What do respiratory function tests tell us?

One of the largest groups of conditions that pharmacists encounter is respiratory diseases and good management involves being able to understand the meaning of pulmonary function tests — and what to do if they are abnormal. In this article Toby Capstick explains the basic lung function tests and helps us understand what aberrant blood gas measurements mean clinically.

Introduction

Respiratory diseases are the third most commonly reported long-term illnesses in Great Britain and are a major burden to the NHS, costing £3billion in 2004.[1] Pulmonary function tests provide objective assessment of lung function. They are an essential component of the management of patients with respiratory disorders, because highly subjective symptoms, such as dyspnoea, are not good indicators of disease severity and progression.[2]

Peak expiratory flow

The peak expiratory flow (PEF) is defined as the highest flow achieved from a maximum forced expiratory manoeuvre started without hesitation from a position of maximal lung inflation.[3] PEF is dependent on airway resistance, particularly in the upper airways and so is used to assist in the diagnosis and monitoring of asthma. At least a 20% variability in PEF, with a minimum change of 60L/min, ideally for three days in a week over a two-week period is highly suggestive of asthma.[4] PEF has no role in the diagnosis of chronic obstructive pulmonary disease (COPD), but may be used to differentiate COPD from asthma.[5]

The normal value for PEF is dependent on sex, age and height, and standard charts are available to read off normal values for individual patients.[6] All asthmatics should be prescribed a peak flow meter and diary to check and record their peak flows so as to recognise deteriorating asthma control early and seek help.[4] Wide diurnal variability in the PEF is indicative of poor asthma control and may be missed if PEF is not checked in the morning before patients use their bronchodilators. A PEF below 50% of the patient's best or predicted best is indicative of acute severe asthma and warrants hospital admission, while a PEF below 33% is a feature of life-threatening asthma.[4]

Spirometry

Spirometry is a physiological test that measures the volume of air exhaled or inhaled by a patient as a function of time (see Figure 1). It can be used as a screening tool for patients at risk of respiratory disease, such as smokers; or individuals exposed to occupational hazards; for diagnostic purposes; for assessing the severity of respiratory disease; or for monitoring disease progression and response to treatment.[3]

Measurement definitions

The total lung capacity (TLC) is the volume of gas in the lungs after maximal inspiration[8] and is related to body size — particularly to standing height.[7]

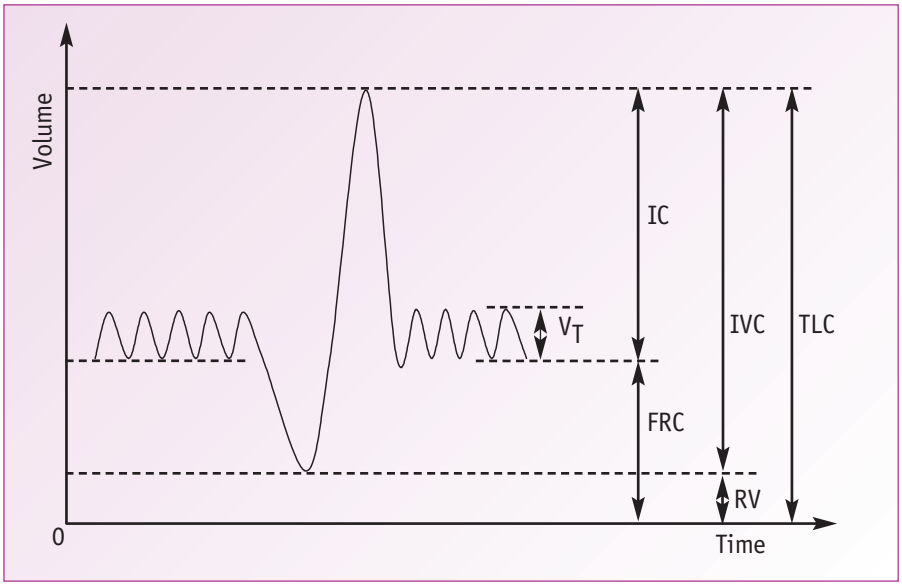
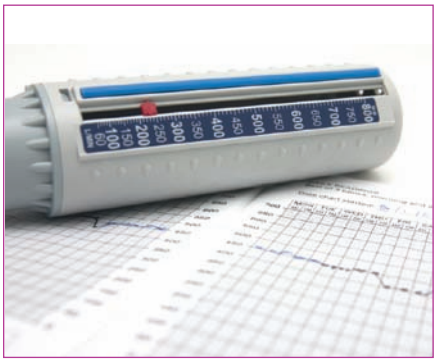


Figure 1: A typical spirometry trace. Key: TLC: Total lung capacity, FRC: Functional residual capacity, IC: Inspiratory capacity, RV: Residual volume, V_T: Tidal volume, IVC: Inspiratory vital capacity.

