

The Physiologic Basis of Spirometry

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Summary

Spirometry is the most useful and commonly available tests of pulmonary function. It is a physiological test that measures individual inhalation and exhalation volumes of air as a function of time. Pulmonologists and general-practice physicians commonly use spirometry in their offices in the assessment and management of lung disease. Spirometric indices are well validated and easily interpreted by comparison with established normal values. The remarkable reproducibility of spirometry results from the presence of compliant intrathoracic airways that act as air flow regulators during forced expiration. Because of this anatomic arrangement, expiratory flow becomes dependent solely on the elasticity of the lungs and airway resistance once a certain degree of expiratory force is exerted. Insight into this aspect of respiratory physiology can help in the interpretation of spirometry. *Key words: spirometry, physiology, forced expiratory volume, FEV₁, lung function, pulmonary function testing.* [Respir Care 2009;54(12):1717–1726. © 2009 Daedalus Enterprises]

Introduction

In pulmonary medicine, when more than a history and physical examination is needed to evaluate a complaint of

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breathlessness or dyspnea on exertion, the next step is almost invariably spirometry. Not only can a properly done and interpreted spirogram aid in diagnosis, but it can help evaluate the severity of a respiratory problem or impairment and, in many cases, assess response to treatment by comparing the spirogram performed before and after an inhaled dose of a bronchodilator. Spirometry requires cooperation between the subject and the examiner, with results dependent upon technical factors and patient effort. The forced vital capacity (FVC), forced expired volume in the first second (FEV₁), and the FEV₁/FVC ratio are very well standardized and validated after study in groups of healthy individuals.¹ The relatively small testing variability of a properly performed spirogram leads to reliable

detection of air flow abnormalities. The simplicity of spirometry hides the subtleties of the physiologic mechanisms at work, especially the processes that result in air flow limitation. These phenomena are responsible for the remarkable consistency of spirometry when it is properly done. This consistency applies once a certain degree of effort is made by the subject, and is very difficult or impossible to falsify. It results from the flow limitation inherent in airway anatomy.

The benchmark studies that described the physiology of forced expiratory maneuvers used for spirometry were published in the 1950s and 1960s. The flow of a forced expiration can be seen as a consequence of the subject's muscle strength and airway resistance, as is the case with a mechanical bellows, but that analogy is seriously incomplete because of 2 fundamental structural features of the respiratory system. First, the lungs are elastic, constantly exerting an inward force against the stiffer chest wall and respiratory muscles. Second, the intrathoracic airways are compressible and subject to intrathoracic pressure generated by forced expiration. The result of this is that, under forced expiration, airway resistance is dynamic and changes with lung volume, effort (transpulmonary pressure), and air flow. This airway resistance is not evenly distributed, but occurs at certain points in the airways, because, as air flows through the airways during forced expiration, the intraluminal pressure diminishes with distance from the alveolus, due to the distributed resistance of the airways. At some point the intraluminal pressure equals the pressure surrounding the airway (the equal pressure point [EPP]), which will be discussed more extensively later in this paper. Beyond the EPP or the segment upstream (ie, from the alveoli to the EPP) the pressure falls below the surrounding pressure, and the affected airway segment is compressed, limiting flow. Thereafter, increased effort raises both the driving pressure and the airway resistance, and the result is that flow becomes subject only to pulmonary recoil pressure that is itself dependent on lung volume.

Background

Flow-Volume Curve

In 1958, Hyatt and colleagues published a benchmark paper that described the functional relationship between transpulmonary pressure, respiratory gas flow, and degree of lung inflation.² The authors introduced the flow-volume curve and a simple means of defining maximal expiratory flow relating to lung volume. They showed that, over the upper half of the vital capacity (VC), the relationship between maximal expiratory flow and degree of inflation was effort-dependent, and over the lower half of the VC, the relationship was determined by physical properties of the lower airways, termed the α flow-volume (α FV) curve.²

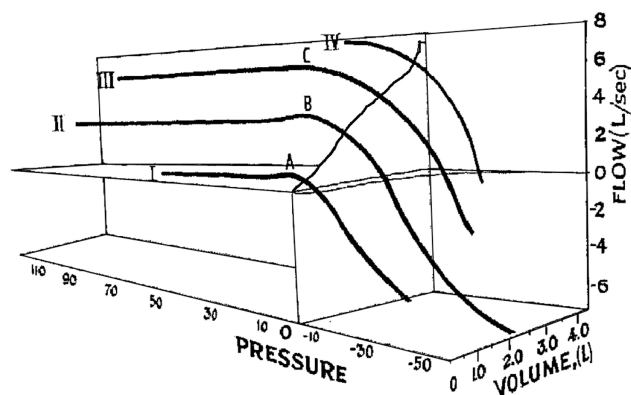


Fig. 1. Isovolume pressure-flow curves placed on a 3-dimensional coordinate system with flow in L/s, volume in L above residual volume, and pressure in cm H₂O. (From Reference 3, with permission.)

The α FV curves produced by the normal subjects and cardiac patients identified similar measurements at different points, without variation.² However, the curves produced by the patients with emphysema demonstrated variability that correlated with clinical status,² thus consistent with worsening airway obstruction in the clinical setting of an acute chronic obstructive pulmonary disease exacerbation.

