Pathophysiology of respiratory disease and its significance to anaesthesia

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Abstract
Significant changes occur in the respiratory physiology of healthy patients during anaesthesia. In patients with underlying respiratory pathology (e.g. chronic obstructive airways disease) these changes in respiratory physiology may lead to clinical problems during the conduct of anaesthesia and the perioperative period. An understanding of the disease processes that can affect the lungs and pleura allows the anaesthetist to account for the potential complications of these conditions and manage the anaesthetic accordingly.

Keywords Acute respiratory distress syndrome; asthma; chronic obstructive pulmonary disease; obstructive; pathophysiology; perioperative management; restrictive; risk stratification; trauma

Preoperative assessment
Symptoms, signs, previous respiratory disease and relevant medications should be identified (Table 1). Patients’ functional capacity should be assessed by evaluating both their subjective and ideally objective exercise capacity. An estimation of the metabolic equivalents (METs) that a patient can achieve is recommended; 1 MET equates to the resting oxygen consumption of a 70-kg man and is approximately 3.5 ml/kg/minute. The ability to climb one flight of stairs is equivalent to approximately 4 METs (or 14 ml/kg/minute of oxygen consumption). The American College of Cardiology/American Heart Association (ACC/AHA) guidelines looking at perioperative cardiac risk stratification deem the inability to achieve 4 METs as an important marker of patients at increased risk of perioperative cardiac complications and those who require further investigation.1 The inability to achieve two flights of stairs identifies patients at increased risk of postoperative cardiorespiratory morbidity and mortality following thoracic and other non-cardiac surgery.2,3

Objective measures of exercise capacity can be used to help stratify risk in patients where pathology is suggested by the history and examination. These measures include the 6-minute walk test, incremental shuttle walk test and, where available, formal cardiopulmonary exercise testing.

Learning objectives
By the end of this article you should be able to:
1. perform a thorough preoperative assessment for respiratory pathology and quantify patients’ risk of respiratory complications following anaesthesia
2. understand the pathophysiological effects of the more common respiratory diseases
3. adapt your anaesthetic practice to allow for these pathophysiological changes.

Patients’ risk of pulmonary complications (Box 1) should be estimated based on patient factors and the operative procedure.4 This may also help to guide the clinician on the need for postoperative critical care.

Pulmonary pathology
Restrictive conditions
These are conditions where lung expansion is restricted. This can be due to lung parenchymal abnormalities, diseases of the chest wall and pleura, or neuromuscular conditions.

Pulmonary fibrosis: fibrosis may be idiopathic or secondary to other respiratory (e.g. pneumoconiosis) and systemic conditions (e.g. rheumatoid arthritis). With all aetiology, inflammation and infiltration of alveolar membranes and bronchiolar walls are found. Cellular exudate collects in the alveoli and fibroblasts form collagen at the damaged areas. Lung parenchyma architecture is altered leading to the formation of air-filled spaces, a reduced surface area available for gas exchange and reduced distensibility.

Mechanical restriction: chest wall deformities (e.g. kyphoscoliosis) cause abnormal crowding of ribs and compression of the lung and pulmonary vasculature resulting in restricted ventilation. In obesity and pregnancy the weight of abdominal and chest tissue impairs inspiration and reduces diaphragmatic excursion. In cases of intra-abdominal pathology, pain and abdominal wall rigidity can also prohibit movement of the diaphragm.

Neuromuscular conditions: conditions such as Guillain-Barré, muscular dystrophies and myasthenia gravis reduce the function of the muscles of respiration, thereby preventing adequate chest wall movement. This leads to atelectasis, reduced clearance of secretions and an increased incidence of pneumonia.

Parkinson’s disease is associated with reduced upper airway tone and may lead to aspiration pneumonia and respiratory failure.

Respiratory conditions usually present in the more advanced stages of neuromuscular disease and are often the cause of death in these patients.

Sedative agents should be used with caution in neuromuscular disease. They can depress brainstem respiratory centre function and central chemoreceptors, resulting in further restriction of muscle movements and hypoventilation.

