MAKING SENSE of Lung Function Tests

Second edition

A hands-on guide

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Ὁ μεν βίος βραχὺς, ἡ δὲ τέχνη μακρὴ, ὁ δὲ καιρὸς ὀξὺς, ἡ δὲ πεῖρα σφαλερὴ, ἡ δὲ κρίσις χαλεπή.

Ἱπποκράτης

Life is short, science is long; opportunity is elusive, experiment is dangerous, judgement is difficult.

Hippocrates

Contents

Preface

Every doctor involved in acute medicine deals with blood gas or lung function data. Although a wealth of information lies therein, much of the content may be lost on the non-specialist. Frequently the information necessary for interpretation of basic data is buried deep in heavy specialist texts. This book sets out to unearth these gems and present them in a context and format useful to the frontline doctor. We accompany the clinical content with underlying physiology because we believe that for a little effort it offers worthwhile enlightenment. However, as life in clinical medicine is busy, we have placed the physiology in separate sections, so that those who want to get to the bottom line first can do so.

This book is not a technical manual, and details of performing laboratory test are kept to minimum to outline the physical requirements for successful compliance. Nor is it a reference manual for the specialist. The aim is to present information in an accessible way, suitable for those seeking a basic grounding in spirometry or blood gases, but also sufficiently comprehensive for readers completing specialist training in general or respiratory medicine.

Acknowledgement

We wish to thank Warwick Hampden-Woodfall for essential IT backup.

Abbreviations

Lung function parameters

Ax	capacitance reactance area (Goldman triangle)
ERV	expiratory reserve volume
FEF	forced expiratory flow
$F_{E_{NO}}$	fractional exhaled nitric oxide
FEV_1	forced expiratory volume within the first second
FRC	functional residual capacity
F_{res}	resonant frequency
FVC	forced vital capacity
G_{aw}	airway conductance
IC	inspiratory capacity
IRV	inspiratory reserve volume
IVC	inspiratory vital capacity
K_{CO}	transfer coefficient (measured using carbon monoxide)
MEP	maximal expiratory pressure
MIP	maximal inspiratory pressure
MVV	maximum voluntary ventilation
PEF	peak expiratory flow
PIF	peak inspiratory flow
R_5	total airway resistance
R_5–R_{20}	peripheral airway resistance
R_{20}	Central airway resistance
R_{aw}	airway resistance
RV	residual volume
sG_{aw}	specific airway conductance
Sniff P_{di}	sniff transdiaphragmatic pressure
SNIP	sniff inspiratory pressure
sR_{aw}	specific airway resistance
TLC	total lung capacity
TL_{CO}	transfer factor (measured using carbon monoxide)

V_A	alveolar volume
$\dot{V}_A$	minute volume of alveolar ventilation
VC	vital capacity
$\dot{V}_{CO_2}$	volume of CO_2 produced by the body per minute
V_D	dead space
$\dot{V}_E$	minute volume of ventilation
V_T	tidal volume
X_5	reactance

Exercise testing

6MWD	6 minute walk distance
6MWT	6 minute walk test
AT	anaerobic threshold
Borg	type of dyspnoea scale
BR	breathing reserve
$\dot{D}o_2$	rate of oxygen delivery to the tissues
ESWT	endurance shuttle walk test
ISWT	incremental shuttle walk test
MVV	maximum voluntary ventilation per minute, usually extrapolated from a 15-second period of forced maximal breathing
RER	respiratory exchange ratio, given by $\dot{V}CO_2/\dot{V}O_2$
RPE	rating of perceived exertion
$\dot{V}_{CO_2}$	rate of oxygen carbon dioxide elimination by the lungs
$\dot{V}_E$	minute volume of ventilation
$\dot{V}_E/\dot{V}_{CO_2}$	ratio of minute ventilation to carbon dioxide elimination by the lungs (ventilatory equivalent for carbon dioxide)
$\dot{V}_E/\dot{V}_{O_2}$	ratio of minute ventilation to oxygen uptake by the lungs (ventilatory equivalent for oxygen)
$\dot{V}_{E_{cap}}$	maximum ventilatory capacity, usually derived from predictive equation using FEV_1
$\dot{V}_{O_2}$	rate of oxygen consumption
$\dot{V}_{O_{2MAX}}$	peak rate of oxygen consumption achieved during a maximal exercise test
$\dot{V}_{O_2}$ @ AT	oxygen consumption measured at the anaerobic threshold
$\dot{V}_{O_2}$/HR	oxygen consumption per heart beat (oxygen pulse)
WR	work rate (measured in watts, W)

Respiratory gas parameters

A–a	alveolar–arterial difference
ABG	arterial blood gas
$\dot{D}o_2$	rate of oxygen delivery to the tissues
HCO_3^-	bicarbonate
P_ACO_2	partial pressure of alveolar carbon dioxide
P_aCO_2	partial pressure of arterial carbon dioxide
P_Ao_2	partial pressure of alveolar oxygen
P_ao_2	partial pressure of arterial oxygen
P_Io_2	partial pressure of inspired oxygen
P_vCO_2	partial pressure of venous carbon dioxide
S_ao_2	oxyhaemoglobin saturation, measured directly by blood gas analysis
S_po_2	oxyhaemoglobin saturation, measured by peripheral pulse oximetry
$S_{\bar{v}}o_2$	mixed venous oxygen saturation, measured in blood from the pulmonary artery
$\dot{V}_{CO_2}$	rate of production of CO_2

