

# Spirometry

Theodore G. Liou · Richard E. Kanner

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**Abstract** Pulmonary function testing is useful for the diagnosis and management of a variety of pulmonary conditions, and the most commonly obtained component is spirometry. Spirometry is most useful in the evaluation of obstructive airway disorders but can be a helpful tool in the management of patients with chest restriction or mixed disease. The utility of spirometry depends on reproducibility, standardization, and quality of testing. Accurate interpretation of test results depends on the availability of reference equations applicable to the subject undergoing testing. This paper reviews basic concepts, testing procedures, and interpretation of a single set of spirometry results as well as results obtained over time and gives an overview of previously published reference equations.

**Keywords** Spirometry · Lung · FEV · FVC · PFT

## Introduction

Pulmonary function testing (PFT) is useful for the diagnosis and management of a variety of pulmonary conditions. The most frequently obtained component of PFT is spirometry. Spirometry involves dynamic measurements of the bellows function of the lung that reflects a patient's ability to

breathe. While these measurements can be made both during inhalation and exhalation, the measurements most frequently used clinically are those made during exhalation.

Spirometry is most useful in the evaluation of obstructive airway disorders as found, for example, in asthma where abnormal findings are reversible or in chronic obstructive pulmonary disease (COPD) where the findings are classically irreversible. It is less helpful in assessing restrictive diseases.

The usefulness of spirometric measurements depends on reproducibility, standardization, and quality. It is an effort-dependent test. Thus, the technician must be well trained and the testing device periodically calibrated. The clinical utility of spirometry is expanded when performed serially to track worsening of disease or efficacy of treatment.

## Lung volumes and capacities

Basic understanding of the measurements produced by spirometry or other pulmonary function tests requires understanding some basic definitions of the compartments of the lung. Four volumes and four capacities are defined to comprise the air contained in or moved by the lung (Fig. 1). By definition, a volume is a compartment that cannot be further sensibly subdivided, while a capacity is composed of two or more volumes.

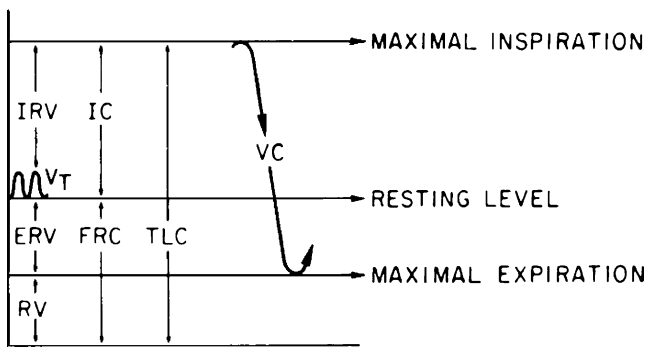
The four volumes of the lung are defined as follows:

1. Tidal volume ( $V_T$ ) or (TV) is the amount of air or of a gas that is inhaled with a normal inspiratory effort from the resting position of the chest and lung. It may be somewhat difficult to measure due to normal variation between breaths or due to a subject's knowledge that he or she is being observed.

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T. G. Liou · R. E. Kanner  
Division of Respiratory, Critical Care, and Occupational  
Pulmonary Medicine, Department of Internal Medicine,  
University of Utah,  
Salt Lake City, UT 84132, USA

T. G. Liou (✉)  
26 North Medical Drive,  
Salt Lake City, UT 84132, USA  
e-mail: ted.liou@utah.edu



**Fig. 1** Lung volumes and capacities in relation to points of maximal inspiration and expiration and the resting level. Vital capacity ( $VC$ ) is an expiratory maneuver. Abbreviations are as follows:  $IRV$ —inspiratory reserve volume;  $V_T$ —tidal volume;  $ERV$ —expiratory reserve volume;  $RV$ —residual volume;  $IC$ —inspiratory capacity;  $FRC$ —functional residual capacity;  $TLC$ —total lung capacity

- Inspiratory reserve volume ( $IRV$ ) is the additional amount of gas that can be inhaled following this normal inspiratory effort. This is an infrequently used measurement and is somewhat difficult to measure because of variation in tidal volume.
- Expiratory reserve volume ( $ERV$ ): after completing a normal expiratory effort that returns the lung and chest wall to the resting position, an additional amount of gas can be exhaled with a voluntary effort that is called the expiratory reserve volume. Thus, the  $ERV$  is the amount of gas that can be exhaled when the expiratory effort begins at the resting position and ends at maximal expiration.
- Residual volume ( $RV$ ): at the point of maximal expiration, there is still a quantity of gas in the lung that cannot be expelled. This remaining volume is the residual volume.

The  $V_T$ ,  $IRV$ , and  $ERV$  may be measured with spirometry. The  $RV$  is not measurable by spirometry (see the lung volume measurements review).

The four capacities of the lung are:

- The total lung capacity ( $TLC$ ) comprises all four volumes.
- The inspiratory capacity ( $IC$ ) is the maximum amount of gas that can be inhaled from the resting position. The  $IC$  is the sum of the  $V_T$  and the  $IRV$ .
- Functional residual capacity ( $FRC$ ): after a normal exhalation to the resting position of the lung and chest wall, the amount of gas remaining in the lung is the  $FRC$ , which consists of the  $ERV$  plus the  $RV$ .
- The vital capacity ( $VC$ ) is the amount of gas that can be expelled from the lung when exhalation starts at the maximal inspiratory level and proceeds to the maximal expiratory level. It is the sum of the  $IRV$ ,  $V_T$ , and  $ERV$  (or  $IC+ERV$ ).

The  $IC$  and  $VC$  may be measured using spirometry. The  $TLC$  and  $FRC$  must be measured using lung volume measurements because both measures include the  $RV$  which cannot be measured by spirometry (see lung volume review).

### Spirometric measurements

The primary result of spirometric measurements is the vital capacity ( $VC$ ), the amount of gas exhaled from a maximal inspiration ( $TLC$  level) to maximal exhalation ( $RV$  level). The raw data for this measurement can be displayed graphically as liters of exhaled gas as a function of time (Fig. 2b). The exhalation can either be forced (Fig. 2b) or unforced.

For a maximal forced effort, typical end points examined are volume exhaled to 1, 3, 6 s, or to end of exhalation. The end of exhalation is identified when the test subject is no longer able to expel additional gas. On a volume–time curve recording the exhalation, the change in volume per unit time drops to approximately zero (Fig. 2b, left side of tracing) [1,2]. Volumes measured for timed end points prior to the end of exhalation are named the forced expiratory volume ( $FEV$ ) in 1, 3, 6 s, or some other number of seconds. The most frequently recorded and used  $FEV$  is the  $FEV$  in 1 s ( $FEV_1$ ).