Consequences of restrictive lung conditions: the following may be seen but will be dependent on the causative condition:
Preoperative assessment and investigation of patients with respiratory pathophysiology

<table>
<thead>
<tr>
<th>Points in history</th>
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<tbody>
<tr>
<td>— Changing or worsening symptoms, e.g. increased cough at night</td>
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<td>— Smoking history (number of pack years)</td>
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<td>— Steroid therapy (frequency of short-course doses or long-term use)</td>
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<td>— Home nebulizers or oxygen therapy</td>
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<td>— Recent or frequent courses of antibiotics</td>
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<td>— Previous admissions to hospital and critical care</td>
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<td>— Symptoms of right or congestive cardiac disease</td>
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<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Cough</th>
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<tr>
<td>— On exertion/at rest</td>
<td>— Sputum production</td>
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<tr>
<td>— Orthopnoea</td>
<td>— Haemoptysis</td>
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<tr>
<td>— Paroxysmal nocturnal dyspnoea</td>
<td>Chest pain</td>
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<tr>
<td>Wheeze</td>
<td>Peripheral oedema</td>
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<tr>
<th>Signs</th>
<th>Observations</th>
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<tr>
<td>— Distressed patient, sitting forward</td>
<td>— Low SpO₂,</td>
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<tr>
<td>— Respiratory rate and pattern</td>
<td>— Tachycardia</td>
</tr>
<tr>
<td>— Tachypnoea, hypoventilation, stridor, abnormal respiratory pattern</td>
<td>— Pyrexia,</td>
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<tr>
<td>— Cyanosis, pletoric facies</td>
<td>— Peripheral oedema</td>
</tr>
<tr>
<td>— Clubbing, tar-staining to fingers or hair</td>
<td>— Hepatomegaly</td>
</tr>
<tr>
<td>— Obesity, pectus excavatum, kyphoscoliosis</td>
<td>— Absent breath sounds</td>
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<thead>
<tr>
<th>Investigations</th>
<th>Blood tests</th>
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<tr>
<td>— Renal function — urea and creatinine (linked to postoperative pulmonary complications when elevated)</td>
<td></td>
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<td>— Albumin (low level has strong association with postoperative pulmonary complications)</td>
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<tr>
<td>— Full blood count — WCC (infection) and Hb (polycythaemia, anaemia) (may be on warfarin, e.g. for PE or pulmonary hypertension)</td>
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<tr>
<td>— Arterial blood gases — oxygen and carbon dioxide concentrations, pH (ABG analysis may differentiate between patients with chronically elevated carbon dioxide levels and patients with acute decompensation)</td>
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| ABG, arterial blood gas; Hb, haemoglobin; INR, international normalized ratio; PE, pulmonary embolism; WCC, white cell count. |

### Table 1

- Increased work of breathing due to reduced lung compliance
  - Initially the patient is able to meet any increase in ventilatory demand by an increase in respiratory rate (tidal volume may be relatively fixed)
  - If the condition (e.g. intra-abdominal pathology or myasthenia gravis) persists, the patient may tire and develop respiratory failure
- A reduced total lung capacity (TLC), functional residual capacity (FRC) and residual volume (RV)
- An increased FEV₁/FVC ratio (>80%) (Although both FEV₁ and FVC are reduced in restrictive conditions, the FVC is reduced to a greater extent)
- Atelectasis
- Hypoxaemia resulting from V/Q mismatching
  - Both dead space and shunt are increased
  - There is disorganized lung architecture due to tissue damage affecting both lung parenchyma and blood vessels, and causing significant changes to both perfusion and ventilation and their relationship to each other
- Reduced diffusion capacity for carbon monoxide
  - This becomes clinically relevant in more advanced disease, as prior to this the lung has a large reserve in terms of diffusion capacity (gaseous exchange occurs rapidly at the start of the blood transit through the pulmonary capillary bed)
  - This manifests as hypoxia at times of increased oxygen demand, such as exercise or during surgery
- Arterial pCO₂ tends to be low or normal
  - There is increased alveolar ventilation (most likely due to stimulation of peripheral chemoreceptors, by low arterial pO₂, or lung receptors)
- Respiratory failure and cor pulmonale (right ventricular failure (RVF) secondary to elevated pulmonary vascular resistance (PVR)).