Gases

CO	carbon monoxide
CO_2	carbon dioxide
He	helium
NO	nitric oxide
O_2	oxygen
ppb	parts per billion

Statistics

LLN	lower limit of normality
SD	standard deviation
SR	standard residual
ULN	upper limit of normality

Societies/Guidelines

ATS	American Thoracic Society
BTS	British Thoracic Society

ERS	European Respiratory Society
GINA	Global Initiative for Asthma
GOLD	Global Initiative for Chronic Obstructive Lung Disease
mMRC	Modified Medical Research Council (Dyspnoea Scale)
MRC	Medical Research Council (UK)
NICE	National Institute for Health and Care Excellence (UK)
SIGN	Scottish Intercollegiate Guidelines Network

Diseases

ALS	amyotrophic lateral sclerosis
COPD	chronic obstructive pulmonary disease
ILD	interstitial lung disease
MND	motor neurone disease
OHS	obesity hypoventilation syndrome
OSA	obstructive sleep apnoea
RTA	renal tubular acidosis

Units

L	litre
min	minute
mmol	millimoles
mmol/L	millimoles per litre
s	second
SI	standard international (units)

Miscellaneous

BODE	BMI, Obstruction, Dyspnoea and Exercise (index)
CK	creatinine kinase
CPAP	continuous positive airway pressure
CSF	cerebrospinal fluid
CT	computed tomography
ICS	inhaled corticosteroid
PEEP	positive end expiratory pressure
REM	rapid eye movement (sleep)

2

Peak expiratory flow

INTRODUCTION

Measurement of the peak expiratory flow (PEF) is one of the most convenient, economical, and commonly performed tests in the management of asthma. The test requires the simplest of measurement equipment and is straightforward to teach and perform.

TEST DESCRIPTION AND TECHNIQUE

The PEF is an easy test for most individuals to master but is dependent upon maximal effort, and so requires cooperation, coordination, and comprehension to produce repeatable and reliable results.

The test involves taking a forceful, full inspiration, immediately followed by short, maximal, explosive expiratory effort into the PEF meter. Expiration does not need to continue past the initial 'blast', as flow will quickly decline beyond this point.

The value recorded is usually the best of three efforts, each of which should be made with acceptable technique.

PITFALLS

- An isolated peak flow reading has limited value in diagnosing the cause of respiratory insufficiency, though it is helpful for monitoring known cases of asthma.
- The PEF can be 'cheated' by spitting into the meter like a blowpipe or pea-shooter. With practice, it is easy to blow the meter to the end of its scale with moderate effort using this technique.

PHYSIOLOGY OF TEST

PEF is the highest velocity of airflow that can be transiently achieved during a maximal expiration from total lung capacity. Because flow is a function of resistance, and the majority of resistance is encountered in the upper airways, the peak flow is an excellent indicator of large airway function.

In addition to airway resistance and effort, the PEF is also a function of lung volume and recoil, both of which increase as the lung is inflated. Therefore, measurements should be made after a full inspiration.

NORMAL VALUES

Normal values for PEF are commonly read from a nomogram, similar to that shown in Figure 2.1.[2] Note that values at all ages are directly related to height, but that males have higher values than females of the same height and age.

These nomograms are constructed from regression equations derived from large population studies. The most commonly used regression equations in Europe are those calculated from the European Community of Coal and Steelworkers (ECCS) study.[3] The equations for calculation of predicted normal values for PEF for males and females are as follows:

Males: PEF ($L \cdot s^{-1}$) = (6.14 × height) – (0.043 × age) + 0.15

Females: PEF ($L \cdot s^{-1}$) = (5.50 × height) – (0.030 × age) – 1.11

PEAK FLOW VARIABILITY IN THE DIAGNOSIS OF ASTHMA

The key to assessment of asthma is a careful history, which in many cases will allow a reasonably certain clinical diagnosis. Nonetheless, as treatment may be required over many years, it is important even in relatively clear cases to try to obtain objective support for the diagnosis where possible.[4]

Confirmation of a diagnosis of asthma hinges upon demonstration of airflow obstruction, varying over short periods of time.

A period of monitoring may be helpful by identifying diurnal variation, which is a hallmark of asthma, to add weight to a diagnosis in uncertain cases. During a period of monitoring, peak flow should be measured at least twice per day, morning and night, and recorded on a peak flow chart similar to that shown in Figure 2.2.