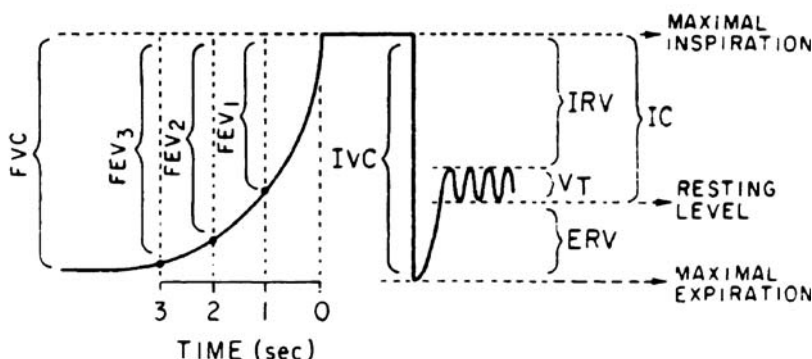
A non-forced vital capacity, usually called a slow vital capacity ( $SVC$ ), is measured from a full inhalation to the point of a full exhalation. The subject is asked to blow steadily until exhalation is complete. Because of lack of reproducibility, timed expiratory volumes are not reported from an  $SVC$  maneuver. The effort is relatively unforced until near the point of end exhalation where additional force is required to expel the last quantity of air [1,2]. Increased force is needed to expel air from the lungs from the relaxed neutral position of the chest where the force of the tendency of the thoracic cage to expand is exactly countered by the tendency of the lung parenchyma to contract [1].

Spirometric measures may also be recorded during inhalation. The inspiratory vital capacity is measured as the volume of gas inhaled slowly and steadily by a test subject from full exhalation to full inhalation. The  $IC$  is the volume of gas inhaled from rest or end of exhalation during tidal breathing to full inhalation.

The direct measurements discussed so far are usually used to derive additional measures of lung function. The ratio of  $FEV_1$  to force vital capacity ( $FVC$ ) is nearly always calculated when spirometry is performed and is expressed as a percentage of  $FVC$ . It is helpful for defining and understanding airway obstruction. A more complex transformation creates the flow–volume loop (Fig. 3). At every point during the  $FVC$  maneuver, the flow rate or the instantaneous slope of the volume time tracing (Fig. 1) is plotted as a function of the cumulative exhaled volume (Fig. 3). The loop is completed when values measured during the immediate



Panel A

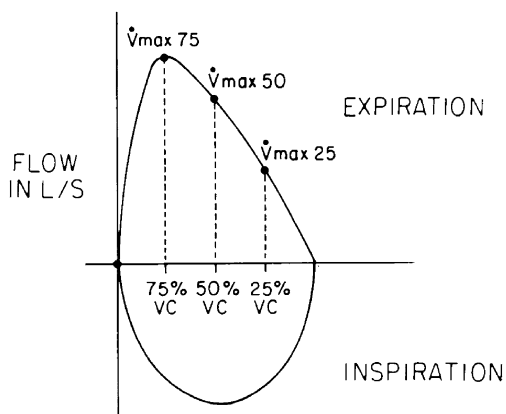


Panel B

**Fig. 2** Spirometry measurements. The figure shows the readout of an analog inverted bell-type spirometer. The X-axis is time and increases to the left; the Y-axis is exhaled volume and increases to the bottom. A test subject exhales into the device raising the bell (a). As the bell rises, it moves a pen in the opposite direction that scribes onto chart paper that is also moving, in this case, from left to right (b). Modern spirometers (a) transform the physical movements of the bell into digital signals to produce volume–time tracings. At the beginning of

the tracing, the subject is performing tidal breathing (*VT*). To begin the forced vital capacity measurement, the subject exhales fully to the dashed line marked *Maximal Expiration*, take a rapid full breath to *Maximal Inspiration*, and holds his breath for a little more than 1 s. On command, the patient exhales as forcefully and quickly as possible. By a little more than 3 s on this tracing, the exhalation is complete as demonstrated by cessation of vertical movement of the trace

maximal inhalation are plotted on the same graph. The flow–volume loop provides a graphical method for determining the maximal flow rate during exhalation and inhalation as well as maximal flow rates at various fractions of the FVC (Fig. 3). In common practice, the inspiratory portion of the flow–volume loop often does not return exactly to the starting volume because patients do not inhale fully unless specifically coached. Even then, the original starting point of full inhalation may not be reached due to the exertion required to complete the earlier parts of each trial.



**Fig. 3** Flow volume curve. The figure shows flow plotted as a function of exhaled volume. The curve is derived from a FVC measurement. As marked, the maximal flow rate at 75%, 50%, and 25% of the VC can be estimated as well as an overall maximal flow rate,  $L_{max}$ , which approximates the  $L_{max}$  shown in the figure

There are other measures that can be obtained from the time–volume tracing. These include peak expiratory flow and maximal mid-expiratory flow. The flow–volume loop allows for measurements of flow at 75%, 50%, and 25% of the expired volume (Fig. 3). Although these values are sometimes helpful in determining the acceptability of a particular effort, they are too variable, both inter- and intra-subject, to recommend for general usage.

A final spirometric measure that is now less commonly obtained is the maximal voluntary ventilation (MVV). MVV measurement has been superseded by the FEV<sub>1</sub> due to good correlation of FEV<sub>1</sub> with MVV and greatly improved ease of FEV<sub>1</sub> measurement. Rather than derivation from a single breath, MVV is the total volume of air exhaled during 12 s of breathing with maximal effort at a rate between 90 and 110 breaths per minute [1,2]. In practice, patients with lung disease may find maximal breathing for 12 s to be exhausting. The most frequent uses of MVV are with pulmonary exercise testing, for determining breathing reserve and in neuromuscular disorders of the respiratory system.

**Reference values for spirometric measurements**

For the FVC and selected times of FEV measurement, equations exist that allow comparison of the patient’s values with measurements derived from normal subjects

of the same age, gender, height, and ethnicity. Many equations allow the option of substituting arm span for height for patients unable to stand due to missing limbs, severe scoliosis, or other abnormality. Sitting height has also been used occasionally to derive normalization equations instead of standing height in selected populations [3,4]. Use of sitting height as a predictor of normal lung function may be less prone to variation due to ethnicity and race than use of standing height [4]. Some sets of prediction values include body weight in reference spirometric equations. The three most frequently used values are expressed as the percent of predicted FEV<sub>1</sub> (FEV<sub>1</sub>%) and the percent of predicted FVC (FVC%) and the FEV<sub>1</sub>/FVC.

The reference equations are derived by performing spirometry in populations of volunteers that are considered to have normal lung function. Typically, a questionnaire is administered to potential study subjects or their parents from a selected geographic, age-related, occupation-related, or ethnic or national group with the intent to find never-smoking individuals without previous lung injury, current pulmonary symptoms, or overt lung disease and to confirm smoking status. Most reference equations are derived after successful exclusion of current smokers. Others are derived from lifetime non-smokers. Due to the prevalence of smoking in some populations, however, smokers may be included in some reference equations [5].

