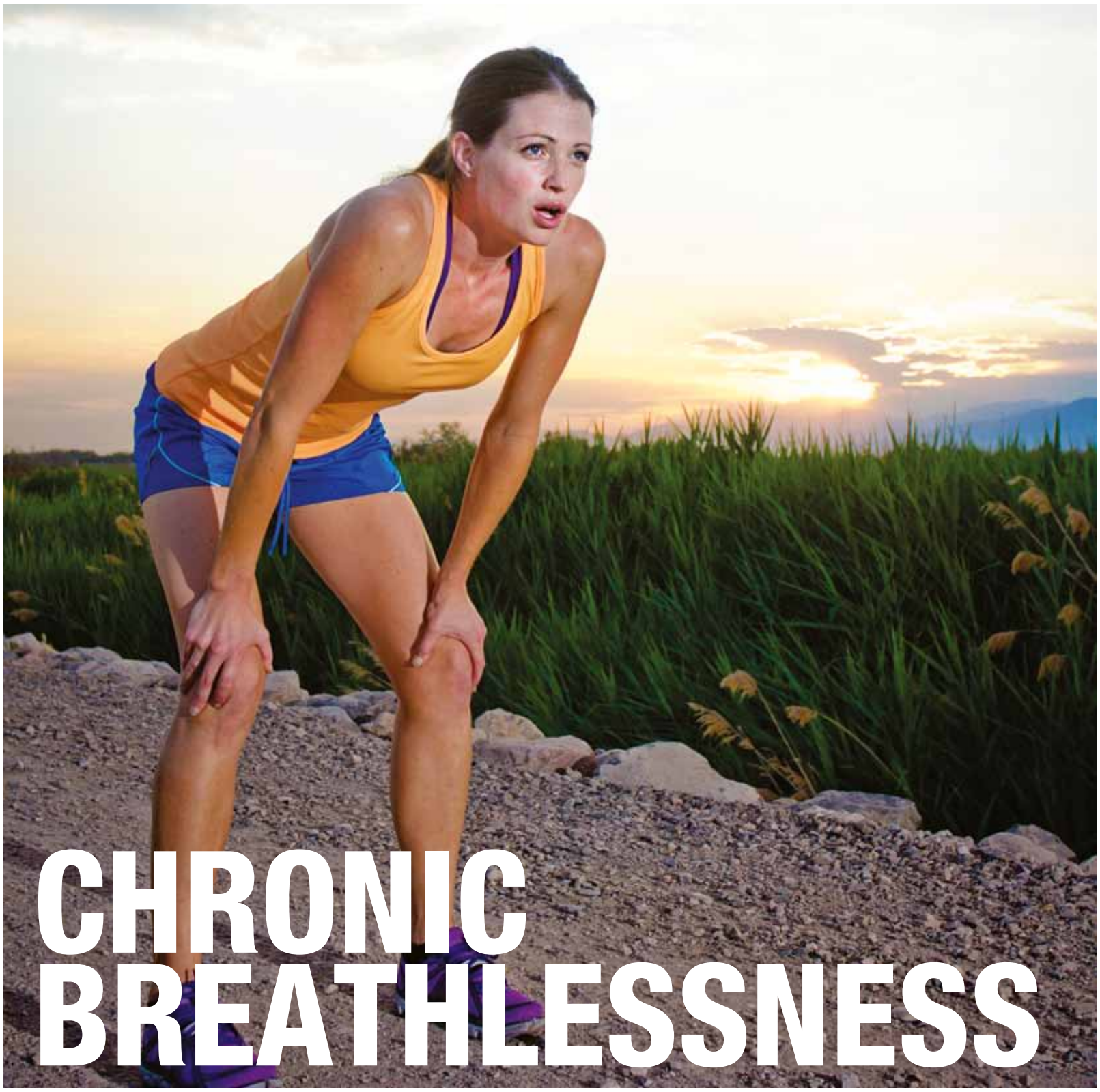
COMPLETE HOW TO TREAT QUIZZES ONLINE
www.australiandoctor.com.au/cpd to earn CPD or PDP points.



CHRONIC BREATHLESSNESS

Introduction

REMEMBER the last time you ran 100m flat out and it left you puffing and panting? Everyone has experienced breathlessness at some stage — it is an unpleasant feeling of breathing discomfort. Having the sensation of dyspnoea during ordinary activities or activities of daily life is abnormal and requires investigation in the primary care setting. In many cases, dyspnoea requires prompt referral to specialists. The good news is that, with a history and a few initial investigations, empiric therapy for the common causes of chronic dyspnoea (see table 1) should quickly improve symptoms.

Isolated shortness of breath is a common complaint representing about one per 100 encounters in general practice. Many patients present late in their disease course because early symptoms are often dismissed as ageing, lack of fitness or putting on a little weight. It is often not until symptoms start to prevent the unavoidable jobs of daily life that patients present for investigation and management.