Blood gas tensions provide information about the integrity of pulmonary gas exchange and acid/base balance. The arterial partial pressure of carbon dioxide ($PaCO_2$) provides information about ventilation, while the arterial partial pressure of oxygen (PaO_2) provides information about the efficiency of gas exchange.

The functional residual capacity (FRC) is the volume of gas present in the lung at the end of expiration during tidal breathing.[8]

The residual volume (RV) is the volume of gas remaining in the lung after maximal exhalation.[8] In the young, the limit of expiration occurs when the ribs cannot move any closer together. However, RV increases with age because of the loss of lung elasticity, which causes airway closure and air-trapping.[9]



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above: *A peak flow meter. This is used to measure the PEF from a maximum forced expiration started without hesitation from a position of maximal lung inflation. People with asthma should check their PEF regularly.*

The inspiratory capacity (IC) is the maximum volume of gas that can be inspired from FRC.[8]

The tidal volume (V_T) is the volume of gas inhaled or exhaled during the normal relaxed respiratory cycle.[8]

The vital capacity (VC) is the volume change between the positions of full inspiration and complete expiration. The measurement may be made during full relaxed inspiration (IVC), full relaxed expiration, or during a forced expiration (FVC).[8]

TLC, FRC and RV cannot be measured using spirometry, because it is not possible to exhale the entire contents of the lungs. However, FRC may be measured using body plethysmography, nitrogen washout or helium dilution techniques and the other values can then be calculated.[8]

Other important data measured during spirometry are the forced vital capacity (FVC), the forced expiratory volume in one second (FEV_1) and the FEV_1/FVC ratio. FVC is defined as the maximal volume of air exhaled with maximally forced effort from a maximal inspiration, while FEV_1 is the maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration.[3]

Relating the measurements to diseases

Obstructive disorders

Obstructive airway diseases affect airflow more than lung volume,[3,7] so that the lung empties more slowly, hence FEV_1 is reduced more than FVC. A diagnosis of airflow obstruction can be made if the FEV_1/FVC ratio is less than 0.7 and FEV_1 is less than 80% of predicted.[5] The reduction in FEV_1 is an indicator of severity (see Table 1), allowing treatment decisions to be made, and is the best predictor of survival in COPD.[3,5]

Table 1. Assessment of the severity of airflow obstruction

Severity	FEV_1
Mild airflow obstruction	50-80% predicted
Moderate airflow obstruction	30-49% predicted
Severe airflow obstruction	<30% predicted

TLC and RV are often increased in obstructive disorders such as emphysema and bronchial asthma.[8] Hyperinflation may occur in emphysema because of the increased pulmonary compliance (increasing TLC), RV is increased because of air-trapping in the lung. This increase in RV is invariably greater than the increase in TLC, so that overall vital capacity is reduced.[9,10]

Table 2. Common causes of acid-base disorders

Respiratory acidosis	**Ventilatory failure and accumulation of CO_2:**
	■ Airways disease, such as COPD, asthma
	■ Chest wall disorders, such as obesity hypoventilation syndrome
	■ Neuromuscular disorders, such as motor neurone disease
	■ Central depression of respiratory drive, such as brain lesion, drugs
	■ Exhaustion, associated with any cause of acute respiratory distress
Respiratory alkalosis	**Hypocapnia:**
	■ Hypoxaemia, resulting in reflex hyperventilation
	■ CNS disorders, such as subarachnoid haemorrhage, trauma, and infection
	■ Anxiety hyperventilation
Metabolic acidosis	■ Diabetic ketoacidosis
	■ Renal failure
	■ Lactic acidosis, such as following tissue hypoperfusion resulting from shock and cardiac arrest
	■ Salicylate poisoning
	■ Diarrhoea
Metabolic alkalosis	■ Acid loss, such as severe vomiting, naso-gastric aspiration
	■ Excessive bicarbonate administration
	■ Excessive mineralocorticoid administration

Restrictive disorders

In restrictive lung disorders, the FEV_1/FVC ratio remains normal, but there is a reduction in TLC. This is either because there is a loss of alveolar volume through, for example, idiopathic pulmonary fibrosis; diseases of the chest wall, pleura or neuromuscular apparatus; or intrathoracic space-occupying lesions.[7] FVC is a more convenient measure of lung function than TLC and can be used to monitor disease progression in restrictive lung diseases.

