SECOND EDITION



# Handbook of Pulmonary & Critical Care Medicine

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CHAPTER

# 4

# Pulmonary Function Tests

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## INTRODUCTION

There is as yet no single test that can provide sufficiently detailed information on all aspects of lung function. Instead, depending on the clinical scenario, one must do one or more procedures to answer a particular question. Further, the available options vary greatly in terms of ease of conducting the test, equipment and technician requirements, test performance characteristics, and procedure cost.

## SPIROMETRY

Spirometry is the most common and most widely used lung function test, although its true potential still needs to be realized. One needs to pay careful attention to follow the standard procedures while performing and interpreting the test. Because the residual volume in lungs cannot be exhaled, spirometric measurements are limited to the vital capacity and its subdivisions (Fig. 4.1).

### Indications and Contraindications

The most common indication for doing the test is a functional evaluation of patients with lung disease. The presence of spirometric abnormalities, as well as the degree of impairment, provides useful information about the disease severity and pulmonary reserve of the patient. Serial measurements can provide information about disease progression, as well as response to prescribed treatment. The test also has an important role in clinical trials. Spirometry is also used as a screening tool for studies in epidemiologic surveys, and to screen at-risk populations for subclinical disease (for example,

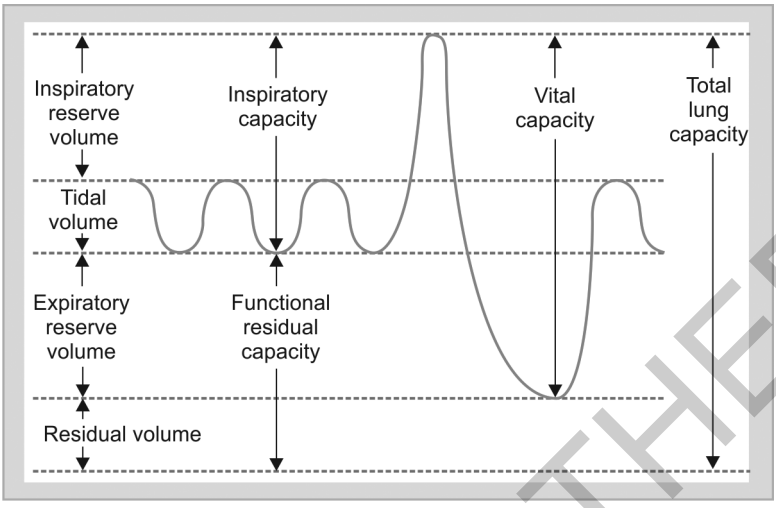


**Fig. 4.1:** Various lung volumes and capacities in relation to the spirometry tracing. Note that residual volume cannot be determined through conventional spirometry.

preoperative assessment, or detecting chronic obstructive pulmonary disease (COPD) among asymptomatic smokers). The test is also utilized in occupational setting, both for detecting work-related respiratory disorders, and for disability assessment in symptomatic people (for example, as part of compensation procedures). Finally, spirometry is an important research tool for understanding pathophysiology and temporal course of several diseases.

Any benefit from the information obtained through this test should be carefully weighed against patient discomfort and risk. The test is better avoided in pregnant and severely dyspneic patients. It should also not be carried out in patients where pressure swings due to a forced expiratory maneuver can worsen existing conditions (such as ruptured tympanic membrane, bronchopleural fistula, ongoing hemoptysis, etc.). Uncooperative patients, and those on life support systems, should also not undergo the test.

## Equipment

A wide range of apparatus, ranging from handheld portable devices to large equipment, and from predominantly manual to completely automated systems, is available to perform spirometry. Although many factors such as cost, patient load, clinical requirements, etc. determine the choice of machine, it is important to use one that confirms to some minimum technical specifications necessary to obtain valid results.