The history is the first point for starting the workup of chronic dyspnoea. Some red flags should prompt more urgent review (see table 2) and closer follow-up.[1] A standard series

cont'd next page

Table 1: Differential diagnoses of chronic breathlessness

System	Common	Uncommon	Rare
Respiratory	Asthma COPD	Interstitial lung disease	Pulmonary hypertension
Cardiovascular	Heart failure with reduced ejection fraction (HFrEF) Heart failure with preserved ejection fraction (HFpEF)	Arrhythmia (eg, AF) Valvular heart disease Congenital heart	Ischaemic heart disease without chest pain
Other	Anaemia Deconditioning Overlap syndrome	Psychogenic	

Table 2: Chronic breathlessness red flags for early specialist referral

Dyspnoea doing activities of daily life or at rest, or rapid decline in exercise tolerance
Haemoptysis
Past history of connective tissue disease
Chest pain
Syncope
Peripheral oedema
Palpitations with breathlessness

INSIDE

THE AUTHORS

DR CLAIRE ELLENDER
fellow, pulmonary hypertension, department of allergy, immunology and respiratory medicine, Alfred Hospital, Prahran, Victoria.

DR MICHAEL STOKES
fellow, advanced heart failure and transplantation, department of cardiology, Alfred Hospital, Prahran, Victoria.

PROFESSOR TREVOR WILLIAMS
professor of respiratory and transplant medicine; department of allergy, immunology and respiratory medicine, Alfred Hospital, Prahran, Victoria.

PROFESSOR DAVID KAYE
cardiologist and transplant physician, department of cardiology, Alfred Hospital, Prahran, Victoria, and Baker IDI, Melbourne, Victoria.

PROFESSOR GRAEME MAGUIRE
professor of respiratory medicine, Baker IDI, Alice Springs, NT.

from previous page
of initial investigations should be done prior in primary care to help confirm the most common causes of chronic dyspnoea (see table 3).

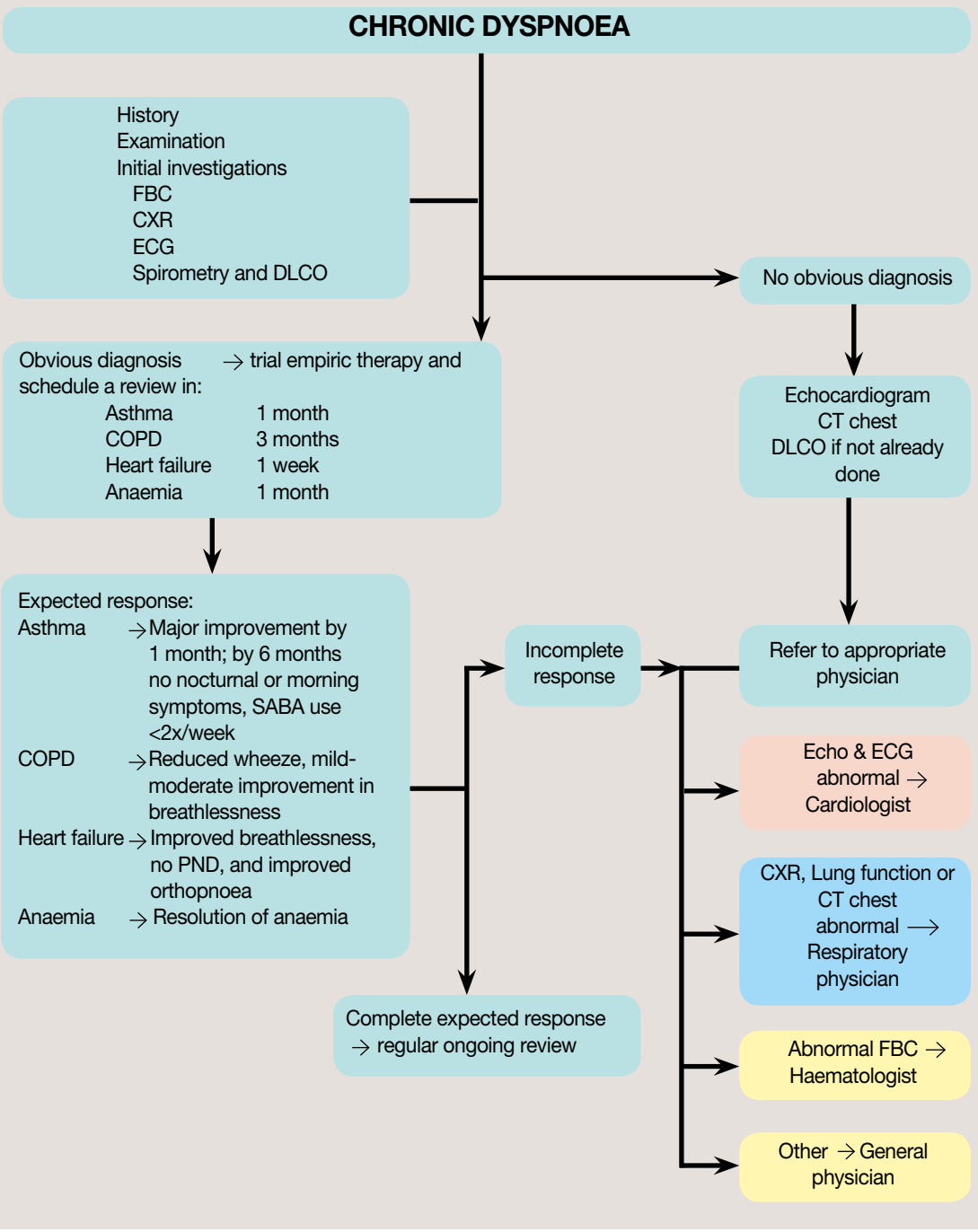
In cases with a clear history and a likely clinical diagnosis, it is appropriate to trial empiric therapy. These cases should always be reviewed in a timely fashion to ensure the symptoms have resolved as expected. In figure 1, we suggest some time frames in which review of symptoms should occur. If the anticipated clinical response is not achieved, these patients require referral to specialist services for further investigation for rarer causes or up-titration therapy once the diagnosis has been confirmed.

