Current Practice in Pulmonary Function Testing

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More than 30 million Americans have chronic obstructive pulmonary disease (COPD) and asthma, with internists, pediatricians, and family physicians providing most of their medical care. Recent management guidelines for asthma and COPD recommend regular use of spirometry for the diagnosis and management of these disorders. Because of the development of easy-to-use office-based spirometers, an increasing number of physicians have ready access to spirometry. Beyond simple spirometry, various tests are available from many pulmonary function laboratories for more detailed evaluation of patients with respiratory disorders. For these reasons, all physicians who care for patients with pulmonary disease must understand basic pulmonary function testing and have a fundamental understanding of more sophisticated tests. A series of performance standards has been developed for improved accuracy and precision of pulmonary function tests. Physicians responsible for administering and interpreting pulmonary function tests, even simple spirometry, must be aware of relevant guidelines. This concise review addresses current indications for pulmonary function testing, provides an overview of the studies commonly available in modern pulmonary function laboratories, and includes comments on basic interpretation and testing standards.


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espiratory disorders are a considerable cause of morbidity and mortality in the United States. Together, asthma and chronic obstructive pulmonary disease (COPD) cost Americans more than $36 billion per year in direct health care costs and twice that amount when indirect costs (lost productivity, premature death, etc) are included.1-4 Currently, more than 17 million Americans have COPD, the fourth leading cause of death in the United States and a major cause of morbidity. A comparable number of Americans have asthma, which not only is the primary cause of school absences in the United States but also has been identified as a global health risk by the World Health Organization.1-4

Clinical pulmonary function testing (PFT) plays an essential role in the management of patients with, or at risk for, respiratory dysfunction. These tests provide objective lung function assessments that the clinician can correlate with highly subjective symptoms such as dyspnea. These tests also yield reproducible, quantitative results, allowing longitudinal monitoring. This is important because respiratory symptoms correlate poorly with disease severity and progression.5,7

Table 1 summarizes the numerous, currently accepted clinical indications for PFT. Among the objectives of PFT endorsed by the American Thoracic Society (ATS) are the description of dysfunction, assessment of severity, and estimation of prognosis in lung disease. Pulmonary function testing is established as an essential diagnostic criterion for specific disorders, including asthma and COPD. Both diseases are characterized by, and their progression related to, exacerbations and periods of stability shown by PFT. When used to monitor patient progress, PFT allows assessment of both beneficial and untoward effects of interventions and can provide early and ongoing surveillance after patient exposures to environmental insults, radiation therapy, and medications with known pulmonary toxicities. Furthermore, PFT is sensitive to various extrapulmonary disorders, including neuromuscular, cardiovascular, and inflammatory processes.5,6,8

Because of its broad utility, the role of PFT has extended beyond the purview of the pulmonary specialist and is increasingly vital in primary care medicine, sports medicine, occupational medicine, and public health. This utility has also gained the attention of third-party payers, who now require preplacement or preinsurance PFT to disclose or quantify occult cardiopulmonary disease in some circumstances. Whether such screening of asymptomatic patients confers health benefits remains controversial. However, physician-initiated screening of selected populations (eg, smokers) apparently allows the identification of pre-
clinical lung diseases, which in turn may allow early inter-
vention while these diseases remain most treatable. Such
intervention for COPD has been shown to improve survival.

Accumulating data from large-scale clinical investiga-
tions, including the third National Health and Nutrition
Examination Survey and the Lung Health Study, have
confirmed the ability of PFT to identify presymptomatic
lung disease in smokers. These data, along with observa-
tions that abnormal PFT results seem to increase the likeli-
hood that smokers will seek medical treatment and attempt
taking up smoking cessation, prompted recommendations from the
National Lung Health Education Program, which promotes
the use of spirometry by primary care physicians. This con-
sensus statement from the American College of Chest Physi-
cians and the National Heart, Lung, and Blood Institute
recommends, in part, the initiation of office-based screen-
ing spirometry by primary care physicians for current
smokers aged 45 years or older or for any smoker with
respiratory complaints. In addition to recommending the
use of screening and symptom-induced spirometry, this
statement endorses spirometry as a tool for global health
assessment.