### Obstructive conditions

Resistance to airflow can be caused by three main mechanisms:

1. Occlusion of the airway lumen, for example secretions
Risk stratification

In 2006, a working party for the American College of Physicians reviewed the evidence for risk factors for postoperative pulmonary complications. They identified the following factors as significant in increasing the risk of postoperative pulmonary complications:

- Age — an independent risk variable, with patients from 60–69 years old at approximately double the risk of younger counterparts, and patients from 70–79 years old at three times the risk
- Chronic obstructive pulmonary disease — most commonly identified risk factor for postoperative complications, but not easily linked with preoperative spirometry values
- Cigarettes — a small increase in risk compared with the non-smoking population. Short-term preoperative reduction in the amount smoked may actually increase the risk of complications
- Congestive heart failure
- ASA score ≥2
- Functional dependency — total dependency is loss of all ADLs and partial requires help from people or equipment
- Altered Glasgow Coma Scale — obtunded patients are more likely to suffer postoperative complications
- Surgical procedure — the following are all associated with increased risk of postoperative complications: prolonged surgery (>3 hours); abdominal, thoracic, head and neck, vascular, neurosurgery and aortic aneurysm repair; emergency operations
- General anaesthesia — associated with increased postoperative complications in some studies

Of note, is that obesity, asthma, and obstructive sleep apnoea are not risk factors for postoperative pulmonary complications. Studies into restrictive lung disease are limited

ADLs, activities of daily living; ASA, American Society of Anesthesiologists.

Box 1

2. Pathology within the airway wall, for example smooth muscle contraction
3. Pathology outside the airway, for example neoplasm

Generalized obstruction

Asthma: the symptoms of asthma develop after antigen exposure to the dendritic cells of the airway. This activates T-lymphocytes resulting in the release of cytokines and an influx of mast cells, basophils, eosinophils, neutrophils and macrophages. These then release mediators such as histamine, prostaglandins and leukotrienes. The result is airway inflammation, constriction and oedema and increased mucous secretion. This causes intermittent, and usually reversible, airflow obstruction and bronchial hyperreactivity. Impairment of ventilatory capacity can often still be demonstrated between attacks however.

Chronic obstructive pulmonary disease (COPD): COPD encompasses emphysema and chronic bronchitis. In emphysema, the alveoli and capillary beds are destroyed by loss of cell wall elastin. The gas exchange surface area is reduced and loss of radial traction causes airway narrowing. In bronchitis, there is chronic inflammation and oedema of the lung parenchyma. Goblet cells produce excess mucous which narrows the airways and plugs form. These plugs and desquamated epithelial cells remain in the lungs due to loss of ciliary function providing an ideal medium for bacterial growth.

Consequences of generalized obstruction: the distinctions between the different causes of generalized obstruction are not always clearly defined. The following can be seen:

