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CLINICAL INVESTIGATIONS FROM THE RACP

Investigating dyspnoea on exertion

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Key points

- **Dyspnoea is a common complaint, most frequently caused by respiratory or cardiac disease.**
- **Multifactorial conditions are frequent; consider the presence of aggravating factors such as obesity, deconditioning, anaemia and anxiety.**
- **Underlying diseases may be serious and irreversible.**
- **The physiology of dyspnoea is complex, but its consideration often helps to clarify the cause of symptoms.**
- **A careful history and examination in combination with simple investigations will often lead to a diagnosis.**
- **Referral for specialist review and complex testing is needed in those in whom the cause is unclear.**
- **The treatment of dyspnoea is often limited to management of its underlying cause, making accurate diagnosis the key to improving patient outcomes.**

In this series, we present authoritative advice on the investigation of a common clinical problem, especially commissioned for family doctors and written by members of the Royal Australasian College of Physicians.

Dyspnoea is a common symptom; shortness of breath was reported by 25% of adults aged 49 to 65 years in a Melbourne community-based survey.[1] It is most often due to respiratory or cardiac disease.[2] Asthma, congestive heart failure, chronic obstructive pulmonary disease (COPD), pneumonia, cardiac ischaemia, interstitial lung disease, pulmonary thromboembolic disease and psychogenic conditions may be the cause of dyspnoea in up to 85% of patients.[3,4] The causes of dyspnoea may be multifactorial in about one-third of patients.[4]

Respiratory disorders are the problems managed most often by GPs (22 per 100 encounters in 2009 to 2010), followed by cardiovascular problems (seen in 17 per 100 encounters).[5] Dyspnoea is a strong independent predictor of mortality in patients with COPD or heart failure.[6] Many of the conditions leading to dyspnoea, including heart failure and COPD, increase in incidence with age, and are worsened by obesity and deconditioning. An ageing, more sedentary and increasingly overweight population (those who were overweight or obese and attending a GP rose from 54.2% in 2000 to 2001 to 60.2% in 2009 to 2010)[2] make it likely that dyspnoea will become an even more prevalent symptom.

Dyspnoea has been defined as a 'subjective experience of breathing discomfort that is comprised of qualitatively distinct sensations that vary in intensity. The experience derives from interactions among multiple physiological, psychological, social and environmental

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factors, and may induce secondary physiological and behavioural responses'.[7] Laboured breathing is expected with exertion; the point at which a person perceives an excessive effort to breathe or becomes aware of an abnormal breathing pattern is subjective, and may not be obvious to an observer.

A complaint of dyspnoea should always be taken seriously. It may be the first symptom of a number of respiratory, cardiac or other diseases, many of which can be serious and irreversible. Almost all conditions causing dyspnoea at rest will be associated with worsening of dyspnoea on exertion (see the box on page 22 for a list of many causes of dyspnoea). In early cardiac and respiratory diseases, dyspnoea is often present only with exertion; however, as the condition advances, dyspnoea occurs with progressively less strenuous activity and ultimately may be present at rest.

This article focuses on chronic dyspnoea (insidious onset or over weeks to months) in adults, predominantly older adults. Patients presenting with acute or subacute dyspnoea (sudden onset or over minutes, to hours or days) should be regarded as a medical emergency, and this is beyond the scope of this article.

CLINICAL ASSESSMENT

History and physical examination

Dyspnoea is a symptom not a diagnosis. Evaluation of the patient with dyspnoea is best conducted in a sequential fashion, with history and physical examination preceding relevant investigations. It is helpful to establish the organ system(s) involved: pulmonary, cardiac, haematological, neuromuscular or other. In a 1989 study of patients with dyspnoea in a pulmonary specialty clinic, use of history, examination and chest radiography was 81% accurate for the four most common diagnoses of asthma, COPD, interstitial lung diseases and cardiomyopathy.[8]

Activities that precipitate dyspnoea should be identified, and their impact on the patient's life assessed. Assessment will clearly be different for an elderly patient experiencing dyspnoea on dressing as compared with a young patient with chest tightness when playing sport. Recall of the level of dyspnoea when conducting common physical tasks, such as dressing, performing household tasks, walking up steps or performing usual exercises, is often helpful. However, patients with chronic disease may gradually adapt their lifestyle, and input from carers can be valuable. Visual analogue scales such as the modified Borg scale (Table 1)[7] or a rating scale such as the Medical Research Council Breathlessness Scale (Table 2)[9] or New York Heart Association Functional Classification (Table 3) can also be used.

Associated symptoms

Dyspnoea often occurs in concert with other symptoms, and their presence helps refine the differential diagnosis. Pain is an important association and may suggest serious pathology. Central chest pain may suggest coronary artery disease or other conditions such as aortic dissection or pneumothorax. Pleuritic chest pain may occur in patients with rib fractures, pneumonia, pulmonary embolism (PE) or pleural tumours. Pain relieved by leaning forward may indicate pericarditis.