ILLUSTRATIVE CASE

Mr B is a 60-year-old man who presents for evalua-
tion of progressive dyspnea. Mr B, a former smoker,
denies wheezing, cough, chest pain, or environmen-
tal exposures but suggests that his symptoms may be
exacerbated in the supine position. Results of his
PFT are shown in Table 2 and Figure 1.

SPIROMETRY

Spirometry measures the volume of air (liters) exhaled or
inhaled by a patient as a function of time. The amount of air
displaced by a maximal exhalation or inhalation maneuver
is called the vital capacity (VC). Flows are measured or
calculated as the rate of volume change as a function of
time (liters/second).

Most of the reported spirometric values are obtained
from a forced expiratory vital capacity (FEVC) maneuver,
which requires the patient to forcefully expel air from a
point of maximal inspiration (total lung capacity [TLC]) to
a point of maximal expiration (residual volume [RV]). The
forced inspiratory vital capacity (FIVC) maneuver requires
forced inhalation from RV to TLC. From the FEVC are
derived such critical values as the forced vital capacity
(FVC), the forced expiratory volume in the first second of
the FVC maneuver (FEV1), and the FEV1/FVC ratio. In
addition to reporting these values, a graphic display of the
flows from the FEVC and FIVC maneuvers plotted as a
function of volume (flow-volume loop) provides a more
comprehensive view of a patient’s respiratory mechanics

<table>
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<th>Table 1. Indications for Pulmonary Function Testing</th>
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<td>Pulmonary disease evaluation</td>
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<td>Symptom-triggered: cough, wheeze, dyspnea (rest, exertional, orthopnea)</td>
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<tr>
<td>Physical examination-triggered: wheeze, crackle, hyperinflation, prolonged expiratory phase, clubbing, cyanosis, altered thoracic structure/motion, altered diaphragmatic excursion, altered respiratory rate or pattern</td>
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<td>Diagnostic test-triggered: abnormalities of arterial blood gas, chest x-ray, oximetry</td>
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<td>Nonpulmonary disease evaluation</td>
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<tr>
<td>Cardiac disease, especially with congestive heart failure or hypoxemia</td>
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<td>Neuromuscular disease, especially with concerns about respiratory muscle weakness</td>
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<tr>
<td>Vascular disease, inflammatory or thrombotic</td>
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<tr>
<td>Inflammatory diseases, including rheumatologic and gastrointestinal diseases</td>
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<tr>
<td>Pulmonary exposure evaluation</td>
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<tr>
<td>Occupational exposures</td>
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<td>Environmental exposures</td>
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<td>History of or current use of medications with pulmonary toxicity</td>
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<td>History of radiation therapy (head, neck, chest, upper abdomen)</td>
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<td>Monitoring</td>
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<td>Pulmonary disease</td>
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<td>Assessment of treatment benefit/adequacy</td>
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<td>Assessment of disease progression</td>
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<td>Determination of prognosis</td>
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<tr>
<td>Detection of subclinical changes in pulmonary function</td>
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<tr>
<td>Pulmonary impact of nonpulmonary disease</td>
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<tr>
<td>Cardiac disease</td>
</tr>
<tr>
<td>Neuromuscular disease</td>
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<tr>
<td>Vascular disease</td>
</tr>
<tr>
<td>Medication effects/pulmonary toxicities</td>
</tr>
<tr>
<td>Screening</td>
</tr>
<tr>
<td>Smokers aged 45 years or older</td>
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<tr>
<td>Smokers with respiratory symptoms</td>
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<tr>
<td>Individuals potentially exposed to occupational hazards</td>
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<td>Global health assessments</td>
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<td>Evaluation of disability</td>
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<td>Preoperative assessment</td>
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<td>Possible lung resection</td>
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<tr>
<td>Thoracoabdominal surgery</td>
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<tr>
<td>Public health/epidemiological evaluations</td>
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</table>

and allows identification of subtle abnormalities and ma-
nearve errors.

