The differential diagnosis of the breathless patient

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Introduction

Breathlessness is the subjective sensation of difficulty in breathing, which may be laboured or uncomfortable. In health it is not always unpleasant and not associated with anxiety or fear. It results from multiple interactions of signals and receptors in the autonomic nervous system, motor cortex and peripheral receptors in the upper airways, lungs and chest wall. Behaviour and emotional state also exert an important influence on the expression of respiratory sensations.

Breathlessness commonly presents in primary care and establishing a diagnosis represents a challenge. Whilst approximately two thirds of cases are due to a pulmonary or cardiac disorder there are other causes that need to be considered. It often has multiple causes particularly in the elderly. As with the symptom of pain, patients use distinct descriptors when describing it. ‘Chest tightness’, ‘choking’, ‘suffocation’ and ‘air hunger’ are some of the terms used. However, the language used to describe it is not specific, and individual descriptions are dependent upon physiological context, personality, social and ethnic factors.

Common causes of breathlessness include asthma, chronic obstructive pulmonary disease (COPD), pneumonia, pulmonary embolism, lung cancer or pleural effusion. Distinguishing between these potential causes requires a careful evaluation of the presenting breathlessness, patient history, physical examination and, in some cases, further investigations.

Taking a history

A careful history will yield important diagnostic clues (Table 1). Key points include the speed of onset and duration of breathlessness. Sudden onset is characteristic of pulmonary embolism or pneumothorax whereas a progressive history associated with fever, cough and purulent sputum would suggest a chest infection. Association with characteristic central chest pain may suggest a myocardial infarction (MI), pleuritic pain may point to pericarditis, and palpitations to an arrhythmia (often fast atrial fibrillation). Acute cause (Table 2) often overlaps with chronic (duration greater than four weeks) (see Table 3). In primary care, telephone triage is an important initial step in assessing the degree of urgency, and adequate training of reception staff and a framework to identify urgent cases is recommended to provide proper care and to minimise risk. Those describing severe breathlessness or sudden onset of chest pain should be directed to the emergency department as an emergency usually by ambulance. Rapid assessment will establish if the patient is unstable (Table 4). Unstable patients requiring emergency hospital care may present with one or more of the following (adapted from reference 2):

- Hypotension
- Altered mental status
- Hypoxia and low oxygen saturation
- Central chest pain
- Unstable arrhythmia
- Stridor and breathing effort without air movement (suspect upper airway obstruction)
- Unilateral tracheal deviation, unilateral breath sounds (suspect tension pneumothorax)
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## Table 1: Diagnostic clues from the history (adapted from references 2 and 4)