COMMON AND LESS COMMON CAUSES OF DYSPNOEA

Common causes

Respiratory
- Chronic obstructive pulmonary disease
- Respiratory infections (upper respiratory tract infections/pneumonia)
- Asthma
- Interstitial lung disease
- Pulmonary malignancy/metastasis
- Pleural effusion/malignancy
- Pulmonary embolism
- Pneumothorax
- Bronchiectasis
- Sarcoidosis

Cardiac
- Acute coronary syndromes/angina
- Congestive heart failure
- Valvular heart disease

Haematological
- Anaemia

Others
- Ageing, deconditioning and obesity
- Pregnancy
- Thyroid disease
- Anxiety/panic attacks
- Ascites
- Acidosis of any cause

Less common causes

Respiratory
- Foreign body aspiration
- Tracheobronchial tumours/goitre
- Pulmonary hypertension
- Hepatopulmonary syndromes
- Pulmonary arteriovenous malformation
- Mesothelioma
- Pleuritis
- Kyphoscoliosis/chest wall deformity

Cardiac/vascular
- Arrhythmias
- Aortic dissection
- Congenital heart disease
- Myocardial disease
- Pericardial disease
- Superior vena cava syndrome/compression

Neurological/others
- Medications/drugs of abuse
- Motor neuron disease
- Guillain-Barre syndrome
- Myasthenia gravis/Lambert–Eaton myasthenic syndrome
- Botulism/tetanus
- Cushings/phaeochromocytoma
- Carbon monoxide/methaemoglobin

TABLE 1. MODIFIED BORG DYSPNOEA SCALE*

Scale	Level of dyspnoea
0	Nothing at all
0.5	Very, very slight (just noticeable)
1	Very slight
2	Slight
3	Moderate
4	Somewhat severe
5	Severe
6	
7	Very severe
8	
9	Very, very severe (almost maximal)
10	Maximal

*Adapted from American Thoracic Society. Dyspnea. Mechanisms, assessment, and management: a consensus statement. Am J Respir Crit Care Med 1999; 159: 321-340.[7]

Palpitations may be experienced by patients with tachyarrhythmias, valvular heart disease or PE, although sinus tachycardia is common with any respiratory distress and with anxiety. Syncope may be present in patients with dyspnoea due to tachyarrhythmia or PE.

Wheeze is a characteristic feature of asthma and COPD and may also be present in patients with bronchiolitis, vocal cord dysfunction, pulmonary oedema or foreign body aspiration. Dry cough is present in many respiratory, and some cardiac, conditions such as COPD, pulmonary fibrosis and pulmonary oedema. A productive cough usually indicates respiratory disease; a chronic productive cough with purulent sputum may indicate COPD or bronchiectasis, and copious clear secretions may be present with bronchoalveolar carcinomas. Haemoptysis may occur with exacerbations of bronchiectasis, pulmonary vasculitis, tuberculosis or malignancy.

Upper airway symptoms such as stridor or voice change suggest upper airway pathology, such as a goitre, or thoracic disease, such as lung cancer. Muscle weakness with dyspnoea suggests an underlying neuromuscular process such as muscular dystrophy or effects of medications such as corticosteroids.

Anxiety is a frequent reaction to dyspnoea of any cause, but anxiety itself may cause dyspnoea in panic or anxiety attacks. Dyspnoea associated with stress may indicate anxiety, hyperventilation or, very rarely, takotsubo cardiomyopathy. Other rare causes of a combination of anxiety, dyspnoea and palpitations include thyrotoxicosis, phaeochromocytoma and systemic mastocytosis.

Position of the patient

Orthopnoea – the presence of dyspnoea when supine, with improvement when upright – is a classic symptom of heart failure and is usually a later symptom than exertional dyspnoea. Orthopnoea can also be present in patients with severe COPD or asthma because the upward shift in abdominal contents further compromises ventilation. Neuromuscular diseases and diaphragmatic paralysis may also be associated with orthopnoea.

Sleep apnoea may cause nocturnal choking and gasping, but is not considered a cause of exertional dyspnoea;

however, patients at risk of sleep apnoea are likely to have comorbidities that can result in dyspnoea on exertion.

Paroxysmal nocturnal dyspnoea is a term applied to acute episodes of severe shortness of breath that wake the patient, usually after one to three hours of sleep. It is a relatively specific symptom of heart failure, and may be accompanied by cough or wheeze, or occasionally the expectoration of pink frothy sputum. Whereas orthopnoea is rapidly relieved by sitting upright, in patients with paroxysmal nocturnal dyspnoea, cough and wheeze often persist for some time afterwards.