Interpretation of abnormal spiograms begins with dif-
f erentiation of obstructive disorders (asthma, emphysema,
chronic bronchitis) from restrictive disorders (fibrosis, chest
wall limitation, pleural disorders, neuromuscular disorders).

The ATS defines airflow obstruction as a disproportio-
nate reduction in maximal airflow with respect to the maxi-
mal volume of air that the patient can displace from the
lungs. Therefore, reductions in the FEV1/FVC ratio (<70%) are
typical of obstructive disorders. The FEV1 is used to
grade the severity of obstruction. Typically, FEV1 and
other values are compared with predicted normal values
derived from population-based reference equations. They
are reported both as raw values and as a percentage of the
predicted or reference values. The forced expiratory flow

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Table 2. Pulmonary Function Testing Results*

<table>
<thead>
<tr>
<th>Tests</th>
<th>Predicted value</th>
<th>Observed value</th>
<th>% Predicted</th>
<th>% Change†</th>
<th>Post-bronchodilator†</th>
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<tbody>
<tr>
<td>Lung volumes</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>TLC (L)</td>
<td>6.82</td>
<td>4.95</td>
<td>73</td>
<td></td>
<td></td>
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<tr>
<td>VC (L)</td>
<td>4.74</td>
<td>2.73</td>
<td>58</td>
<td></td>
<td></td>
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<tr>
<td>RV (L)</td>
<td>2.08</td>
<td>2.22</td>
<td>107</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV/TLC (L)</td>
<td>30.5</td>
<td>44.9</td>
<td>147</td>
<td></td>
<td></td>
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<tr>
<td>Spirometry</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>FVC (L)</td>
<td>4.74</td>
<td>2.13</td>
<td>45</td>
<td>2.36</td>
<td>+10</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>3.69</td>
<td>1.64</td>
<td>44</td>
<td>1.80</td>
<td>+10</td>
</tr>
<tr>
<td>FEV₁/FVC (L)</td>
<td>77.9</td>
<td>76.8</td>
<td>99</td>
<td>76.3</td>
<td></td>
</tr>
<tr>
<td>MVV (L)</td>
<td>142</td>
<td>40</td>
<td>28</td>
<td></td>
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<tr>
<td>Maximal respiratory pressures</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>P₁ max (mm Hg)</td>
<td>–110</td>
<td>–54</td>
<td>49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pₑ max (mm Hg)</td>
<td>206</td>
<td>99</td>
<td>48</td>
<td></td>
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<tr>
<td>Diffusing capacity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D₁CO₂‡</td>
<td>28.7</td>
<td>27</td>
<td>94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vₐ (L)</td>
<td>6.57</td>
<td>4.53</td>
<td>69</td>
<td></td>
<td></td>
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<tr>
<td>Oximetry</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resting O₂ sat (%)</td>
<td>96</td>
<td>91</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise O₂ sat (%)</td>
<td>96</td>
<td>84</td>
<td>NA</td>
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</tbody>
</table>

*Test results for Mr B, aged 60 years; height, 177.8 cm; weight, 104.1 kg; body mass index, 32.9. D₁CO₂ = diffusing capacity of lung for carbon monoxide; FEV₁ = forced expiratory volume in the first second; FVC = forced vital capacity; MVV = maximum voluntary ventilation; NA = not applicable; O₂ sat = oxygen saturation; P₁ max = maximal expiratory pressure; Pₑ max = maximal inspiratory pressure; RV = residual volume; TLC = total lung capacity; Vₐ = alveolar volume; VC = vital capacity.

†Values shown are the only ones of importance in this column.
‡Unit is mm CO₂·min⁻¹·mm Hg⁻¹.