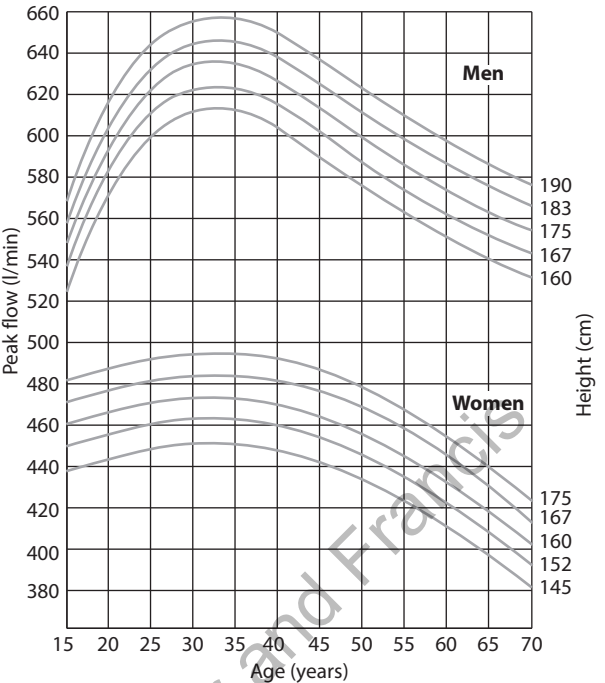


Figure 2.1 Peak flow nomogram showing normal peak flow values for males and females by age and height. During childhood, peak flows are similar for boys and girls of the same height. During adolescence, the two curves diverge, so that the predicted peak flow is greater for a short man than for a tall woman. Hence, the two sets of curves have no overlap. (Reproduced from Gregg I and Nunn AJ, *Br Med J*, 3, 282–284, 1973. With permission from the BMJ Publishing Group.)

Daily diurnal PEF variability is calculated from twice daily PEF as

$$\frac{\text{Each day's highest} - \text{Same day's lowest}}{\text{Mean of that day's highest and lowest}}$$

The above equation should be applied to the highest and lowest results for each day, to produce a daily percentage variability over the period of monitoring. All of the percentages should then be averaged, over at least 1 week.[4]

The threshold of significance of diurnal PEF variability depends upon how many readings are taken per day, as the more readings are taken, the

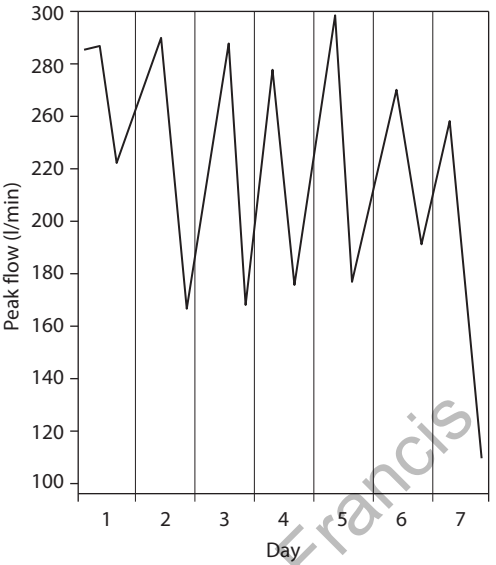


Figure 2.2 Diurnal peak flow variability. Peak flow only has a slight diurnal variability in normal subjects, with the lowest values usually seen in the early hours of the morning. The wide variation in this asthmatic is seen during very poor control, with a final dangerous deterioration.

greater the likelihood that the true daily maximum and minimum PEF will be identified. Thus, if two daily readings are taken (morning and night) then a variability of 10% is significant, whereas a variability of 20% is required where four or more readings are recorded. A four-time daily monitoring schedule would be difficult for most patients to maintain.

Notwithstanding the above, the sensitivity of peak flow variability monitoring for diagnosing asthma is not high, at around 25%.[4] Moreover, patients with other causes of obstructive lung disease may also show some degree of peak flow variability, reducing the specificity of variability monitoring as a diagnostic test. Greater sensitivity may be gained by monitoring peak flow for a 2-week period prior to treatment, followed by 2 weeks after commencement. However, the time required to calculate this is not insignificant.

Electronic peak flow devices are available which record the time at which readings are made and automatically calculate the variability. Use of such devices ensures that readings are made at appropriate times.

Very wide variability in daily PEF readings is a feature of poorly controlled or brittle asthma. Brittle asthmatics may exhibit PEF variability of 40% or more. Large variability in PEF is also observed in the recovery phase of acute severe asthma and indicates ongoing lability. A patient who has been admitted to hospital with acute asthma should not be discharged until the diurnal variability in PEF is less than 25%.

Peak flow monitoring is an essential tool in the diagnosis of occupational asthma. The portability of the peak flow metre enables convenient serial readings to be made during the working day, so that the effects of occupational exposure may be measured at the time of contact with the suspected sensitising agent.

ASSESSMENT AND MANAGEMENT OF ASTHMA

Asthmatics should have their own self-management plan to guide escalation of treatment, based on any deterioration of peak flow and clinical symptoms. All patients with severe asthma should have their own peak flow metre and a familiarity of their own range of values.[4]

The PEF reading gives an objective and early warning signal of the need to increase therapy or seek medical intervention.

A sudden deterioration in the peak flow of an asthmatic may occur during exacerbations and be a premonitory warning of such. In a patient suffering an acute exacerbation of asthma, a PEF of less than 75% of their normal best value (or the patient's predicted, whichever is less) suggests a moderate exacerbation. A PEF of less than 50% of best or predicted is a feature of acute severe asthma. A patient with a PEF of this order, particularly when it persists after bronchodilator therapy, should be admitted to hospital. A PEF of less than 33% of a patient's normal best or predicted value indicates life-threatening asthma.

Severity of acute asthma, as gauged by PEF, is summarised in Table 2.1.

Table 2.1 Severity of acute asthma by peak expiratory flow

Severity of acute asthma exacerbation	% of normal best or predicted
Moderate exacerbation	50%–75%
Acute severe exacerbation	33%–50%
Life-threatening exacerbation	<33%

PITFALL

Diurnal variation may be missed if PEF is not measured first thing in the morning, prior to bronchodilator therapy.