Peripheral oedema is an indication for early referral.

Table 3: Investigations with their associated red flags

Primary care tests	
Test	**Look for:**
1. FBC	Low haemoglobin
2. Chest x-ray	Cardiomegaly Consolidation Fibrosis
3. ECG	Arrhythmia ST segment elevation Left bundle branch block
4. Respiratory function tests with diffusion capacity for carbon monoxide (DLCO) if available	Obstruction to suggest asthma / COPD Restriction to suggest interstitial lung disease (ILD) Reduced DLCO (with normal spirometry) could suggest pulmonary hypertension
If no obvious diagnosis then	
5. Echocardiogram	Severe systolic dysfunction (ie, EF <30%) suggests heart failure Severe aortic or mitral stenosis Pericardial effusion Pulmonary hypertension
Specialist initiated tests	
Respiratory provocation tests	Asthma
CT chest	Parenchymal lung disease
V/Q scan	Pulmonary embolism or chronic thromboembolic pulmonary hypertension
B-type natriuretic peptide (BNP) or N-terminal fragment (NT-pro BNP)	Greater than 300 suspicious of heart failure; NB not Medicare-rebated

Figure 1: Treat and review workup of dyspnoea.



Respiratory causes of breathlessness

COPD

COPD is a common cause of breathlessness, but it is important to remember that only a minority of even heavy smokers develop severe COPD. The diagnosis should be made on the basis of history (breathlessness, sputum and smoke exposure) plus airflow limitation on spirometry — that is, FEV_1/forced vital capacity less than 0.7.[2]

Non-pharmacological therapies are extremely helpful but often under-utilised in treating breathlessness in COPD. After confirming the diagnosis the next step is smoking cessation, which has been shown to reduce loss of lung function, reduce exacerbations and thus aid breathlessness. Flu vaccination is recommended annually and pneumococcal vaccination for patients over 65 with COPD and a single revaccination after five years. Maintaining physical activity, including pulmonary rehabilitation, is indicated at all severities, even with end-stage disease. Pulmonary rehabilitation reduces dyspnoea by improving peripheral muscle fatigability and respiratory muscle mechanics and has been shown to significantly improve quality of life.

Table 4: Guide to initiating therapy in COPD

	Short-acting beta$_2$ agonist (SABA)	Short-acting muscarinic antagonist (SAMA)	Long-acting beta-agonists (LABA)	Long-acting muscarinic antagonist (LAMA)	Inhaled corticosteroid (ICS)
Mild	✓ **SABA** Salbutamol Terbutalin **OR** ✓ **SAMA** Ipatroprium		✗	✗	✗ not indicated
Moderate — no exacerbations			✓ **LABA** **AND** ✓ **LAMA** Option of combinations: • Vilanterol /umeclidinium (Anoro) • Indacaterol /glycopyrronium (Ultibro)		✗ not indicated
Moderate — severe with exacerbations					✓ **ICS** Beclomethasone Budesonide Fluticasone Option of combinations: • Budesonide/eformoterol (Symbicort) • Fluticasone/salmeterol (Seretide) • Fluticasone/vilanterol (Breo)
Pneumonia / infections					✗ cease

Adapted from GOLD guidelines 2015[2]

Pulmonary rehabilitation reduces dyspnoea by improving peripheral muscle fatigability and respiratory muscle mechanics.

The wide range of inhalers currently available to treat COPD may make it difficult knowing where to start. It is important to manage patients' expectations because many report being disappointed in the lack of symptom improvement. A step-wise approach is shown in table 4.

In exacerbations of COPD, an action plan for prompt treatment is important because severe infections can significantly reduce a patient's lung function. Certainly, judicious prescribing of antibiotics is important, recognising that every infection can have devastating consequences to functional state and conditioning in patients with poor lung function. Thus, the balance of risks vs benefits with

moderate to severe COPD would lead us to utilise antibiotics for exacerbations, except where exacerbations are mild or clearly have viral aetiology. Collecting sputum helps guide antibiotic selection, especially where an exacerbation is slow to respond or has incomplete resolution.