After sufficient sampling of normal patients, reference equations can be derived that can be used to predict normal values for other individuals matching the characteristics of the volunteer population. Methods for deriving the reference equations vary according to the distribution of data from the normal volunteers. Unfortunately, there is no uniform method for deciding the form of the normalizing equations, and some exploratory statistical modeling must be performed to determine the most satisfactory fit of the data. Linear equations are preferred due to easier interpretation of the equations and improved ease of application for normalizing spirometry results. Often, however, linear equations do not fit the data from normal volunteers well. This typically leads to the use of non-linear equations that normalize spirometric measures according to the aforementioned age, height, and sometimes other variables such as weight but with non-linear terms such as the square of height. See, for example, Hankinson et al. [6]. Nevertheless, with the ubiquity of automation in modern spirometry equipment, application of these more complex equations is usually not difficult.

The ideal population for derivation of reference equations is normal never-smoking volunteers drawn from the local community served by a particular pulmonary laboratory [1]. Equations derived from such an ideal group include the effects of local environmental factors and geographic variations in genetic background. Application

of local reference equations depends on an assumption that there is a reasonable degree of homogeneity in the population served by the pulmonary laboratory. However, local reference or normalization equations are often not available [1] and may not be appropriate for communities with a great deal of genetic or environmental diversity or for an individual visiting the community or otherwise not representative of the local reference population. While the raw FEV and FVC measurements are unaffected, interpretation in settings where appropriate reference equations are unavailable must proceed with caution. The Medical Director of the laboratory needs to determine which reference equations best fit the population that is being served.

Separate sets of equations exist for children, adults, children and adults together, White, Black, Hispanic, and numerous other ethnic groups, national groups, and even groups by occupation, for example, South African male bankers [7]. Table 1 includes a partial listing of reference equations available for a wide variety of groups published in peer-reviewed journals in English. Application of these equations typically calculates the predicted normal values and the predicted lower limits of normal.

It is important to avoid errors in applying reference equations by extrapolation beyond the limits of the underlying data. For example, applying equations that were designed to predict adult values of FEV<sub>1</sub> and FVC to measurements from an 8-year-old patient will lead to serious errors in interpretation. Similarly, use of equations derived from normal Caucasian men and women on values from Hispanic or African-American patients may lead to errors. Conversely, it is rare, but not impossible, for the same equations to apply to diverse populations [8].

Because of the diversity of physiology worldwide, there remain many individuals for whom reference equations are not available to assist in interpretation of results. In these subjects, extrapolation may be applied cautiously and may be of some use. For example, a scaling factor of 0.88 was suggested in the past as a correction when using Caucasian male reference equations on results obtained from African-American males in the US [9]. Recommendations such as these may be superseded by the derivation of specific reference equations when enough normal individuals in the population have been found, as, for example, has been done for African-Americans and Hispanics in the US [6]. Other extrapolation factors, derived for other clinically identifiable groups, may be found in the literature [10]. Any use of scaling factors should be noted as part of the formal interpretation of pulmonary function.

Even when appropriate equations appear to exist, subtle errors are possible. For example, application of reference equations derived from elderly Chinese subjects in Hong Kong several decades ago [11] may lead to erroneous interpretations when applied to values obtained from

**Table 1** The table lists papers from peer-reviewed journals in English that present reference equations and reference values for various populations

Reference and number	Year published	Number of subjects	Population studied
Berglund et al. [32]	1963	296 M 201 F	Healthy and normal patients aged 7 to 70, Sweden
Ferris et al. [33]	1965	355 M 914 F	Healthy and current non-smokers from Berlin, New Hampshire
Harrison et al. [34]	1969	217 M 121F 228 Boys	Normal adults 18–50 years old residing at Debarech, Adi-Arkai, and Geech, Ethiopia (1,500-, 3,000-, and 3,700-m elevation, respectively); normal school boys (228) aged 6 to 23 years from Debarech and Adi-Arkai
Morris et al. [35]	1971	517 M 471 F	Healthy non-smoking adults, Portland, OR
Cherniack and Raber [36]	1972	870 M 452 F	Never smokers with no history of lung disease or symptoms, Winnipeg, Manitoba, Canada
Knudson et al. [37]	1976	291 M 455 F	Healthy, never-smoking, non-Hispanic normal Caucasians, aged 9–79 years, Tucson, Arizona
Cotes et al. [3]	1979	120 M 134 F	Healthy boy and girl twins aged 8–16 years from Cardiff, Wales, UK; presents equations that use sitting height as a predictor of lung function
Gibson et al. [38]	1979	6,511 M 6,275 F	Non-smoking Australian adults
Hsu et al. [39]	1979	Mexican–American 259 M 297 F Caucasian 335 M 382 F African-American 216 M 311 F	Mexican–American, Caucasian and African-American healthy non-wheezing children from Houston
Crapo et al. [40]	1981	125 M 126 F	Non-smoking, urban adults at 1,400 m above sea level, Salt Lake City, Utah
Viljanen et al. [41]	1982	296 M 257 F	Non-smoking Scandinavian adults
Burrows et al. [42]	1983	377 M 539 F	Never smokers from the Tucson Epidemiological Study of Airways Obstructive Disease
Hsi et al. [4]	1983	Mexican–American 259 M 297 F Caucasian 335 M 382 F African-American 216 M 311 F	Mexican–American, Caucasian and African-American healthy, non-wheezing children from Houston; presentation of equations that use sitting height as a predictor
Mengesha and Mekonnen [43]	1985	143 M 117 F	Non-smoking, healthy Ethiopian adults
Roca et al. [44]	1986	443 M 427 F	Non-smoking, urban Mediterranean adults, Barcelona, Spain; equations were validated in 1998 [45]
Udwadia et al. [46]	1986	472 M 288 F	Non-smoking, healthy, urban Indian adults, Bombay, India
Ayub et al. [47]	1987	116 M 114 F	Non-smoking, healthy, urban and rural Pakistani adults