KEY POINTS

- Diurnal variability in PEF is a hallmark of asthma.
- Peak flow measurements are essential for assessing the severity of acute asthma.
- Peak flow variability monitoring may be useful in the management of some asthmatics.
- Peak flow variability monitoring may be useful in the diagnosis of asthma.
- There are many causes of a low PEF other than asthma.
- Peak flow monitoring is requisite for assessment of suspected occupational asthma.

7

Static lung volumes and lung volume subdivisions

INTRODUCTION

Dynamic lung volume tests such as spirometry are limited to measurement of volumes of gas which may be inspired or expired from the lungs. However, a residual volume (RV) of gas remains within the lungs, even at full expiration. Measurement of this volume provides additional information to supplement the spirometric values, see Figure 7.1.

Lung volumes which cannot be measured by spirometry alone are termed *static* lung volumes. Measurement of static lung volumes may be helpful to evaluate the cause of a reduced forced vital capacity (FVC), particularly if there is suspicion of a mixed restrictive/obstructive defect.

Static volumes are measured less often than gas transfer and may not always be performed in a routine lab assessment, unless requested for a specific indication.

MEASURED INDICES/KEY DEFINITIONS

Measurement of functional residual capacity (FRC) also allows calculation of lung volume subdivisions and derived parameters. Figure 7.1 shows a spirometry trace with all lung volume subdivisions. The major indices calculated during the measurement of static lung volumes are shown in Table 7.1.

The total lung capacity (TLC) is the sum of the vital capacity (VC) and the RV, so TLC = RV + VC.

The RV is often expressed as the proportion of TLC, thus RV/TLC. This ratio represents the proportion of the lungs which is not available for ventilation (but does participate in gas exchange). As such, it is an indirect index of gas trapping.

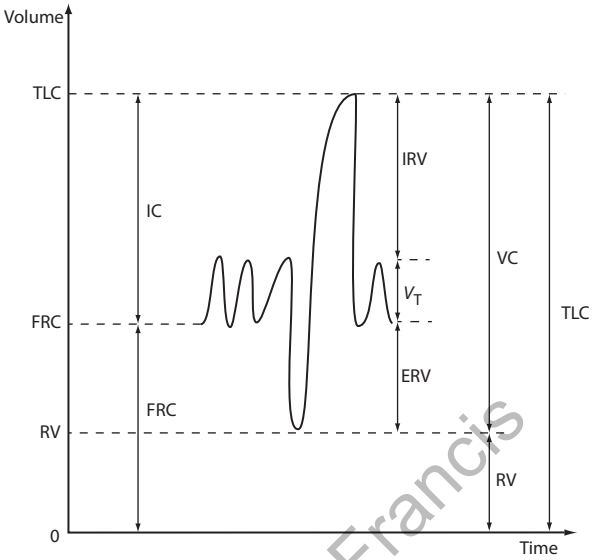


Figure 7.1 Spirometry showing lung volume subdivisions. Note that spirometry cannot measure residual volume, nor any lung volume subdivisions of which residual volume is a component. TLC, total lung capacity; FRC, functional residual capacity; RV, residual volume; IRV, inspiratory reserve volume; V_T, tidal volume; ERV, expiratory reserve volume; VC, vital capacity; IC, inspiratory capacity.

Table 7.1 The principle lung volume subdivisions

Abbreviation	Parameter	Description
RV	Residual volume	The volume of gas remaining in the lungs at the end of a maximal expiration.
TLC	Total lung capacity	The total volume of gas in the lungs at full inspiration.
FRC	Functional residual capacity	The volume of gas remaining in the lungs at the end of a normal resting tidal expiration.
ERV	Expiratory reserve volume	The volume of gas which can be expired from end tidal expiration (FRC) to residual volume.
IC	Inspiratory capacity	This is the volume of gas which can be inspired from FRC to TLC.

TEST DESCRIPTIONS/TECHNIQUES

A variety of methods exist for measurement of static lung volumes, each of which requires differing levels of comprehension, cooperation, and compliance to produce accurate and meaningful results. The three main techniques for measuring static lung volumes are helium dilution, nitrogen washout, and whole-body plethysmography.

Helium dilution

Helium dilution is the easiest method to perform, but is not the cheapest due to the relative expense of helium gas. There are no contraindications, and the only real pre-requisite is the ability to maintain an effective mouthpiece seal. Some patients will find breathing from a mouthpiece for an extended period of time unpleasant which may influence their normal tidal breathing.

The test begins with a period of normal tidal breathing to establish a consistent end-expiratory volume (FRC), at which point the patient is connected to a closed circuit containing the test gas (Figure 7.2). This gas contains a known concentration of helium, along with sufficient oxygen for the test duration, with the balance made up of nitrogen. The breathing circuit also contains a carbon dioxide absorber such as soda lime to prevent the accumulation of carbon dioxide. Tidal breathing continues until the concentration of helium in the breathing circuit stabilises, indicating equilibration between lungs and the circuit, and relatively thorough mixing and even distribution throughout the lungs. The patient then performs a VC manoeuvre (full inspiration followed by full expiration, or vice versa) to complete the measurement.

At the point where the patient is switched into the breathing circuit (assumed to be at FRC), certain values are known:

V_1 is the volume of the breathing circuit and bag.