Most commercially available spirometers nowadays are computerized systems that employ a transducer to convert a mechanical signal to an electrical one, and display the output in a fashion understood by the operator. These equipment can be divided into two broad categories: (1) volume displacement spirometers and (2) flow-sensing spirometers. The former work with volume as the primary output, and flow is a derived parameter. Such machines can have

a water seal, a dry-rolling seal, or a bellows type design. Flow sensing devices can either be electronic turbines, or use electronic pneumotachometers (sensors that estimate airflow from the change in pressure occurring across a suitable resistance), which in turn can have a flow-resistive, a heated wire, or an ultrasonic design. As opposed to volume displacement spirometers, these machines measure flow as the primary signal, which is time-integrated to yield volume estimates.

## Reference Values

The basic purpose of pulmonary function testing is to identify persons with abnormal lung function. To know what is abnormal, we must first define what is normal. Predicted normal values can be obtained from studies carried out in healthy subjects. They are usually in the form of a regression equation describing the predicted value as a function of gender and anthropometric data (e.g. height, weight, etc.), and differ greatly with ethnicity. Any value below the predicted normal is not necessarily reduced, since the normal value is a range rather than a fixed point. This introduces the concept of "lower limit of normal" or LLN, which can be defined in several ways. The simplest (and most widely used) method is to use a fixed percentage of predicted value. For example, a value less than 80% of predicted FEV1 can be considered abnormal. However, there is very little statistical or physiological basis for such an approach. A more valid approach is to use lower 95% confidence limits of the regression equation, or subtract 1.645 times the standard error of estimate of the regression equation from the predicted value, to define the LLN. Any value below the corresponding LLN is considered abnormal. It is very important to use norms derived from individuals largely similar to the patients being generally tested at any pulmonary function laboratory. Therefore standard Caucasian norms, often incorporated into spirometer softwares, should be avoided, and locally appropriate reference equations preferred wherever available.

## Interpretation and Patterns in Common Disorders

Interpreting lung function data is not just about looking at numbers generated by the spirometer. Both the volume-time curve and the flow-volume loop must also be evaluated with regard to their technical quality, size and shape, and various components, before making a final interpretation. Often such graphical analysis provides additional important information not obtainable from the numerical data. If available, the postbronchodilator graphs should also be similarly evaluated and compared to baseline curves. The clinical data provided in the requisition form is equally important in helping to reach any conclusion, especially in borderline situations.

Broadly, the interpretation of spirometric data involves only three numerical variables: FEV1, VC and FEV1/VC. The largest observed values of FEV1 and VC available from among at least three acceptable and reproducible tests should be used as the key parameters for interpretation, even if these individual observations are derived from different test maneuvers. If both forced and relaxed VC maneuvers have been performed, the larger value of VC

amongst the FVC and SVC measurements should be used for interpretation. The large numbers of other variables, often available from computerized spirometer outputs, usually provide no additional information, and are best excluded from a standard interpretative algorithm.

Any spirometry record with normal FEV1, VC and FEV1/VC (i.e. all values more than their corresponding LLN values) should be interpreted as normal. Any spirometry record with FEV1/VC value below its predicted LLN should be interpreted as having an obstructive abnormality. This approach is superior to the use of fixed cut-offs in correctly identifying patients with airflow limitation, especially among the elderly.

Any spirometry record with a normal FEV1/VC (i.e. value above corresponding LLN), coupled with a reduced VC (i.e. value below corresponding LLN), is suggestive of a restrictive abnormality. In situations where statistically valid LLN figures are not available (or not practical to use, as in field settings), observed VC ratio less than 80% of predicted value is often used to define reduction in VC. Restrictive defects are common in conditions with loss of functioning lung parenchyma (e.g. diffuse parenchymal lung diseases, lung collapse/atelectasis, pneumonia, after lung resection). Such defects are also observed in neuromuscular diseases (due to reduction in generation of force needed for a FVC maneuver) as well as disorders of chest wall and pleura (e.g. massive pleural effusion, pleural fibrosis, obesity, and kyphoscoliosis). True restriction is defined as reduction in total lung capacity. A mixed (obstructive plus restrictive) defect also cannot be diagnosed solely based on spirometry. A disproportionately low VC in face of a reduced FEV1/VC can either represent air trapping (with consequent increase in RV at the expense of VC, as in severe emphysema), or a true reduction in TLC (as in COPD with pneumonia). There is no universally accepted scheme of severity categorization.

