Key points

- The spirometric measurements of most clinical value are FEV_1 and VC.
- FEV_1 and VC are used for diagnosis, assessment of severity, and monitoring progress and response to treatment.
- FEV_1 and VC are a valuable guide in the prognosis of many diseases, not only respiratory.
- The greatest clinical value of maximum flow–volume curves is the recognition of central (upper) airway narrowing.

Spirometry: then and now

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Educational aims

- To outline the historical development and rationale of the measurements commonly made during forced expiration.
- To review the diagnostic specificity of these measurements and their continuing value in clinical respiratory medicine.
- To review the prognostic information conveyed by measurements of FEV_1 and VC in various respiratory and non-respiratory diseases.

Summary

Measurements of VC were first made in the 18th Century, and they had been reported in large numbers of healthy subjects and patients with respiratory disease (tuberculosis) by the middle of the 19th Century. However, little use was made of the VC in clinical medicine until the second half of the 20th Century. The FEV_1 was first described about 50 years ago. Although used widely by respiratory physicians, the value of both these simple measurements remains under-appreciated by non-specialists. Their main roles are in aiding diagnosis by pattern recognition, assessing severity of disease, and monitoring progress and/or the effects of treatment. The valuable prognostic information conveyed by FEV_1 and VC has been demonstrated in several conditions, both respiratory and non-respiratory.

Spirometry, the measurement of volumes of air breathed in and out, is widely used in the assessment of patients with respiratory disease. Nowadays, in practice, "spirometry" is usually equated with measurements during forceful expiration: in particular, the forced expiratory volume in one second (FEV_1) and the vital capacity (VC) or forced vital capacity (FVC). In addition, various indices of maximum flow may be recorded at the same time. Simple forced expiratory measurements are important in the diagnosis and evaluation of patients with respiratory symptoms, and they carry a remarkable amount of prognostic information in several conditions. The VC has a venerable history, but the FEV_1 is of more recent origin. For more than a century, measurements were made with the classical, but cumbersome, water-filled spirometer. Since the1950s, this has gradually been replaced, first by more portable dry bellows instruments and then by miniature spirometers; the latter measure flow, which is integrated electrically to give volume.

Pre 1840

The earliest measurements of respiratory volumes are usually attributed to the Italian mathematician and "iatrophysicist", Giovanni Alfonso Borelli (1681). His very crude estimates were made with a cylindrical glass tube, up which liquid was sucked, with the volume calculated from the bore of the tube and the height of the meniscus. Due to pressure changes within the tube, the measurements were considerable underestimates; he calculated the tidal volume as 15 "cubic fingerbreadths" (246 mL) and the expiratory reserve volume as a further 20 cubic fingerbreadths (328 mL).

Much more realistic volumes were reported in the early 18th century by the English clergyman, Stephen Hales (1727). He recorded the maximum volume of air which he could expire into a bladder (figure 1), with the measurement made by subsequent displacement of water, according to the principle of Archimedes. His estimate of what was later called the VC was ~220 cubic inches (3.6 L). (Early estimates of lung volume were expressed at ambient temperature, pressure and saturation (ATPS), ~10% less than volumes at BTPS.) Curiously, Hales's results are hidden away in a monograph entitled, "Vegetable Staticks", which is devoted mainly to experiments on the sap of vegetables. By describing a method for collecting gas above water, Hales made another important contribution to the later development of spirometry. However, he developed this for studying the products of combustion from a stove and he does not appear to have used the technique for respiratory measurements. His other major claim to physiological fame was as the first to make direct measurements of blood pressure, which he did in the femoral artery of a horse.

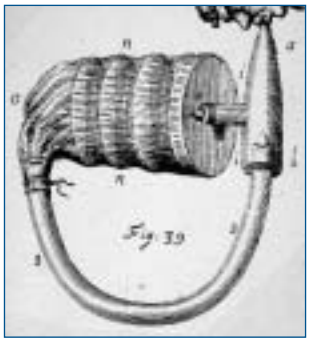


Figure 1
Bladder described and used by Stephen Hales for collection of expired air.

The classical water-filled spirometer was developed from the gas holder or "gazometer" with which the great chemists of the late 18th Century, such as Priestley, Lavoisier and Watt, performed their pioneering work on oxygen, carbon dioxide and other gases. This type of instrument was soon modified for use in humans, initially using mercury but later water. Of particular note was the "mercurial air holder" developed by William Clayfield (figure 2); this incorporated the important feature (used also by Lavoisier in his gazometer) of a balancing counterweight, which reduces the resistance of the instrument, and later became standard. Clayfield worked at the Pneumatic Institute in Bristol (UK), where the great chemist Humphry Davy started his career. Davy is noted particularly for the discovery of nitrous oxide ("laughing gas") and he realised that, in order to interpret the results of his experiments on nitrous oxide, he needed to know the absolute capacity of his lungs. In addition to measuring VC using Clayfield's spirometer, he rebreathed a gas mixture containing hydrogen, the dilution of which allowed him to estimate residual volume. He recorded his own VC as 213 cubic inches (3.5 L) and his residual volume as only 41 cubic inches (670 mL), but he commented that "this capacity is most probably below the medium, my chest is narrow, measuring in circumference but 29 inches" (John Hutchinson (1846) later queried whether this unrealistic measurement might have been a misprint of 39 inches (99 cm)).