In 1960, Fry and Hyatt demonstrated that the α FV curve is relatively unaffected by a marked increase in upper airway resistance in normal subjects.³ They reported that the basic element of 3-dimensional graphic representations of pulmonary ventilation mechanics was the isovolume pressure-flow curve.³ Figure 1 illustrates the isovolume pressure-flow curves obtained by the authors in relation to flow, volume, and pressure on a 3-dimensional coordinate system. This 3-dimensional representation included transpulmonary pressure, respiratory flow, and lung inflation.³ The α FV curve was easily obtainable and reproducible, moderately dependent upon effort, essentially unaffected by wide variations in upper airway resistance, determined by the physical properties and dimensions of the intrathoracic pulmonary system, and greatly altered in emphysematous subjects.³

Starling Resistor

Two studies identified evidence that the driving pressure for expiratory air flow from the lungs is the difference between alveolar and mouth pressures (ΔP).^{3,4} At constant lung volumes, the expiratory flow rate increases as ΔP increases, until a critical pressure ($\Delta P'$) is reached, at which point expiratory flow rates are at their maximum.^{3,4} In 1967, Pride and colleagues further expanded on these principles and reported a method of simultaneously measuring alveolar pressures and expiratory air flow at constant lung volume.⁵ Expiration was interrupted in subjects at a selected lung volume, and then the subject increased alveolar

pressures by an effort against a closed valve until the pressure reached a preset level, at which time the valve was reopened.⁵ The pressure at the mouth immediately before valve opening was measured by a pressure transducer.⁵ When maximum expiratory flow was reached in an isovolume pressure-flow curve, a “waterfall” or Starling resistor effect developed in the airways.⁵ The term “waterfall” effect is used as an analogy to the concept that the volume of water going over a waterfall is independent of the height of the waterfall, so the downstream segment has no effect. A Starling resistor is a compressible tube surrounded by the same pressure used to drive flow through the tube. Once the driving pressure reaches a certain point, an upstream and downstream segment forms that is separated by a point of narrowing. Two physiological phenomena are characteristic of this situation: (1) flow becomes independent of the downstream pressure, leading to this “waterfall effect” and subsequent collapse, and (2) self-developed oscillations form in the downstream segment. Expiratory flow-limitation is an example of the first characteristic, and snoring seen in obstructive sleep apnea is an example of the second. Using the waterfall model, simple equations have been developed to relate the roles of elastic recoil of the lung, airway resistance, and bronchial collapsibility in determining maximum expiratory flow, airway resistance, and $\Delta P'$.⁵

Equal Pressure Point

In 1967, Mead and colleagues developed a relationship between static elastic recoil of the lungs and the maximum rate at which gas is expelled, which they termed the maximum flow-static recoil curve.⁶ The point where the pressure at the inner wall of the airway is equal to the pleural pressure was defined as the equal pressure point (EPP).⁶ The authors demonstrated that isovolume pressure-flow curves depict a relationship between pleural pressure and flow at a particular lung volume, which was previously described,²⁻⁴ but then they showed how these curves are interpreted in relation to EPP. During forced expirations, the authors reported lateral pressures at points within the airways that equaled pleural pressure, and the pressure drop from the alveoli to these points approximated the static recoil pressure of the lungs.⁶ This concept of the flow-limiting segment modeled the intrathoracic airways as an upstream segment, the alveoli to the EPP, in series with a downstream segment, the EPP to the mouth. The distribution of pressures in the airways of the upstream segment behaved as a Starling resistor, regulating the flow as expiratory effort varied.

Elastic Recoil

The most important concept to grasp is that forced expiratory flow is not limited by expiratory muscle effort

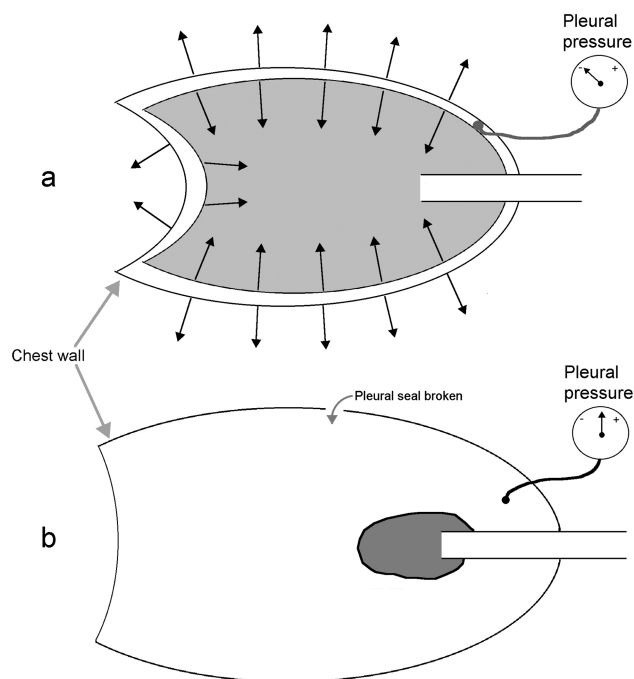


Fig. 2. A: Cartoon of lung and chest wall, showing elastic tension of each (thin, black arrows). The lung is shaded gray. The negative pleural pressure results from the opposing pull of the chest wall and lung. It remains negative during passive or mildly forced expiration, as the lung tends to pull in on itself, even as it is allowed to grow smaller. The situation changes during forced expiration, as will be shown in Figure 4. The pleural pressure is transmitted throughout the lung, so that when the pleural pressure is negative (relative to the air pressure surrounding the body), so is the parenchymal pressure. B: Pleural seal breached allowing lung and chest wall to assume their un-apposed positions. Pleural pressure approximates atmospheric pressure.

(once it achieves a certain level), but by the elasticity of the lungs. In fact, the velocity of exhaled air is determined by the degree of previous lung inflation and, therefore, the strength of the inspiratory muscles. This is counterintuitive because we only feel the active muscle effort associated with forced exhalation.

