Dyspnoea is defined as a sensation of difficult breathing. It is common in hospitalised patients and is often a harbinger of serious and potentially fatal pathology. The pathophysiology of dyspnoea involves complex interactions between peripheral and central receptors and cognition. Given the myriad causes of dyspnoea, a systematic approach to diagnosis is important. A good history and systemic examination are necessary as it is important to quickly identify the cause and treat it promptly. Investigations are numerous but chest radiography and electrocardiography are among the commonest and most useful. It is important to understand the mechanisms underlying dyspnoea to treat breathless patients successfully.

**PATHOPHYSIOLOGY**

The pathophysiology of dyspnoea involves complex interactions between peripheral and central sensory receptors and cognition. It is thought that physiological, psychological, behavioural, social, and environmental factors play a part in the pathogenesis and modulation of dyspnoea. The sense of effort involved in breathing has recently been recognised as having an important role in dyspnoea, and is thought to result from a number of closely related sensory and cognitive phenomena.

When an increased urge to breathe fails to correct oxygenation, ventilation and acid-base status, dyspnoea ensues.
Table 1 Physiological mechanisms involved in dyspnoea

<table>
<thead>
<tr>
<th>Physiological mechanism</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase in effort of breathing due to increased airflow</td>
<td>Asthma or COPD with negative effects on respiratory muscle performance</td>
</tr>
<tr>
<td>resistance or decreased respiratory compliance,</td>
<td></td>
</tr>
<tr>
<td>aggravated by hyperinflation</td>
<td></td>
</tr>
<tr>
<td>Increase in dead space ventilation due to decreased</td>
<td>Lung hyperexpansion, vascular occlusion from pulmonary emboli</td>
</tr>
<tr>
<td>regional lung perfusion relative to ventilation</td>
<td></td>
</tr>
<tr>
<td>Stimulation of chemoreceptors by hypoxaemia or hypercapnia</td>
<td>Ventilation-perfusion mismatch in pulmonary emboli, metabolic alkalosis, increased temperature, or sepsis</td>
</tr>
<tr>
<td>Reduction in central or neural drive to the inspiratory</td>
<td>Central nervous system depressant drugs</td>
</tr>
<tr>
<td>muscles</td>
<td></td>
</tr>
<tr>
<td>Reduction in respiratory muscle function</td>
<td>Guillain-Barré syndrome and myasthenia gravis, general deconditioning accompanied by lactic acidosis during exercise with stimulation of ventilation</td>
</tr>
<tr>
<td>Possible stimulation of vagal irritant receptors</td>
<td>Asthma</td>
</tr>
<tr>
<td>Possible stimulation of C-fibres</td>
<td>Pulmonary oedema</td>
</tr>
</tbody>
</table>

COPD, chronic obstructive pulmonary disease.

Table 2 Causes of dyspnoea based on onset of symptoms

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute airways obstruction</td>
<td>COPD</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Pleural effusion</td>
</tr>
<tr>
<td>Acute respiratory distress syndrome</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>Vascular heart disease</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>Anaemia</td>
</tr>
<tr>
<td>Mitral valve rupture</td>
<td>Renal failure</td>
</tr>
<tr>
<td>Flail chest</td>
<td>Neuromuscular dysfunction</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>Psychogenic</td>
</tr>
<tr>
<td>Pulmonary embolus</td>
<td></td>
</tr>
</tbody>
</table>

COPD, chronic obstructive pulmonary disease.

Table 3 Results of the lung function tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Sitting</th>
<th>Measured</th>
<th>% Predicted</th>
<th>Supine</th>
<th>Measured</th>
<th>% Predicted</th>
<th>% Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC(l)</td>
<td>4.05</td>
<td>1.79</td>
<td>44</td>
<td>1.32</td>
<td>33</td>
<td></td>
<td>−26</td>
</tr>
<tr>
<td>FEV₁ (l)</td>
<td>3.14</td>
<td>1.39</td>
<td>44</td>
<td>0.96</td>
<td>31</td>
<td></td>
<td>−31</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>0.78</td>
<td>0.78</td>
<td>100</td>
<td>0.73</td>
<td>94</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FEV₁, forced expiratory volume in one second; FVC, forced vital capacity.

CASE HISTORY

A 75 year old white man presented to the cardiology clinic with a nine month history of progressive breathlessness, fatigue, and generalised weakness. He noticed his breathlessness was worse on lying flat. He was an ex-smoker with a 20 pack year smoking history. No other significant past medical history was elicited.

Physical examination showed a thin male in sinus rhythm. Use of accessory muscles was noted with a respiratory rate of 24 breaths/min. A soft pansystolic murmur suggestive of mitral regurgitation was heard. Some fasciculations were seen over the shoulders and upper extremities.