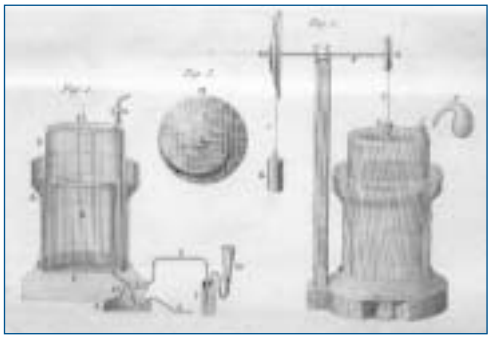


Figure 2
The "mercurial air holder" of William Clayfield (1800).

An alternative approach to measurement of respiratory volumes was that of Boerhaave, who "caused a man to be put into a large tub of water above his shoulders and desired him to make a strong inspiration"; he then measured the rise in the level of the liquid after "dilatation of the chest". This was, in effect, the forerunner of the body plethysmograph, although the subject's head was excluded from the tub and he inspired directly from the room. The Edinburgh physician, Robert Menzies, reports using Boerhaave's method with the subject immersed in a "hog's head" (wine barrel) filled with water, but his attempt to measure inspiratory capacity was frustrated by the water overflowing and running down the outside of the barrel. Menzies' "Dissertation on Respiration" of 1799 illustrates this and other methods used around that time (figure 3).

Perhaps the earliest description of measuring lung volumes in disease was by Edward Kentish (1814) using his "pulmometer" (figure 4), a device consisting of a graduated Bell jar inverted in water, into which gas was introduced *via* the top (rather than from below as in a conventional

Fig. 1 was described originally by Edmund Goodwyn and shows that the subject inspired *via* tube E, sucking water into container D *via* tubes a, b, c from trough G, and the volume of water thus aspirated was calculated by weighing. Fig. 2 shows balloon-like "allantoids", from which, or into which, air was breathed with subsequent measurement by water displacement (fig. 5), using the principle devised by Stephen Hales. Fig. 4 shows Boerhaave's hogshead, in which the subject sat immersed to the neck.

Figure 3
Illustrations from the "Dissertation on Respiration" of Robert Menzies (1790).

spirometer). As with Borelli's earlier measurements, the volumes will have been limited by the increasing pressure in the jar. Kentish reported that "Mr. S., a 17-year-old male with phthysis, could inhale only 2 pints of air. From his stature he ought, if his lungs had been sound, to have inhaled 7 pints if not more", observations which clearly show that he appreciated the need for comparison with reference values. Kentish went on to record that, at autopsy 3 weeks later, his lungs "appeared quite full with tubercles, from the size of a filbert, gradually down to the appearance of millet seed....The inferior or pendulous part of the lungs had become hardish or fleshy; when a cut piece of the lung was thrown into water it sunk to the bottom.....Had the state of this young man's lungs been measured at an earlier period by the pulmometer, some means of arresting the progress of the disease might have been attempted", a comment which clearly anticipates the value of spirometry in screening for early disease. Kentish also reported a reduced volume in a patient with pleural effusions due to heart failure ("dropsy of the chest"), with an increase in the volume after the effusions resolved, an early observation of extrapulmonary volume restriction.

A similar instrument was used by Charles Thackrah (1831), a physician often regarded as the father of occupational medicine. He recognised that the volume he recorded (the VC) "does not show the mere capacity of the lungs", but "is the compound of the capacity of the air cells and the power of the respiratory muscles". He reported that the average volume of air which 19 dragoons "could throw out at one full expiration" was 217 cubic inches (3.56 L). Of his subjects, nine were officers (possibly better nourished?) and their average VC was 240 cubic inches (3.94 L), while a "tall young cornet [brass instrument] player "threw out" 295 cubic inches (4.84 L) and this is the largest expiration we have known".

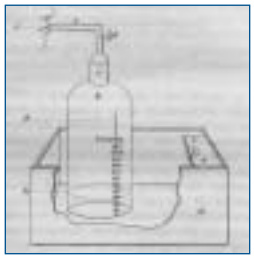


Figure 4
The "pulmometer" of Edward Kentish (1814).