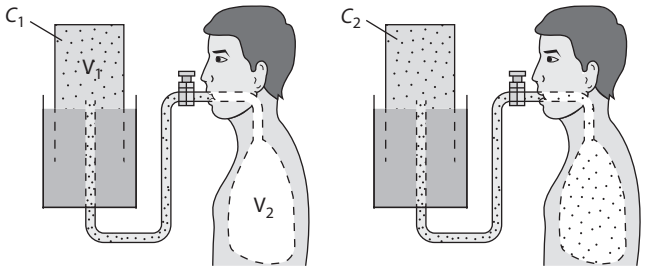
C_1 is the concentration of helium in the breathing circuit and bag.

V_2 is the (unknown) volume of gas within the lungs at the beginning of the test (FRC).

The concentration of helium in the lungs is 0%.

At the end of the measurement, V_1 is unchanged, but C_1 will be reduced by dilution with the gas in the lungs which contained no helium.

C_2 is the final concentration of helium within the breathing circuit, measured at the end of the test.



$$C_1 \times V_1 = C_2 \times (V_1 + V_2)$$

Figure 7.2 Method of measuring total lung capacity by helium dilution.

The total gas volume in the lungs and the bag combined is given by $V_1 + V_2$. As the breathing circuit is closed and no helium is added or lost:

$$C_1 \times V_1 = C_2 \times (V_1 + V_2)$$

Rearranging:

$$V_2 = \frac{V_1(C_1 - C_2)}{C_2}$$

As the measurement was commenced with the patient at FRC, V_2 gives a measurement of FRC.

Once the volume of FRC is known, it is easy to calculate the remaining lung volume subdivisions, thus:

$$\text{RV} = \text{FRC} - \text{ERV}$$

$$\text{TLC} = \text{RV} + \text{VC}$$

Alternatively, TLC can be calculated by adding FRC to inspiratory capacity (IC), measured from spirometry.

Nitrogen washout

Like helium dilution, this technique involves breathing from a closed circuit for a period of time and then performing a VC manoeuvre to provide values for IC, expiratory reserve volume (ERV), and VC. There is no difference in the measurement procedure from the point of view of the patient.

The principle of measurement differs slightly, using nitrogen rather than helium as the test gas. The methods differ in that the tracer gas (nitrogen) exists in the lungs whereas helium does not.

At the point where the patient is switched into the closed circuit (again at FRC), only the concentration of nitrogen within the lungs is known (80%), and this becomes C_L. From this point, the patient breathes 100% oxygen, which continues long enough to 'wash out' the vast majority of nitrogen from the lungs (usually 7 minutes). At the end of the test, the total volume of expired gas is measured, which becomes V_E. The concentration of nitrogen in this expired gas is also measured and becomes C_E. Measurement of FRC, which in this case becomes V_{FRC}, is then easily derived using the following equation:

$$V_{FRC} \times C_L = V_E \times C_E$$

Rearranging:

$$V_{FRC} = \frac{V_E \times C_E}{C_L}$$

Once this value is obtained, then calculation of other lung volume subdivisions is made as for helium dilution.

Whole-body plethysmography

Measurement is made in a closed whole-body plethysmograph or body box for short (Figure 7.3). This method is generally considered the gold standard, though those who suffer with claustrophobia may be unable to tolerate the procedure. The apparatus required is more bulky (and expensive) than that required for dilution methods. The principle of measurement depends upon Boyle's law, which states that in a closed container, the pressure of a fixed mass of gas is inversely proportional to the volume. In other words, if volume halves, pressure doubles.

The test procedure starts with the patient breathing normally in and out through a standard mouthpiece. Once a consistent breathing pattern and

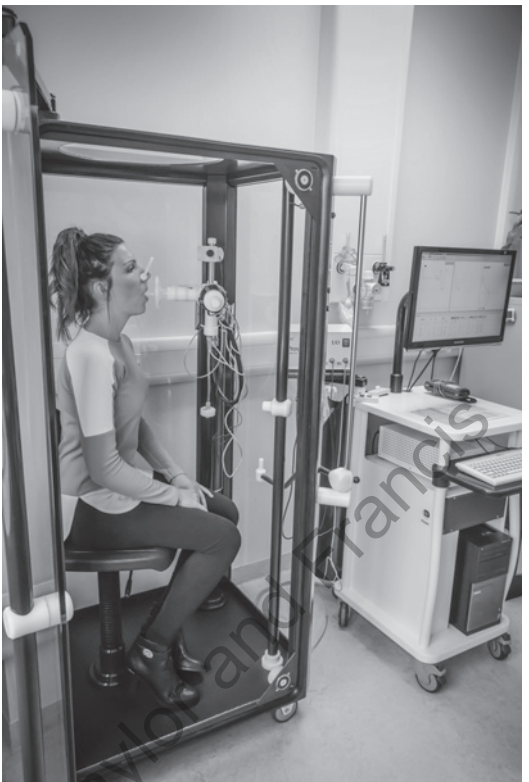


Figure 7.3 Whole-body plethysmograph (or body box for short). (Courtesy of P Pearson and D Gore.)

end-expiratory volume have been established, a shutter is closed at end expiration, following which the patient makes several panting efforts in and out against the shutter. These efforts expand and compress the gas in the lungs according to Boyle's law. The shutter is then released, allowing the patient to take a maximal inspiration to TLC.