To better comprehend this concept, it helps to see the lung and chest wall as elastic structures balanced against one another. The lung is stretched in partial expansion, balanced against the chest wall, which is held in partial compression (Fig. 2A). If allowed to disconnect from one another, as in an open pneumothorax, a normal, healthy lung will spontaneously contract to a size less than residual volume,⁷ expelling its air by the force of the potential energy stored in its elastic tissue, much like releasing a stretched rubber band (see Fig. 2B and Fig. 3).

At the same time, the chest wall will spring outward, without the involvement of muscle activity. With the mental image of reconnecting the lung and chest wall, one can envision that the lung is stretched on inspiration, storing elastic energy created by the inspiratory muscles, and then,

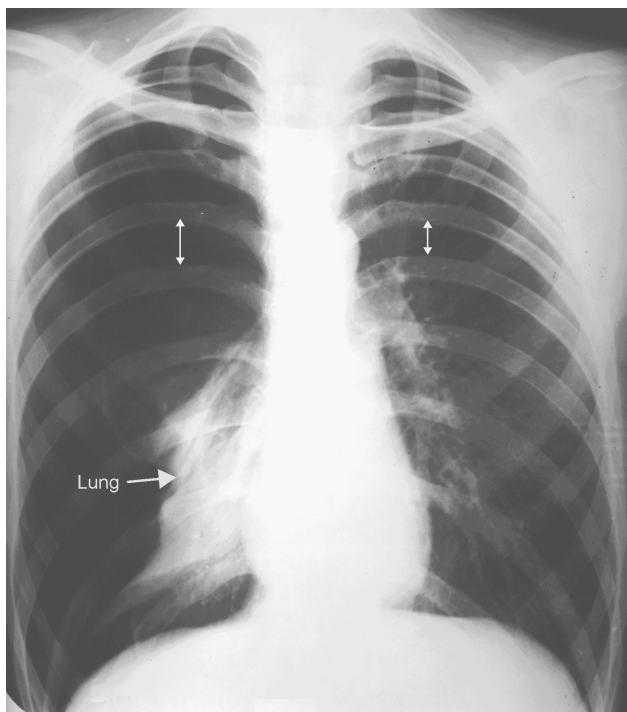


Fig. 3. Antero-posterior chest radiograph of a man with a complete pneumothorax of the right lung. Notice the small, airless lung and increased size of the right chest wall, as shown by the increased intercostal distance on the side of the pneumothorax (double-headed arrows).

during expiration, allowed to passively retract until it reaches equilibrium with the passive elasticity of the chest wall. A deeper breath leads to greater stretch and faster air flow, which defines quiet breathing but not forced expiration.

One can theorize that forced expiration should overwhelm the elastic recoil of the lung and force the lung to empty faster. This concept occurs at high lung volumes, approximately 80% of vital capacity or higher, and would be true for the entire expiration if the airways were rigid. However, they are really quite pliable; even the cartilaginous airways have a membranous portion that, under external pressure, can invaginate, substantially narrowing the lumen. The smaller airways, imbedded within the parenchyma, reduce in size as well, causing expiratory flow to decrease with lung volume.

At high levels of expiratory effort, the flow-limiting segments form as illustrated in Figure 4. At the start of an FVC maneuver, the muscle-generated pressure is applied to the lung parenchyma and airways, with the airways held open by the surrounding elastic tissue. As air flow proceeds toward the mouth, the driving pressure within the airways is expended, overcoming airway resistance. At some point, the intraluminal pressure falls below the pressure that surrounds the airway. Beyond this point the involved airways are partially constricted or “choked,” lim-

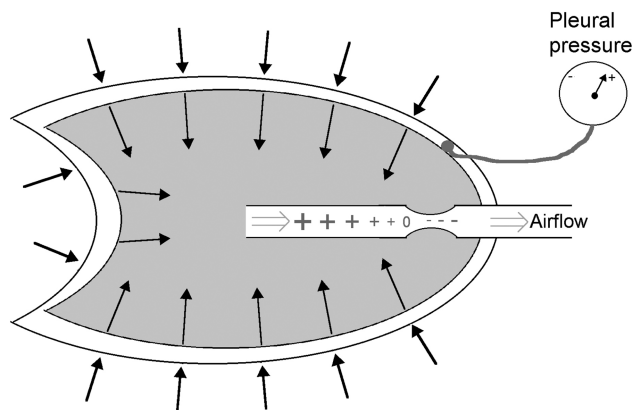


Fig. 4. Cartoon of chest during forced expiration. Pleural pressure is now positive, but the air flow through the bronchial tree is regulated by the choke segments that form when the intra-airway pressure falls below the surrounding pressure in the lung tissue. See text.

iting the air flow. This is the Starling resistor effect or “waterfall,” as previously discussed. Changes in expiratory effort will change the position and luminal size of the choke point, so that extra effort produces extra obstruction, but air flow remains steady, reflecting only the degree of lung inflation. This variability in resistance is caused by conditions around the choke point and upstream, toward the lung periphery. Downstream conditions toward the mouth have no controlling effect on air flow. This is the reason it has been likened to a waterfall, as there too, downstream conditions (the height of the waterfall) do not affect water flow.