Platypnoea – the worsening of dyspnoea when upright, and improvement when supine – is rare, but is characteristic of hepatopulmonary syndrome and left atrial myxoma. It is also encountered with bilateral phrenic nerve palsy, where lying supine places a weakened diaphragm at a relative mechanical disadvantage compared with the upright state.

TABLE 2. MEDICAL RESEARCH COUNCIL (MRC) BREATHLESSNESS SCALE*

Grade	Degree of dyspnoea
0	No dyspnoea except with strenuous exercise
1	Dyspnoea when walking up an incline or hurrying on the level
2	Walks slower than most on the level or stops after 15 minutes of walking on the level
3	Stops after a few minutes of walking on the level
4	Dyspnoea with minimal activity such as getting dressed, too dyspnoeic to leave the house

*Adapted from Fletcher CM. The clinical diagnosis of pulmonary emphysema—an experimental study. Proc R Soc Med 1952; 45: 577-584.[9]

TABLE 3. NEW YORK HEART ASSOCIATION (NYHA) FUNCTIONAL CLASSIFICATION FOR HEART FAILURE

NHYA class	Symptoms
I	No limitation of physical activity
II	Slight limitation of physical activity
III	Marked limitation of physical activity
IV	Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest

Timing and pattern

Dyspnoea appearing during the working week and resolving during periods away from work is suggestive of occupational asthma. Although exercise will usually worsen dyspnoea of any cause, excessive breathlessness can occur with prolonged aerobic exercise or worsen shortly after exercise. Seasonal or episodic dyspnoea related to cold air, pollens or nonspecific irritants is suggestive of asthma or reactive airways disease. Intermittent dyspnoea may also be due to cardiac arrhythmias or PE.

Additional medical history

Patients presenting with dyspnoea should be asked about their family history; it is useful to know if there is a history of diseases such as α-1 antitrypsin deficiency or thrombophilia. Obesity is frequently associated with dyspnoea, because of the increased physical load, reduced diaphragmatic excursion and increased cardiorespiratory demands, often coupled with deconditioning. A normal pregnancy may be associated with dyspnoea, but pregnancy may also unmask previously undiagnosed medical conditions, such as pulmonary hypertension or valvular heart disease.

Risk factors for PE should be sought; a significant proportion of patients with PE may not be symptomatic enough to seek medical attention, and over time this can lead to a subacute presentation with dyspnoea or even frank pulmonary hypertension when the pulmonary vascular bed becomes sufficiently injured. Known malignancy may be associated with dyspnoea due to local airway obstruction, pleural effusion, lymphangitis and anaemia and is itself a risk factor for PE. Previous thoracic radiotherapy may cause radiation pneumonitis, usually within six months of treatment, or fibrosis in the longer term.

Patients with connective tissue and autoimmune diseases are at risk of complications causing dyspnoea, such as pulmonary hypertension, PE, interstitial lung disease, myocarditis or pericarditis. Recurrent pneumonia may be associated with immunodeficiency, gastro-oesophageal reflux disease with aspiration or local airway obstruction with benign or malignant tumours or foreign bodies.

Many medications may cause or contribute to dyspnoea via various mechanisms, direct and indirect. Interstitial lung disease is a well-recognised complication of the use of amiodarone and methotrexate but cardiopulmonary side effects (e.g. pulmonary infiltrates, pulmonary hypertension, opportunistic infections and valvular heart disease) may occur with many medications including immune-modulators and antineoplastic agents. Metabolic acidosis may be induced

IMPORTANT COMPONENTS OF A RESPIRATORY HISTORY

- Smoking history, passive smoking exposure
- Complete occupational history
- Use of medications or illicit drugs known to cause cardiac or respiratory disease
- Exposure to toxic inhaled substances at home (including hobbies) and at work
- Family history of cardiac and respiratory diseases
- Risk factors for coronary artery disease
- Risk factors for thromboembolic disease
- History of connective tissue and autoimmune disease
- Immunisation history
- Recent and remote travel history
- Previous use of cardiac and respiratory medications and treatments
- Risk factors for HIV infection
- History of immunosuppressive therapy and radiation exposure
- Presence of upper respiratory tract and/or gastro-oesophageal symptoms
- History of sleep disorders and risk factors for sleep apnoea
- Provoking and relieving factors
- Timing of dyspnoea in relation to triggers
- Accompanying symptoms

by the use of reverse-transcriptase inhibitors. Bradycardia may be caused by the use of digoxin, calcium-channel blockers and β-blockers; β-blockers, oral or topical, may also worsen airflow obstruction in patients with asthma.