Asthma

Asthma is another common differential for chronic breathlessness. With modern combination ICS, this condition should respond quickly (ie, within one month to inhaler therapy), and if symptoms persist, then it is important to quickly reassess the diagnosis, adherence to therapy or refer to specialists for review. A detailed history about symptom severity is really important as all patients should be able to achieve good asthma control within six months (see table 5).[3]

Pharmacotherapy for asthma works quickly and effectively in most cases (see table 6 for treatment guide). If a patient does not have substantial improvement in symptoms after one month of therapy, then the diagnosis is not correct, they are not taking therapy or there are comorbidities that need identifying and treating. After a month of therapy, ongoing symptoms in asthma would warrant referral to a specialty clinic.

Additional therapies — such as mast cell stabilisers (montelukast), theophylline or chromones — should be reserved for prescription after specialist review. Non-pharmacological therapy in asthma is also important. Advice about smoking cessation is essential. Identifying and controlling comorbid conditions that can exacerbate asthma is also helpful; for example, therapy for allergic rhinitis and gastro-oesophageal reflux disease.

Table 5: Asthma severity and symptom control

Good control/Mild asthma	Poor control/Severe asthma
Infrequent (fewer than two days a week) symptoms	Frequent need for reliever
No nocturnal cough	Nocturnal symptoms of cough and wheeze
Sleeps through night easily	Wakes through night, uses reliever first thing in the morning
Regular preventer use and optimal technique	Poor preventer technique and adherence
No exercise limitation • No comorbidities • Allergic rhinitis • Sinusitis • Gastro-oesophageal reflux	Symptoms limit exercise tolerance • Untreated comorbidities • Allergic rhinitis • Sinusitis • Gastro-oesophageal reflux

Adapted from *Australian Asthma Handbook*[3]

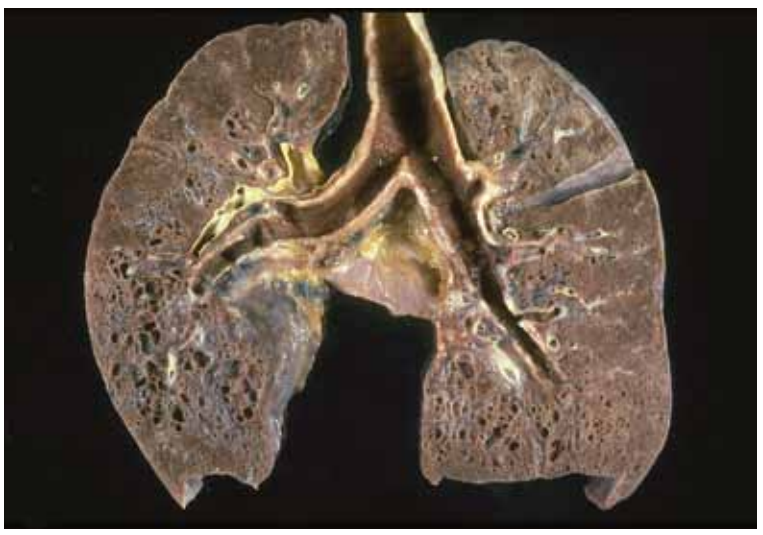
Table 6: Asthma inhaler therapies

	SABA	ICS	Combination
	Salbutamol Terbutaline	Beclomethasone Budesonide Fluticasone	ICS / LABA • Budesonide/eformoterol (Sympbicort) • Fluticasone /salmeterol (Seretide) • Fluticasone /vilanterol (Breo) • Fluticasone/eformoterol (Flutiform)
Symptoms less than twice a month and no flares in the past 12 months	✓		
Symptoms less than twice a month but a flare requiring steroids in the past two years	✓	✓ Low dose	
Symptoms more than twice a month	✓	✓ Low dose	
Nocturnal symptoms	✓	✓ Low dose and uptitrate to control	
Poor control of symptoms	✓	✓ High dose	

Adapted from *Australian Asthma Handbook*[3]

Interstitial lung disease

Interstitial lung disease is a broad term that encompasses many forms of diffuse parenchymal lung disease. Dyspnoea is the most common presenting complaint. The classification of these conditions is complicated and resembles alphabet soup: usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP) and idiopathic pulmonary fibrosis (IPF).[4] A CT chest is important, and as soon as a suspicious finding is detected, an early referral to a respiratory physician should be made for evaluation of treatment options before irreversible fibrosis occurs. Previously, there were limited treatment options for the common form of idiopathic pulmonary fibrosis (ILD); however, the past 12 months have seen the introduction of new treatment options, including pirfenidone and nintedanib.