**Table 1** (continued)

Reference and number	Year published	Number of subjects	Population studied
Chatterjee et al. [48]	1988	104 M	Healthy, non-smoking men associated with Calcutta University, Calcutta, India
Neukirch et al. [49]	1988	Polynesian 180 M 190 F European 202 M 179 F Chinese 135 M 121 F	Chinese, European, and Polynesian children (mean age 14.4) attending school in Tahiti
Shamssain [50]	1988	275 M	Healthy Libyan men
Woo and Pang [11]	1988	129 M 210 F	Healthy, elderly Chinese men and women including non-smokers, ex-smokers, and current smokers in Hong Kong
Wu and Yang [51]	1990	78 M 102 F	Elderly Chinese (age>60 years), Taiwan
Olanrewaju [52]	1991	131	School children and adolescents, Nigeria
Roberts et al. [53]	1991	83 M 96 F	Non-smoking urban Caucasian adults, London, England
Shamssain [54]	1991	973 M 1,026 F	Non-smoking black school children, Umtata, Republic of Transkei, South Africa
Smolej-Narancic et al. [55]	1991	327 M 582 F	Non-smoking adults, Eastern Adriatic Islands, Former Yugoslavia
Rao et al. [56]	1992	71 M 25 F	Healthy, non-smoking adults, Gujarati, India
Singh et al. [57,58] <sup>a</sup>	1992	1385 M 614 F	Healthy, non-smoking adolescents and women, Malaysia
Thompson et al. [5]	1992	126 M (107 smokers) 103 F (78 smokers)	Smoking and non-smoking Australian Aborigines, North Queensland, Australia
Chia et al. [59]	1993	277 M 175 F	Healthy Chinese, Malaysian, Indian adults, Singapore
Shamssain [60]	1994	1,624 M 1,376 F	Non-smoking, healthy Xhosa black adults, Umtata, Republic of Transkei, South Africa
Chowgule et al. [61]	1995	354 M 278 F	Normal urban Indian children, Bombay, India
Gore et al. [62]	1995	165 M 249 F	Lifetime non-smoking Caucasian adults, Adelaide, Australia
Udupihille [63]	1995	328 M 367 F	Non-smoking Sinhalese Sri Lankan adults
Brändli et al. [64]	1996	1,267 M 1,890 F	Never-smoking white Swiss adults aged 18–60 years from the Swiss Study on Air Pollution and Lung Diseases in Adults
Huang et al. [65]	1996	506 F	Never-smoking adult Chinese women, Taiwan
Louw et al. [7]	1996	796 M	Healthy black and white male South African bank workers
Quintero et al. [66]	1996	214 M	Healthy, non-smoking male Nicaraguan workers (106 industrial, 53 farm, 55 office workers)
Chin et al. [67]	1997	Chinese 60 M 115 F Malay 37 M 58 F	Chinese, Malaysian and Indian never-smoking adults without history of lung disease, Singapore



**Table 1** (continued)

Reference and number	Year published	Number of subjects	Population studied
		Indian	
		49 M	
		87 F	
Pan et al. [68]	1997	511 M 1,516 F	Never-smoking healthy adult Chinese in the Cardiovascular Disease Risk Factor Two Township Study, Taiwan
McDonnell et al. [69]	1998	199 M 366 F	Healthy never-smoking Seventh Day Adventists aged 43–79 years from San Francisco, Los Angeles and San Diego, California, USA
Crapo et al. [8]	1999	176 M 168 F	Healthy, non-smoking urban Mongolian adults, Ulan Bator, Mongolia
Hankinson et al. [6]	1999	Caucasian 898 M 1,383 F	Asymptomatic, lifelong non-smokers, children and adults, US (NHANES III study)
		African–American 1,027 M 1,481 F	
		Mexican–American 1,116 M 1,523 F	
Baltopoulos et al. [70]	2000	38 M 33 F	Elderly Greek adults, Greece
Dejsomritrutai et al. [71]	2000	1,655 M 2,299 F	Healthy never-smoking adults from across Thailand
Hnizdo et al. [72]	2000	18,524 M	15,772 black and 2,752 white male gold miners, South Africa
Ip et al. [73]	2000	392 M 460 F	Non-smoking, native-born Chinese children 7–19 years old with no history of lung disease from seven schools in Hong Kong
Vijayan et al. [74]	2000	246 M 223 F	Healthy children and adolescents, South India
Kivastik and Kingisepp [75]	2001	527 M 643 F	Non-smoking Estonian school children
Langhammer et al. [76]	2001	362 M 546 F	Healthy never-smoking adults from Norway aged 20–80 years
Manzke et al. [77]	2001	213 M 187 F	Hospitalized children without lung disease, Germany
Marion et al. [78]	2001	190 M 253 F	Healthy American Indians from 14 different tribes from Central Arizona, Southwestern Oklahoma, Central South Dakota and northeastern North Dakota in the US
Milivojevic-Poleksic et al. [79]	2001	39 M 62 F	Adult Pacific Islanders from Auckland, New Zealand; 87% never smokers, 13% <10 pack years smoking
Virani et al. [80]	2001	195 M 202 F	Healthy, non-smoking Indian adults, Pondicherry, India
Zverev and Gondwe [81]	2001	230 M 284 F	Urban, healthy Malawian school children, Blantyre, Malawi
Boskady et al. [82]	2004	326 M 246 F	Healthy, non-smoking adults without cardiopulmonary disease from Mashhad, Iran
Mohamed et al. [83]	2002	58 M 60 F	Non-smoking healthy Italian young adults, Italy
Golshan et al. [84]	2003	1,793 M 1,420 F	Never-regular-smoking Persian children and adults, Isfahan, Iran
Havryk et al. [85]	2003	130 M 119 F	Children and adult Sherpas without lung disease and less than five pack years smoking from Khunde and Khumjung, Nepal (3,840-m elevation).

**Table 1** (continued)

Reference and number	Year published	Number of subjects	Population studied
Mustajbegovic et al. [86]	2003	1,162 M 1,320 F	Healthy, never-smoking, urban and rural adults, Croatia
Pérez-Padilla et al. [87]	2003	2,076 M 1,943 F	Children from schools in Mexico City, Mexico (2,240-m elevation)
Zapletal and Chalupov [18]	2003	102 M 71 F	Preschool (age 3–6 years) Czech children, Czech Republic
Al-Riyami et al. [88]	2004	382 M 455 F	Non-smoking, healthy children attending primary, intermediate and secondary schools in Al-Khod, Oman
Boskabady et al. [89]	2004	208 M 185 F	Non-smoking children without cardiopulmonary disease aged 8–18 years from Mashhad, Iran
Falaschetti et al. [90]	2004	2,497 M 3,556 F	Healthy, never-smoking English adolescents (>16 years old) and adults, England (1995/1996 Health Survey for England)
Fulambarker et al. [91]	2004	226 M 137 F	Never-smoking, healthy Asian–Indian adults living in Chicago, IL, USA
García-Río et al. [92]	2004	179 M 279 F	Elderly non-smoking European adults, Madrid, Spain
Kotaniemi and Kataja [93]	2004	213 M 227 F	Healthy, non-smoking (57% former smoking) adults from Finland
Trabelsi et al. [94]	2004	581 M 533 F	Asymptomatic non-smoking Tunisian children, Tunisia
Ostrowski et al. [95]	2005	49 M 87 F	Healthy Polish adults older than 40 years including smokers and ex-smokers, Lublin, Poland
Zhang et al. [96]	2005	184 M 159 F	3–6 year old Chinese children, Shenzheng, China <sup>‡</sup>
Ip et al. [12]	2006	494 M 595 F	Healthy, non-smoking Chinese adults, Hong Kong, China
Johannessen et al. [97]	2006	237 M 278 F	Healthy never-smoking Caucasian Norwegian adults 26 to 82 years old in the Hordaland County Cohort Study, Norway
Nku et al. [98]	2006	600 F	Healthy non-smoking Nigerian adult women, south eastern Nigeria
Pesant et al. [22]	2007	61 M 67 F	Caucasian children aged 3–5 years without history of lung disease from 11 daycare centers in Sherbrooke, Quebec, Canada
Piccioni et al. [21]	2007	406 M 360 F	3–6 year old children from 20 kindergartens, Turin, Italy