John Hutchinson

All these measurements were made in individuals or small groups, and they pale into insignificance alongside the mammoth work of John Hutchinson (1811–1860), whose contributions in this area were unequalled for more than 100 years. Hutchinson was born in Newcastle upon Tyne (UK) in 1811, and qualified in Medicine in London. In the 1830s and 1840s, he practised as a medical assessor for the Britannia Life Assurance Company; during this time, he accumulated an enormous number (>4,000) of measurements of VC from healthy subjects and patients with lung disease. Inevitably at that time, the condition from which the patients were suffering was tuberculosis (TB). Indeed, Hutchinson showed that measurement of VC was much more sensitive for the detection of TB than auscultation *via* a stethoscope (which had been invented by Laennec some 30 years earlier). This was 50 years before the introduction of radiography and 40 years before Robert Koch discovered the tubercle bacillus. Hutchinson is sometimes described as the inventor of the spirometer and the first to measure VC, but, as discussed previously, neither claim is correct. He was not even the first to report measurements in patients with lung disease, but

Figure 5
Hutchinson's spirometer and method of measuring vital capacity (1846).

he did establish spirometry as an important clinical tool. He refined the water-filled spirometer to make it suitable for everyday use (figures 5 and 6), he documented the normal variation of VC with age, sex and body size (using height as the index of size as is still used today), and he showed the clear reduction in VC demonstrable even in early disease (figure 7). He greatly extended Thackrah's work on variation in different occupations. He published extensively and his magnum opus (1846), running to more than 120 pages, contains a wealth of information and observations that are still relevant today. The healthy subjects he studied included "sailors, fire-fighters, policemen, paupers, artisans, soldiers, printers, draymen, pugilists, and wrestlers, giants and dwarfs, gentlemen, girls, and diseased cases". Although not the first to report measurements of VC, he gave it its name, and, in his role as an insurance company doctor, he proposed that the measurement of VC be used to predict life expectancy. Sadly, even today, the insurance industry often relies on the tape measure rather than the spirometer!

Probably because of his extensive work on spirometry, Hutchinson was, in 1850, appointed assistant physician to the newly opened Brompton Hospital for Consumption in London (UK), but he remained there for only a short period before emigrating to Australia, where he worked as a general practitioner in the newly discovered gold fields. Ten years later he moved to Fiji, where he died.

Although Hutchinson's work was acclaimed when he was working in London, it seems not to have been widely adopted and, indeed, shortly after his departure from the Brompton Hospital,

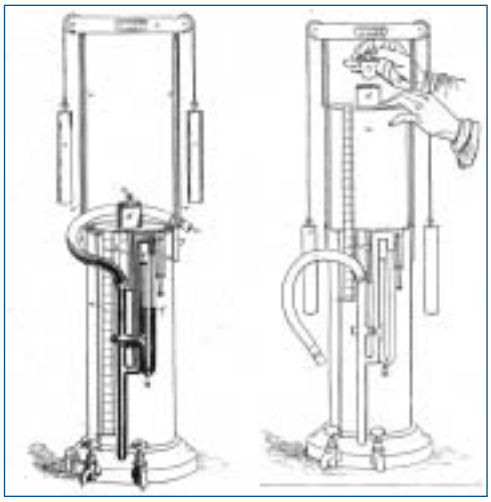


Figure 6
Hutchinson's spirometer empty and full; the device is emptied by removing a brass stopper.

one of his erstwhile colleagues published a detailed critique of the "fallacies" of the spirometer. By 1875, in a case report from the Brompton Hospital published in *The Lancet*, it was noted that "the spirometer had not been of late much used at the Brompton Hospital as these instruments require a great deal of education on the part of the patient, particularly nervous women".

1850–1950

Sporadic reports of other devices for measurement of VC were published in the latter part of the 19th Century. These included the following, as shown in figure 8: Mitchell's device is a miniature version of the domestic "dry gas meter"; MacMunn's device is simply a distensible bag