Transmural Pressure

In 1975, Jones and colleagues reported the ability to predict flow during the plateau phase of the flow-volume curve in a dog model.⁸ After deriving an equation so that maximum flow could be calculated from the area and transmural pressure of the flow-limiting segment, the authors demonstrated that when maximum flow was kept constant, the area of the flow-limiting segment varied with transmural pressure.⁸ This relationship was confirmed by the area-transmural pressure curves, which yielded flows identical to those measured during maximum expiration.⁸ The gradual fall in flow during the plateau phase was due to flow limitation in more compliant segments located further upstream.⁸ In another study that same year, also in a dog model, Jones et al assessed the effect of changing airway mechanics on maximum expiratory flow, and demonstrated that vagal stimulation resulted in an increase in small-airway resistance, the EPP moved further toward the alveoli, and maximum flow was reduced, compared to control studies.⁹ Changes in lung recoil pressure and up-

stream resistance were vital in the determination of the position of EPP as flow accelerates to the peak.⁹

Wave Speed Theory

In 1977, Dawson and Elliot further explained the mechanism responsible for the flow-limiting behavior of the choke segment, when they proposed their wave speed theory of flow limitation.^{10,11} The basis of their theory is that a mass flow of a fluid (air, in this case) cannot exceed the velocity of the pressure differential that drives it (air cannot flow faster than the speed of sound in the same air). Dawson and Elliot presented evidence that this mechanism was operational in airways under conditions of forced expiration. This is not the speed of sound in air as usually understood (340 m/s), but, rather, the speed of a pressure wave along the airways, where the compliant airway walls and air contained in them interact as one physical system. Because of the airway mass and elasticity, the speed of the pressure wave is much slower than sound speed in air alone. The flow rate occurring at wave speed is described by the following formula:

$$\dot{V}_c = \left(A^3 \frac{dB}{dA} / q\rho \right)^{1/2}$$

in which \dot{V}_c is air flow, A is the area of the choke point, B is the transmural pressure, dB/dA is the stiffness of the choke segment, q is the correction factor for Poiseuille flow, and ρ is the gas density.

Simplifying, we see that the air flow velocity varies directly with airway cross-sectional area and stiffness, but negatively with gas density. This makes sense, although the differential term for choke point stiffness (dB/dA) cannot be measured *in vivo* and so is an estimate. Several researchers have tested this theory and found their results to be “consistent” with wave speed limitation.¹²⁻¹⁶ In 1985, Webster and colleagues¹² addressed what they thought was a critical weakness of Dawson and Elliott’s.¹¹ They proposed a theory describing a mechanism for the dissipation of energy when effort exceeded what was needed for maximal flow. These authors used a 2-dimensional mathematical model to approximate the physical characteristics of the trachea, to predict that aerodynamic flutter occurs in the zone of supercritical flow, as described in wave speed theory. Such aerodynamic flutter in the supercritical zone provided a potential means for energy dissipation at maximal flow. This also may explain the high-frequency tone heard with flow limitation.¹²

In a canine model, Mink and colleagues demonstrated, in localized lung disease, that wave speed limitation is reached in proximal airways if flows from the different regions are high enough and a choke point occurs more centrally rather than peripherally; however, if flows are

low, then wave speed is reached peripherally and a choke point common to all lung regions does not occur.¹³ In 1993, in 5 healthy adults, Kano et al tested the hypothesis that wave speed could be reached at peak expiratory flow (PEF); they were unable to reject this hypothesis using maximal forced expiratory effort maneuvers with the neck fully flexed and extended, after breath-holds at total lung capacity of 2 seconds and 10 seconds, and with esophageal pressure measurements, as well as using PEF measurements with a spirometer and pneumotachograph.¹⁴ A breath-hold at total lung capacity could increase airway wall compliance by allowing stress-relaxation of the airway and reduce the wave speed achievable.¹⁴ In healthy and asthmatic subjects, Pedersen and colleagues used an esophageal balloon and a Pitot-static probe positioned in 5 locations between the mid-trachea and right lower lobe to obtain dynamic area-transmural pressure curves that were then used to determine wave speed in the central airways at PEF, but the authors could not exclude that wave speed is also reached in the more peripheral airways.¹⁵

There remains some controversy, and it is possible that both flow-limitation theories (choke point and wave speed) operate together or under different conditions.^{17,18} In 1980, Hyatt and colleagues obtained static pressure-volume curves and deflation pressure-area curves of the first 3 to 4 airway subsegmental divisions in 9 normal excised human lungs.¹⁷ They found that the wave speed theory predicted flow over much of the vital capacity, but other mechanisms may limit flow at low lung volume. More recently, using a nonlinear dynamic morphometric model of respiratory mechanics during artificial ventilation, Barbini et al demonstrated that coupling between dissipative pressure losses and airway compliance resulted in the onset of expiratory flow limitation in normal lungs when driving pressure was significantly increased with the application of subatmospheric pressures to the outlet of the ventilator expiratory channel.¹⁸ Wave speed limitation remained predominant at even higher driving pressures.¹⁸

Effort

In an important study, Krowka and colleagues demonstrated a positive relationship between PEF and effort in 5 normal subjects, using flow-volume curves as a noninvasive index of expiratory effort with correlation of effort obtained via esophageal balloon.¹⁹ The investigators then measured the difference between the largest FEV₁ and the FEV₁ from the maneuver with the highest PEF during 10 test sessions in 10 normal subjects.¹⁹ The FEV₁ difference was always ≥ 0 mL, with a mean FEV₁ difference of 110 mL for all sessions, which decreased to 80 mL when the maneuvers with poorly reproducible PEF or FVC values were discarded.¹⁹ The authors concluded that the FEV₁ is inversely dependent on effort and that maximal effort