- Indices of expiratory flow are reduced
  - This includes the forced expiratory volume in 1 s (FEV1), forced expiratory flow (FEF25–75%) and forced expiratory volume as a percentage of vital capacity FEV1/FVC% (usually <70%)
  - The FVC may also be reduced during an acute attack due to premature airways closure towards the end of expiration
- Increased airways resistance resulting in an increased expiratory time and work of breathing
- TLC, FRC and RV are increased (due to gas trapping behind obstructed airways)
- Lung compliance is reduced in emphysema due to loss of elastic tissue and destruction of alveolar walls
- Arterial hypoxaemia due to ventilation-perfusion inequality
  - In COPD, emphysema tends to result in an increase in dead space (due to changes in airway and capillary bed structure) and bronchitis causes an increase in shunt (secondary to narrowing and oedema of the airways)
  - The degree of arterial hypoxaemia depends predominantly on the amount of blood flow to areas that have low V/Q ratios (i.e. low blood flow to these regions results in minimal shunting and mild hypoxaemia, whereas high blood flow causes severe hypoxaemia)
  - Arterial hypoxaemia is common in asthmatics, even in a mild acute episode, and is due to reduced alveolar ventilation resulting in an increase in shunt.
- Hypoxic pulmonary vasoconstriction (HPV) and collateral ventilation reduce shunt and dead space
  - HPV is constriction of the pulmonary vasculature (mainly the pre-capillary arterioles), in response to a low oxygen level in the alveoli (low P,O₂) and is designed to divert blood away from underventilated alveoli in order to reduce shunt
  - HPV is affected by many physiological factors (including acid–base disturbance, prostacyclins and autonomic nervous system stimulation) and importantly, is reduced by halogenated anaesthetic agents and vasodilating drugs (which may therefore worsen hypoxaemia in susceptible patients due to an increase in shunting of blood)
  - Collateral ventilation occurs through holes between alveoli and small airways, allowing ventilation to areas with proximal obstruction of the supplying bronchioles
- Hypercarbia is usually a late sign
  - It is more common in patients with COPD than asthma
  - This is initially compensated for by an increase in minute ventilation but with disease progression there is a reduced sensitivity to the increased level of carbon dioxide and the blood level rises
- Hypoxic ventilatory drive to compensate for a chronically elevated CO₂ in COPD
- Respiratory failure and right ventricular failure.
Localised obstruction

**Tracheal obstruction**: stridor is the main symptom and is a potentially life-threatening emergency. Clinical features will depend on the degree (partial or complete) and location (e.g. glottic or sub-glottic) of the obstruction.

**Bronchial obstruction**: obstruction has many causes including foreign bodies (e.g. peanuts) and bronchial tumour. The right main bronchus is affected more frequently than the left due to the more acute angle which the left side makes with the trachea. Complete obstruction can result in absorption atelectasis and collapse distal to the obstruction. Compensatory hyperinflation of adjacent lung may be seen. Perfusion of the unventilated lung is reduced by HPV and the increased PVR (secondary to narrowed extra-alveolar vessels due to the mechanical effect of loss of lung volume). This helps to reduce the degree of shunt but residual blood flow to the unventilated lung area will still contribute to the hypoxaemia seen.

Infection and lung abscess formation are late complications.

**Infection and inflammation**

**The common cold**: results in an increased risk of airway hyperreactivity and lower respiratory tract infection (RTI). There are rare case reports of viral myocarditis as a consequence of anaesthesia at the time of RTI. The following symptoms should lead the clinician to consider postponement of an elective procedure:
- productive cough
- pyrexia
- general malaise
- signs on chest auscultation
- concurrent chest disease
- elevated white cell count.

**Pneumonia**: pathogens enter the airways either by aspiration of nasopharyngeal contents, inhalation or haematological spread. Once present within the lungs, the host’s macrophages are overwhelmed leading to activation of the inflammatory cascade. Alveolar oedema develops and blood and fibrin enter the alveoli. Epithelial and goblet cells are damaged and deposited in the airway and consolidation occurs. This results in impaired gaseous exchange secondary to damage and oedema of the alveolar wall. There is increased work of breathing, hypoxia and hypercarbia.

**Acute respiratory distress syndrome (ARDS)**: ARDS is characterized by the following:
- acute onset
- bilateral infiltrates on chest X-ray
- reduced PaO₂:FiO₂ ratio ≤26.7 kPa
- absence of left ventricular failure (identified either by pulmonary artery wedge pressure (PAWP) ≤18 mmHg or absence of clinical evidence of left atrial hypertension).

ARDS has both pulmonary (e.g. pneumonia) and non-pulmonary causes (e.g. pancreatitis) and is characterized by diffuse alveolar damage and lung capillary endothelial injury. The pathophysiology is complex and is divided into an early exudative phase (Figure 1) and a later fibro-proliferative phase.