The flow-volume loop may also provide a clue to underlying pathology. A small and concave or scooped curve suggests obstructive disorder. A small curve with steep slope suggests restriction. A small and flat curve suggests central airway obstruction. In disorders with variable intrathoracic obstruction, only the expiratory component of the loop is flat, whereas in disorders with variable extrathoracic obstruction, only the inspiratory component is flat. Both components are flat in lesions causing fixed airway obstruction.

Bronchodilator responsiveness (BDR) is considered to be present if the increase in FEV1 and/or VC (15–30 minutes after inhalation of 400 μg salbutamol) in the postbronchodilator study is both more than 12% and more than 200 mL over baseline values. Although an oversimplification, patients with asthma tend to have BDR much more frequently than those with COPD. It must be noted that lack of BDR does not necessarily imply poor clinical response to bronchodilators in either condition.

## PEAK EXPIRATORY FLOW

Peak expiratory flow (PEF) is defined as highest flow achieved from a maximum forced expiratory maneuver started without hesitation from a position of

maximal lung inflation. It can be measured either as a part of the spirometry procedure on the same instrument (with values derived from the flow volume curve), or separately using peak flow meters. The first meter specifically designed to measure this index of lung function was developed more than 50 years ago (Wright meter). Subsequently, a more portable, lower cost version (the "Mini-Wright" peak flow meter) was developed, and other designs and copies have since then become available across the world.

Although PEF is fairly well reproducible for an individual, the normal range of PEF in healthy individuals is rather wide. As a result, predicted values of PEF cannot be used to detect lung disease, since there is substantial overlap between values in patients with lung diseases and normal persons. Further, since PEF recordings are both flow and volume dependent, they tend to get reduced in both obstructive and restrictive disorders. Hence in general notion that diminished PEF is a marker of airway obstruction is also not correct. While a normal PEF can reliably rule out airway obstruction, a low PEF does not necessarily indicate the same. The degree of reduction in PEF does not correlate well with the severity of obstruction described by the degree of reduction in FEV1. PEF measurements generally underestimate the degree of airway obstruction, as determined from FEV1 measurements.

## STATIC LUNG VOLUMES

Since spirometry cannot measure RV, it is not possible to determine FRC and TLC from this test. Other techniques are needed for the purpose. These methods are generally based on principles in which airflow velocity plays no role (in contrast to spirometry), and hence the term "static lung volumes" is often used for these measurements. Three techniques may be used: (a) open circuit nitrogen washout, (b) closed circuit inert gas dilution, and (c) whole body plethysmography. Determination of static lung volumes is helpful in ascertaining true restrictive physiology, and differentiating between obstructive and restrictive disorders. Comparison between TLC estimated through gas dilution and plethysmographic methods can also quantify the extent of air trapping within the lungs.

### Whole Body Plethysmography

In contrast to gas dilution techniques, plethysmography measures the total volume of air in the thoracic cavity, including gas trapped in bullae and other noncommunicating spaces (e.g. air within pleura or esophagus). Plethysmographically determined FRC is therefore often referred to as thoracic gas volume (TGV). Although several different types of body plethysmographs are available, the "volume constant" type is the most widely used.

### Interpretation

A decrease in TLC is diagnostic of a restrictive defect. In parenchymal restriction (e.g. lung fibrosis), RV and TLC are reduced proportionately,

resulting in a normal RV/TLC ratio. In extrapulmonary restriction (e.g. chest wall or neuromuscular disorders), RV is usually normal (or sometimes even increased), resulting in an increased RV/TLC ratio. On the other hand, TLC might be increased in acromegaly, or in conditions like emphysema, as a result of air trapping. An increase in RV/TLC ratio, with an obstructive defect on spirometry, is a good indicator of air trapping. In conditions characterized by non-communicating air in the lungs (e.g. emphysema, bullae, etc.), whole body plethysmography provides a better estimate of the lung volume, since gas dilution techniques measure only the volume of air that is freely exchanged during breathing. In fact, the difference in volumes calculated by the two techniques may provide some indication to the volume of noncommunicating air present in the lungs. Estimation of static lung volumes is also necessary to diagnose mixed obstructive-restrictive defects, with a combination of reduced FEV1/VC ratio and reduced TLC.