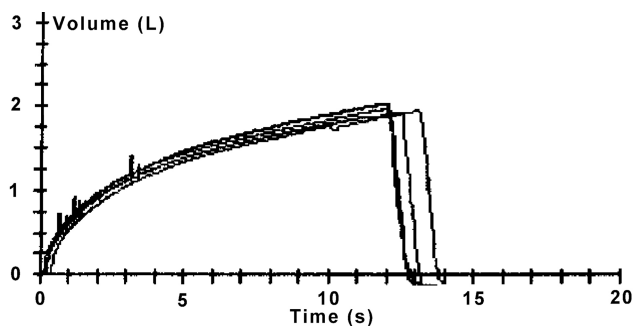


Fig. 5. Three superimposed forced vital capacities, demonstrating the remarkable reproducibility of near maximal efforts.

decreases FEV₁ because of the effect of thoracic gas compression on lung volume during standard spirometry. The flow-volume curves of superimposed efforts facilitate the recognition of submaximal efforts.¹⁹

The Process of Spirometry

The result of these physiologic processes is that, when done properly, spirometry is remarkably consistent, and repeated tests will look almost identical (Fig. 5), graphically confirming adequate effort. One major limitation of spirometry is its dependence on patient effort, with high potential for error if effort is suboptimal. Thorough explanation of the procedure to the patient prior to performing spirometry, followed by active encouragement during it, will yield more accurate and consistent results. The interpreter should recognize if an error is present, and the magnitude of that error. An examination of a flow-volume loop shows that, after the initial blast, the air flow decreases smoothly as the lungs empty, reflecting the progressive decrease in lung elastic recoil and shrinking of the flow-limiting segments (Fig. 6). A proper effort is nearly always accompanied by polyphonic wheezes audible at a distance from the mouth, that are probably generated at the choke points in the larger airways,²⁰⁻²² as they are squeezed to near closure.

Determining the starting point of the FVC is straightforward when the exhalation is optimal, when a volume-time curve is available, and tidal volume breathing leading up to the FVC maneuver is displayed. In other situations, for purposes of timing, the back-extrapolation method is used to determine the start of the test (Fig. 7). The back-extrapolation traces back from the steepest slope on the volume-time curve, as illustrated in Figure 7. To achieve an accurate time zero and to assure the FEV₁ comes from a maximal effort curve, the back extrapolated volume must be 5% of the FVC or 0.150 L, whichever is greater.²³

The traditional way of evaluating the FVC maneuver is by displaying the volume change against time. The FVC and FEV₁ can be directly measured from such a plot. The

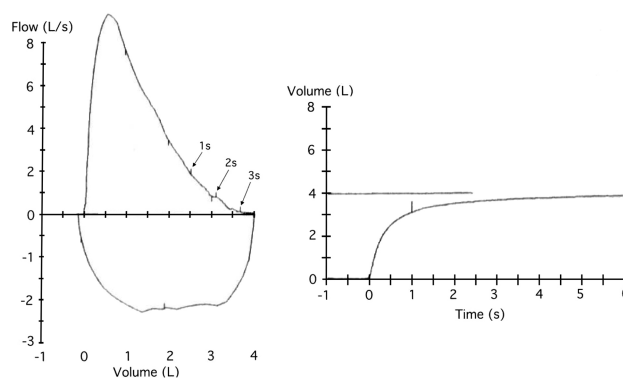


Fig. 6. Flow-volume loop (left) and volume-time trace (right) of a healthy subject. This displays the slope of the volume-time trace with respect to volume. Because time is on neither axis in a flow-volume loop, time ticks are usually added to show the 1-second, 2-second, and 3-second points. Otherwise, the information is the same as the volume-time display, although instantaneous flows at defined volumes are much easier to measure from the flow-volume loop.

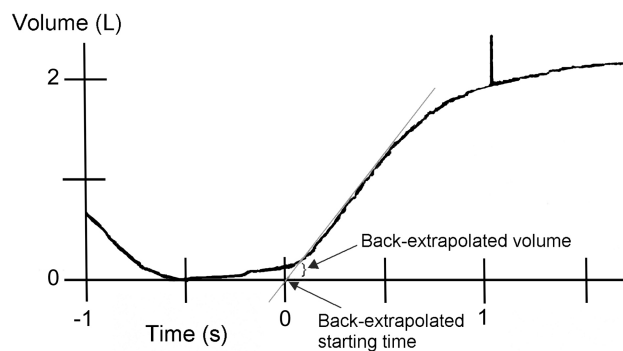


Fig. 7. Back-extrapolation method of determining a reasonable starting point when initial expiratory effort is suboptimal but the remainder of the forced vital capacity maneuver is adequate.

instantaneous flow at any time on this plot can be estimated from the steepness (rate of change, or slope) of volume change with time. If this slope itself (in L/s) is plotted against exhaled volume, then we get a flow-volume loop, from which flow at any volume can be directly measured, although time as an independent variable is lost. This alternative method of examining the FVC is useful for the easily perceived visual patterns that suggest certain pathology (Fig. 8).

Central and Upper Airway Obstruction

The effect of central and upper airway (trachea and above) obstruction on the flow-volume loop depends on whether the obstruction is within the thoracic cavity (and therefore subject to intrathoracic pressure changes) or outside of it, and whether it is fixed or variable. This creates 3 basic patterns that, in their pure state, are specific to the