Papers were identified using PubMed at [www.pubmed.gov](http://www.pubmed.gov) and from citations within papers; the list is not exhaustive but rather concentrates on listing papers of continuing clinical relevance and of wide diversity in background of study subjects. We selected original works that had the primary intent of deriving reference equations for spirometry. Papers of the well-studied North American Caucasian population that are no longer clinically applied, for example, because they predate American Thoracic Society standards for performing spirometry, are mostly omitted. An extensive, but also incomplete, list of older literature reporting reference equations can be found in Quanjer et al. [99]. Numbers of subjects refers to those left after application of inclusion and exclusion criteria within each paper and may be approximations for papers where variable numbers of patients participated in different parts of each study. Unless specified, smokers may have been included in derivation of reference equations presented. Some papers present equations for additional values beyond FEV<sub>1</sub> and FVC. Particular details of the studied populations that may be of special interest, such as altitude [34,40,85,87] or particular occupations [7,72] are briefly noted in the last column

<sup>‡</sup> The data and equations for female subjects appear to be identical between these two publications by the same authors

elderly Chinese subjects in Hong Kong today or when applied to Chinese subjects from other parts of China or other parts of the world [12]. While these patients may share a common genetic heritage, local environmental factors, for example, improved access to food, may cause significant differences in spirometric results.

### Technical aspects of spirometry

Spirometry should be performed on equipment that is calibrated at least daily using a calibrated 3 l gas syringe. Spirometric equipment should be checked daily or at least weekly for air leaks [1,2,13]. Air leaks can significantly



decrease FVC although smaller leaks have little effect on measurements of FEV<sub>1</sub> [13]. More frequent calibrations and air leak checks should be performed for equipment that is moved as for field studies or when large numbers of subjects are tested as in mass screening programs. Equipment should be kept in a room maintained at a comfortable room temperature to help maintain calibration in addition to improving patient performance.

There are two major types of spirometers, volume displacement spirometers and flow integrated pneumotachographs. As the name implies, volume displacement spirometers measure the actual volume exhaled by a test subject during an FVC or SVC maneuver. These spirometers are large and have moving parts but hold their calibration extremely well. Flow integrated pneumotachographs are electronic devices that are typically small and without moving parts. These measure volume by performing integration of flow rates by time—essentially the opposite of calculating flow rates from the volume–time measurements and tracings. Pneumotachographs are more likely to need frequent calibration than volume displacement spirometers. Because of their portability, these spirometers are likely to be used under more variable conditions than their larger and more mechanical counterparts.

Regardless of type of spirometer, the American Thoracic Society (ATS) and European Respiratory Society (ERS) standards require that a spirometer be capable of accumulating a minimum volume of 8 l over a minimum of 15 s. A spirometer must have an accuracy of the greater of  $\pm 3\%$  of readings or  $\pm 0.050$  l with flows of between 0 and 14 l/s. At 14 l/s, the total resistance to airflow must be less than 1.5 cm H<sub>2</sub>O per liter per second [2]. Manufacturers are responsible for producing spirometers that meet these minimum requirements and must disclose actual performance characteristics.

Spirometers used to measure MVV must comply with additional performance requirements to assure quality. The spirometer must have a flat amplitude–frequency response ( $\pm 10\%$  from baseline) from 0 Hz to greater than or equal to 4 Hz at flow rates up to 12 l/s. In calibration using a pump to generate mechanical breaths [2], the spirometer must be able to measure volumes delivered by flow rates up to 250 l/min with an accuracy of the greater of  $\pm 10.5\%$  or 20 l/min [2].

All spirometric measurements should be reported at body temperature (37°C), ambient pressure, saturated with water or body temperature pressure-saturated. The correction methods differ according to the type of spirometer, volume displacement or flow pneumotachograph, and whether measurement is of inhalation or exhalation. The actual correction takes into account the ambient barometric pressure and local humidity. The vast majority of modern spirometers perform these functions automatically. Additional attention may be required however if ambient temperature or humidity or barometric pressure is rapidly changing [1,2].

## Obtaining spirometric measurements

Prior to actual spirometry, patient- and test-specific information should be gathered in order to facilitate instrument calibration and interpretation of results. The patient's height (without shoes), age, gender, weight, and ethnicity or racial background should be collected. For patients with kyphoscoliosis or inability to stand for other reasons such as missing limbs, an approximation to height should be substituted using arm span. This method has been investigated and found to be sufficient in several populations of different background for patients with osteoporosis or vertebral-fracture-induced changes in height [14–17]. Another alternative, when reference equations are available, is to use sitting height [3,4]. Any time the calculations are performed using variant methods, a note should be included in the formal PFT report declaring the variance.

Patient positioning and comfort are key elements for obtaining reliable spirometry measurements. Spirometry should be performed with the subjects in a sitting position with the head held in a neutral position. Uncomfortable room temperatures, tight clothing, or uncomfortable seating can all lead to inaccurate measurements. Artifacts due to temperature and body positioning variations have been well described [9].

Patient cooperation is vital for completion of testing that produces results amenable to interpretation. Patients may be unable to cooperate fully for a number of reasons including age less than 5–6 years (although there are clearly exceptions [18–22]), lack of common language with the technician administering the test or mental or physical impairment of some type. Patients may also be unwilling to cooperate because of non-medical issues including malingering in hopes of some type of secondary gain or fear of loss of qualification for employment. In many of these cases, spirometry will not be reproducible and will thus not be interpretable. The ordering physician, not the pulmonary function laboratory, must undertake resolution of these issues.

Finally, the nature of patients undergoing spirometry is such that many will be using medications that can affect results. Patients should be asked, if possible and safe, to refrain from use of bronchodilators prior to testing or certain inhaled medications such as hypertonic saline for patients with cystic fibrosis. For patients unable to refrain, a comment including the type of medication and interval between dosing and spirometric testing should be included in the report.

## Testing procedures

SVC testing should precede FVC testing. A total of four trials is the maximum recommended by the ERS/ATS working group in order to prevent muscle fatigue and associated artifacts [2]. The technician should assure that

the patient is seated comfortably; the mouth piece is properly inserted; lips are sealed around the mouth piece and a nose clip is in proper position. After observation of tidal breathing, the technician asks the patient to exhale completely to residual volume, inhale to total lung capacity, and exhale again to residual volume. On each trial, the technician should coach the patient to maintain a steady flow of gas and should observe for leaks, obstructions to airflow such as by glottic closure, and end of exhalation. Coughing or interspersed inhalations may invalidate the trial.