Social factors

A history of smoking with documentation of pack-years smoked is essential. A history of use of illicit drugs (such as marijuana or cocaine) should be sought if appropriate because these drugs can cause significant respiratory and cardiac disease.[10,11] Occupational history is essential, both in identifying triggers of episodic dyspnoea, for example solvents, fumes, dust, moulds or animals, but also for identifying more quantifying possible chronic exposures to agents associated with chronic lung diseases such as interstitial lung disease, hypersensitivity pneumonitis, asthma, silicosis and asbestos-related lung diseases. A history of past or recent travel may be associated with various infections including tuberculosis or parasitic diseases. The box on this page lists some important components of a respiratory history.

Clinical examination

Initial examination of the patient should include measurement of vital signs. Respiratory rate is an often under appreciated sign, and is best measured over a period of at least 30 seconds. In hospital settings, a raised respiratory rate (more than 20 breaths/minute) suggests the patient is probably unwell; a respiratory rate of more than 24 breaths/minute suggests the patient may be seriously unwell.[12] Observation of the patient while walking may show dyspnoea on mild exertion, an indicator of significant disease, or more specific features such as the pursed lip breathing of COPD. Mechanical factors such as arthritis or muscle weakness may be associated with increased sensation of effort during exertion.

General examination should include evaluation for anaemia, thyroid disease, muscle weakness and obesity. A thorough cardiovascular examination should be performed, looking specifically for signs of cardiac failure, arrhythmias, pulmonary hypertension and valvular heart disease. Respiratory examination should include assessment of the upper airway and the lower respiratory tract. Signs such as clubbing, cyanosis and tracheal deviation should be sought. Chest inspection may show kyphoscoliosis or scars from previous surgeries.

Wheeze is frequently absent in stable airways disease, so absence of wheeze does not exclude airflow obstruction. The sensitivity of physical examinations for detecting mild to moderate COPD is poor.[13] Physical features commonly found in patients with advanced disease are hyperinflation of the chest and soft breath sounds. Right heart failure may complicate severe lung disease. Crackles may be present in pulmonary oedema, bronchiectasis and interstitial lung disease.

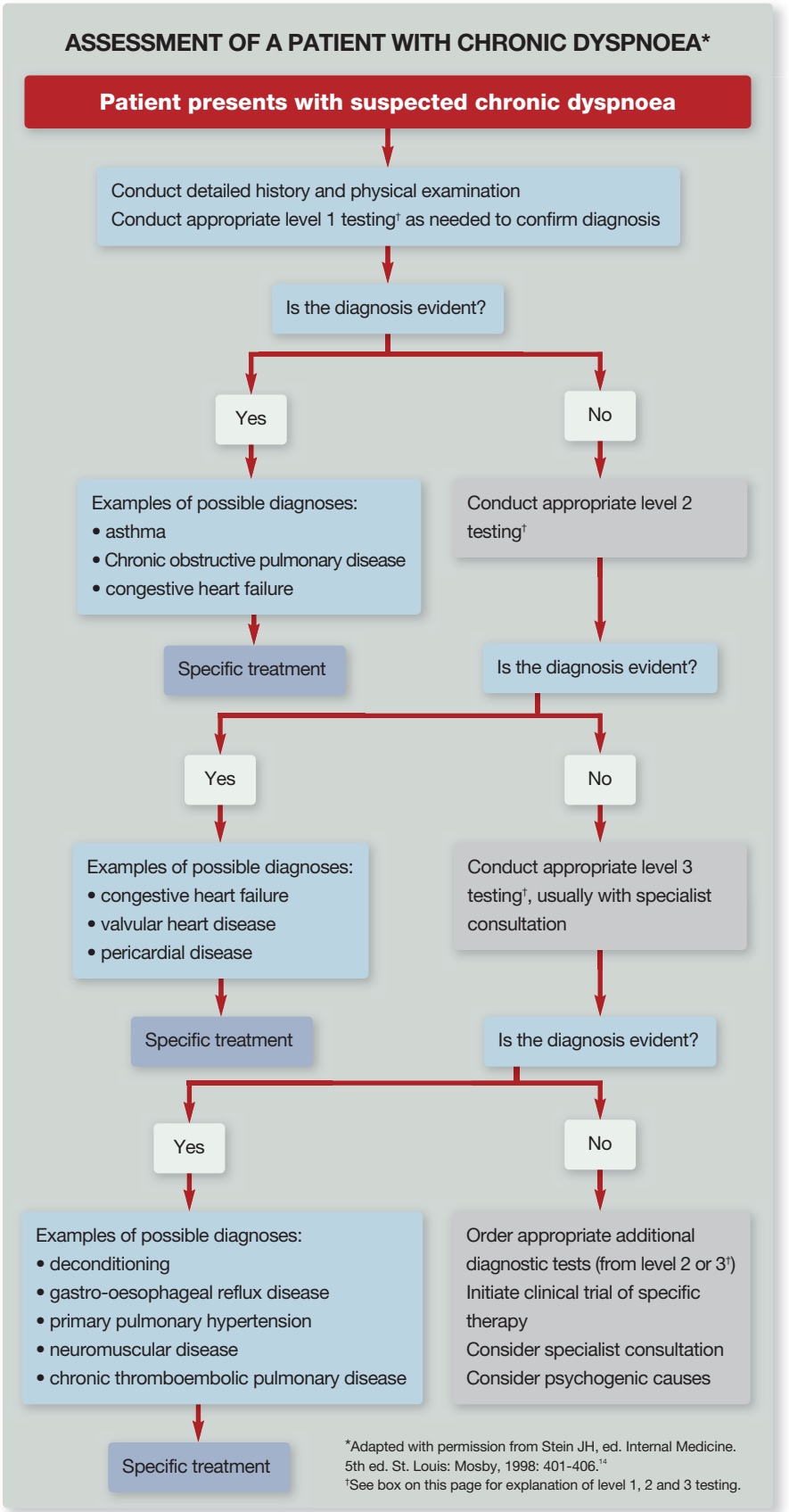
Examination of the patient's legs is useful to look for peripheral oedema and deep venous thrombosis. Abdominal examination is helpful if distension causing respiratory compromise is possible; the presence of ascites, tumours or, most commonly, obesity should be noted.