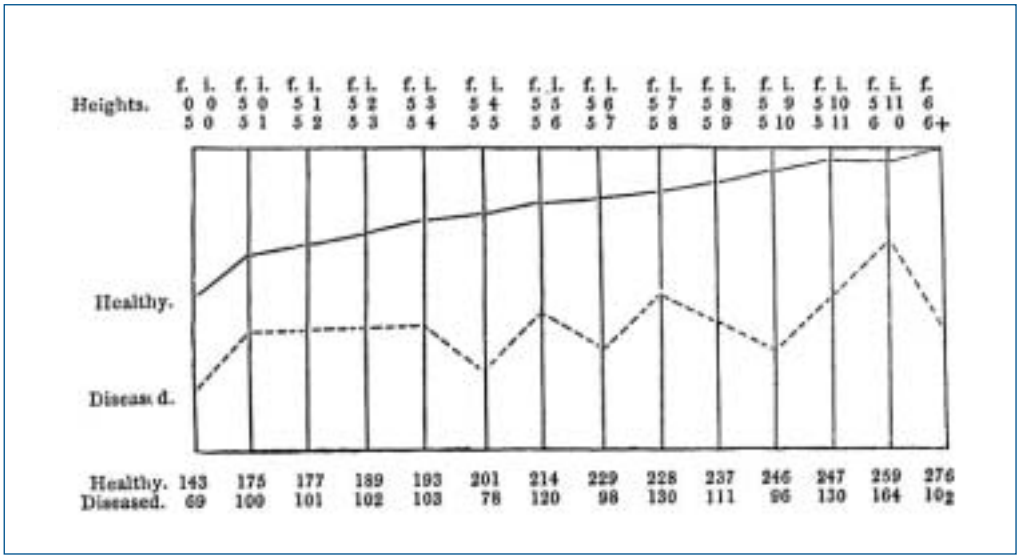


Figure 7
The relationship between VC (average given at bottom in cubic inches) and height (in feet and inches) in health and disease. Hutchinson 1846.

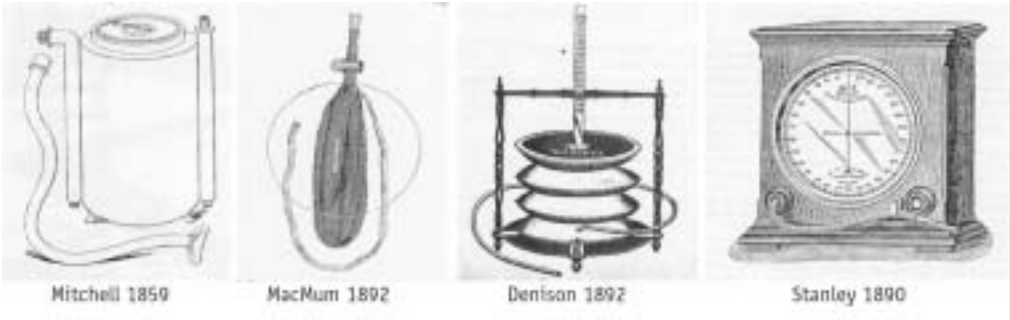


Figure 8
Four instruments for measurement of VC described in the late 19th Century.

with a tape measure to measure its circumference; Dennison's is a simple rubber bellows; and Stanley's device has an internal wheel, which revolves under water turning the hand on the dial.

By the early 20th Century, there had been a resurgence of interest in the measurement of respiratory volumes, but this was driven largely by the need to measure metabolic rate, particularly in patients with thyroid disease. The apparatus designed for this function by both Benedict and Knipping (figure 9) is similar to Hutchinson's spirometer. There appears to have been more sustained interest in spirometric measurements in the USA and, in 1925, Myers published a monograph detailing the various conditions in which VC was reduced, demonstrating its sensitivity, but relative lack of specificity (table 1).

A resurgence of interest in respiratory measurements in Europe in the 1920s was driven by three factors: the problems experienced by aviators during the First World War, the need for objective measurements following the introduction of statutory compensation schemes for workers with industrial lung disease, and, probably most importantly, the rise of thoracic surgery as a viable speciality and the need to evaluate patient fitness. Respiratory physicians were still concerned almost exclusively with the problems of TB and, as late as 1933, a paper published in *The Lancet* emphasised the sensitivity of VC in the detection of TB (even though this was now 50 years after the recognition that TB was an infectious disease). It appeared that little had changed since the time of Hutchinson nearly a century earlier.

During the 1930s, there was increasing recognition of asthma as a clinical problem, and also a burgeoning awareness of the importance of emphysema (almost certainly because of the boost in cigarette consumption during the First World War 20 years earlier). The maximum voluntary ventilation was introduced by Hermannsen in 1933 and became popular, particularly in presurgical assessment. In 1938, Barach reported examples of spirometric recordings in a patient with "asthma and acute pulmonary emphysema" before and after nebulised adrenaline (epinephrine), which clearly showed the increased rate of expiration after a bronchodilator and may represent the first published bronchodilator response (figure 10). The classic studies of Cournand and Richards (1941) and, subsequently, Baldwin and colleagues led to the classification of ventilatory abnormalities and the recognition of "obstructive" and "restrictive" patterns.