Interstitial lung disease resulting from sarcoidosis.
Source: Yale Rosen http://bit.ly/1MY50RZ

Pulmonary hypertension can be classified into five categories[5]

Group 1	Pulmonary arterial hypertension (formerly known as primary pulmonary hypertension); rare; requires treatment with new specific medications; managed by pulmonary hypertension–designated prescribing clinics
Group 2	Pulmonary hypertension secondary to left heart disease; not uncommon; generally, treatment is directed at underlying heart disease by a cardiologist
Group 3	Pulmonary hypertension secondary to lung disease; frequently complicates severe lung disease; treatment of underlying disease with oxygen therapy as indicated by a respiratory physician
Group 4	Chronic thromboembolic pulmonary hypertension; may be surgically curable but requires specialty referral and lifelong anticoagulation with warfarin
Group 5	Pulmonary hypertension with multifactorial mechanisms; rare; requires review by a pulmonary hypertension–designated centre

Pulmonary arterial hypertension

Pulmonary hypertension is an umbrella term for a group of conditions characterised by raised pulmonary pressures. This condition is often initially diagnosed on echocardiogram, with right ventricular systolic pressure (RVSP) or pulmonary artery systolic pressure greater than 35mmHg.[5] Dyspnoea is a common presenting complaint, but pulmonary arterial hypertension should also be considered in patients with syncope, chest pain, palpitations, fatigue or signs of right heart failure.[6] Any patient with pulmonary hypertension on echocardiogram should be referred to a respiratory physician or cardiologist for further workup.

Cardiac causes of breathlessness

Heart failure

HEART failure is defined as a complex clinical syndrome characterised by structural and/or functional cardiac disorders that lead to impairment of the ability of the ventricles to fill (diastolic) or eject (systolic) blood. Heart failure is a condition that carries a high morbidity and mortality. Early identification and institution of appropriate treatment are important for good patient outcomes.

Dyspnoea on exertion is almost universal, but late presentations with dyspnoea at rest are unfortunately not uncommon. Other clinical manifestations include fatigue, decreased exercise tolerance and fluid retention. Clinical examination may reveal signs of congestion (ie, pulmonary, hepatic and peripheral) or evidence of organ hypoperfusion secondary to reduced cardiac output (ie, cool peripheries, confusion and abdominal organ ischaemia).

The clinical syndrome of heart failure can be further subdivided into those with heart failure with reduced ejection fraction (HFrEF) and an increasingly recognised group of patients with heart failure with preserved ejection fraction definition (HFpEF).[7] There are no major differences in the initial clinical presentation of those with HFrEF and HFpEF, but important differences in the epidemiological profile do exist between these two patient groups. HFpEF can be a particularly challenging condition to diagnose, particularly as comorbidities are commonly present (eg, obesity), which alone are associated with dyspnoea.

Heart failure with reduced ejection fraction

HFrEF is identified in those presenting with the clinical syndrome of heart failure with identified left ventricular ejection fraction of less than 40%. The reduced ejection fraction is identified on cardiac imaging, usually transthoracic echocardiography but also may be seen on nuclear imaging or cardiac MRI. There is a broad range of conditions associated with HFrEF (see table 7).

Identification of HFrEF should prompt referral to a cardiologist for assessment and management. GPs can greatly assist in providing support and patient education with regard to non-pharmacological measures, such as fluid restriction, avoidance of exacerbating factors (eg, dietary sodium and alcohol restriction, avoidance of NSAIDs) and monitoring signs of fluid overload. A significant proportion of patients with HFrEF have associated sleep disorders, and these should be screened for and treated where appropriate.

Table 7: Causes of HF-REF

Common	Ischaemia (about 50% of new cases) Hypertension
Less common	Idiopathic dilated cardiomyopathy Familial dilated cardiomyopathy
Uncommon	Valvular heart disease Alcohol-associated cardiomyopathy Inflammatory cardiomyopathy (ie, post-viral myocarditis) Peripartum cardiomyopathy Drug-induced (ie, anthracyclines, cyclophosphamide, paclitaxel) Thyroid dysfunction Chronic arrhythmia
Rare	Sarcoidosis Inherited muscle disorders (ie, muscular dystrophy, Friedreich's ataxia)

Therapy consists of measures to control congestion (ie, diuret-

cont'd page 24

from page 21

ics, fluid restriction) and disease-modifying pharmacotherapy (ACE inhibitors, beta blockers and mineralocorticoid receptor antagonists).[8] Rarely, a specific aetiology may necessitate the use of disease-modifying therapy (eg, corticosteroid therapy in myocarditis or sarcoidosis).

Heart failure with preserved ejection fraction

HFpEF as a cause of chronic dyspnoea is increasingly identified in those presenting with the clinical syndrome of heart failure with an intact left ventricular systolic function (ie, LVEF greater than 50%). The primary pathophysiology appears to be left ventricular stiffness reducing the rate of left ventricular filling in diastole, often complicated by pulmonary hypertension. About 40-50% of the heart failure population has a diagnosis of HFpEF. The key message to remember is to have a high index of suspicion for HFpEF in patients with chronic breathlessness and the comorbidities listed in the box, "HFpEF comorbidities and risk factors". This will avoid missing the diagnosis.