Investigations included electrocardiography, which showed sinus rhythm and a normal axis with left ventricular hypertrophy on voltage criteria; echocardiography, which showed mild mitral regurgitation and good left ventricular function; and chest radiography, which showed hyper-inflated lung fields but no other acute changes. Arterial blood gases on room air were: pH 7.40, carbon dioxide pressure 6.1 kPa, oxygen pressure 10.0 kPa, and bicarbonate 32 mmol/l. The results of lung function tests are shown in table 3.

Comment⁷⁻¹⁰

The symptoms are non-specific and could be caused by heart failure or lung disease. The lung function tests, however, suggest a severe restrictive impairment and decreased respiratory muscle strength. The marked decrease in supine lung function is suggestive of diaphragmatic weakness. The progressive nature and physical findings raise the possibility of amyotrophic lateral sclerosis and this was confirmed by clinical and electrophysiological studies.

Features that raise the suspicion of a neuromuscular disorder as a cause for shortness of breath include: (1) absence of cardiopulmonary disorder and (2) relatively normal physical examination, electrocardiography, chest radiography, and echocardiography.

The most successful approach to diagnosis is to focus on the circumstances surrounding dyspnoea and its progression from rest to exertion.

AETIOLOGY

Some relationship has been found between the type of sensation experienced by patients and the underlying pathophysiological mechanisms involved in the diagnosis.

Given the myriad causes of dyspnoea, a systematic approach to diagnosis is imperative.

The following broad categories cover most of the common causes of breathlessness and should be considered when taking a history and devising a differential diagnosis:

- Pulmonary.
- Cardiac.
- Neuromuscular.

Ruptured ventricular septum, mitral valve rupture, or pulmonary oedema.

CHRONIC DYSPNOEA

Dyspnoea that has already been present for some time is more common and may worsen slowly over months or even years before a patient seeks medical advice. The occurrence of chronic dyspnoea increases consistently with age, as the prevalence of its two most important causes, chronic congestive heart failure and COPD, also increase with age.¹¹⁻¹² The most successful approach to diagnosis is to focus on the circumstances surrounding dyspnoea and its progression from rest to exertion.
• Haematological.
• Metabolic and endocrine.
• Renal failure.
• Others such as anxiety, obesity, lack of fitness, trauma, and panic attacks.

PULMONARY CAUSES OF BREATHLESSNESS
Chronic obstructive airways disease, a spectrum of diseases that encompasses asthma, emphysema and chronic bronchitis, is among the most common causes of dyspnoea. Few patients fit exclusively into one category. In addition, an exacerbation of cystic fibrosis and acute infection secondary to lung carcinoma can produce dyspnoea. These conditions are associated with airflow limitation that causes an increase in respiratory work and thus the oxygen expenditure of breathing.

Chronic hypercapnia seen in patients with chronic bronchitis can blunt the hypoxic drive to breathe, resulting in relatively less dyspnoea for a given degree of hypoxaemia; by contrast the emphysematous patient puffing away looks worse than he really is and may have well preserved oxygenation despite tachypnoea and laboured pursed lip breathing. In asthmatic patients, inspiratory and expiratory wheezes are commonly heard during chest auscultation.

CARDIAC CAUSES OF BREATHLESSNESS
Dyspnoea caused by engorged pulmonary vasculature and interstitial pulmonary oedema is common in heart failure. Acute cardiogenic pulmonary oedema may occur as a result of heart failure and its symptoms may mimic those of asthma. Valvular heart disease, particularly aortic stenosis and mitral regurgitation, may cause gradually worsening dyspnoea. Occasionally acute mitral regurgitation may result from papillary muscle dysfunction or rupture and, because there is no compensatory increase in left atrial and ventricular compliance, may result in cardiogenic shock necessitating urgent surgical intervention.

NEUROMUSCULAR CAUSES OF BREATHLESSNESS
Neuromuscular disorders may produce dyspnoea and are characterised in more extreme forms by alveolar hypoventilation with resultant hypercapnic respiratory failure (see case history).

PSYCHOGENIC CAUSES OF BREATHLESSNESS
Dyspnoea is an unsettling and fear provoking symptom. Both acute and chronic breathlessness generate anxiety which may exacerbate the sensation of dyspnoea; as the sole aetiology of symptoms, it remains a diagnosis of exclusion.

DIAGNOSIS AND MANAGEMENT
Dyspnoea is poorly related to objective tests of respiratory function. One approach to diagnosis is based on the circumstances in which dyspnoea occurs. Indices are now available to assess the intensity of dyspnoea, such as the Baseline Dyspnoea Index [1] that provides a description of the actual impairment, as well as an estimate of the magnitude of effort. A second approach, derived from advances in psychophysiology, permits monitoring of the changes in the sensation induced by physical exercise. Both a visual analogue scale and a categorical Borg scale [2] [3] are useful for assessing these parameters.