(25%-75%), or FEF₂₅₋₇₅ is the mean expiratory flow rate in the middle half of the FVC maneuver. It is a sensitive but nonspecific indicator of airway obstruction. If inspiratory flows are reduced out of proportion to expiratory flows, variable extrathoracic (upper airway) obstruction may be inferred.

A reduction in the FVC with a normal or elevated FEV₁/FVC ratio is suggestive of restriction. Measurement of lung volumes gives more definitive evidence of the presence of restriction. When a restrictive disorder is identified, severity is graded by the reduction in observed FVC compared with the predicted value.

The maximum voluntary ventilation (MVV) maneuver requires maximal inspiratory and expiratory effort over 12 to 15 seconds to estimate maximum ventilatory capacity in liters per minute. The MVV is typically 30 to 40 times the patient’s FEV₁ but may be reduced by upper airway obstruction, respiratory muscle weakness, or poor maneuver performance (ie, due to poor instruction, poor understanding, poor effort, coughing, or other disease-related factors).

Spirometry performed after inhalation of a bronchodilator may help predict response to therapy and has prognostic importance for both COPD and asthma. The ATS defines a significant bronchodilator response as an increase in either FEV₁ or FVC of 12% or more and 0.2 L or more from baseline. Spirometry after bronchoprovocation challenge with methacholine, exercise, or other exposure is useful in identifying airway hyperreactivity. Most protocols require a 20% decrease in FEV₁ to consider a bronchoprovocation challenge positive. Other forms of bronchoprovocation (cold air, exercise) will seldom be positive when the methacholine challenge is negative.

Although population-based reference equations are required for initial spirogram interpretation, comparison to prior studies is essential in spirometric monitoring of individual patients. Longitudinal comparisons, performed to account for normal age-dependent decline in lung function, often reveal trends that reflect changes in disease activity. Identification of such trends is crucial to the management of patients with asthma, COPD, pulmonary fibrosis, and lung transplants.

Spirometric results correlate strongly with morbidity and life expectancy. Compared with other medical tests, spirometry is safe, quick, and inexpensive. However, it is highly effort dependent and requires cooperation between the patient and administering technician to ensure data quality. For this reason, the ATS has issued several statements regarding technician training, equipment quality, and standardization of technique. The clinician must understand that a single value (eg, FEV₁) does not reveal the complete clinical picture for patients with complex diseases such as COPD. Similarly, the variability that is characteristic of asthma may require repeated spirometric assessment, rather than reliance on a single testing session.
Mr B’s spirometry shows proportional reductions in expiratory flows (ie, preserved FEV/FVC ratio), suggesting restriction. There is no indication of airways obstruction and no substantial change in flows after bronchodilator use. The MVV reduction without an altered FIVC suggests possible respiratory muscle weakness.

LUNG VOLUMES
Although spirometry can measure inhaled and exhaled volumes, it cannot determine the total amount of air in the lungs at full inspiration (TLC), the amount of air remaining in the lungs at the end of quiet (tidal) expiration (functional residual capacity), or the amount of air remaining after maximal expiration (RV). These volumes can be determined by any of 3 techniques: (1) inert gas dilution, in which volumes are calculated from the equilibrated concentration of a known volume and concentration of gas, usually helium; (2) nitrogen washout, in which volume calculations are based on expired nitrogen concentrations before and after breathing pure oxygen; and (3) body plethysmography, which uses Boyle law ($P_1V_1 = P_2V_2$) to determine lung volumes from pressure and volume changes during respiration in a sealed box. Although each technique has technical limitations, all are physiologically sound methods of providing accurate results.

The TLC is reduced in restrictive disorders, whether because of pulmonary parenchymal disorders or chest wall abnormalities (pleural effusion, chest deformity, muscular weakness). The TLC may be normal in obstructive disorders or may be elevated (hyperinflated) due to air trapping. In patients with hyperinflation, the RV and RV/TLC ratio are typically increased.15 Restriction caused by parenchymal processes (eg, fibrosis) typically yields reductions in all lung volumes, similar to their proportional reductions in spirometric values. In contrast, neuromuscular weakness and some cases of chest wall limitation cause reductions in TLC but increases in RV and the RV/TLC ratio. Because of the increased RV/TLC ratio, these restrictive disorders may be confused with obstructive disorders. A skilled interpreter must be mindful of this potentially confusing pattern.