Initial investigations

A suggested algorithm for the evaluation of patients with chronic dyspnoea and an accompanying box are presented on page 26.[14]

Pulse oximetry allows detection and monitoring of hypoxaemia, and many physicians now consider it to be a routine vital sign. Oximeters are relatively inexpensive and can be portable; they are generally a useful tool in the clinic setting. Oximetry can be performed at rest and on exertion. Hypoxaemia in a patient with dyspnoea indicates significant disease, acute or chronic. However, dyspnoea does not equate to hypoxaemia; many patients with dyspnoea are not hypoxaemic, and chronic hypoxaemia can be present without dyspnoea.

Arterial blood gases give further information on gas exchange and should be performed if hypoxaemia is present. Hypercapnia can occur with COPD, other obstructive airway diseases and neuromuscular diseases. Hypocapnia may be present with any process that leads to



INVESTIGATIONS OF A PATIENT WITH CHRONIC DYSPNOEA*

Level 1 investigations

- Pulse oximetry
- Arterial blood gas
- Full blood count
- Metabolic profile
- Chest radiography
- Electrocardiogram
- Spirometry

Level 2 investigations

- Echocardiogram
- Pulmonary function testing
- Bronchial provocation testing
- High-resolution computed tomography
- Brain-natriuretic peptide
- Holter monitor
- CT pulmonary angiogram/ ventilation-perfusion (V/Q) scan

Level 3 investigations

- Cardiac catheterisation
- Cardiopulmonary exercise testing
- Bronchoscopy
- Oesophageal pH
- Lung biopsy
- Neuromuscular investigations
- Abdominal imaging

*Adapted with permission from Stein JH, ed. Internal Medicine. 5th ed. St. Louis: Mosby, 1998: 401-406.[14]

hyperventilation, such as PE, and with anxiety states. Acidosis, either due to acute hypercapnia or secondary to a metabolic process such as ketoacidosis or renal failure, will drive ventilation and dyspnoea.

Chest radiography

Chest radiography should be performed, if possible, in most patients with dyspnoea requiring assessment and in most patients with clinical chest findings. Heart failure, lung parenchymal disease, pleural diseases, chest wall abnormalities and malignant disease may be seen. It is a useful test when abnormal but it is not a sensitive test. For example, in patients with early or mild interstitial lung diseases, about 10% have a normal chest x-ray.[6]

Electrocardiography

In patients suspected of having cardiac disease or who are at high risk of cardiac disease, an electrocardiogram (ECG) should be performed. A normal ECG makes the diagnosis of heart failure unlikely.[15] ECG changes are common in patients with heart failure and are often nonspecific, but they can prove helpful if signs of ischaemia or arrhythmias are seen. ECG may show changes suggestive of right (COPD, pulmonary hypertension) or left (hypertension, valvular heart disease) atrial or ventricular enlargement, or pericarditis.

Spirometry

Spirometry can be used to distinguish between normal and abnormal lung function, to detect and quantify an obstructive ventilatory defect and to assess the degree of reversibility after use of an inhaled bronchodilator. The presence and severity of airflow limitation in patients with COPD cannot be determined by clinical signs, and objective measurement by spirometry is vital. Peak expiratory flow measurement is a simple screening test for airflow obstruction. It is not a sensitive measure of airway function in patients with airways disease because it has a wide range of normal values.[16] It is also entirely dependent on effort and technique. If spirometry is within normal ranges, then COPD is effectively excluded. Asthma, bronchiectasis and bronchiolitis may also cause an obstructive ventilatory defect.