During the acute phase, an increased diffusion distance due to alveolar-capillary oedema and reduced ventilation of affected alveoli causes shunting and hypoxaemia. Reduced lung compliance is seen. Further lung damage can result from oxygen toxicity and barotrauma induced by mechanical ventilation.

**Trauma**

**Rib fractures and flail chest**: rib fractures are painful and may result in a restrictive-like ventilatory pattern. With multiple rib fractures a flail chest may result. This is an area of the thoracic cage that has become functionally separated from the rest due to fractures in two or more adjacent ribs in at least two places. Paradoxical movement of the chest wall segment is seen; inward movement of the flail segment is seen as the chest wall moves outwards during inspiration and vice versa in expiration.

A flail chest is often associated with underlying lung contusion.

**Lung contusion**: lung contusion is ‘bruising’ of the lung parenchyma as a result of trauma. Lung capillary damage leads to parenchymal oedema and blood collecting within the alveolar space. This results in reduced gas exchange and hypoxaemia, increased pulmonary vascular resistance and reduced lung compliance. Blood within the alveoli also generates an inflammatory response. Both pneumonia and ARDS may develop.

**Haemothorax and pneumothorax**: large volumes of gas or blood in the pleural space compress adjacent lung tissue. This results in atelectasis and collapse, increased intrathoracic pressure and loss of negative intrapleural pressure. Mediastinal shift with a precipitous fall in cardiac output may result. Tension pneumothorax can occur if the defect in the lung functions as a ball and socket valve, allowing gas into the intrapleural space but preventing its release.

A chest drain should be inserted prior to induction of anaesthesia if a pneumothorax is present. Even a small pneumothorax may enlarge significantly when exposed to positive pressure ventilation. Significant amounts of blood can be lost into the pleural space (up to 30–40% of blood volume in each hemithorax). Thorough preoperative assessment including assessment of haemodynamic status and haemoglobin concentration should be performed. Cross-matched blood must be available. If there are sudden changes in cardiovascular parameters during surgery then the anaesthetist must also be vigilant to the development of a tension pneumothorax or a problem with the chest drain.

**Pulmonary vascular conditions**

**Pulmonary embolus (PE)**: this is thrombus from deep vein thrombosis, fat, amniotic fluid or injected material that enters the pulmonary circulation. The pathophysiological effect depends on its size and location:
- Large emboli may occlude the proximal pulmonary arteries causing acute haemodynamic compromise as forward flow from the right heart is prohibited
- Small PEs may go clinically unrecognized until symptoms of RVF develop secondary to the long-term increased PVR caused by capillary occlusion
- A moderate-sized PE may cause infarction of lung parenchyma. PE under general anaesthesia may be difficult to diagnose. The following should be looked for:
  - sudden fall in end-tidal CO₂ concentration (more easily identifiable during positive pressure ventilation)
  - tachypnoea (in the spontaneously breathing patient)
  - tachycardia
  - hypotension
  - hypoxaemia
  - pallor
- normal airway pressures are usual (as the embolus affects lung perfusion, not ventilation).
Pulmonary hypertension (PH): this may be primary (idiopathic) or secondary to cardiac or pulmonary disease. It is defined as a mean pulmonary artery pressure (PAP) >15 mmHg.7 Primary PH is poorly understood pathologically, but increased smooth muscle in the pulmonary arteries is seen. The secondary causes are:

- increased left atrial pressure e.g. mitral stenosis
- increased pulmonary blood flow e.g. ventricular septal defect
- increased pulmonary vascular resistance, due to vasoconstriction, obstruction or obliteration e.g. thrombo-embolic disease.

Hypoxaemia may develop on exertion and is present at rest in advanced cases. The condition results in RVF secondary to chronically elevated PAP.