The diffusion capacity of the lung for carbon monoxide ($DL_{,CO}$)[11] is used to estimate the patient's ability to absorb oxygen from the alveoli and monitor the severity of lung disease. $DL_{,CO}$ is commonly reduced in diffuse lung diseases associated with restrictive disorders, such as fibrosis and sarcoidosis, but tends to be normal in neuromuscular disorders or diseases associated with chest wall.[7]

Interpreting blood gases

Blood gas tensions provide information about the integrity of pulmonary gas exchange and acid/base balance. The arterial partial pressure of carbon dioxide ($PaCO_2$) provides information about ventilation, while the arterial partial pressure of oxygen (PaO_2) provides information about the efficiency of gas exchange. Causes of respiratory and metabolic disorders of acid-base balance are listed in Table 2.

Carbon dioxide

The concentration of CO_2 dissolved in the blood is regulated by chemoreceptors to maintain a $PaCO_2$ in the range 4.7 to 6.0 kPa,[12] which is achieved primarily through the control of the rate and depth of breathing.[9,10] Type 2 respiratory failure exists if PaO_2 is less than 8kPa and is accompanied by hypercapnia (high $PaCO_2$) and indicates ventilatory failure. The possible causes of respiratory acidosis are listed in Table 2. Hypercapnia may also be caused by increased dead space resulting from the loss of effective alveoli available for gas exchange, for example in acute lung injury and acute respiratory distress syndrome (ARDS). However, this is normally compensated for by an increase in ventilatory rate.[10] Raised $PaCO_2$ may also be caused by an increased production of CO_2 that might occur during sepsis, thyrotoxicosis, malignant hyperthermia or rhabdomyolysis. However, this is uncommon unless there is co-existing ventilatory failure.[10]

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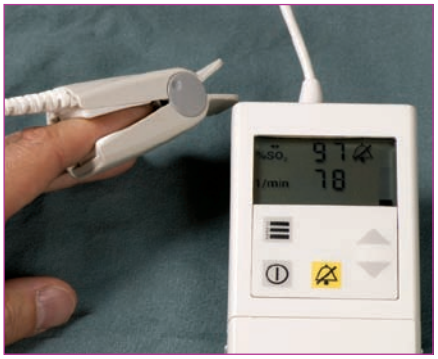

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above: *A pulse oximeter is useful for measuring the percentage of arterial haemoglobin that is oxygenated.*

Oxygen

PaO_2 is dependent on age, posture, body mass index and the concentration of inspired oxygen, but is generally in the range 10–13.3kPa. Hypoxaemia is defined as a PaO_2 of less than 10kPa[10,12] and respiratory failure describes the situation when PaO_2 is less than 8kPa. In a perfect system, PaO_2 would be 21kPa, matching the partial pressure of oxygen in atmospheric, dry air (PO_2). However, inspired gas is humidified in the upper airways and is then further diluted in the alveoli with CO_2 produced in the body. The alveolar partial pressure of oxygen (PAO_2) is therefore dependent on the concentration of inspired oxygen, ventilation (because hyperventilation reduces $PaCO_2$ and thus alveolar $PACO_2$, which therefore raises PAO_2) and the respiratory quotient (the ratio of CO_2 produced/O_2 consumed). The alveolar-arterial oxygen gradient does not vary much with age, but is generally less than 2.6kPa.[12] Greater differences than this generally indicate ventilation to perfusion mismatch, rather than impairment of diffusion, even in fibrotic lung diseases where the blood-gas barrier is abnormally thickened.[10]

Ventilation to perfusion mismatch may occur if blood perfuses alveoli that are not ventilated, so that $PaCO_2$ and PaO_2 remain the same as venous blood. This occurs in pulmonary consolidation, for instance, or if there are well-ventilated alveoli that receive no blood perfusion, such as occurs in acute pulmonary embolism or anatomical shunt — as found in some congenital heart diseases.[10]

A more convenient way of measuring oxygenation is the use of pulse oximetry, which measures the percentage of arterial haemoglobin that is oxygenated (SpO_2).[10] SpO_2 is approximately 95–97% at normal PaO_2, but the relationship between the two is not linear, and so SpO_2 is not significantly affected by a fall in oxygen tension until the PaO_2 drops below 8kPa (when SpO_2 = 90%).[9,10,12] Under conditions of acidosis, raised $PaCO_2$ and raised temperature the dissociation curve shifts to the right causing haemoglobin to have a reduced affinity for oxygen at the same tension of oxygen in the blood. This facilitates the delivery of oxygen to tissues with a high demand. In the pulmonary circulation, where CO_2 concentration is lower, the curve shifts back to the left, causing haemoglobin to have a greater affinity for oxygen and so improving oxygen binding.[10]

Patients with asthma or COPD should only be prescribed inhalers after they have received training and education on how to use their device, and have demonstrated satisfactory technique.