Acute dyspnoea
The first step in evaluating dyspnoea in the adult patient is to determine the degree of severity and hence degree of urgency of treatment. Immediate evaluation of the airway, arterial oxygenation, mental status, and work of breathing are essential. Vital signs including respiratory rate are recorded to determine the presence of haemodynamic compromise.

Pulse oximetry is useful for evaluating the oxygen status of dyspnoic patients, however, it does have limitations. Delivery of oxygen to tissues is determined by three factors:
• The oxygen saturation, or amount of oxygen being carried by haemoglobin.
• The amount of haemoglobin present in the blood.
• How well the oxygen is being transported around the body.

Of these factors, only oxygen saturation is demonstrated by the pulse oximeter by measuring arterial haemoglobin saturation. It does this using red and infrared light to determine the colour of haemoglobin passing through arterioles in the area beneath the probe. Fully saturated haemoglobin is a brighter colour than partly or completely desaturated molecules. [4] Because the pulse oximeter uses colour to determine saturation, the measurements are subject to error in certain circumstances. The presence of nail polish, tattoos, or jaundice can all affect the oximeter reading. [5] Poor blood flow to the area, a dirty probe, or incorrect attachment can cause false readings (low) as can the presence of carbon monoxide (high). [6]

Measurement of arterial blood gases is more interventional but will provide quantification of defects in oxygenation, ventilation, and acid-base balance.

Indications for arterial blood gas analysis include [7] [8]:
• The need to evaluate the adequacy of ventilatory (arterial carbon dioxide pressure), acid-base (pH and carbon dioxide pressure), and oxygenation (arterial oxygen pressure and oxygen saturation) status and the oxygen carrying capacity of blood (arterial oxygen pressure, oxygenated haemoglobin, total haemoglobin, and dyshaemoglobins).
• The need to quantitate the patient’s response to therapeutic intervention and/or diagnostic evaluation (for example, oxygen therapy, exercise testing).
• The need to monitor severity and progression of the disease process.

Contraindications include:
• Negative results of a modified Allen test (collateral circulation test) indicate the need to select an alternative puncture site.
• Arterial puncture should not be performed through a lesion or through or distal to a surgical shunt (for example, patient on haemodialysis).
• If there is evidence of peripheral vascular disease an alternate site should be selected.
• A coagulopathy or a medium to high dose anticoagulation therapy (for example, heparin, coumarin, streptokinase and tissue plasminogen activator but not aspirin) is a relative contraindication for arterial puncture.

Chronic dyspnoea
Dyspnoea is cited as one of the main symptoms by patients referred to cardiology and respiratory clinics. In practice it is often difficult to distinguish between cardiac and pulmonary causes of dyspnoea, bearing in mind that some patients experience simultaneous dysfunction in both systems. Physical findings, such as pulmonary rales, wheezing and jugular venous distension, may be apparent. An accurate diagnosis is crucial because inappropriate treatment can exacerbate symptoms. For example, a diuretic used to treat...
cardiac dyspnoea can cause acid-base disturbances and hypotension in patients with pulmonary induced dyspnoea. Similarly, sympathomimetic amines and β-agonists can induce arrhythmia in patients with dyspnoea due to congestive heart failure.

Altogether 50% of patients who are having palliative care will have some exertional dyspnoea, which increases to 70% of patients in the last six weeks of life.22 Hyperventilation due to panic attacks and tachypnoea with acidic breathing in acidosis may mimic dyspnoea. Fatigue, fear, and panic also exacerbate dyspnoea. Cachexia and weakness of the patient can present as dyspnoea on exertion.

**Assessment**

The history should include pertinent questions about the characteristics of dyspnoea, especially descriptive qualities, onset, frequency, severity, and activities that provoke symptoms.13 The New York Heart Association (NYHA) classification provides a more objective assessment of the severity of dyspnoea. Recent studies have shown that NYHA class and quality of life scores are closely correlated; with a remarkably consistent and significant incremental deterioration of quality of life due to heart failure with declining NYHA class.20 Alleviating factors should be determined and may include elevating the head of the bed or administering bronchodilators or diuretics. Associated manifestations may include cough, sputum production, chest pain, palpitations, or abdominal pain. These findings provide important clues, which narrow the range of clinical possibilities. A careful review of medications should be followed by a systematic physical examination. This begins with inspection and palpation of the head, neck, and chest. Auscultation of the chest provides information about airflow through the lung fields. The cardiac examination is done with special focus on signs of heart failure or valve dysfunction; the presence of a third heart sound or a displaced apex beat suggests heart failure. Examination of the abdomen may confirm hepatomegaly or ascites and of the extremities confirm oedema.21

**Diagnostic studies**

The order in which diagnostic studies are obtained is dictated by the differential diagnosis after history and physical examination.