The equation required to calculate FRC is slightly more complicated than the dilution or washout techniques, but the principle is similar. At the start of the measurement, the box volume and pressure and alveolar pressure (which with an open glottis is the same as that measured at the mouth) are known. Using these known parameters, the volume of gas in the lung can

be calculated from changes in box volume and pressure and mouth pressure during closed-shutter panting.

Comparison of methods

Each of these methods employs a different concept and consequently measures a slightly different physical volume. Washout and dilution techniques measure only that gas in the alveoli and airways which is in communication with the breathing circuit. In severe obstructive diseases, gas trapped in closed airways mixes poorly with that in the circuit. Consequently, helium dilution and nitrogen washout may underestimate static lung volumes in subjects with obstructive airways disease.

By contrast, whole-body plethysmography measures all the gas present within the thoracic cavity which is subject to the pressure changes of the closed-shutter panting manoeuvre. This includes any gas trapped behind closed airways and bullae (Figure 7.4), but may also include intestinal gas. This leads to an overestimate of TLC, although error is not usually large. In those with severe obstruction, changes in lung compliance may also

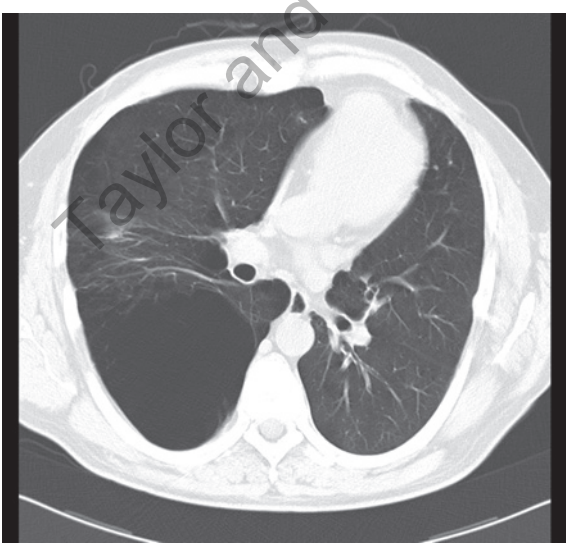


Figure 7.4 Computed tomography (CT) of an emphysematous bulla. The volume of this bulla would not be included in the volume of TLC measured by a dilution method, which would underestimate the true TLC.

interfere with accurate pressure transmission from the lungs to the mouth during the panting manoeuvre. Nonetheless, measurement of static lung volumes by whole-body plethysmography in obstructive airways disease is more accurate than that measured by gas dilution or washout techniques.

The difference between TLC measured by dilution or washout, and that measured by whole-body plethysmography provides a useful additional index of the extent of any gas trapping in obstructive airway disease.

The only situation where dilution or washout techniques may be preferable to whole-body plethysmography is where the patient is unable to manage this technique due to claustrophobia, habitus, or disability.

PHYSIOLOGY OF LUNG VOLUMES

Total lung capacity

During inspiration, the chest wall musculature expands the lungs against the force of their elastic recoil, which would otherwise tend to deflate them, like a balloon. As the lungs expand they become progressively stiffer, i.e. their compliance is reduced. The lungs reach TLC when the force generated by the inspiratory respiratory muscles is no longer able to overcome the force generated by the elastic recoil of the lungs and chest wall.

Residual volume

In young healthy subjects, expiration can progress no further when the ribs are opposed, so that the RV is determined by the anatomical mechanics of the chest wall. This typically occurs at an RV of approximately 25% of TLC.

However, with increasing age, airway closure occurs during deep expiration, resulting in gas trapping at progressively higher RVs, and thereby forms the limiting factor to expiration. Typically, RV may occur at up to 40% of TLC in the elderly. As such, the RV is one of the few lung volumes that increase with age. This gas trapping may be increased markedly in those with emphysema.

Functional residual capacity

This is the volume within the lungs at the end of a passive expiration. Expiration during normal tidal breathing is a passive manoeuvre, achieved by relaxation of the respiratory musculature against an open glottis. FRC

occurs at the point at which outward recoil of the chest wall balances the inward recoil of the lungs.

Therefore, FRC reflects the compliance of the lungs and chest wall, both of which may be affected by disease. The FRC will also be reduced when a subject moves from an upright to a supine posture, as the abdominal contents push against the diaphragm in the supine position (particularly in the obese).

The FRC is an important concept, as it provides a reservoir which maintains blood oxygenation during any pause in breathing or apnoea.

Closing capacity

Closing capacity is a volume which is not routinely measured by pulmonary function testing, but is important conceptually. Closing capacity is the lung volume at which airway closure begins to occur during expiration. It is physiologically significant because closure of airway units causes them to become unventilated, the consequence of which is ventilation–perfusion mismatch and a reduction in arterial oxygen tension.

Notably, the closing capacity increases with age. By the age of 75 years in a healthy individual, the closing capacity exceeds the FRC in the upright position, meaning that some airway closure occurs all of the time. This is one of the principle reasons for the gradual decrease in arterial oxygen tension seen with ageing. Closing capacity is more likely to exceed FRC in the supine position, in which FRC is lower (though closing capacity unchanged).

NORMAL VALUES

Static lung volume indices are compared to predicted values or standard residuals in a similar way to the majority of lung function test results. Likewise, the relationships between some lung volume subdivisions change predictably with age and in disease.