Mr B’s plethysmography shows restriction (reduced TLC), but there is also an increased RV/TLC ratio. Spirometric results indicate that the restriction is severe (FVC <50% of predicted value).

DIFFUSING CAPACITY
Spirometry and lung volumes elucidate the mechanics of ventilation but do not address the gas-transfer function of the lung. With use of a highly diffusible gas (carbon monoxide [CO]) as a surrogate for oxygen, the diffusing capacity of lung for CO ($D_{LCO}$) estimates the patient’s ability to absorb alveolar gases. The $D_{LCO}$ reductions occur in disorders of the pulmonary parenchyma, vascular abnormalities, reductions in effective alveolar units (eg, lung resection, emphysema), and anemia. Conversely, conditions resulting in an increased effective pulmonary blood volume cause an elevated $D_{LCO}$. Patients with asthma often have an increased $D_{LCO}$, probably and primarily due to an increased pulmonary blood volume. Other conditions resulting in an elevated $D_{LCO}$ include obesity, left-to-right intracardiac shunt, polycythemia, and postexercise physiology.

Mr B’s $D_{LCO}$ is relatively preserved.

MAXIMAL RESPIRATORY PRESSURES
Maximal respiratory pressures (MRPs) help in the evaluation of patients with neuromuscular causes of respiratory dysfunction. Both inspiratory and expiratory pressures are reduced in generalized neuromuscular disease (eg, amyotrophic lateral sclerosis) or in poor maneuver performance. Maximal inspiratory pressure is selectively reduced with diaphragmatic dysfunction. Patients with spinal cord inju-
ries but intact phrenic nerves have respiratory pressure reductions predominantly affecting expiratory pressures. This information may be helpful in determining the etiology of respiratory symptoms but has an equally important prognostic role. The MRP can help evaluate airway protective capacity (ie, the ability to generate adequate cough), predict successful weaning from mechanical ventilation, and assess the severity and progression of neuromuscular weakness.

Mr B’s MRPs are severely reduced, suggesting neuromuscular weakness or poor performance.

OXIMETRY

With use of noninvasive pulse oximetry, arterial oxyhemoglobin saturation can be estimated at rest and after standardized step exercise. Desaturation measured at either time point is a sensitive indicator of gas exchange abnormalities. Also, oximetry has been used to screen for opportunistic pneumonias in patients with acquired immunodeficiency syndrome and is helpful in titration of oxygen therapy.

Mr B has a gas exchange abnormality, showing abnormal rest oximetry and further desaturation with exercise.

EXERCISE TESTING

Dyspnea during exertion is a common symptom. Various exercise protocols have been developed to distinguish among a broad variety of causes of this nonspecific complaint. Cardiopulmonary exercise testing (CPX) engages subjects in graded exercise to a defined end point or to exhaustion. Population-based reference equations and baseline spirometric data are used to predict patients’ cardiac, ventilatory, and gas exchange responses to exercise. Comparison of actual performance to predicted values can usually distinguish between cardiac and pulmonary causes of exercise limitation. Cardiopulmonary exercise testing may be more invasive than other forms of PFT and requires more patient effort. This, combined with additional costs of staffing, equipment, and space, makes CPX somewhat less widely available than the other testing described in this review. However, CPX can be extremely helpful in assessing unexplained dyspnea and in reassuring some patients by excluding cardiac or pulmonary disease when deconditioning is the primary cause of their dyspnea.