Chest radiography is a readily available, inexpensive, and important screening tool when a pulmonary cause of dyspnoea is suspected. Bedside spirometry is also readily available and non-invasive and recent reports suggest that peak expiratory flow (PEF) might be a useful adjunctive tool in differentiating cardiac from respiratory dyspnoea. In particular, the calculation of Dyspnoea Differentiation Index, defined as \[ \text{PEF} \times \text{arterial oxygen pressure}/1000 \] provided a more accurate diagnosis of the cause of dyspnoea than an emergency room physician.22

Cardiopulmonary exercise testing may help differentiate cardiac and respiratory limitation, as well as documenting deconditioning and psychogenic dyspnoea.15 The measurement of dyspnoea and leg discomfort during exercise testing using the Borg visual analogue scale, providing useful information about limiting symptoms. This perceptual scale complements physiological data and is a useful measure of the severity of pretreatment symptoms and of response to treatment.21

If cardiac dysfunction is suspected, electrocardiography is a sensitive screening tool for a variety of conditions, including cardiac ischaemia, infarction, and arrhythmias. An electrocardiogram is a simple, non-invasive assessment of left ventricular wall motion, ejection fraction, valve function, and pulmonary artery pressures. The finding of a normal electrocardiogram makes left ventricular systolic dysfunction, the commonest cause of heart failure, very unlikely; when access to echocardiography is limited, the electrocardiogram can assist prioritisation.24 The debate on the prevalence of left ventricular diastolic dysfunction remains unresolved, especially in elderly patients.

Management of terminally ill dyspnoeic patients is just as important and it may not be appropriate to pursue intensive investigations. However chest radiography, haemoglobin, and electrocardiography are relatively non-invasive and worth considering if there is acute deterioration.

**DISCUSSION**

Dyspnoea is one of the most common symptoms particularly in the elderly and is a frequent cause of hospitalisation.23 It should not be attributed to the ageing process alone and warrants careful evaluation to distinguish its many causes, the commonest being cardiac and respiratory.28

It is important to identify the cause of dyspnoea and treat appropriately. An inquiring mind and a high index of clinical suspicion is always helpful. Dyspnoea is one of the most common and disabling symptoms for patients with chronic pulmonary and cardiac disease and is also an important outcome variable for clinical and research evaluation in heart and lung disease for which the primary goal is the reduction of breathlessness. As dyspnoea increases, quality of life decreases;27 variables with the strongest correlation with quality of life include dyspnoea, NYHA class, and life stresses.

Dyspnoea in the terminally ill can be most distressing for both patient and family. In addition to treating the specific causes for dyspnoea, this group of patients may benefit from measures as outlined below28:

**General**

- Reduce exertion by using a wheelchair and bedside commode.19
- Prop patient up with a pillow and attempt to distract by reading or watching television.
- Open the window and use an electric fan for facial cooling.
- Learn relaxation techniques, meditation, and breathing exercises.

**Drug management**

- Use of humidified air and mucolytic agents such as acetylcysteine or bromhexine for management of tenacious secretion.
- Excessive secretions can be reduced by use of anticholinergic drugs.
- Morphine and other opioids have a direct affect on the brainstem respiratory centre.29 They reduce respiratory drive and alter central perception of breathlessness.
- Steroids can reduce peritumour oedema with improvement in obstruction.
- Anxiolytics like midazolam have been recommended for panic associated with dyspnoea.
- Local anaesthetic agents, lignocaine and bupivacaine, can be administered by nebuliser and may improve dyspnoea.30

**Oxygen**

Most patients do not require continuous oxygen when there has been optimal management with morphine and anxiolytics. However, it should be available if acute dyspnoeic attacks are likely, such as in end stage chronic airways disease, cardiac failure or thromboembolism, or if the patient remains extremely anxious despite efforts to counsel and control symptoms.
SUMMARY
Respiration is unique in that, of all the vital functions, it alone is regulated not only by automatic centres located in the brainstem but also by voluntary signals initiated in the cortex. Insofar as individuals have some control over their breathing, sensations arising from respiratory activity affect the rate and pattern of breathing as well as an individual’s functional status.

While the initial goal of clinicians is to remedy the physiological derangements producing the sensation, there are many individuals with chronic cardiopulmonary disorders for which the underlying pathophysiology cannot be corrected. This in turn, frequently results in long term disability for the patient. A better understanding of the mechanisms, assessment, and treatment of dyspnoea is necessary if clinicians are to improve their ability to monitor and treat patients with breathlessness.  

REFERENCES