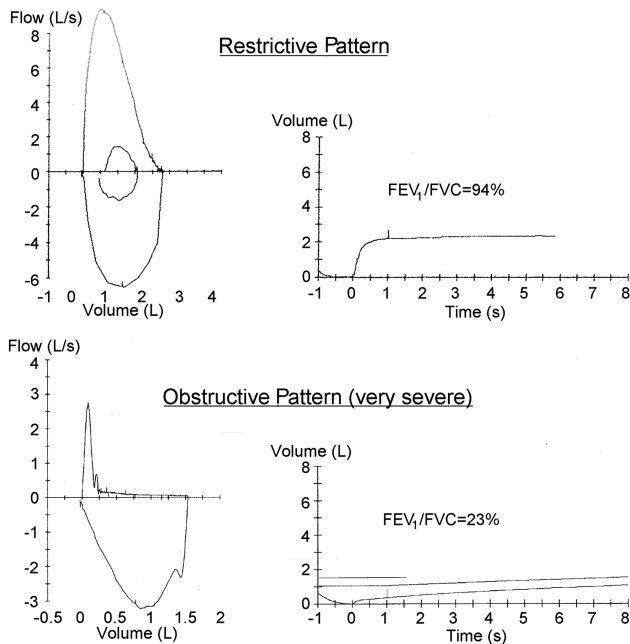


Fig. 8. Spirometry patterns from patients with restrictive lung disease and obstructive lung disease. Although the loop patterns on the left are more visually striking, they do not accurately convey the relative duration of the efforts; the volume-time tracing shows that the patient with airways obstruction perseveres for an expiratory time of 19.5 seconds, whereas the patient with restrictive disease expels his entire vital capacity in little more than 1 second.

type and location of the pathology and are easily understood from the physiology involved. A fixed obstruction, such as is seen with a tracheal stenosis or tumor, will limit air flow in both directions, whether it is in the chest or upper airway, and the loop will appear similar in either case. Flexible or floppy segments, such as those seen in tracheomalacia, will widen or narrow in response to the relative pressure differences between the airway lumen and surrounding tissue, generating either a variable intrathoracic or variable extrathoracic obstruction, depending on the location of involvement. Miller and Hyatt²⁴ defined 3 classic flow-volume loop patterns that have been published extensively elsewhere, but we feel this is more easily understood when shown graphically, as in Figure 9, where the conditions are idealized for clarity.

There are no actual standard definitions or measurements pertaining to flow-volume loop patterns for the diagnosis of central or upper airway obstruction, but there are several measurements that may predict or suggest it. Miller and Hyatt²⁵ described the ratio of the maximum expiratory flow at the half-way point in the forced expiratory maneuver (MEF_{50%}) to the maximum expiratory flow at the half-way point in the forced inspiratory maneuver (MIF_{50%}) to address maximal flow during inspiration and expiration while performing spirometry, using interval smaller orifices in the respiratory circuit while

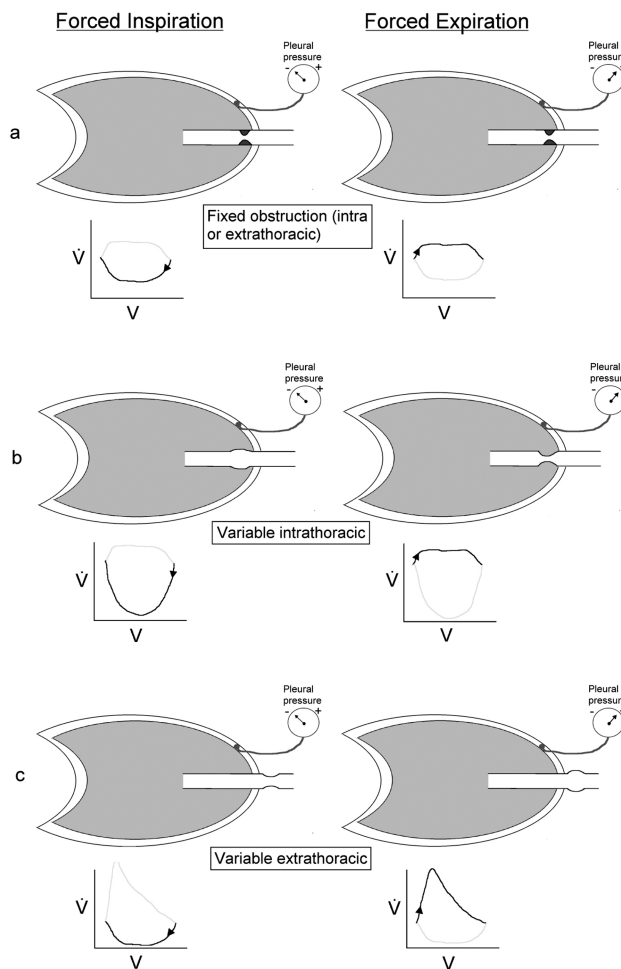


Fig. 9. Typical shapes of the flow-volume loop in different kinds of central or upper airway obstruction. In each panel, the darker segment of the flow-volume loop indicates the portion of the maneuver depicted above each loop. \dot{V} is the flow. V is the volume. The constricted airway segments are stenotic or floppy tracheal segments and are not meant to show choke segments, as in Figure 3 (although they look similar here for simplicity). Arrows and signs indicating pressure changes are omitted to avoid clutter of the figures. During forced inspiration, intra-airway pressure is lower than atmospheric pressure, and pleural pressure is lower than both. During forced expiration, intra-airway pressure is higher than atmospheric pressure, and pleural pressure is greater than both. The loops are idealized. In actual patients, some degree of ambiguity is often present, so the interpreter must have a high index of suspicion. Note that patients are often not coached to take a forceful inspiration, so the inspiratory portion of the loop is often rather flat, even in healthy subjects. When upper airway obstruction is suspected, the pulmonary function technician should be asked to coach both maximal expiratory and inspiratory efforts.