## DIFFUSING CAPACITY OF LUNGS

Measurement of pulmonary diffusing capacity allows us to assess the ability of lungs to transport gas from inspired air to the red blood cells in pulmonary capillary network. It is, however, a misnomer, since gas transfer does not depend solely on diffusion across the alveocapillary membrane, and it is not a "capacity" in that there is no theoretical maximal limit. Many laboratories therefore employ the term "transfer factor" instead.

The diffusing capacity for carbon monoxide (DLCO) is the generally measured index. This is because carbon monoxide uptake is easily measurable, and the gas essentially follows the same pathway as oxygen during transport from alveolar air to red blood cells, and ultimate binding to hemoglobin. DLCO is the uptake of carbon monoxide from lungs per unit time per unit of carbon monoxide driving pressure. The test is usually performed for screening for diffuse lung diseases and pulmonary vascular disorders, precise characterization of airflow limitation, differential diagnosis and severity assessment of restrictive ventilatory defects, disability evaluation, and preoperative assessment. There are no absolute contraindications. However, for technical reasons, most machines cannot measure DLCO in individuals with an extremely low VC (usually <1.5 L) or severely dyspneic patients unable to hold breath for a sufficient time. The test cannot be performed on many patients receiving supplemental oxygen, as this needs to be discontinued before and throughout the test procedure.

### Methodology

Diffusing capacity for carbon monoxide can be measured using a single breath method, an intrabreath method, or a rebreathing technique. The first is most commonly used, as it is simpler and better standardized. DLCO is calculated from the total lung volume, breath-hold time, and the initial and final alveolar carbon monoxide concentrations. It is a product of the subject's total lung capacity and rate of carbon monoxide uptake during the breath-hold time. An

estimate of the total lung capacity and the initial alveolar carbon monoxide concentration is obtained from the tracer gas concentration in exhaled gas.

The test can be repeated after an interval of at least 5 minutes. Generally, a mean value is reported from two acceptable tests whose results agree within 2 mL/min/mm Hg.

### Interpretation

In contrast to other pulmonary function tests, observed DLCO values must be normalized to key nonrespiratory variables. Hemoglobin concentration is important as it removes the carbon monoxide from the blood, thus providing a nearly constant gradient for gas transfer. Anemic patients may thus have a lower DLCO, and the measurement should therefore be corrected for this factor in such patients. Smokers tend to have a small baseline level of blood carbon monoxide, and thus the transfer gradient may be less than for nonsmokers. If available, blood carboxyhemoglobin levels may be used to compensate for this anomaly.

As with other lung function tests, the patient's result is interpreted by comparing it with a corresponding reference value. It must be noted that the degree of variability of DLCO (both for a given subject and for the population) is much higher than the results of other lung function tests. In case serial tests are performed, a DLCO result can also be compared to previous values to detect any sizeable change. Normalizing the DLCO to patient's alveolar volume may provide additional information about the reason for an abnormal result. When alveolar volume is reduced (either because of true restriction or due to noncommunicating air spaces), the ratio of DLCO to alveolar volume is relatively preserved. The ratio is however decreased if alveolar volume is increased (as in emphysema) or normal (as in anemia, or nonperfusion of ventilated alveoli).

## EXERCISE TESTING

Exercise testing is generally indicated for (a) evaluation of exercise intolerance, (b) evaluation of unexplained breathlessness, (c) preoperative assessment, and (d) formulation of exercise prescriptions. Detailed evaluation can give some clue about whether the underlying disorder is predominantly cardiovascular or respiratory in origin. Exercise testing can range from gross and crude assessments to highly detailed and standardized evaluation using computerized equipment. The two most regularly employed types of exercise testing for evaluating pulmonary diseases are the 6-minute walk test (6MWT) and a formal complete cardiopulmonary exercise testing (CPET).