An abnormal inspiratory flow volume loop may suggest extrathoracic airways obstruction, and should prompt further assessment of the patient's upper airway. Reductions in both forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) suggest a restrictive defect, and warrants full pulmonary function testing, with measurement of lung volumes and gas transfer factor.

LABORATORY INVESTIGATIONS

Laboratory investigations are often of limited value in finding the cause of dyspnoea. However, haemoglobin levels should be measured; anaemia may cause or contribute to dyspnoea. Polycythaemia can complicate chronic hypoxaemia. A raised white blood cell count and/or erythrocyte sedimentation rate may indicate occult infective or inflammatory conditions. Measurement of electrolyte levels can reveal renal disease or acid-base derangement, such as high bicarbonate levels in patients with chronic hypercapnia. Thyroid function testing should be performed if hyperthyroidism or hypothyroidism is suspected, and autoantibody tests should be conducted if connective tissue disease is likely.

Measurement of levels of brain natriuretic peptide (BNP) and N-terminal (NT) pro-BNP are increasingly used as part of the assessment of patients with suspected heart failure. A BNP level of less than 100 pg/mL or NT pro-BNP level of less

than 400 pg/mL make a diagnosis of heart failure unlikely in untreated patients.[17]

SELECTIVE INVESTIGATIONS

For patients with no clear diagnosis after history, examination and initial testing, further investigations are needed; this will often be through specialist consultation.

Suspected pulmonary disease

Pulmonary function testing

In addition to spirometry, detailed pulmonary function testing can measure gas transfer functioning of the lung, lung volumes and respiratory muscle strength. Reduced gas transfer factor is seen in a number of pulmonary parenchymal or vascular diseases, such as interstitial lung disease, emphysema, pulmonary hypertension and thromboembolic pulmonary disease. Lung volumes may be reduced in interstitial lung disease or musculoskeletal diseases such as kyphoscoliosis, or may show evidence of gas trapping with chronic airflow obstruction. Neuromuscular diseases may lead to a combination of a restrictive defect and reduced respiratory muscle strength.

Suspected asthma

Asthma is most commonly diagnosed in childhood (often on clinical grounds given inherent challenges in performing paediatric spirometry), but can occur at any age. Many adolescents experience remission of childhood asthma symptoms, but may have recurrence several years later. In this setting, although a characteristic history and response to medications is highly suggestive of asthma, formal spirometric assessment is always useful to confirm what may have initially been a clinical diagnosis in childhood, and to quantify its severity.

Most patients with asthma causing dyspnoea on exertion also have asthma symptoms at other times, and can have unrecognised or under-treated asthma. In a patient not previously known to have asthma but with a suggestive history and examination, the diagnosis can be usually confirmed by spirometry (or less formally by peak flow measurements) before and after bronchodilator use.

Exercise-induced asthma typically develops five to 15 minutes after brief exertion, or about 15 minutes into prolonged exertion, and resolves with rest after 30 to 60 minutes. This time course is different to simple exertional dyspnoea, which usually develops shortly after onset of exertion and settles within five minutes of stopping. Exercise-induced asthma is most common and intense when cold dry air is inhaled, such as when playing winter sports.

If asthma remains clinically likely but the diagnosis is not clear-cut, for example spirometry is normal or there has been no response to asthma treatment, then bronchial provocation

testing can be performed. These tests might be viewed as being similar in concept to exercise stress testing in a patient suspected of having angina but with a normal resting ECG. Contraindications to provocation testing exist, so specialist or laboratory consultation is recommended.

'Direct' provocation tests use nonspecific pharmacological agents such as methacholine to induce bronchoconstriction. They are sensitive tests for diagnosing asthma, but are not specific. False-positive results can be seen in patients with recent respiratory tract infections, COPD and smokers. Also, a negative methacholine challenge does not exclude exercise-induced asthma.

A minority of patients may have bronchoconstriction strictly limited to exercise. 'Indirect' challenge tests act via the release of airway inflammatory mediators, generally by dehydration of the airway surface. They are less sensitive than direct challenges for diagnosing asthma, but are more specific. Indirect tests include eucapnic voluntary hyperventilation and mannitol inhalation. Eucapnic voluntary hyperventilation is the most sensitive test for diagnosing exercise-induced bronchoconstriction; a positive challenge is highly specific for current exercise-induced asthma, although a negative challenge cannot fully exclude asthma.

Peak flow diaries and home monitoring may be useful in proven cases of asthma or where clinically suspected asthma cannot be demonstrated with spirometry or bronchial provocation challenge testing, both for diagnosis and measuring response to treatment.