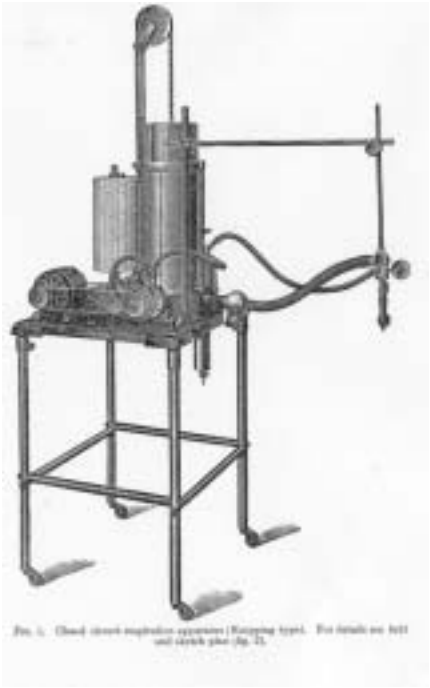


Figure 9
The classical water-filled spirometer of Knipping used for metabolic measurements.

Table 1 Conditions with reduced VC

Cardiac disease
Hypothyroidism
Emphysema
Asthma
Pleurisy
Pneumothorax
New growths
Pulmonary abscess
Pneumonia
Pulmonary TB
Old pleural adhesions
Deformities of the thorax
Ossification of the costal cartilages

In addition "malingering, lack of cooperation and will power must be considered". Taken from Myers 1925.

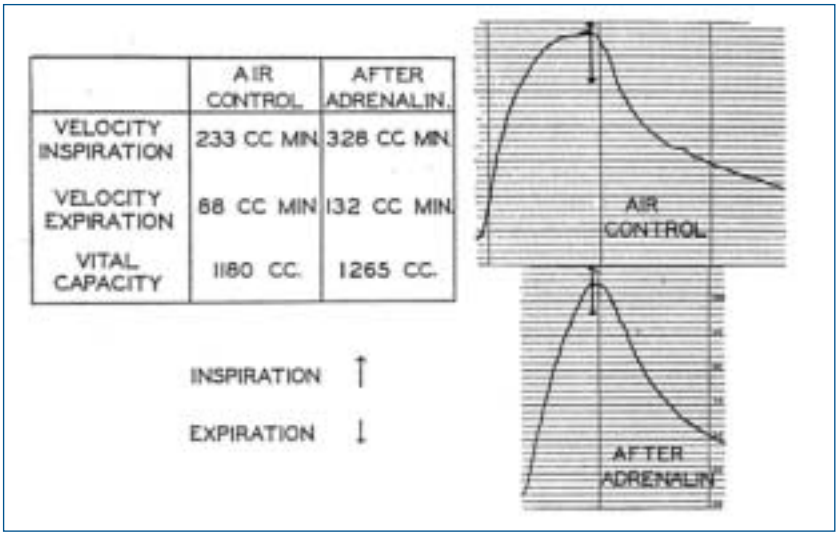


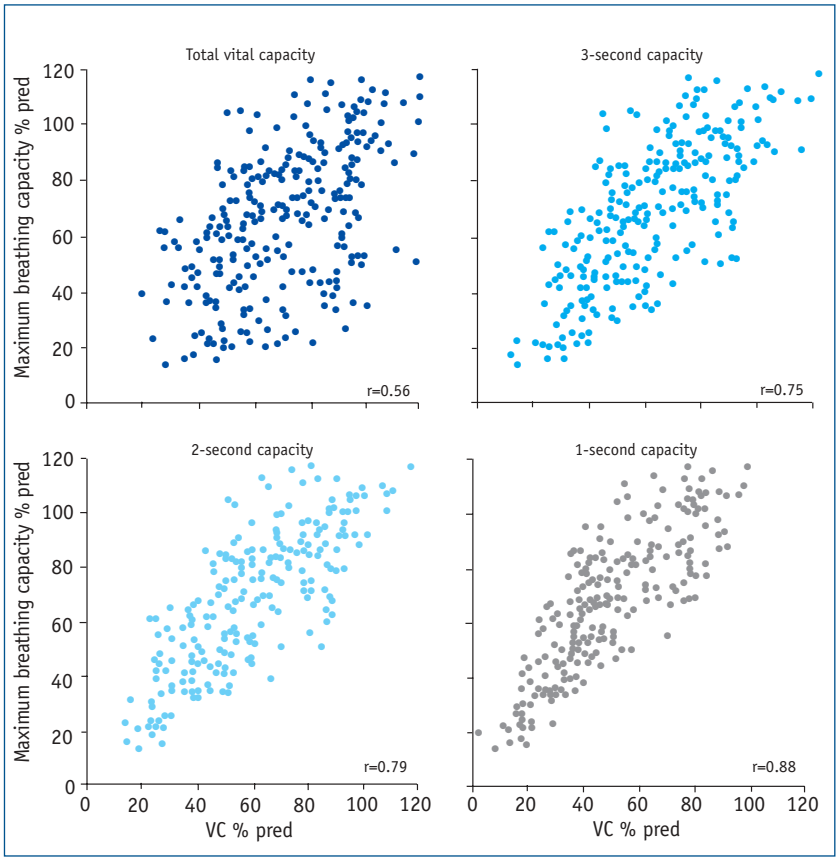
Figure 10
Effect of nebulised adrenaline on expiratory flow and VC. Barach (1938).