performing a flow-volume loop procedure. The flow during the midpoint of inspiration measured at 50% of the FVC (MIF_{50%} or FIF_{50%}) is usually greater than the maximal expiratory flow at 50% of the FVC (MEF_{50%} or FEF_{50%}), so the MEF_{50%}/MIF_{50%} ratio is typically < 1. In variable extrathoracic lesions the ratio is increased, while

in variable intrathoracic lesions the ratio is diminished, at ≤ 0.2 .²⁶

Empey used this same technique of reducing the orifice diameter to demonstrate that an increased ratio of FEV₁ to PEF was highly suggestive of central or upper airway obstruction, with the FEV₁/PEF index required value being > 10 mL/L/min.²⁷ Using these small orifices inserted into mouthpieces of patients without upper airway obstruction, Empey demonstrated upper airway obstruction in normal patients at an orifice ≤ 6 mm in diameter, which resulted in the FEV₁/PEF index > 10 mL/L/min required to develop upper airway obstruction; all patients with upper airway obstruction had a FEV₁/PEF index > 10 mL/L/min.²⁷

Rotman and colleagues evaluated yet another ratio; when the FEV₁/FEV_{0.5} was ≥ 1.5 , a central or upper airway obstruction should be considered.²⁸ The authors compared patients with upper airway obstruction, defined as obstruction at or proximal to the carina, to patients with chronic obstructive pulmonary disease, using measurements obtained via body plethysmography, and demonstrated that 4 values usually distinguished patients with upper airway obstruction: (1) forced inspiratory flow at 50% of the VC (FIF_{50%}) ≤ 100 L/min; (2) the ratio of forced expiratory flow at 50% of the VC to FIF_{50%} (FEF_{50%}/FIF_{50%}) or MEF_{50%}/MIF_{50%} ≥ 1 ; (3) FEV₁/PEF > 10 mL/L/min; and (4) FEV₁/FEV_{0.5} ≥ 1.5 .²⁸

In our opinion, spirometry occupies a status similar to that of auscultation. They are both mature, well established techniques that have changed little over many decades. Although simple to perform, their value relies critically on the experience and knowledge of the operator. Like auscultation, spirometry evaluates lung function rather than structure, and so effectively complements imaging techniques. A working knowledge of the determinants of flow limitation is helpful in interpreting spirometry.

Interpretation

First and foremost in the performance and interpretation of spirometry is the issue of test accuracy and quality. The American Thoracic Society (ATS) and the European Respiratory Society (ERS) published standard recommendations on spirometric technique and lung function testing in 2005.²⁹ Avoidance of spirometric testing is recommended within 1 month of a myocardial infarction or in patients with chest or abdominal pain, oral or facial pain exacerbated by a mouthpiece, stress incontinence, or dementia or confused state.²⁹ The goal of tests is to obtain accurate results that are in agreement between the measurement result and the actual true value. Reproducibility is vital to achieve accurate measurements, so individual measurements should be obtained under the same conditions, including same method, same instrument, same observer,

Table 1. Common Derived Parameters Generally Reported by Pulmonary Function Analyzers*

Parameter	Description
FVC	Forced vital capacity
FEV ₁	Forced expired volume in the first second
FEV ₁ /FVC	Ratio expressed as a percent of the FVC
FEV _{0.5}	Forced expired volume in the first half second (Measurable but not standardized, and of questionable value)
FEV ₆	Forced expired volume in the first 6 seconds (used as a surrogate for the FVC in patients with severe airway obstruction and long forced expiratory time)
FEF _{25-75%}	Average flow during the middle half of the FVC (of controversial value in detecting small airway disease)
PEF	Maximal flow during the FVC
$\dot{V}_{\max 50\%}$	Instantaneous flow at 50% of the FVC
$\dot{V}_{\max 75\%}$	Instantaneous flow at 75% of the FVC

*Only the first three are of undisputed utility, as the others have not been studied in as many diverse large groups as the first three. Clearly, an infinite number of other derived parameters can be reported for air flows in shorter or longer time periods than the FEV₁, or instantaneous flows at any percentage of the FVC, but there is no evidence that this would be of benefit.

same location, same condition of use, and repeated over a short period of time.²⁹

As stated in the introduction, the FVC and FEV₁, along with their respective ratios, are the best validated parameters derived from the spirogram. Innumerable measurements can be made from the time-volume curve and flow-volume loop, and many have been evaluated in an attempt to find better indices of lung function or indicators of small airway disease. Table 1 lists most of the parameters that have been formally studied. The subject of small airway disease and the decades-long search for a test to detect it is beyond the scope of this paper, as it involves more than spirometry. Automated pulmonary function machines will easily report many of the measurements on this list, along with predicted normal values. There is little evidence that any of them provide information about the patient not already evident in FVC and FEV₁, along with their respective ratios.

The only exception is the forced midexpiratory flow rate (FEF_{25-75%}), which has undergone the most scrutiny of any of these "lesser" tests (Fig. 10). Whether it is helpful or not remains controversial, even after decades of research. The reason for this variability is that the failure to completely empty the lungs will drive the middle half of the curve toward the portion with the steepest slope and so increase the value of the FEF_{25-75%} even though the FEV₁ would be unaffected so long as the maximal effort lasted at least 1 second. Despite controversy and years of research, the use of FEF_{25-75%} further illustrates the ever-changing recommendations for spirometry. Fixed standard