A diagnosis of HFpEF can be difficult to confirm because many of these patients only have symptoms on exercise. Initial cardiac investigations, such as baseline transthoracic echocardiography, may not provide a clear diagnosis. Features to look for on transthoracic echocardiography reports are summarised in table 8.

Elevation of the cardiac biomarkers BNP or NT-proBNP is also potentially useful, but this testing is currently not available in the primary care setting.[9] A BNP greater than 500ng/L indicates a high probability of heart failure.

Evidence of pharmacological therapy providing prognostic and mortality benefit in HFpEF is scant.[10] Because of the tendency for HFpEF patients to possess comorbidities, a high level of diligence should apply to assessment and management of sleep disorders, obesity, airways disease and deconditioning.

Clinical trials in HFpEF have largely failed to provide quality evidence of significant clinical benefit for agents used in HFrEF, such as ACE inhibitors, angiotensin receptor blockers, beta blockers and spironolactone. The key message is risk factor modification, including the following:

- Weight loss
- Blood pressure control (targeted to less than 130/80)
- Glycaemic control in those with diabetes
- Management of congestion with diuretics
- Management of coronary artery disease
- Management of AF
- Cardiac rehabilitation

Given the paucity of evidence for drug therapy in HFpEF, it is hoped that a number of ongoing clinical trials assessing new drug targets will provide new therapeutic strategies in this difficult-to-treat condition.

Valvular heart disease

Valvular heart disease can commonly present with chronic breathlessness.[11] It encompasses a wide range of valvular pathologies in different clinical settings. Suspicion of valvular heart disease should be raised in the presence of dyspnoea and other relevant clinical findings, such as a murmur or clinical findings suggestive of heart failure. A patient's age and epidemiological profile may provide useful information about the possibility of certain aetiologies. Degenerative or calcific valvular defects (eg, severe calcific aortic stenosis or severe functional mitral regurgitation with co-existing ischaemic heart disease) are much more common in the older population. Younger patients with valvular lesions are much more likely to have a primary valvular abnormality (eg, mitral valve prolapse or bicuspid aortic valve).

Transthoracic echocardiography is the appropriate investigation to assess the aetiology of a murmur and the severity of the associated valvular pathology. Identification of a significant valvular lesion requires assessment by a cardiologist. Refer patients where a moderate or more severe valvular lesion is identified.

Infective endocarditis is a condition that can involve any of the four heart valves and presents with dyspnoea. This can present acutely or subacutely, and patients may present with a fever and a murmur. Other associated symptoms may include night sweats, weight loss, joint pains or evidence or embolisation. Infective endocarditis carries significant morbidity and mortality and thus necessitates urgent cardiology referral.

HFpEF comorbidities and risk factors

Age
Female sex
Systemic hypertension
Diabetes mellitus
Chronic renal failure
Obstructive sleep apnoea
Obesity

Congenital heart disease

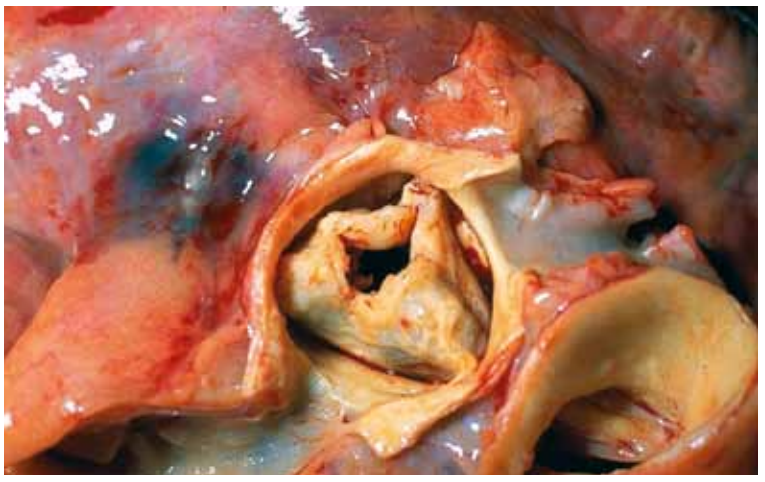
A growing population of adults have congenital heart disease that was diagnosed and treated with a surgical or percutaneous corrective procedure at a young age. These patients are often at risk of late complications from their diagnosis and may present as an adult many years later with dyspnoea, fatigue, palpitations, syncope or poor effort tolerance. Many patients have the misconception that they had a 100% curative procedure in childhood, so a significant proportion of patients (up to 50%) with congenital heart disease are lost to cardiology follow-up during the transition from childhood clinics to adulthood.[12]

Congenital heart defects, such as atrial septal defect or patent ductus arteriosus, not diagnosed in childhood may present later in life with dyspnoea. These patients also require referral to an appropriate cardiology service to formulate their management strategy, including medical therapy options, need for repair of defects, and the frequency and appropriate testing required for follow-up.