1950 to date

The FEV_1 was described independently by Tiffeneau and Pinelli in Paris (1947) and Gaensler in the USA (1951). Both authors argued that the "useable" part of the expired VC was the early part as, during performance of the maximum breathing capacity (MBC) manoeuvre, expiration was unlikely to continue for >1 second or so before the subject took his next inspiration. Gaensler examined the relationship between the MBC and various timed forced expiratory volumes (figure 11), demonstrating that the FEV_1 correlated better than 2-second or 3-second capacities or the total VC. From that time, the FEV_1 (sometimes $FEV_{0.5}$ or $FEV_{0.75}$) became regular measurements obtained along with the VC or FVC.

Maximum flow–volume curves were first described in 1960, and gave an elegant visual synthesis of maximum expiratory and inspiratory flow over the whole FVC range. The maximum mid-expiratory flow (MMEF or $FEF_{25–75}$) actually antedates flow–volume curves, as it does not require rapidly responding equipment and it can be obtained graphically from the volume–time spirogram (figure 12). The measurement has always been more popular in North America than in Europe; it is not specific for airway narrowing, as it is also reduced with restrictive ventilatory defects and it has a much wider normal range than FEV_1 and FVC. Later indices derived from forced expiration include moments analysis in the time domain and the FEV_6. The former, although of theoretical interest, has not confirmed its early promise. The FEV_6 has recently been advocated as an alternative to the FVC, with the advantage that patients with prolonged expiration need to sustain forced expiration for a much shorter period.

Figure 11
The relationships between MBC and various timed "VC" measurements, showing the closest correlation with the one-second capacity (FEV_1). Data taken from Gaensler (1951).



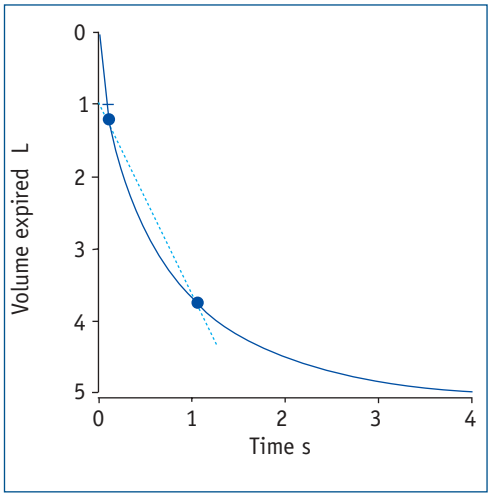


Figure 12
A schematic spirogram of a healthy subject with VC 5 L showing derivation of MMEF ($FEF_{25–75}$) as the average flow over the mid-VC range (slope of broken line). •: 25 and 75% FEF.

The present day

In healthy subjects, the FVC and VC are effectively interchangeable, but, in patients with airway disease, FVC is often less than the VC delivered in a more relaxed manoeuvre, probably because of the effects of compression of thoracic gas with forceful expiratory efforts and the inability to sustain the effort for a prolonged period. An obstructive ventilatory defect can be defined in terms of a reduction in the ratio of FEV_1 to either FVC or VC; the forthcoming European Respiratory Society/American Thoracic Society guidelines favour use of the VC. A restrictive ventilatory defect may be suggested by reduced FEV_1 and VC and a normal ratio, but requires measurement of absolute lung volumes (by inert gas dilution or whole body plethysmography) for confirmation.

Modern miniaturised spirometers (figure 13) are a great improvement, in terms of convenience and portability, over bellows or water-filled devices. Unfortunately, the capacity of the software has often run ahead of the information value of the many indices that can now be recorded, confusing the non-specialist and sometimes distracting from the most relevant information. Maximum flow–volume curves are visually attractive and offer advantages of pattern recognition in certain situations, *e.g.* narrowing of the central airway (figure 14). They also allow visual representation of the adequacy of a subject's effort in the early part of forced expiration, but they are not necessary for routine assessment of patients with known diffuse airway narrowing (as in asthma or chronic obstructive pulmonary disease (COPD)). It is often forgotten that the pattern of diffuse airway narrowing is essentially an exaggeration of the normal effects of ageing; increasing concavity of the curve to the "x" axis, occurs with both increasing age and increasing severity of airway obstruction (figure 14). The shape of the flow–volume curve does not distinguish airway obstruction due to asthma from COPD (including emphysema). Although maximum expiratory flow at small lung volumes is, in theory, sensitive to milder degrees of airway narrowing, it is also subject to considerable variation in the healthy population, so that its "signal-to-noise" ratio is much lower than that of the FEV_1.