Chest imaging

High-resolution CT has become the standard test for the evaluation of patients with interstitial lung disease and bronchiectasis. High-resolution CT is not recommended as a general screening test but in patients with evidence of gas-exchange abnormalities, such as reduced gas transfer factor or hypoxaemia at rest or on exercise, unsuspected interstitial disease may be found. Chest CT with contrast is used for the diagnosis of vascular abnormalities, such as aortic dissection, aneurysm and PE and diagnosis of pulmonary pathology such as lung malignancy, and pleural, mediastinal and chest wall diseases. The main disadvantages of CT are radiation exposure and contrast administration.

CT pulmonary angiography has become a standard test for suspected thromboembolic disease, both in acute and chronic situations. Chronic thromboembolic disease is an uncommon condition, but one that is important not to miss. Patients with this condition often present with gradually worsening dyspnoea rather than the sudden symptoms associated with acute PE.

CT pulmonary angiography is being used more often than ventilation-perfusion scanning in many centres, because CT pulmonary angiography provides the ability to directly visualise emboli and to detect abnormalities that may provide an alternative diagnosis. However, a normal perfusion scan essentially rules out pulmonary emboli[18] and this scan may be useful when intravenous contrast agents (necessary in CT pulmonary angiography) are contraindicated or problematic, such as in patients with advanced renal disease or an allergy to iodine; or where the patient or clinician seek to minimise radiation exposure (especially an issue in young females).

Suspected cardiac disease

Echocardiography

In the assessment of patients with heart failure and for diagnosing most cardiac causes of chronic dyspnoea, echocardiography is the preferred diagnostic method. It is safe and noninvasive, although it does require skilled operation and interpretation. It can assess systolic and diastolic left and right heart functions, wall motion and dilation, valvular function, and the presence or absence of a pericardial effusion. Echocardiography may also be able to give an estimate of pulmonary artery pressure.

In about two-thirds of patients with heart failure and reduced systolic function, coronary artery disease is the underlying cause.[17] There are a number of investigations available for suspected coronary artery disease, including exercise ECG, stress echocardiography, myocardial perfusion imaging, CT coronary angiography and coronary angiography. The choice of investigation will depend on the patient's pretest probability of disease, ability to exercise, gender, age and need for a therapeutic as well as a diagnostic procedure.

Assessment of heart function has traditionally focused on systolic function, with diastolic function considered to be less relevant. However, diastolic function is also important, with epidemiological studies showing that about half of patients who develop heart failure have a normal or preserved left ventricular ejection fraction (more than 40 to 50%).[19] Patients with diastolic dysfunction are generally older than 65 years, with many older than 80 years, and are predominantly women. Patients with diastolic dysfunction also have a high prevalence of coexistent conditions, such as hypertension (60 to 80%), obesity (30 to 50%), diabetes (30 to 50%) or atrial fibrillation (20 to 40%). Dyspnoea on exertion in this patient group is likely to be multifactorial, with contributions from comorbidities as well as diastolic dysfunction.

Suspected pulmonary arterial hypertension

Pulmonary hypertension most commonly occurs secondarily to left-sided heart disease or chronic respiratory disease, and elevation of pulmonary arterial pressure is generally in the mild to moderate range in patients with these conditions. Pulmonary arterial hypertension is a rare condition and is often difficult to diagnose.

The onset is usually gradual, with symptoms seemingly out of proportion to the physical examination.

The cause of pulmonary arterial hypertension is:

- idiopathic in about 50% of patients
- related to connective tissue disease in 25% of patients
- due to congenital heart disease, HIV infection, portal hypertension and drugs or toxins in the remaining 25% of patients.[16]

Auscultation for a loud pulmonary component of the second heart sound is an important step in diagnosis. The mean time between symptom onset and diagnosis is 2.8 years, mean age at diagnosis is currently 53 years and 79.5% of affected patients are female.[20]

ECG can be normal in patients with pulmonary arterial hypertension but may show signs of right heart disease. Chest radiography can show prominent proximal pulmonary arteries and peripheral oligaemia, right ventricular hypertrophy and right atrial enlargement, but these signs may be subtle. Echocardiography is the initial cardiac imaging test of choice, but may overestimate or underestimate the true pulmonary pressures. Right heart catherisation is the gold standard test, but is only performed in specialised centres and after careful review.

Cardiopulmonary exercise testing

Cardiopulmonary exercise testing (as distinct from testing for exercise-induced bronchospasm and stress testing to identify myocardial ischaemia) is useful in some patients with otherwise unexplained exertional dyspnoea. It is not an initial test, but may help distinguish between pulmonary, cardiac or other patterns of disease when other tests are inconclusive. Patients are maximally exercised on a treadmill or bicycle ergometer, while their cardiac and respiratory variables are monitored, and results are then compared with reference values. There are contraindications to testing and specialist or laboratory consultation is suggested.