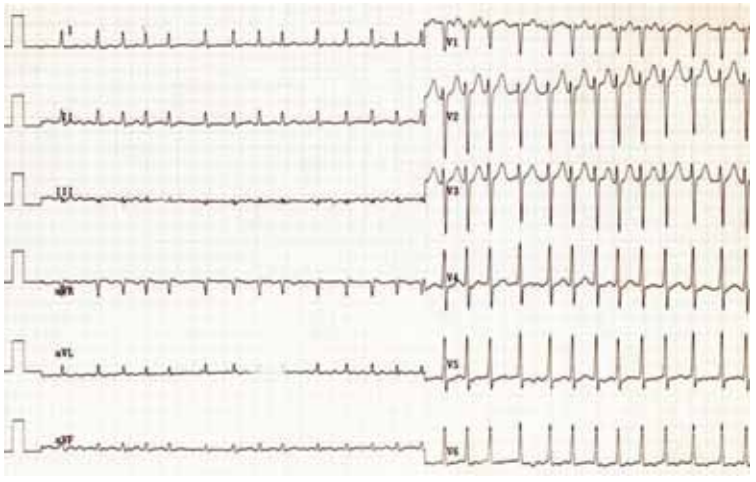
Each state has a cardiac service specialising in adult congenital heart disease. Ideally, adult patients with congenital heart disease should be referred to the nearest expert centre for review by a team with experience in this complex area.

Table 8: Echocardiography findings in suspected heart failure

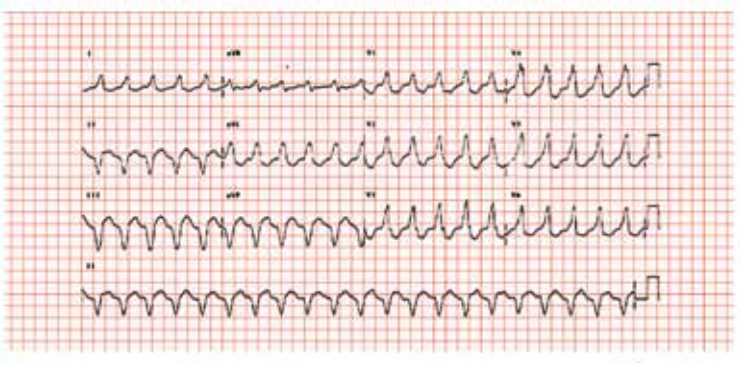
Echo feature	Report finding suspicious for heart failure
Chamber size and wall thickness	Left atrial and/or biatrial enlargement Left ventricular dilation/Hypertrophy
Left ventricular ejection fraction	Reduced
Right ventricular function	Reduced
Valvular function	Moderate or severe regurgitation/Stenosis
Pulmonary pressures	RVSP greater than 35mmHg Pulmonary artery systolic pressure greater than 35mmHg
Regional wall motion abnormalities	Abnormal (ie, hypokinesis, dyskinesis, akinesis)
Diastolic function assessment	"Suspicious for diastolic dysfunction" or "features consistent with elevated filling pressures"; may also be reported as "restrictive filling pattern" or "pseudonormal diastolic filling pattern" E/E' ratio greater than 15: E is the mitral inflow early diastolic velocity as measured on pulse wave doppler. E' is the early diastolic mitral annular velocity as measured on tissue doppler. A ratio of greater than 15 is suggestive of raised left atrial pressure, which may indicate diastolic dysfunction



Gross pathology of rheumatic heart disease: aortic stenosis. Aorta has been removed to show thickened, fused aortic valve leaflets and opened coronary arteries from above. Autopsy.
Source: http://bit.ly/1Tp2CTU CDC



Atrial fibrillation.
Source: Meddoc http://bit.ly/1BeMgHM



Ventricular tachycardia.
Source: Michael Rosengarten http://bit.ly/1BjaOPE

Arrhythmias

Arrhythmias are a less common cause of dyspnoea that may present in primary care. Arrhythmias that may present with dyspnoea include supraventricular, atrial and ventricular arrhythmias. While the most common presenting symptom of an arrhythmia is palpitations, the patient may also experience dyspnoea, fatigue, presyncope and syncope. Arrhythmias may be associated with other underlying structural heart abnormalities (eg, valvular heart disease or hypertrophic cardiomyopathy). The following is a list of the arrhythmias that may present with dyspnoea:

1. Atrial flutter
2. AF
3. Supraventricular arrhythmias (including AV-nodal re-entry tachycardia, atrioventricular re-entry tachycardia and atrial tachy-cardia)
4. Ventricular tachycardia
5. Third-degree heart block (or complete heart block)

An ECG, Holter and echocardiogram are the pertinent initial investigations. Early referral should be made for a cardiology review if these investigations show a new arrhythmia, myocardial ischaemia, second-degree heart block or abnormalities in ventricular function on echo. Urgent referral with contact to the local cardiology unit should be made if ventricular tachycardia, complete heart block or ventricular pauses are detected. Baseline screening blood tests including thyroid function tests may provide useful baseline data. Other investigations that may increase the yield of capturing an arrhythmia include seven-day event monitors and, in situations of high clinical suspicion, an implantable loop recorder.

