be useful in detecting early changes in the lung parenchyma, before well-defined anatomic emphysema is present. Perhaps the real correlation between structure and function will be found at a more subtle level. Indeed, Cosio and colleagues[20] have presented evidence that there are significant microscopic changes in the lung parenchyma of healthy, "pre-emphysematous" smokers, in whom increases in the size of alveolar fenestrae were demonstrated. These lesions corresponded anatomically to the regions where centrilobular emphysematous changes would be typically seen in smokers. Indices of elastic recoil, in particular $P_{L,90,}$ correlated significantly with the mean area of the fenestrae. These findings led to the concept of "ultramicroscopic emphysema," which refers to increased size, irregular shape, and increased numbers of alveolar pores and fenestrae in smokers with negligible or absent gross emphysema. It is of note that these findings have recently been reproduced experimentally in guinea pigs exposed to cigarette smoke,[21] where a correlation was found between the number of pores and static compliance measured between 0 and 15 cm H_2O of transpulmonary pressure, as well as with TLC, FRC, and RV.

Another approach to the detection of early lung destruction in emphysema, again from the Cosio laboratory, was the development of the destructive index (DI), introduced as a light microscopic index of parenchymal damage in smokers.[22] Using point counting, Saetta and colleagues[22] calculated the ratio between the percentage of destroyed space and the total alveolar and ductal space. DI was able to differentiate the lungs of smokers from those of nonsmokers and was more sensitive than a preexisting index, the mean linear intercept (L_m). DI also showed a fair correlation with the functional indices, including the elastic properties. This index was refined further by Eidelman and colleagues,[23] who demonstrated that DI could be separated into two components: DI_b, which measures the breaks in alveolar septa, and DI_e, which measures the true emphysematous spaces. Only DI_b was significantly increased in the lungs of smokers and thus appeared to be a microscopic precursor of the subsequent gross destruction of the proximal portion of the lobulus.[23] This finding again reinforces the importance of heterogeneity of lung destruction in emphysema.

What of the relationship between lung mechanics and destruction? In 1989, Eidelman and colleagues reported a systematic study of heterogeneity of mechanical properties of the lung in smokers and subjects with α_1-antitrypsin deficiency.[24] Although some smokers exhibited the expected decrease in elastic recoil, increased compliance, and changes in shape of the *P–V* curve, as described by Macklem and Becklake[8] and similar to that seen in the α_1-antitrypsin–deficient subjects, others, despite decreased elastic recoil pressure, showed a significantly less accentuated slope of their *P–V* curves. In other words, they exhibited reduced rather than increased compliance. Similarly, the k factor was not increased in these subjects. It is of interest that the

patients whose lungs appeared to be stiffer also showed the most severe airflow limitation. This observation suggested the hypothesis that lung destruction in the smokers may be heterogeneous in a manner corresponding to the anatomic abnormalities present. Those with *P–V* curves resembling that seen in α_1-antitrypsin deficiency might have evidence of panlobular emphysema in their lungs, whereas the others could have a predominantly centrilobular pattern. Kim and colleagues[25] investigated this at a microscopic level, confirming the presence of centrilobular and panlobular patterns. Subsequent studies suggested that those individuals with the unexpected decrease in compliance all had the centrilobular variant.[26,27] These finding are consistent with the notion that distribution, rather than the severity of emphysema, influences the shape of the *P–V* curve.

Asthma

The notion that pulmonary mechanics may be abnormal in asthma is more controversial than it is for emphysema. Asthma is generally considered to be primarily an airway disease in which inflammation leads to increased capacity for airway smooth muscle shortening and intermittent bronchoconstriction. Although there is some evidence that the peribronchial parenchyma is inflamed in asthma,[28,29] asthma remains a disease of the tracheobronchial tree. Nevertheless, there is a long history of reports of abnormal lung mechanics in asthmatic patients. More than 30 years ago, Woolcock and Read[30] reported that VC is reduced in asthma. This change was associated with increased RV, FRC, and TLC, as might also be found in emphysema patients (see Figure 8-1). In our experience, in the present-day world of frequent use of inhaled corticosteroids, increases in TLC are rare among asthmatic patients. Nevertheless, the central issue, from the point of view of pulmonary elastic properties, is whether the increases in lung volume that may occur in uncontrolled asthma merely represent gas trapping behind closed airways or rather reflect loss of elastic recoil as occurs in emphysema.

There have been reports of abnormal *P–V* curves in asthma, both in remission and during acute exacerbations, with the principal finding being loss of elastic recoil. Decreases in recoil have been described as transient, reverting to normal after therapy with corticosteroids.[31] Among reports of lung static mechanical properties in asthma, there is a consensus that the compliance in the tidal volume range is unchanged, with a normal slope at FRC. When alterations are seen, they tend to affect the recoil at higher lung volumes.[31–35] A limitation of many studies of elastic recoil in asthma relates to technical difficulties with plethysmographic measurements of lung volumes in the setting of airflow obstruction. These limitations were not recognized until the 1980s, after many of these studies were completed. Nevertheless, Gelb and colleagues[36] have presented new interesting data in this regard. In a group of patients with moderate-to-severe chronic persistent asthma undergoing optimal treatment, and with no signs of emphysema, there is actually a marked loss of elastic recoil, and this loss of elastic recoil accounted for 34 to 50% of the decrease in maximum expiratory flow at 70 and 80% TLC. Based on these data, the authors have hypothesized that airflow limitation in asthma may result from mechanisms in the far periphery of the lung, involving structural changes in the parenchyma and distal airways, rather than being limited to the more proximal airways. These findings are consistent with observations from the Denver group, who have described inflammatory involvement of the alveolar and distal airways in transbronchial biopsy specimens from asthmatic subjects.[28,29,37] Macrophages, $CD4^+$ lymphocytes and eosinophils were detected, and in some cases[28,29] there was a correlation between alveolar infiltrate and decline in lung function. It is certainly conceivable that inflammation in the lung periphery could ultimately lead to damage or disruption of stromal components of the lung, including elastic fibers, and this would account for the loss of elastic recoil, whereas bronchoconstriction per se has been shown to increase the dynamic elastance without affecting the static *P–V* curve.[38] Changes in lung stiffness have the potential to alter coupling between the lung and the airways, leading to enhanced responsiveness, particularly in the supine position[39] or at night.[40]