<table>
<thead>
<tr>
<th>Clues from symptoms or history</th>
<th>Possible diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nocturnal cough; intermittent breathlessness; wheezing; triggering asthma factors; allergic rhinitis</td>
<td>Asthma</td>
</tr>
<tr>
<td>Pleuritic chest pain</td>
<td>Pericarditis, pulmonary embolism, pneumothorax, pneumonia, empyema</td>
</tr>
<tr>
<td>History of hypertension; CAD; MI; diabetes; orthopnoea; nocturnal paroxysmal dyspnoea; oedema</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Recent trauma; surgery; pregnancy; prolonged immobility</td>
<td>Pulmonary embolism</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>Pulmonary embolism, malignancy, bronchiectasis, pulmonary vasculitis/pneumonia; mitral stenosis; arteriovenous malformation</td>
</tr>
<tr>
<td>Orthopnoea; weakness; hoarseness of voice</td>
<td>Neuro-muscular weakness; diaphragmatic dysfunction</td>
</tr>
<tr>
<td>Tobacco dependency</td>
<td>COPD, congestive heart failure, malignancy</td>
</tr>
<tr>
<td>Indigestion, dysphagia, cough after eating</td>
<td>GERD, aspiration (foreign body)</td>
</tr>
<tr>
<td>Postprandial dyspnoea</td>
<td>GERD, aspiration, food allergy; coronary artery disease</td>
</tr>
<tr>
<td>Recurrent pneumonia</td>
<td>Lung cancer, bronchiectasis, aspiration, organising pneumonia</td>
</tr>
<tr>
<td>Drug exposure</td>
<td>Beta blockers aggravating airways disease Amiodarone / nitrofurantoin / Methotrexate lung fibrosis Illicit drugs (e.g., heroin): talcosis</td>
</tr>
<tr>
<td>History of immunosuppressive disease or therapy; acquired immunodeficiency syndrome</td>
<td>Opportunistic infections: Pneumocystis carinii pneumonia; bacterial (tuberculosis; Legionella); viral (cytomegalovirus); or fungal (Aspergillus)</td>
</tr>
<tr>
<td>Exposure to inorganic dust, asbestos, or volatile chemicals</td>
<td>Pneumoconiosis; silicosis; berylliosis; coal workers lung; asbestosis</td>
</tr>
<tr>
<td>Organic exposure to dust (birds, laboratory workers)</td>
<td>Hypersensitivity pneumonitis (bird fancier’s lung)</td>
</tr>
<tr>
<td>Stress/emotional problems</td>
<td>Hyperventilation/dysfunctional breathing</td>
</tr>
</tbody>
</table>

**Table 2: Differential diagnosis of acute breathlessness in adults (NICE 2020)**

| Cardiac | Silent MI, cardiac arrhythmia, acute pulmonary oedema, cardiac tamponade, chronic heart failure |
| Pulmonary | Asthma, COPD, pneumonia, pulmonary embolism, pneumothorax/tension pneumothorax, pleural effusion, lung/lobar collapse, bronchiectasis, interstitial lung disease, lung or pleural cancer |
| Other causes | Anaemia, diaphragmatic splinting, anxiety-related breathlessness |

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease; MI, myocardial infarction
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Table 3: Differential diagnosis of chronic breathlessness

<table>
<thead>
<tr>
<th>Cardiac</th>
<th>COPD, asthma, interstitial lung disease, pleural effusion, malignancy (primary or metastatic), bronchiectasis, upper airway obstruction (laryngeal disease, tracheal stenosis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>COPD, chronic obstructive pulmonary disease; GAD, generalised disorder; GERD, gastroesophageal reflux disease; PTSD, post-traumatic stress</td>
</tr>
<tr>
<td>Other causes</td>
<td>COPD, chronic obstructive pulmonary disease; GAD, generalised disorder; GERD, gastroesophageal reflux disease; PTSD, post-traumatic stress</td>
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</table>

Physical examination

Examination should be systematic and should include a general observation looking for respiratory distress, anaemia, cyanosis, clubbing or lymphadenopathy (Table 5). Nasal passages and pharynx should be examined to look for evidence of obstruction and the neck should be palpated for an enlarged thyroid gland and evidence of any tracheal deviation. The thorax should be examined for chest deformity or kyphosis and the movements should be observed for evidence of any asymmetry. Percussion may indicate dullness over a pleural effusion or hyperresonance over a pneumothorax. Auscultation of the chest should look for the presence of bronchial breathing or added sounds such as rhonchi, crepitations or stridor. Cardiovascular examination may identify abnormalities such as an abnormal heart rate or rhythm, hypertension, displacement of the apex, murmurs and added heart sounds. The presence of carotid bruits or diminished peripheral pulses should be noted. The legs should be examined for oedema and evidence of deep vein thrombosis. A systolic murmur may indicate aortic stenosis or mitral regurgitation and the presence of a third heart sound, a displaced apex beat and a raised JVP could indicate the presence of cardiac failure. Non-cardiac and non-pulmonary disease should be considered in patients with minimal risk factors and no clinic evidence of cardiac or pulmonary disease.