The predicted TLC varies directly with height, but is greater in men than women of the same height. A TLC of less than 80% of predicted or with a standard residual more than 1.64 below the mean is considered abnormal (see Chapter 1).

The RV is also compared with predicted norms. For example in the average male (1.78 m, 70 kg), with a TLC of around 7 L, RV should lie in the range 1.5–2 L.

The RV is commonly expressed as the proportion of TLC which it occupies, i.e. RV/TLC. This value changes naturally with age, rising from 20%–25% in youth to approximately 40% by the age of 70.

Multiple factors affect the normal value of FRC, including posture, body weight, and gender. Generally though, FRC occurs at about 50% of TLC, but also increases with age (see above). In the supine position, the force of the abdominal viscera against the diaphragm reduces the FRC by approximately 25%.

PATTERNS OF ABNORMALITY

Figure 7.5 shows the pattern of lung volume subdivisions seen in various different disease states.[22]

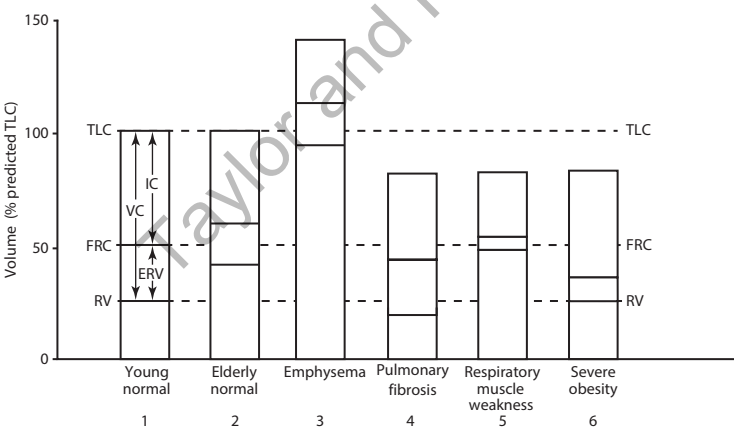


Figure 7.5 Typical changes in lung volume subdivisions by disease. Volume expressed as percent predicted TLC. Horizontal lines indicate FRC. (2) With ageing RV and FRC both increase, so that VC falls within the same TLC. (3) In emphysema the TLC increases, with greater proportional increases in RV and FRC making for a reduction in FVC. (4) In intrapulmonary restriction RV tends to fall or remain unchanged, whereas in muscle weakness (5) RV tends to increase. (6) In obesity, an increase in ERV is characteristic. (Modified from Gibson G, In J Hughes, N Pride [eds.], *Lung Function Tests: Physiological Principles and Clinical Applications*, London, WB Saunders, 1999.)

Relationship between VC and TLC

Reduction of TLC is the defining feature of a restrictive defect (see Table 3.4 for a list of causes). The relative change of other lung volume subdivisions provides additional information, which may indicate the cause of the reduction in TLC.

A reduced TLC is usually associated with a reduction in VC, from which its presence may be suspected by spirometry. However, a reduction in VC is not always associated with a reduced TLC. In up to 50% of cases in which a reduced VC is detected by spirometry, the TLC is normal.[12,23] The reduction of VC in such cases is caused by an increase in the RV, within the same envelope of TLC (see Figure 7.1).

An obstructive defect may frequently be associated with a reduction of VC, due to trapping of gas in small airways thereby increasing the RV. Under these circumstances, the TLC measured by whole-body plethysmography will be normal or even increased.

Conversely, VC may be maintained despite a reduction in TLC, if the RV is reduced. This may occur early in the course of interstitial lung disease (ILD), though it is rare.

Obstructive lung disease

Emphysema causes the greatest elevations of RV seen, due to gas trapping, which prevents complete expiration. During the early course of obstructive airways disease, the RV increases at the expense of FVC, without any increase in TLC (gas trapping). Later in the course of disease, TLC also rises (hyperexpansion).

The FRC is also elevated in obstructive airway disease (hyperinflation) as the greater compliance of emphysematous lungs makes for a reduction of recoil, shifting the lung volume at which inward and outward recoil pressures equilibrate.

Interstitial lung disease

The RV is usually relatively unaffected by ILD, or only reduced in proportion to TLC, so that the RV/TLC remains approximately normal, or only slightly elevated.

The FRC is reduced by ILD, though proportionately less than other lung volume subdivisions.

Miscellaneous

Obesity causes loss of FRC, leading to loss of ERV. Therefore, tidal breathing occurs at smaller FRCs.

The RV is increased in patients with expiratory muscle weakness, due to the reduced force that can be developed to expel air from the lungs. Likewise, the RV/TLC is also increased.

In left ventricular insufficiency, the RV is also increased because pulmonary congestion reduces the compressibility of lung tissue.

Table 7.2 summarises the key changes in static lung volume and lung volume subdivision indices.

SPECIFIC CONSIDERATIONS

Anaesthesia

Induction of anaesthesia brings about a further reduction of FRC to 15%–20% below that which occurs in a supine subject. The reduction is seen whether neuromuscular blockade is used or not, and occurs with all anaesthetic drugs. Thus, anaesthesia reduces the FRC to around the level of the closing capacity, which has practical considerations for maintaining oxygenation in the anaesthetised patient.