Anaesthetic considerations

Preoperative management

Patients may present for surgery with an acute episode of respiratory disease. Unless surgery is urgent, postponing it until this has fully resolved should be strongly considered. When postponement is not possible, preoperative optimization of the condition with physiotherapy, oxygen therapy, antibiotics and nebulized bronchodilators for example should be attempted. Sedative drugs should be used with caution and avoided where possible as they may lead to a deterioration in respiratory function by causing hypoventilation and inhibition of coughing.
Type of anaesthesia and analgesia
Consider the use of regional anaesthesia, peripheral nerve block and local anaesthesia as alternatives to general anaesthesia and to help ensure good postoperative analgesia. Be aware of any complications and specific contraindications when performing regional anaesthesia. For example, inter-scalene brachial plexus block may result in respiratory failure due to phrenic nerve blockade in patients with underlying respiratory disease.

Intraoperative opioids may cause decreased respiratory effort postoperatively due to central nervous system depression. This hypoventilation, caused by both a reduction in respiratory rate and tidal volume, will lead to hypercarbia. This can further depress the central nervous system and result in hypoxaemia and respiratory failure, particularly in susceptible patients with underlying disease (e.g. severe COPD).

Airway management: airway manipulation should be kept to a minimum in patients at risk of airway hyperreactivity. The use of a laryngeal mask airway (LMA) rather than an endotracheal tube (ETT) may reduce the incidence of laryngospasm and bronchospasm. It should be remembered however that an ETT also offers certain advantages including allowing tracheobronchial suctioning and more complex ventilation strategies.

Direct laryngoscopy may be difficult due to lesions of the oropharynx or larynx. Intubation using a fibreoptic scope may not appropriate if there is partial obstruction of the airway as the scope may actually occlude the remaining airway. A gaseous induction should be considered in these circumstances. Lesions distal to the ETT may cause persistent obstruction following successful endotracheal intubation.

Ventilation strategies: patients with respiratory pathology may require manipulation of their ventilation settings dependent upon the underlying condition. For example, use of an increased FiO₂ and application of positive end expiratory pressure, or PEEP (to recruit underventilated alveoli), in a patient with pneumonia or use of a lung-protective strategy (small tidal volumes (6 ml/kg)), increased respiratory rates and tolerance of any resulting hypercapnia (permissive hypercapnia) for a patient with suspected or confirmed ARDS.

Cardiac output and haemoglobin concentration should be maintained to maximize oxygen delivery to the tissues.

Extubation: suction bronchial secretions and perform lung recruitment manoeuvres prior to extubation. Always proceed with caution as airway hyperreactivity increases the risk of bronchospasm and laryngospasm.

Venous-thromboembolism (VTE) prophylaxis
All patients should have their VTE risk assessed and appropriate prophylaxis administered. Remain vigilant to conditions or clinical situations that can lead to an increased risk of embolism (e.g. open venous sinuses for air embolism, fractured long bones for fat embolism).

Postoperative management
Patients felt to be at increased risk of perioperative respiratory morbidity (see Box 1) should be cared for in an appropriate environment postoperatively e.g. high dependency or intensive care.

The following strategies can be employed in the perioperative period to help reduce respiratory complications following surgery:
- chest physiotherapy
- nursing in semi-recumbent or upright position
- incentive spirometry
- early mobilization
- encouragement to cough and deep breathing exercises
- humidified oxygen
- good analgesia.

REFERENCES

7 West JB. Pulmonary pathophysiology: the essentials. 7th edn. Crawfordsville: Lippincott Williams & Wilkins, 2008.

FURTHER READING


(This link takes you to the BTS’s library of guidelines which is an invaluable tool for the management of respiratory disease. It contains guidelines for many conditions and situations, including the management of oxygen therapy and asthma).


(The guidelines for prophylaxis in preventing venous thromboembolism in patients in hospital and undergoing surgery).

West JB. Pulmonary pathophysiology: the essentials. 7th edn. Crawfordsville: Lippincott Williams & Wilkins, 2008.

(A follow-on text from West's Respiratory Physiology that gives comprehensive details of the pathophysiology of respiratory disease, with a particularly useful section on the lung function tests and what they mean).