Figure 13
Use of a modern miniature spirometer.

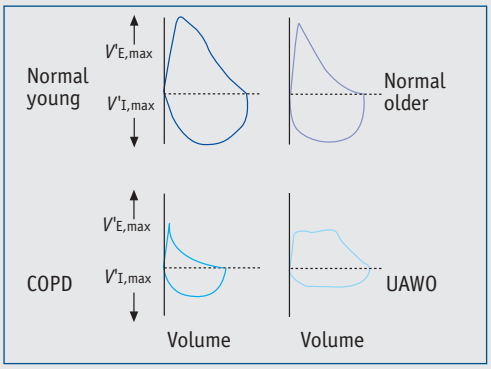


Figure 14
Schematic maximum expiratory and inspiratory flow–volume curves in healthy younger and older subjects, and diffuse airway obstruction (COPD) and upper (extra-thoracic) airway obstruction (UAWO).

Forced expiratory measurements have the advantages that they are easy to perform, the equipment is simple and portable, and the FEV_1 and FVC have good reproducibility and extensive normal reference values. In clinical practice, spirometry is used to aid diagnosis, to assess severity and to monitor progress and treatment. In addition, the measurements contain a remarkable amount of prognostic information, as demonstrated in several studies in a variety of conditions. They have withstood the test of time, but they may suffer from being regarded as somewhat mundane and old-fashioned measurements. They are criticised for poor sensitivity and are sometimes unjustly denigrated. Admittedly, they give an incomplete picture of the physiological abnormality in particular diseases and clinical situations, *e.g.* in trials of COPD treatment, other indices may be more appropriate as end-points or guides to prognosis. However, a note of caution is necessary. Some studies conclude that other measurements, such as simple walk tests, may be better related to important end-points (*e.g.* therapeutic benefit or mortality) than the FEV_1. However, the population in such studies is often pre-defined by a certain level of spirometric values, and, consequently, it is not surprising that, *within such a population*, other measurements (such as the 6-minute walk) turn out to be better predictors of outcome than FEV_1 itself. (If, instead of defining the subjects in terms of FEV_1, they were defined by exercise performance, the contrary conclusion would probably be drawn, *i.e.* the level of exercise performance would then turn out to be a poor guide to outcome.)

Prognostic value of spirometric volumes

Several studies across the range of severity of airway obstruction in patients with asthma and COPD have shown that the FEV_1 is the single most powerful predictor of survival (figure 15). Similarly, in cystic fibrosis, data from the pre-transplantation era showed that the FEV_1 and/or FVC were the best predictors of mortality. Not surprisingly, patients with lower spirometric volumes have a poorer prognosis after lung resection for cancer. Less obviously, FEV_1 appears also to relate to the risk of developing lung cancer: in a population of patients with COPD or "chronic bronchitis" matched for age, occupation and initial smoking status, those with FEV_1 initially <70% predicted had a significantly greater mortality than those with FEV_1 >85% predicted.

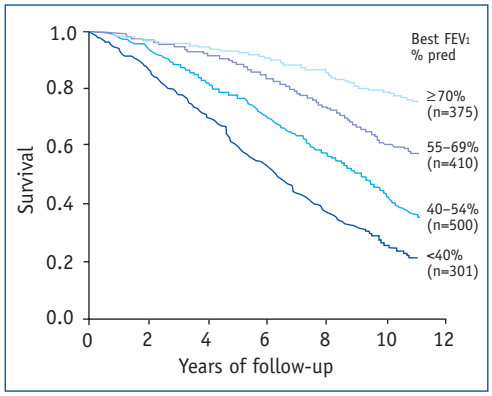


Figure 15
The value of FEV_1 in predicting survival with COPD. Data taken from Hansen et al. (1999).

Similar prognostic value is seen in studies of patients with restrictive abnormalities, but here the VC or FVC is usually the chosen index. Thus, in cryptogenic fibrosing alveolitis (idiopathic pulmonary fibrosis), cross-sectional studies show a good correlation with survival and, in addition, change in VC over the first 6 months of follow-up is also predictive. In addition, in systemic sclerosis, the FVC is highly predictive of survival and, in one study, was actually better than the severity of pulmonary hypertension. Spirometric measurements are widely used in patients with generalised neuromuscular disease, with VC clearly related to survival in motor neurone disease, Duchenne muscular dystrophy and other forms of muscular dystrophy.

Most surprising, but a very consistent finding in community studies, has been the association between spirometric volumes and death from ischaemic heart disease. This was shown first in the Framingham study and has been found consistently in several studies since (figure 16). More recently, it was shown that longitudinal measurements of *change in* spirometric indices are also predictive, with a higher rate of decline in FEV_1 associated with increased mortality from coronary heart disease. This finding was independent of smoking and, in this study, the relative risk conferred by a rapidly declining FEV_1 was actually greater than that associated with either smoking or blood cholesterol level. The precise mechanism(s) responsible for this striking association have not been identified.