FVC testing should be performed with a comfortably seated patient (Fig. 2a); tight clothing should be loosened. Because this procedure is more difficult to perform, the technician should explain FVC testing thoroughly until the subject can demonstrate that he/she understands what they are being asked to perform. The mouthpiece should be checked for proper insertion beyond the subject's teeth and for leaks. A nose clip should be in place. The patient is instructed to breathe normally for several breaths then to exhale maximally. Once the technician determines that full exhalation has been reached (by observing the pattern of the tracing), the patient is instructed to inhale maximally. Once inhalation is determined to be complete, the technician should vigorously coach the patient to "blow as hard and as fast as possible," repeating the command continuously throughout the effort [1,2]. It is recommended that the loudness and urgency of the coaching to "blow" be at a level somewhat embarrassing to the technician [1].

For very young children, special methods have been used to assist measurement. Obtaining spiograms may be possible with special attention to teaching and coaching [23]. Games involving various types of images that change with blowing into a spirometer have been shown to be successful aids for obtaining spirometry that conforms to American Thoracic Society and European Respiratory Society standards in young children [19,20,22]. It is useful to remember, however, that spirometry rarely provides the critical information for diagnosis and management; thus, undue stress of a young child to obtain adequate spirometry may not be worthwhile.

FVC testing is acceptable if three reproducible trials are produced [1,2,24]. Trials are considered reproducible if the differences in values between measurements are less than or equal to 0.15 l [2] or 5% of the measurement [1]. Up to four trials are recommended as the exertion required may cause muscle fatigue and artifacts that can decrease the values during succeeding trials [24]. A rest period of more than 1 min between trials is recommended to reduce the effect of muscle fatigue [2].

A technician may deem a trial unacceptable if he or she observes coughing, inhalations interrupting the forced exhalation, Valsalva maneuvers (glottic closures), early termination of expiration, a leak, obstructed mouth piece (by the

tongue or false teeth, for examples), or an unsatisfactory start of expiration including hesitation or false starts [1].

MVV testing has largely been superseded by FEV<sub>1</sub> measurement. The latter test is far easier to perform for patients and to administer for technicians, requires less stringent calibration of equipment, and correlates well with MVV. However, MVV may still be required in some specific cases. A single MVV maneuver should last for at least 12 s but no more than 15 s. An exact time should be recorded. In contrast to the FVC measurement, patients should be standing comfortably. Like the previous measurements, patients should be wearing a nose clip and have the mouthpiece properly held in the mouth with a good seal by the lips. The technician should watch for patient fatigue or even distress, try to coach the patient to "keep going," and maintain a respiratory rate of 90 to 110 breaths per minute throughout each trial. The number of breaths thus required ranges from 18 to about 28 over 12 to 15 s. A rate below 65–70 breaths per minute is unlikely to yield an acceptable trial. Each breath during the test should be approximately half of the patient's FVC, which is typically greater than the patient's usual resting V<sub>T</sub>. Leaks, hesitation, Valsalva maneuvers, and mouth piece obstructions are all likely to lead to underestimation of the MVV [1,2].

Measurements of FEV<sub>1</sub> and FVC before and after treatment with a short-onset bronchodilator may be helpful in identifying reversible airways obstruction. Patients must be asked whether they have already taken bronchodilators prior to visiting the pulmonary laboratory. If so, the test may still proceed, but the likelihood is reduced of finding improvement after bronchodilators are administered as part of testing. Recording prior bronchodilator treatment is important for later interpretation of results.

FEV<sub>1</sub> and FVC are measured as described above. The subject is then given a dose of albuterol by metered dose inhaler or similar rapid-onset bronchodilator and allowed to rest. After sufficient time for a bronchodilator effect, usually 15 or 20 min, spirometry is repeated. Changes in spirometry are calculated as the percent and absolute volume change after bronchodilators compared to baseline values. Thus, a change in FEV<sub>1</sub> from 2.0 to 2.2 l is a 10% and 200-ml increase. Testing after additional doses of bronchodilator is not done.

### Technical analysis of spirometric measures

Measurements of FEV<sub>1</sub>, FVC, SVC, and other spirometric measures require clear identification of both the start and end of expiration and reproducibility. The start of expiration is determined by back extrapolation [1,2]. While the FVC is simply a displacement of volume; the FEV<sub>1</sub> and all other timed FEV measurements require a starting time. Back

extrapolation from the point of maximal expiratory flow identifies the defined start of exhalation. The times for determination of FEV<sub>1</sub> and other FEV measurements begin at the extrapolated start of expiration. When there is no need to measure more than the FEV<sub>1</sub> (as in methacholine challenge testing, see the Bronchoprovocation Review in this issue), there is no need to continue the test beyond the time required for the FEV measurement and complete the FVC maneuver other than to ensure that there is no decrease in effort before the FEV measurement is completed.

Most modern electronic spirometers now perform back calculation automatically. However, it is useful when equipment is new to manually confirm that back calculation is being performed correctly. To find the start of exhalation manually, on a volume–time curve, a line is drawn at the point of peak expiratory flow parallel with the curve at that point (with a slope equal to the peak expiratory flow). The intersection of this line with the maximum inspiratory level identifies the start of exhalation. The volume difference between maximum inspiration and the actual FVC curve at the extrapolated start of exhalation is called the extrapolated volume. This must not exceed 10% of FVC or 100 ml or the trial is considered suboptimal [1]. An extrapolated volume above 250 ml makes the trial unacceptable.

The end of an FVC trial is determined in one of two ways. First, patients may complete exhalation. This is shown by a plateauing of the volume–time curve demonstrating a lack of additional change in volume for one or more seconds during the FVC maneuver as long as the exhalation has lasted three or more seconds for children less than 10 years of age or six or more seconds for patients older than 10 years. Second, patients may end their tests when it becomes uncomfortable to exhale further, or the technician may terminate the test because of patient distress. Trials that exceed 15 s should be terminated as they do not generate additional useful clinical information and raise the risk of complications including light-headedness, syncope, increased discomfort, and exhaustion [2]. Flow–volume loops best demonstrate poor performance in the early part of the expiratory maneuver while time–volume tracings are better for evaluating performance during the latter part of the study. Most modern spirometers provide both tracings.

In MVV testing, there is no agreed upon standard for repeatability, but trials that differ by more than 20% should be considered for repeating. Because the test is potentially exhausting, patients should be allowed to rest several minutes between trials and trials should be limited to three or four [2].

### Interpretation and clinical uses of spirometry

Spirometry is most useful for diagnosing diseases that cause airway obstruction. However, it can be useful in chest

restriction or a combination of these limitations to normal function. Spirometry may also be helpful to track progression of disease and assess the effectiveness of therapy over time.