Investigations

Following a careful history and physical examination, certain tests should be carried out in order to confirm a diagnosis or to provide further information. Routine blood tests should include a full blood count, urea and electrolytes, random blood sugar and thyroid function tests, a normal B-type natriuretic peptide (BNP or NT proBNP) rules out heart failure. ECG may reveal abnormal heart
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rate or rhythm. There may be evidence of ischaemic changes, ventricular hypertrophy or pericardial disease. Heart failure is unlikely in the presence of a normal ECG. If BNP and/or ECG are abnormal the patient should be referred for echocardiography, which will help to confirm the presence of valve abnormality as well identifying left ventricular systolic dysfunction, left ventricular hypertrophy and raised pulmonary arterial pressure. Chest x-ray may reveal chest wall abnormalities, evidence of pleural disease, neoplastic lesions, interstitial lung disease, cardiomegaly or cardiac failure. Pulse oximetry abnormalities may indicate desaturation at rest or after exercise – an indicator of gas exchange abnormalities. Serial peak flow monitoring will identify variable airway obstruction and spirometry may show evidence of obstructive and restrictive lung disease. Fractional exhaled nitric oxide levels can support a clinical suspicion of asthma. Capnography or blood gas analysis may reveal hypocapnia indicative of hyperventilation.

Remote assessment of breathlessness

Where initial face to face assessment of a patient presenting in primary care with breathlessness is not possible or appropriate, assessment can be undertaken remotely via telephone or video messaging. While there are currently no validated tests for the remote assessment of breathlessness in patients presenting with breathlessness the ability of a patient to complete full sentences and the recently proposed algorithm from the Centre for Evidence-Based Medicine (CEBM) are helpful.

In response to the COVID-19 situation and the challenge of face to face evaluations, the CEBM proposed an algorithm for the remote assessment of breathlessness in the acute primary care setting. The algorithm takes into account the patient’s own description of their problem, asks specific questions to enable the patient to describe their breathing in more detail and focuses
Table 6: Centre for Evidence-Based Medicine (CEBM) recommendations for the remote assessment of breathlessness

| 1 | Ask the patient to describe the problem with their breathing in their own words and assess the ease and comfort of their speech. Ask open-ended questions and listen to whether the patient can complete their sentences “How is your breathing today?” |
| 2 | Align with NHS111 symptom checker, which asks three questions (developed through user testing but not evaluated in formal research):
   - “Are you so breathless that you are unable to speak more than a few words?”
   - “Are you breathing harder or faster than usual when doing nothing at all?”
   - “Are you so ill that you’ve stopped doing all of your usual daily activities?” |
| 3 | Focus on change. A clear story of deterioration is more important than whether the patient currently feels short of breath. Ask questions like
   - “Is your breathing faster, slower or the same as normal?”
   - “What could you do yesterday that you can’t do today?”
   - “What makes you breathless now that didn’t make you breathless yesterday?” |
| 4 | Interpret the breathlessness in the context of the wider history and physical signs. For example, a new, audible wheeze and a verbal report of blueness of the lips in a breathless patient are concerning |

on recent changing in breathing in the context of the patients wider clinical picture (Table 6).

Who should we refer?

Patients should be referred for specialist opinion when:
- the underlying cause cannot be established definitively and referral is indicated for further investigation
- symptoms are disproportionate to the apparent severity of the disease
- symptoms do not respond to therapy in order to confirm the diagnosis or alter therapy in order to alleviate symptoms.

References

14. CEBM. Are there any evidence-based ways of assessing dyspnoea (breathlessness) by telephone or video? Available at: https://www.cebm.net/covid-19/are-there-any-evidence-based-ways-of-assessing-dyspnoea-breathlessness-by-telephone-or-video/

Further reading:
The IMPRESS Breathlessness Algorithm, developed by the PCRS in collaboration with the British Thoracic Society, provides additional guidance on managing the patient presenting with breathlessness. Available at: https://www.respiratoryfutures.org.uk/resources/impress-breathlessness-algorithm/

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