Results may exclude some conditions that would otherwise require more invasive testing to evaluate. For some patients a specific diagnosis can be made by the finding of a specific pattern of abnormality. Unfortunately, many causes of dyspnoea do not have specific findings on standard test protocols. In particular, exercise testing is insensitive in distinguishing cardiac disease from deconditioning. However, a normal result is very helpful, suggesting no serious cardiac or respiratory disease and can support limitation of further diagnostic testing.

ADDITIONAL INVESTIGATIONS

Further investigations will be guided by the results of initial and selective testing, and may include:

- bronchoscopy or lung biopsy to evaluate lung lesions
- Holter monitoring for potential arrhythmias
- nerve conduction studies or muscle biopsy for neuromuscular disease
- abdominal imaging for ascites
- pH monitoring for gastro-oesophageal reflux disease.

SUMMARY

Dyspnoea is a common symptom, and diagnosis is best made by a structured approach based on initial history and examination. Simple investigations should precede more invasive or complex tests. Dyspnoea is often multifactorial in origin and the presence of a coexisting factor, such as deconditioning, obesity, anaemia or anxiety, should be considered in patients who continue to experience dyspnoea despite maximal therapy. Treatment is directed at the management of the underlying cause and at general symptomatic measures, such as weight loss and rehabilitation programs. MT

REFERENCES

A list of references is available on request to the editorial office.

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REFERENCES

1. Abramson M, Matheson M, Wharton C, et al. Prevalence of respiratory symptoms related to chronic obstructive pulmonary disease and asthma among middle aged and older adults. Respirology 2002; 7: 325-331.
2. Gillespie DJ, Staats BA. Unexplained dyspnea. Mayo Clin Proc 1994; 69: 657-663.
3. DePaso WJ, Winterbauer RH, Lusk JA, Dreis DF, Springmeyer SC. Chronic dyspnea unexplained by history, physical examination, chest roentgenogram, and spirometry. Analysis of a seven-year experience. Chest 1991; 100: 1293-1299.
4. Michelson E, Hollrah S. Evaluation of the patient with shortness of breath: an evidence based approach. Emerg Med Clin North Am 1999; 17: 221-237, x.
5. Britt H, Miller GC, Charles J, et al. General practice activity in Australia 2000–01 to 2009–10: 10 year data tables. General practice series no 28. Cat no GEP 28. Canberra: Australian Institute of Health and Welfare; 2010.
6. Nadel JA, Mason RJ, Murray JF. Murray and Nadel's textbook of respiratory medicine. 5th ed. Philadelphia: Elsevier Saunders; 2010.
7. American Thoracic Society. Dyspnea. Mechanisms, assessment, and management. Am J Respir Crit Care Med 1999; 159: 321-340.
8. Pratter MR, Curley FJ, Dubois J, Irwin RS. Cause and evaluation of chronic dyspnea in a pulmonary disease clinic. Arch Intern Med 1989; 149: 2277-2282.
9. Fletcher CM. The clinical diagnosis of pulmonary emphysema – an experimental study. Proc R Soc Med 1952; 45: 577-584.
10. Howden ML, Naughton MT. Pulmonary effects of marijuana inhalation. Expert Rev Respir Med 2011; 5: 87-92.
11. Schwartz BG, Rezkalla S, Kloner RA. Cardiovascular effects of cocaine. Circulation 2010; 122: 2558-2569.
12. Cretikos MA, Bellomo R, Hillman K, Chen J, Finfer S, Flabouris A. Respiratory rate: the neglected vital sign. MJA 2008; 188: 657-659.
13. Mosenifar Z. Chronic obstructive pulmonary disease. Available online at: http://emedicine.medscape.com/article/297664-overview (accessed September 2011).
14. Stein JH, ed. Internal medicine. 5th ed. St Louis: Mosby; 1998. p.401-406.
15. Davie AP, Francis CM, Caruana L, Sutherland GR, McMurray JJ. Assessing diagnosis in heart failure: which features are any use? QJM 1997; 90: 335-339.
16. Kelly CA, Gibson GJ. Relation between FEV1 and peak expiratory flow in patients with chronic airflow obstruction. Thorax 1988; 43: 335-336.
17. Jayasinge R, Murdoch D, Sivakumaran S. New-onset dyspnoea in the young adult: consider the serious causes. Medicine Today 2011; 12(2): 38-46.
18. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). The PIOPED Investigators. JAMA 1990; 263: 2753-2759.
19. Bonow RO, Mann DL, Zipes DP, Libby P. Braunwald's heart disease: a textbook of cardiovascular medicine. 9th ed. Philadelphia: Saunders Elsevier; 2011.
20. Badesch DB, Raskob GE, Elliott CG, et al. Pulmonary arterial hypertension: baseline characteristics from the REVEAL Registry. Chest 2010; 137: 376-387.