### Airway obstruction

Airway obstruction is most commonly defined as a reduction in the ratio of FEV<sub>1</sub> to FVC due to a reduction in FEV<sub>1</sub>. (Alternate definitions may use FEV<sub>0.5</sub> or another timed FEV measurement.) In airway obstruction, the rate of air flow during exhalation is slowed. In severe airway obstruction, parts of the diseased lung may never empty causing a rise in the FRC. Rises in FRC and RV may lead to decreases in FVC, thus masking to some extent the severity of airway obstruction by limiting the drop in the ratio of FEV<sub>1</sub> to FVC. Table 2 provides current specific definitions of airway obstruction and severity from the ERS/ATS.

Common causes of airway obstruction include asthma and COPD. Bronchiectasis is a somewhat less common disease characterized by airway obstruction. Cystic fibrosis is the most common lethal genetic disease among US Caucasians and is characterized by saccular bronchiectasis, progressive airway obstruction, and early death primarily due to end-stage lung disease. It is primarily seen in referral centers. In this group of diseases, spirometry may be a useful adjunct for diagnosis, management, or both.

Reversible airway obstruction is the key feature of asthma. Consequently, a single spirometry test is less useful than a series of spirometric measurements over time. Such a series of spirometry tests may be helpful for managing disease and monitoring the effects of treatment. In a patient with suspected asthma, spirometry that demonstrates airway obstruction followed by spirometry that shows reversal of airway obstruction by a bronchodilator can be extremely helpful to confirm the diagnosis. It is important to note that spirometry diagnoses reversible airway obstruction and does not specifically diagnose asthma. When a patient is suspected to have asthma but has normal spirometry, post-bronchodilator spirometry is unlikely to identify patients with airway obstruction. Infrequently, a patient with normal values on spirometry responds and has a significant increase in spirometric measures.

In COPD, some degree of airway obstruction is irreversible by definition, but there may also be a component of reversibility that is useful to identify as that suggests that bronchodilator treatment may be helpful. Repeated spirometric measures over time can track the worsening severity of airway obstruction and the effectiveness of routine therapies such as regular long-acting bronchodilators or corticosteroids or more dramatic therapies such as lung transplantation.

**Table 2** Defining and grading spirometric abnormalities

Finding	Definition	Severity of abnormality	FEV <sub>1</sub> % finding
Airway obstruction	FEV <sub>1</sub> /FVC < fifth percentile	Mild	>70
Chest restriction <sup>a</sup>	FVC or VC < 80% of predicted	Moderate	60–69
	FEV <sub>1</sub> /FVC > 85%	Moderately severe	50–59
	Flow–volume loop has convex expiratory limb	Severe	35–49
		Very severe	<35

Adapted from Pellegrino et al. [100]. The finding and grading of severity of airway obstruction are dependant on the proper application of the appropriate normalization equations (Table 1)

Spirometry showing decreased FVC is not proof of chest restriction but is suggestive. Chest restriction is defined based on abnormality of TLC (please also see chapter on lung volume measurements)<sup>a</sup>

Patients with bronchiectasis and cystic fibrosis typically have some degree of irreversible airway obstruction with a variable amount of reversible airway obstruction. In these patients, spirometry can be quite useful for tracking long-term decline in lung health. Spirometry, particularly the FEV<sub>1</sub>, can be extremely useful for identifying an acute exacerbation of either disease. FEV<sub>1</sub> has been used as a criterion for selecting patients for lung transplantation in both bronchiectasis and cystic fibrosis, and it has been used quantitatively to predict 5-year survival outcomes in cystic fibrosis [25–28].

In the acute care setting for acute exacerbations of asthma and sometimes COPD, bedside spirometric testing of FEV<sub>1</sub> may be useful to demonstrate the effect of acute bronchodilator treatments and to track improvement over hours after administration of systemic steroid therapy. Used this way, spirometry may assist in making patient care decisions whether to admit to the hospital or discharge to home. Peak flow meters have often been used in these types of settings due to their easy portability, but they are prone to inaccuracy. There can be a marked training effect that may falsely indicate improvement. With patients wishing to appear sicker or healthier than reality, peak flow measurements are susceptible to easy manipulation and may even be reproducibly incorrect.

For patients hospitalized for acute exacerbations of asthma, COPD, bronchiectasis, and cystic fibrosis, tracking of FEV<sub>1</sub> may be useful as a way to gauge the effectiveness of therapy. Finding an improvement of 10% from admission values for FEV<sub>1</sub> is an easily calculated rough measure often employed in these situations. However, standards for determining significant improvement under these conditions are not well established and, when patients have been admitted without a significant fall in FEV<sub>1</sub> from baseline values, treatments are unlikely to create a rise in measurements.

#### Central airway obstruction

A few patients with airway obstruction have localized disease in the central or large airways rather than more

generalized disease as is the case in asthma or COPD. Vocal cord paralysis, tumors impinging on the larynx or trachea or involving airway structures, scarring from prior surgery, or intubation or occasionally foreign objects can cause a specific pattern of airway obstruction detectable on spirometry [29]. The essential defect on spirometry is the reduction in peak flow during inspiration, expiration, or both.

These obstructions are categorized by behavior as fixed or variable. Fixed obstructions affect airflow whether a patient is inhaling or exhaling and are not further categorized. Variable obstruction is present either during inhalation or exhalation but not both. Such an obstruction may be localized as either intrathoracic or extrathoracic by spirometry. The localization refers to whether the walls of the obstructed portion of airway are subject to the intrathoracic or pleural pressures generated by active breathing or to the extrathoracic, ambient, or barometric pressure.

A variable intrathoracic obstruction is partially or completely relieved during inhalation because the intrathoracic pressure is lower than central airway pressures leading to dilatation of the obstructed airway. During active exhalation, intrathoracic pressure exceeds pressures in the central airways tending to collapse those airways and potentially leading to severe obstruction to airflow at the lesion causing the variable central airway obstruction. A variable extrathoracic obstruction behaves in an opposite manner. It is relieved during exhalation when airway pressure exceeds barometric pressure leading to dilation of the central extrathoracic airway. During inspiration, the barometric pressure exceeds airway pressure leading to a tendency to collapse the airway, especially at the lesion causing the variable obstruction.

On physical exam, patients with central airway obstruction may wheeze. However, the patterns seen on spirometry are quite distinct from those of asthma or other generalized forms of airway obstruction. Figure 4 shows the shapes of three flow–volume loops that correspond to the three

possible types of central airway obstruction. Detection of these patterns requires that the inspiratory portion of the FVC maneuver be performed as carefully as the expiratory portion. This may entail additional instructions to ensure adequate performance of that part of the FVC maneuver. Typically, an abnormal spirogram demonstrating a pattern consistent with central airflow obstruction is confirmed with direct laryngoscopic examination or other similar study.