FRC in patients receiving ventilatory support: PEEP and CPAP

Mechanical ventilatory support works by providing positive airway pressure to inflate the lung. This is by contrast to spontaneous ventilation, during which the respiratory muscles inflate the lungs by transmission of *negative* pressure from the pleura to the airways. Expiration, under both conditions of spontaneous and mechanical ventilation, is effected passively by the recoil

Table 7.2 Characteristic changes in lung subdivisions in lung disease

Defect	TLC	RV	RV/TLC
Obstructive	↑	↑	↑
Restrictive – ILD	↓	↔/↓	↔/↑
Restrictive – muscle weakness	↓	↑	↑

of the lungs and chest wall, which generates positive airway pressure and thereby outward airflow. Therefore, the patient undergoing mechanical ventilation experiences positive airway pressure throughout the respiratory cycle.

Positive end-expiratory pressure (PEEP) is routinely applied to patients with acute respiratory failure who are undergoing mechanical ventilation. PEEP is a small pressure applied to the airway during expiration, against which a patient must breathe to exhale. This has the favourable effect of increasing FRC. A higher inspiratory pressure is then utilised to elevate the inspiratory volume by the same amount as the increase in FRC, maintaining an equivalent tidal volume.

A similar technique may be employed in the care of spontaneously breathing patients who require respiratory support. Continuous positive airway pressure (CPAP) applies additional positive pressure throughout the respiratory cycle and may be administered through a face mask. Inspiration, under these circumstances is driven by negative pleural pressure but augmented by the additional positive airway pressure. CPAP therefore aids inspiration, whilst providing a resistance to expiration which increases FRC.

The effect of both PEEP and CPAP is to increase FRC. In patients with respiratory failure, this has several advantages:

1. The increase in FRC relative to closing capacity increases the amount of lung that is ventilated throughout the respiratory cycle, thus improving ventilation–perfusion matching and oxygenation (see section 'Closing capacity').
2. Consolidated lung segments tend to collapse at low volumes and the elevation of FRC recruits such segments into participation in ventilation and arterial oxygenation.
3. In patients with pulmonary oedema, the increased volume of ventilated lung increases the capacity of the pulmonary interstitium for water and helps to reduce the volume of alveolar oedema.
4. In patients with stiff and poorly compliant lungs, the increase in FRC shifts the lung to a more favourable point on the pressure–volume compliance curve, so that less work of breathing is required to produce equivalent ventilation.
5. Face-mask CPAP is also used to treat obstructive sleep apnoea (OSA, Figure 7.6). In patients with OSA, the pharynx collapses during sleep, under the negative pressure of inspiration. By maintaining positive airway pressure throughout the respiratory cycle, the upper airway is splinted open during inspiration.

Figure 7.6 Continuous positive airway pressure treatment for obstructive sleep apnoea. (Courtesy of Resmed Limited.)

CLINICAL PEARLS

- In many cases where the FVC is reduced, measurement of TLC does not demonstrate a restrictive defect. Reduction of FVC may otherwise occur in obstructive airways disease, when gas trapping increases the RV, at the expense of FVC. A reduction in FVC may be seen in 40% of chronic obstructive pulmonary disease (COPD) cases. In a large series of reported pulmonary function tests, a reduction in TLC was confirmed in only 10% of those with a reduced FVC, an increased RV accounting for the reduced FVC in the other 90% of cases.[12]
- Measurement of static lung volumes may be useful for evaluating more complex mixed defects, but in order of importance probably comes after spirometry, the flow–volume loop and gas transfer.
- Measurement of lung volumes is requisite to assessment for lung volume reduction surgery, which may occasionally be helpful for patients with severe emphysema, as hyperexpansion (increased TLC) and gas trapping (increased RV) are amongst the criteria.
- There is little role for performing serial measurement of static lung volumes over a period of time to track the course of a subject's condition, neither in obstructive nor ILD. Once the distribution of static

volumes has been determined, any deterioration is likely to correlate with the decline in the values of dynamic lung volumes, measureable by spirometry.

- If a subject has normal spirometry and normal gas transfer, then these findings provide a robust diagnosis of normality. Little would be gained in most situations by measuring static volumes as a further screening measure.
- The IC/TLC ratio may provide a useful index of severity of COPD, as it provides a measure of hyperinflation. This ratio has proven more predictive of mortality than FEV_1 in at least one study of patients with COPD.[24] IC also correlates with exercise tolerance in patients with COPD.
- Many patients with airways disease make a positive volume response to bronchodilator, even if there is no measureable increase in FEV_1. Such a response may be evidenced by an increase in IC whilst RV, TLC and FRC may reduce toward their normal values, measureable only by recording static lung volumes.[18] Moreover, this increase may correlate with an improvement in symptomology. Therefore, lack of response of FEV_1 to bronchodilator does not preclude benefit.
- When a restrictive defect is caused by muscle weakness, the RV is often increased, by contrast to ILD, where the RV is usually either unchanged or slightly reduced.
- The volume which is most susceptible to change in patients with obesity is the ERV, which may be dramatically reduced. A reduction in TLC and VC may also be seen, but is usually limited to around 10%.

KEY POINTS

- Tests of static lung volumes measure indices which cannot be accessed by simple spirometry alone.
- A reduction of TLC is the defining feature of a restrictive defect.
- Many subjects with a reduced FVC do not have a reduction of TLC, i.e. they do not truly have a restrictive defect.
- In patients with obstructive airway disease, gas dilution and washout measurements commonly underestimate TLC compared with whole-body plethysmography.