Another mechanism of potential relevance occurring in asthma involves the important role of surfactant as a determinant of pulmonary mechanical behavior. Murine data suggest that surfactant may be altered in allergic inflammation,[41] and this suggestion is supported by a modest amount of data from humans.[42] It is known that alveolar surfactant, through the action of its components surfactant protein-B (SP-B) and, to a lesser extent, SP-C, contributes to the mechanical stability of the alveoli and distal airways, thus preventing air trapping through distal airway closure. In heterozygous SP-B–deficient mice, airway closure is enhanced, leading to increased RV, whereas their homozygous counterparts die soon after birth.[43] Moreover, Th2 cytokines prominent in asthma, such as interleukin-4 (IL-4) and IL-5, may alter the function of SP-B[44] and SP-C.[45] Finally, in addition to their implications for lung mechanics, changes in surfactant could have immunomodulatory implications; some components of surfactant bind allergens, so these are not available to bind IgE.

Fibrotic Lung Disease

Although idiopathic pulmonary fibrosis (IPF) is the prototype of these disorders, there are many etiologic categories of fibrosis that share the mechanical consequence of decreased lung volumes (restriction) with increased lung recoil or decreased compliance. IPF is characterized by progressive distortion of the lung architecture, with inflammation and accumulation of fibrotic tissue, eventually leading to the development of what is termed "end-stage lung." In its advanced stages, this type of lung disease is characterized by the so-called "honeycomb" pattern, with diffuse fibrosis, loss of recognizable architectural organization, cystic lesions, and traction bronchiectasis. The functional counterpart of these changes is decreased TLC, usually accompanied by a reduction in RV.[46,47] The mechanical similarities among these diseases lead to similarities in the appearance of the *P–V* curve, which is shifted downward and to the right (see Figure 8-2B).

It is noteworthy that the decrease in the volume of the airspaces is accompanied by an increase in tissue volume, due to collagen deposition, and so the total intrathoracic volume might in some cases be less altered than would be predicted from the gas volume evaluation alone.[4] Although compliance is decreased, the shape of the *P–V* curve is less affected, at least as reflected in the *k* factor calculated from exponential curve fitting.[46]

As with emphysema, the diagnostic utility of measuring the *P–V* curve in parenchymal restrictive disease is less of an issue than in the past. The high-resolution CT scan is now central to the diagnosis of interstitial lung diseases, including IPF. Nevertheless, the *P–V* curve can be a sensitive and effective approach to diagnosis, particularly in difficult cases with multiple disease processes. For example, in a group of patients with progressive systemic sclerosis, none of whom had signs of pulmonary involvement shown by standard radiography or reduction of TLC, the static compliance was reduced in one-third of cases.[48]

Extrapulmonary Diseases

In neuromuscular diseases resulting in weakness of the respiratory muscles, the involvement of inspiratory and expiratory muscles results primarily in changes in lung volumes, typically a decrease in both VC and TLC,[49,50] the severity of which correlates with the degree of muscle impairment. However, reduction in the amplitude of volume excursion is not the only feature of the *P–V* curve in neuromuscular disease. A decrease in the slope of the *P–V* curve can often be observed (see Figure 8-1), suggesting a reduction in lung compliance, the principal determinant of which appears to be the frequent presence of microatelectasis within the parenchyma. A change in the passive properties of the chest wall has also been reported, and in children, in particular, an increase in chest wall compliance has been demonstrated.[51] This change, probably attributable to the higher amount of cartilage in the thoracic cage,[52] can represent a potential determinant of thoracic deformation. In elderly subjects, however, the chest wall is stiffened, possibly through accumulation of fibrotic tissue among the muscle fibers, leading to a reduction in chest wall compliance. The rib cage in quadriplegic patients also appears to be significantly stiffer than in normal subjects.[53] In addition, it has been suggested that patients with chronic neuromuscular disease eventually develop a decrease in chest wall outward elastic recoil (or increase in transthoracic pressure),[54] which can result in a decrease in FRC, often observed in these patients.[49,50] An alternative or complementary explanation of the decrease in FRC is that the measured FRC does not represent the true relaxation volume of the respiratory system in patients with neuromuscular disease but rather a lower volume actively reached by the subjects, so that the subsequent inspiration can benefit from the descent of the diaphragm and the relaxation of the abdominal muscles.[4] Deformities of the thoracic cage, such as severe scoliosis or pleural thickening, can also impair ventilatory function directly by impairing pulmonary inflation, resulting in a restrictive syndrome. It remains unclear, however, whether some of these abnormalities can be attributed to changes in the elastic properties of the lung.[4]

CONCLUSIONS

Although the measurement of *P–V* curves has gone out of fashion, this remains a useful technique for the measurement of the functional state of the lung. Particularly in the context of emphysema research, the *P–V* curve appears to be a relatively simple means of detecting evidence of lung destruction before it is evident on CT scans and of differentiating among patterns of destruction in the lung that may be of pathophysiologic importance. In difficult cases with mixed radiologic patterns of disease, the *P–V* curve may be the only means to determine the physiologic basis of a patient's disordered breathing.

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