### Basic Modalities

Stair climbing remains the most basic exercise test that asks patients to climb stairs till they get limited by symptoms. There is, however, no consensus on how to standardize the procedure, and several variations (such as climbing at own

pace or at brisk pace, climbing with or without holding handrails) are used. Results are generally reported as number of stairs or number of flights of stairs.

Step tests ask the subject to walk up and down on a stool or bench at a specified rate. Several variations exist with regard to height of steps, number of steps, and the frequency of step-ups. The most popular is the Master two-step test. The test is well-suited to field use, and subjects can achieve close to their maximal exercise capacity.

The 6MWT is a simple procedure that assesses the maximum distance that a subject can walk on flat surface at his/her own pace in 6 minutes. The test provides a global estimate functional capacity, but does not provide any specific information on individual systems (cardiac, pulmonary, hematologic, and musculoskeletal) involved in exercise. The test is also sensitive to patient effort. The 6MWT is the most popular among the basic exercise tests as it is simple, practical and well standardized, and involves an activity familiar to almost everyone. A measured corridor, usually about 30 meters, is used, and the subject walks to and fro in this space at a self-determined pace. If a long corridor is not available, the test can be performed on a treadmill, although pacing and control are not as optimal and the distance walked is usually less. The test has good reproducibility and good correlation with other measures of functional status. For this reason, the 6MWT is the preferred investigation when a complete CPET is not available. Norms for healthy Indian men have recently become available.

The shuttle walk test uses an audio signal from a metronome to dictate the walking pace. Walking speed is incrementally increased every minute while the subject walks to and fro on a 10-meter straight path. The test is terminated when the subject can no longer maintain the required speed. Hence, the test correlates better with maximal symptom limited tests such as the CPET, rather than the submaximal tests like 6MWT. However, the test is more complicated than 6MWT, and may result in more frequent cardiac complications in the absence of electrocardiographic monitoring.

Exercise testing may sometimes be used to diagnose airway hyperreactivity due to exercise in patients with unexplained dyspnea. Exercise induced bronchospasm (EIB) is described as a self-limiting bronchospastic event occurring immediately after strong exercise. Typically, greater than 10–15% reduction in FEV1 and/or FVC is observed. EIB is caused by loss of heat, water, or both, from the airways during exercise.

## Cardiopulmonary Exercise Testing

The CPET is a more complex investigation that involves exercise at incrementally increasing intensity. The test is terminated when symptoms limit further exercise, or the maximal exercise capacity is achieved. A computerized protocol provides breath-by-breath information on respiratory gas exchange, airflow, oxygen consumption, carbon dioxide production, and cardiac variables (such as heart rate, blood pressure, etc.). The subject exercises on either a treadmill or on a bicycle ergometer; the latter may however be preferable as work rate can be directly measured.

Electrocardiographic and noninvasive blood pressure monitoring accompanies the test. In addition, oxygen saturation is continuously monitored through pulse oximetry. Real-time data on ventilatory and gas exchange parameters is obtained by asking the subject to breathe through a mouthpiece connected to a spirometer and metabolic cart. Flow, volume, and exhaled oxygen and carbon dioxide concentrations are measured. Either incremental or constant work protocol can be used. The test is terminated when the subject (a) gets exhausted, fatigued or distressed, (b) develops signs of cardiovascular instability (ischemia, arrhythmia, substantial blood pressure elevation, etc.), or (c) develops significant hypoxemia.

Although data for a large number of monitored and calculated variables is generated, interpretation and clinical correlation depends on judicious integration of all available information. No single parameter is diagnostic of a cause for exercise limitation. Four basic measurements are critical in describing the response to exercise: oxygen consumption, carbon dioxide production, heart rate, and minute ventilation. Under steady state conditions, measured oxygen uptake ($VO_2$) equals metabolic oxygen consumption, and measured carbon dioxide output ($VCO_2$) is the same as its metabolic production. Both $VO_2$ and $VCO_2$ can be mathematically computed from expired gas concentrations.

The test is highly sensitive in identification of subclinical disease than other lung function tests conducted at rest. Therefore, CPET can be performed for preoperative assessment, disability evaluation, and selection of candidates for heart and/or lung transplantation. The test is also useful in determining whether breathlessness results from cardiac or pulmonary component among patients who have disorders of both organ systems.