#### Chest restriction

Chest restriction is an inability to reach a normal TLC with inspiration. Spirometry does not measure the TLC, but an indirect consequence of a low TLC is a reduced FVC. FVC is more easily measured than TLC. Nevertheless, because FVC is not a direct measure of chest restriction, a suggestion of chest restriction may need to be confirmed with direct TLC measurement with lung volume measurements. Although the FVC is typically decreased with chest restriction, the FEV<sub>1</sub> to FVC ratio is preserved. The flow–volume loop may appear normal in shape except that the size of the loop is reduced.

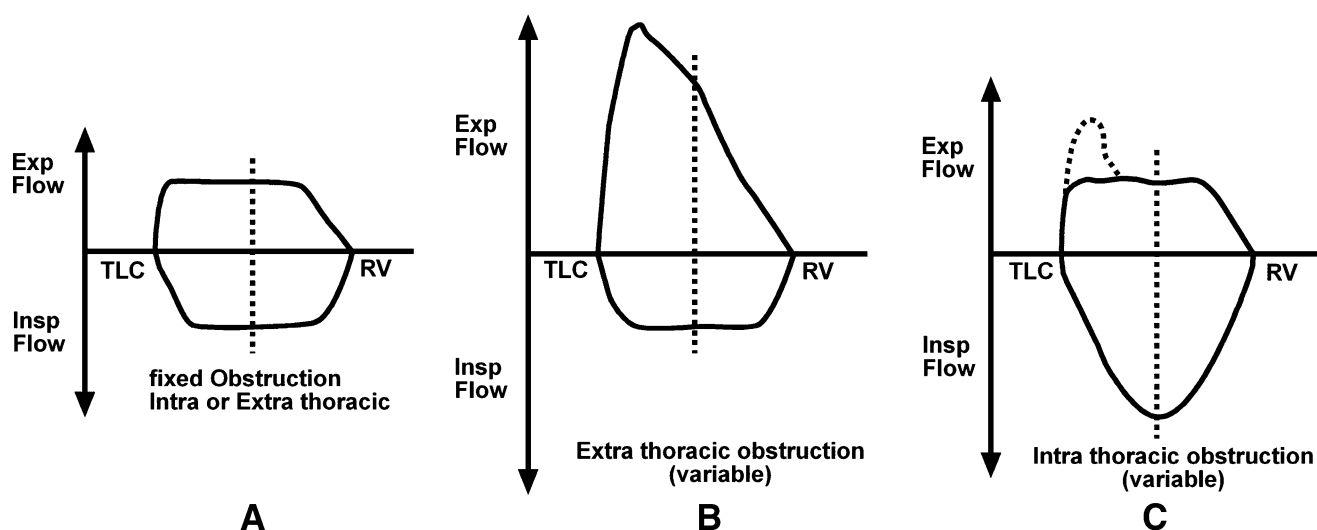
Diseases characterized by chest restriction are less common than diseases that cause airway obstruction. These include diseases that reduce respiratory muscle strength including paralysis of either or both hemi-diaphragms, cervical spine injuries, myasthenia gravis, and other neuromuscular disease. Other diseases lead to chest restriction by increasing the stiffness of the lung parenchyma or reducing the mobility of the thoracic cage. These include idiopathic and other causes of pulmonary fibrosis, pulmonary edema of any type, amiodarone, chemotherapeutic and other drug toxicities,

paralytic agents, poisons and toxins, kyphoscoliosis, extreme morbid obesity, and scar formation from severe and extensive burns of the chest. External binders applied to the abdomen or chest itself or extremely tight clothing may occasionally be a cause of chest restriction.

Pulmonary function testing can be useful for providing adjunctive information for these diseases by providing a measure of the severity of chest restriction. Over time, spirometry may help reveal disease progression by showing gradual worsening of chest restriction, as in cases of idiopathic pulmonary fibrosis and scoliosis. Chest restriction may wax and wane in diseases such as myasthenia gravis that are characterized by exacerbations, and repeated measurements of FVC may help to track changes that occur on a day-to-day or longer basis. For patients with an FVC that drops below 800–1,000 ml, the measurement may help guide timing of initiation of ventilatory support. Conversely, for ventilated patients with an FVC that rises past 800–1,000 ml, the measurement may facilitate a decision to extubate a patient to allow for unencumbered breathing. Under these circumstances, typical testing methods are usually impractical and measurements are made using less accurate bedside methods or through ventilator circuits.

#### Comparing studies over time

Many clinicians use serial measures of spirometry to track the progression of lung disease due to either airway obstruction or restriction. Individual drops in spirometric measures often differ from rates derived from cross-



**Fig. 4** Patterns of central airway obstruction. **a** shows fixed obstruction where both expiratory and inspiratory flow rates are limited. **b** shows variable extrathoracic obstruction affecting only

inspiration, and **c** shows intrathoracic obstruction affecting only expiratory flow. From Kashima [29], with permission. Redrawn by B Stephan, Medical Graphics and Photography, U of Utah



sectional studies, so clinicians should be cautious interpreting changes for individuals and comparing those changes to the average change for patients with the same disease [30]. For example, spirometric values in patients with cystic fibrosis tend to decrease over time. The average drop in FEV<sub>1</sub> is approximately 2% per year but varies markedly from patient to patient. FEV<sub>1</sub>% in these patients is directly linked to 5-year predicted survival, and a decreasing value suggests worsening prognosis [28].

Interpretation of a series of measurements of spirometry is not as well described as for a single measure. ERS/ATS criteria suggest that a 10% change in FEV<sub>1</sub> or FVC is significant. However, that interpretation may be compromised if the serial values are obtained using different machines even within a single laboratory or especially if the values are obtained at different facilities. While most laboratories now adhere to ERS/ATS standards, small variations in techniques and small differences in measurement ability in different machines may result in significant machine-to-machine or center-to-center differences when none truly exist [9]. To minimize these differences due to procedures and techniques for obtaining PFTs, rigid adherence to ERS/ATS guidelines is recommended. When practical, identical machines and procedures should be used for each patient for whom serial PFTs are performed.

In following patients with COPD, it was noted that in two studies performed within 60 days in stable patients the difference between the FEV<sub>1</sub> measurements fell within 225 ml in 90% of the subjects. Thus, in comparing two tests on the same patient with COPD performed within a 2-month period of time, the use of a change of more than 225 ml denotes a change in the patient's status [31].

## Summary

Spirometry provides evidence of airway obstruction or chest restriction. Such evidence may be useful for diagnosis of a variety of diseases that compromise the normal physiology of breathing. The usefulness of spirometry depends upon the reproducibility and accuracy of measurements. Reproducible and accurate measurements rely on good quality control of testing and adherence to standard procedures for obtaining PFTs such as those provided by the ATS. The development of many sets of reference equations (Table 1) to support better interpretation of spirometry results has increased the usefulness of testing for diverse populations of patients. Spirometry may be helpful for detecting changes in disease over time and may be helpful for making decisions to start, continue, change, or stop therapy.

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