SPECIAL SITUATIONS

Obesity

Patients who are obese and have dyspnea often wheeze and are commonly diagnosed as having asthma. A recent study found that the most obese 20% of a study population had higher rates of clinical asthma diagnoses and bronchodilator use than the rest of the population. However, spirometry showed that the same obese persons had less evidence of airflow obstruction than did less obese persons. Obese patients are prone to dyspnea as a result of increased chest wall impedance, which causes increased work in breathing. The role of spirometry is crucial in the diagnosis of asthma in obese patients, perhaps even more than in nonobese patients, to facilitate the appropriate administration of bronchodilators to those (and only to those) patients for whom they are indicated.

Preoperative Assessment

Pulmonary function testing is commonly used for preoperative risk stratification. Vital capacities less than 50% of predicted, FEV₁ values less than 50% of predicted or less than 2 L (especially <0.8 L), and MVV reductions with respect to FEV₁, hypercapnia, and hypoxemia have all been associated with increased risk of perioperative pulmonary complications. No study has shown improved surgical outcomes with preoperative spirometry, but because of its predictive role, spirometry is used often to guide perioperative management of patients with increased risk of respiratory complications, such as smokers or patients with respiratory symptoms. Since respiratory complications are common after thoracic and upper abdominal surgery, PFT often is obtained before these procedures. For elective lung resection, PFT is performed virtually universally (and correlated with vascular or radiographic studies, if necessary) to estimate postresection pulmonary reserve and to guide perioperative care.

SUMMARY

Pulmonary function testing has well-established utility, and its use in the management of COPD and asthma by generalists is expected to increase. It has been shown clearly that PFT has greater precision than use of either symptoms or physical examination for assessment of the severity of lung disease. For certain lung diseases, including asthma and COPD, PFT is recommended for both diagnosis and management. Numerous investigations have shown a high degree of sensitivity of PFT for nonpulmonary diseases. In fact, data from the Framingham Heart Study suggest that spirometric changes have greater prognostic importance than do many cardiac tests in establishing prognoses in congestive heart failure.

Cost-effectiveness analyses have not been performed to evaluate PFT in disease management. Spirometry and oximetry are inexpensive and provide a great deal of diagnostic information compared with other tests. Spirometry is recommended for the diagnosis, periodic assessment, and management of asthma and COPD. Spirometry and oxim-
etry are increasingly important tools in primary care medicine. Other pulmonary function tests fall into the realm of more specialized pulmonary centers and practitioners.

Mr B showed a severe restrictive process without evidence of obstruction. Reductions in Mr B’s MVV and MRP (without associated FIVC truncation), likely aggravated by his obesity, suggest neuromuscular weakness as the primary cause of his dyspnea. Clinical evaluation revealed bilateral diaphragmatic paralysis and diffuse weakness, apparently due to chemotherapy-associated neurotoxicity. Eventual improvement in the neuropathy was associated with improvement in lung volumes and gas exchange abnormality, suggesting that Mr B’s ventilatory limitation was the primary contributor to his hypoxemia.

REFERENCES

Questions About PFT

1. Which one of the following can cause an increased DLCO?
   a. Pulmonary fibrosis
   b. Emphysema
   c. Pulmonary embolism
   d. Asthma
   e. Lung resection surgery

2. Upper airway obstruction characteristically reveals an altered FIVC flow-volume curve and which one of the following?
   a. Reduced TLC
   b. Reduced MVV
   c. Reduced RV
   d. Reduced DLCO
   e. Reduced maximal expiratory pressure

3. Which one of the following is most suggestive of an obstructive disorder?
   a. FEV1/FVC ratio of <70%
   b. FVC <70% of predicted
   c. TLC <70% of predicted
   d. DLCO <70% of predicted
   e. Maximal inspiratory pressure <70% of predicted

4. Which one of the following suggests air trapping in chronic obstructive pulmonary disease?
   a. Increased RV/TLC ratio
   b. Decreased TLC
   c. Decreased DLCO
   d. Decreased RV
   e. Increased maximal inspiratory pressure

5. Which one of the following can be determined by spirometry?
   a. TLC
   b. Functional reserve capacity
   c. RV
   d. DLCO
   e. VC

Correct answers: 1. d. 2. b. 3. a. 4. a. 5. e