## OTHER TESTS

### Airway Hyperresponsiveness

Airway hyperresponsiveness (AHR), a characteristic feature of bronchial asthma, is an increased sensitivity of airways to a variety of inhaled agents. AHR is classically measured using inhalation challenges with airway constrictor agonists, such as histamine or methacholine, which result in direct bronchoconstriction. Recently, inhaled mannitol solution has also become available for this purpose and acts by inducing osmotic changes in the airway. Exercise can also be used to test for AHR.

### Airway Resistance

Airway resistance can be clinically estimated using several approaches such as interrupter technique, forced oscillation technique, and whole body plethysmography. The interrupter technique is the simplest, and requires monitoring airway pressure and airflow. Airway resistance is not normally determined for clinical purposes, but may provide additional information in the evaluation of patients suspected to have obstructive disorders. The range of normal airway resistance is not well defined, and generally values higher than 2.8 cm $H_2O$/L/s are considered abnormal.

## Pulmonary Mechanics

The elastic properties of the lungs are determined by relating alterations in volume of air in the lungs to the corresponding changes in the lung's recoil. A body plethysmograph is usually used to determine the static pulmonary mechanics. Lung recoil force is measured as the transpulmonary pressure. This is the difference between the alveolar and pleural pressures; the former is measured at mouth under static conditions with shutter at mouth closed and glottis open, and the latter is quantified through pressure measurement from a thin balloon placed in the lower third of esophagus and connected to a pressure transducer.

## Respiratory Muscle Function

Estimation of maximal respiratory pressures is a simple technique to assess global respiratory muscle function. A manometer is used to record highest pressures during maximal inhalation and exhalation, which can be sustained for at least 1 second. Maximal expiratory pressure (MEP) is roughly twice as much as maximal inspiratory pressures (MIP). The test is commonly used during evaluation of respiratory muscle weakness in patients with neuromuscular disorders. It is also used as one of the several parameters to assess weaning potential in patients receiving mechanical ventilation. Abnormal muscle strength is identified by comparing observed values to reference data; such data is also available for the Indian population. Values are generally higher among men, and decline with age. A reduction in both MIP and MEP indicates generalized skeletal muscle weakness. A low MIP with normal MEP suggests isolated inspiratory muscle weakness (usually diaphragmatic). Isolated expiratory muscle weakness (normal MIP and low MEP) is rare.

The sniff nasal inspiratory pressure (SNIP) is a noninvasive test of inspiratory strength. The test is performed by wedging a catheter into one nostril and asking the subject to sniff through the other nostril. Pressure measured in the obstructed nostril. The SNIP correlates strongly with transdiaphragmatic pressure and the MIP, but provides no information on expiratory muscle function.

Transdiaphragmatic pressure can be measured after insertion of esophageal and gastric balloon catheters. This allows functional assessment during inspiration, expiration, a sniff, a cough, or phrenic nerve stimulation. Although the technique is highly complex and invasive, it is the best measure of respiratory muscle strength. However, a wide normal range limits its clinical utility.

# Handbook of
# Pulmonary & Critical Care Medicine

***Salient Features***

- Presents a concise, yet fairly comprehensive information for day-to-day use
- Abridged form of *Textbook of Pulmonary & Critical Care Medicine* (2nd edition)
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- It is reader-friendly with simple language
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- Useful for educators, pulmonologists, internists, intensivists, pediatricians, medical students and practitioners, who are treating patients with lung diseases.

**SK Jindal** MD FAMS FNCCP FICS FCCP is a distinguished Clinician and Medical Teacher. He is an Emeritus Professor (Pulmonary Medicine), Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India, with a long teaching and research career. He has extensively contributed to the specialty with the introduction of the 1st postdoctoral course (DM) course in Pulmonary and Critical Care Medicine in India. He has authored several books, published a large number of research papers and served on the Editorial boards of many scientific and professional journals. He has been variously honored with fellowships and awards for life-time achievements by several national and international organizations including the Outstanding Educator Award of American Thoracic Society in 2011.

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