Respiratory disease and abnormal arterial blood gas measurements

In asthmatics arterial blood gases (ABGs) should be checked to assess the severity of an asthma attack if SpO_2 is less than 92%, or if there are other features of life-threatening asthma. They should be repeated two hours after starting treatment if the initial PaO_2 is less than 8 kPa, unless SpO_2 is greater than 92%; or if the initial $PaCO_2$ was normal or raised; or if the patient deteriorates.[4]

All patients experiencing an exacerbation of COPD should have their ABGs checked to assess severity and determine the need for hospital treatment. Patients with a pH $\geq$ 7.35 or $PaO_2 \geq 7$ may be managed at home provided that other signs and symptoms are favourable.[5] Supplemental oxygen is given to maintain adequate levels of oxygenation (SpO_2 >90%) without precipitating respiratory acidosis or hypercapnia.[5] However, the more oxygenated a patient with COPD becomes, the greater the magnitude of subsequent acidosis is, and so the PaO_2 should be maintained at 7.3–10 kPa (SpO_2 85–92%) to avoid the dangers of hypoxia and acidosis.[15] ABGs should be repeated regularly, according to the patient's response to treatment, until they are stable, otherwise pulse oximetry is acceptable for patients with non-hypercapnic, non-acidotic respiratory failure.[5]

Patients with COPD should be prescribed long-term oxygen therapy (LTOT) if their PaO_2 <7.3 kPa, or <8 kPa if they also have polycythaemia or cor pulmonale when their ABGs are checked on two occasions at least three weeks apart.[5]

Use a systematic approach to interpreting blood gases

The interpretation of blood gas data should be approached in a structured manner[10,12] as follows:

1. Determine whether there is acidosis (pH <7.35) or alkalosis (pH >7.45).
2. Determine whether $PaCO_2$ is high or low. CO_2 combines with water to form carbonic acid and so $PaCO_2$ is raised in respiratory acidosis, and low in respiratory alkalosis. If the change in $PaCO_2$ does not match the abnormality in pH, there is a metabolic component to the disorder and the change in $PaCO_2$ is compensatory.
   - Respiratory acidosis — $PaCO_2$ >6.0kPa
   - Respiratory alkalosis — $PaCO_2$ <4.7kPa.
3. Determine whether the alkali bicarbonate is high or low. In metabolic alkalosis bicarbonate is raised, and it is low in metabolic acidosis. If the change in bicarbonate does not match the abnormality in pH, there is a respiratory component to the disorder and the change in bicarbonate is compensatory.
   - Metabolic acidosis — arterial bicarbonate <22 mmol/L
   - Metabolic alkalosis — arterial bicarbonate >26 mmol/L.
4. Assess arterial oxygenation to determine the extent of hypoxaemia, documenting the inspired oxygen concentration.
5. Respiratory or metabolic compensation will occur to some extent to correct the primary disorder. For example in respiratory acidosis, metabolic compensation occurs by increasing renal reabsorption of bicarbonate in an attempt to normalise the arterial pH. In metabolic acidosis, respiratory compensation occurs by increasing ventilation to remove CO_2 in an attempt to normalise pH. Metabolic compensation takes days to occur, while respiratory compensation takes hours.

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Inspiratory flow and the use of inhaler devices

Patients with asthma or COPD should only be prescribed inhalers after they have received training and education on how to use their device, and have demonstrated satisfactory technique.[4,5] However, many studies have demonstrated that technique is frequently poor. One review reported the frequency of physician assessed 'good' technique to range from 5% to 86% of patients for pressurised metered dose inhalers (pMDIs),[13] which are the most

commonly prescribed inhaler device. Even immediately after verbal instruction and demonstration of different inhaler devices, optimal technique was only achieved in 78% of patients using pMDIs, 87% using turbohalers and 90% using accuhalers.[14]

A common error made by 26–70% of patients using pMDIs is their failure to inhale slowly and deeply.[13] Appropriate device selection can be assisted by using an In-Check DIAL inspiratory flow meter (Clement Clarke Ltd, Harlow, UK), which

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mimics the internal resistance of a range of inhaler devices allowing the measurement of inspiratory flow rate and ensuring the patient can inhale through a device at its optimal inspiratory flow rate.[16,17] Optimum inspiratory flow rates for pMDIs, turbohalers and accuhalers are 25–60L/min, 60–90L/min and 30–90L/min respectively.[18] This is important information because high inspiratory flow rates with pMDIs result in decreased total lung deposition, and for turbuhalers only 8% of elderly COPD patients may be able to generate the optimal inspiratory flow of >60L/min, while 19% cannot generate the minimum (30L/min) inspiratory flow.[16]

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All patients experiencing an exacerbation of COPD should have their ABGs checked to assess severity and determine the need for hospital treatment. Patients with a pH >7.35 or PaO_2 >7 may be managed at home provided that other signs and symptoms are favourable.

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