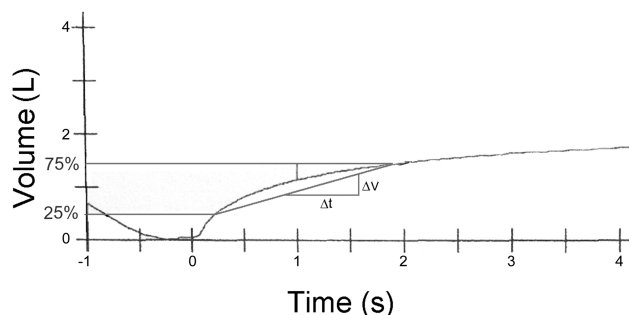


Fig. 10. Diagram showing how the forced midexpiratory flow rate ($FEF_{25-75\%}$) is measured from a volume-time tracing. Because the middle half of the expired volume determines the $FEF_{25-75\%}$, an incomplete forced vital capacity maneuver will shift the $FEF_{25-75\%}$ toward the earlier part of the curve and raise its value, because the rate of change in expired volume is greatest near the beginning of the effort.

cutoffs are no longer recommended, especially with age, ethnic, and sex differences.³⁰ In regards to using the $FEF_{25-75\%}$, we recommend not using it, but many clinicians do. If the $FEF_{25-75\%}$ is used for clinical care, we suggest using it for trends rather than true diagnostic purposes.

The ATS established the first statement regarding standards at the Snowbird workshop in 1979,³¹ with subsequent updates to these standards in 1987³² and 1994.³³ The first initiative for spirometry standardization in Europe was formulated by the European Community for Steel and Coal in 1983,³⁴ which was later updated as the official statement of the ERS on spirometry in 1993.³⁵ Airway obstruction is assessed based on the FEV_1/FVC ratio, with these previous guidelines recommending a fixed ratio of 70% as the cutoff for normal. More recent recommendations by the ATS and ERS Task Force³⁰ discussed the advantage of using VC rather than FVC; thus, the ratio of FEV_1 to VC is capable of accurately identifying more obstructive patterns than its ratio to FVC, since FVC is more dependent on flow and volume histories, as demonstrated by Brusasco et al.³⁶ Celli and colleagues demonstrated that the use of fixed cutoffs, such as an FEV_1/FVC ratio $< 70\%$ for airway obstruction, tended to markedly misclassify subjects who were over 50 years of age.³⁷

The ATS and ERS Task Force thus recommended that a decrease in a major spirometric parameter, including FEV_1 , VC, and FEV_1/VC , below their relevant 5th percentiles is consistent with a pulmonary defect.³⁰ Problems develop when these parameters lie near to the upper and lower limits of normal, leading to a failure to describe the function status, so the authors suggested additional studies, such as bronchodilator response, diffusion capacity, gas-exchange evaluation, respiratory muscle strength measurements, or exercise testing.³⁰ Briefly, a diagnosis of obstruction requires an FEV_1/VC ratio of < 5 th percentile of predicted, while restriction requires a total lung capacity

Table 2. Severity of Spirometric Abnormality, Based on Forced Expired Volume in the First Second*

Degree of Severity	FEV_1 (% of predicted)
Mild	> 70
Moderate	60–69
Moderately severe	50–59
Severe	35–49
Very severe	< 35

*As recommended by the American Thoracic Society and European Respiratory Society Task Force.²²
 FEV_1 = forced expired volume in the first second.

of < 5 th percentile of predicted and a normal FEV_1/VC ratio; a mixed defect, where there is coexistence of obstruction and restriction, is defined when both FEV_1/VC ratio and total lung capacity are < 5 th percentile of predicted.³⁰ If an obstructive defect is determined to be present, the severity of the obstruction is determined by percent of predicted of the FEV_1 , as outlined in Table 2.³⁰ The physiological response of the lower airways to a bronchodilator involves the airway epithelium, bronchial smooth muscle, inflammatory mediators, and nerve cells, so individual responses to a bronchodilator can be variable. The ATS and ERS Task Force recommended to test either a single dose of bronchodilator agent in a pulmonary function testing laboratory or after a clinical trial conducted over 2–8 weeks, with a defined significant positive bronchodilator response in percent change from baseline and absolute changes in FEV_1 and/or FVC being $> 12\%$ and 200 mL, respectively.³⁰

It is important to remember that the comparison of pulmonary function values to the “predicted” values (reported as percent of predicted) is useful only for persons whose lung function was unknown before the test in question. The predicted values are those of healthy populations of similar age, race, and sex. The percent of predicted values help the interpreter decide whether the patient significantly departs from the normal group. In the case of a patient for whom previous studies exist, subsequent tests should relate to the previous ones. For example, a person who suffers a fall in FEV_1 from 110% predicted to 85% predicted, while technically still within the normal range, is clearly deteriorating. His or her real normal value is the best previously recorded. Excessive importance should not be placed on the predicted values that are inevitably printed out by most every spirometer.

Other statistical parameters could also be monitored rather than percent of predicted, including z scores or standard deviations of spirometric measurements, which can account for variability. The key factor is to be consistent in what parameter is monitored. Our suggestion is to follow the FEV_1 , which is the most repeatable parameter that changes in both obstructive and restrictive lung diseases.

A short-term, 2-point change in the FEV₁ > 12% percent of predicted and > 0.2 L are usually statistically significant and are probably clinically relevant.³⁰ Changes in the FEV₁ less than these criteria may be as important, but depend on the reproducibility of the pre-bronchodilator and post-bronchodilator results.³⁰

Summary

The physiologic basis of spirometry includes the measurement of individual inhalation and exhalation volumes of air as a function of time. This simple lung function measurement, which has well established normal values, is very effective and well validated in diagnosing and monitoring upper and lower airway abnormalities, including numerous lung diseases. This article summarizes the complex respiratory physiology of spirometry, which is dependent on the elasticity of the lungs and airway resistance and is determined by the degree of expiratory force exerted. Understanding this complicated physiology is very important in the field of respiratory care and the interpretation of spirometry.

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