Spirometric measurements have stood the test of time and remain a remarkably inexpensive and simple means of assessing respiratory and general health. This is widely appreciated by the respiratory community but much less so in non-specialist circles. Spirometry is at last being introduced into primary care but we still have a major educational task in encouraging our colleagues towards its more general adoption.

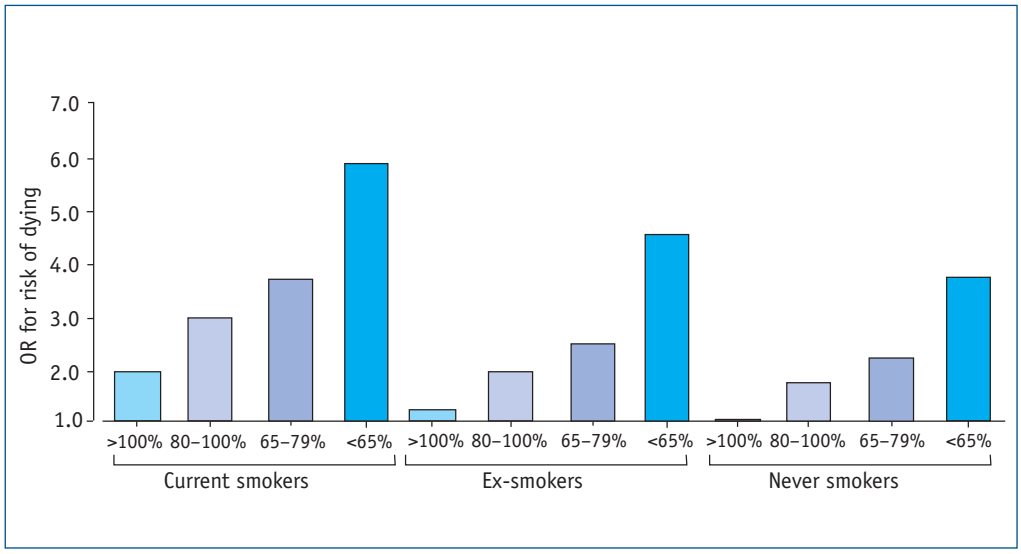


Figure 16
Odds ratios (OR) for risk of death from cardiovascular disease related to smoking category and FEV_1 (% predicted); the OR increases as FEV_1 declines, independently of smoking history. Modified from Tockman et al. (1989).

Educational questions

1. How are expired volumes measured by modern miniature spirometers?
2. Does the finding of a proportional reduction of FEV_1 and VC (*i.e.* normal FEV_1/VC ratio) necessarily imply a restrictive ventilatory defect?
3. What is the difference between forced and "relaxed" VC?
4. Why, in paediatric practice, is $FEV_{0.75}$ or $FEV_{0.5}$ sometimes preferred to FEV_1?
5. Does a reduction in maximum mid-expiratory flow (MMEF) (*i.e.* $FEF_{25–75}$) necessarily imply airway obstruction?
6. Why is FEV_6 being promoted as a potentially useful spirometric measurement?
7. In what way may a single recording of maximum flow–volume curves distinguish asthma from emphysema?
8. How do maximum flow–volume curves differ with extra- and intra-thoracic narrowing of the trachea?

Suggested further reading

Historical

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Predictive value of FEV_1 and VC

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Suggested answers

1. Usually by electrical integration of a flow signal.
2. No, it is suggestive but not diagnostic; a restrictive defect implies a reduced total lung capacity.
3. In healthy individuals there is usually no appreciable difference. VC (as defined by Hutchinson) is the maximum volume which can be expired following full inspiration. In subjects with diffuse airway obstruction the FVC often underestimates the true or "relaxed" VC because of dynamic airway narrowing and thoracic gas compression during very forceful efforts. Use of FEV_1/VC is preferred to FEV_1/FVC for recognition of airway obstruction.
4. Children normally have very rapid lung emptying during forceful expiration such that FEV_1 may be close to VC. An earlier timed measurement may then be a more sensitive guide to airway narrowing.
5. No, it is also reduced with a restrictive ventilatory defect.
6. As a surrogate for FVC, particularly in patients with airway obstruction in whom forced expiration can be very prolonged (*e.g.* ≥15 seconds) and uncomfortable.
7. It does not.
8. Both tend to show similar "blunting" of the maximum expiratory curve, but a small early "peak" may be seen with more distal obstruction. In addition, narrowing of the intra-thoracic airway characteristically has a proportionately greater effect on expiratory than inspiratory flow in the mid-VC volume range, while the converse is true with narrowing of the extra-thoracic airway.