Drug therapy depends on the aetiology but includes beta blockers; calcium-channel blockers; and antiarrhythmic agents, such as amiodarone and sotalol. However, the choice will be critically dependent on associated myocardial structure, function and electrophysiology. Pacemakers or automatic implantable cardioverter defibrillator therapy may be indicated in other settings, and electrophysiology testing (to allow diagnosis and catheter ablation of an arrhythmic focus) may be appropriate in a range of scenarios (eg, supraventricular tachycardia due to AV-nodal re-entry tachycardia).

Ischaemic heart disease

Ischaemic heart disease does not commonly present primarily with breathlessness; however, there are a number of patient groups and clinical scenarios where this may occur. Ischaemic heart disease develops when there is a mismatch between myocardial oxygen supply and consumption, secondary to an epicardial coronary stenosis from an occlusive atherosclerotic plaque, acute coronary thrombosis, occlusive coronary spasm or dissection, or microvascular dysfunction of the coronary circulation.

While acute chest pain is the classical presentation of an acute coronary syndrome, patients may present with acute dyspnoea, particularly in diabetics and in the elderly. These two groups of patients are also at risk for angina equivalent, whereby patients with myocardial ischaemia present with dyspnoea or fatigue in the absence of chest pain.

Identification or suspicion of ischaemic heart disease should prompt referral to a cardiologist for assessment of suitability for myocardial revascularisation and risk factor modification.

Other causes and contributors to breathlessness

Iron deficiency

IRON deficiency carries prognostic significance and is a therapeutic target with many conditions causing dyspnoea. Iron plays an important role in skeletal muscle metabolism, and iron repletion in those with deficiency can improve cognitive, symptomatic and exercise performance.

Iron deficiency is diagnosed when the serum ferritin is less than 100mcg/L or between 100mcg/L and 299mcg/L when the transferrin saturation is less than 20%. These values are suggestive of iron deficiency, regardless of whether anaemia identified on haemoglobin measurement is present.

A significant proportion of patients with heart failure and pulmonary hypertension are iron deficient (26-37%), and replacement of iron via IV infusion provides a safe and effective means of repletion. This provides symptomatic benefit, improved quality of life scores and improved exercise capacity.[13]

Anaemia

Anaemia contributes to dyspnoea by reducing the oxygen-carrying capacity of blood and leads to increased cardiac output. The exact mechanism of breathlessness is unclear, but increased cardiac output may alter pulmonary venous pressures and thus stimulate pulmonary stretch fibres, causing the sensation of dyspnoea. Anaemia may contribute to dyspnoea at a haemoglobin of less than 100g/L or less than 130g/L in patients with comorbid respiratory and cardiac conditions.

Obesity and deconditioning

Obesity and deconditioning can be contributors to or primary causes of dyspnoea. Both should, however, be used as a diagnosis of exclusion. Obese people report dyspnoea more frequently than age-and-smoking-matched non-obese controls.

It is hypothesised that there are two mechanisms: (i) increased basal metabolic rate and total body oxygen consumption increase as weight increases, causing increased respiratory muscle work, even at rest; and (ii) a reduction in functional residual capacity due to the effect of the abdominal contents on the position of the diaphragm. Obesity as a cause of dyspnoea would be expected in patients with a BMI greater than 35 or greater than 30 if there were other contributory comorbidities.

Deconditioning is another diagnosis of exclusion and should only be considered after the other major differentials have been thoroughly investigated. After initial investigations have come back within normal limits, the next investigation to help clarify this diagnosis is a cardiopulmonary exercise stress test and should be followed up by a respiratory physician or cardiologist. A structured exercise program should be recommended, and then after a period of 3-6 months, the cardiopulmonary exercise stress test can be repeated to see if measures, such as the peak oxygen uptake and anaerobic threshold, are within normal limits.[14]

Overlap conditions

In a patient presenting with dyspnoea, consideration must be given to multiple diagnoses contributing to symptoms. Dyspnoea may present in patients who are obese, have significant lower-limb osteoarthritis that limits their exercise capacity, are physically deconditioned from lack of physical activity or who have significant depression and/or anxiety. Other contributors to dyspnoea may include haematological (ie, anaemia, malignancy), metabolic (significant liver or renal impairment), endocrine disorders (eg, thyroid disease), neurological (eg, neuromuscular disorders), as well as underlying malignancy of various origins.

Obstructive airways disease is commonly associated with ischaemic heart disease and can also frequently be associated with HFrEF and HFpEF. Particularly with HFpEF, the delineation of the condition that is primarily responsible for dyspnoea in these patients can be clinically challenging. Clinically useful tests in this scenario include BNP/NT-proBNP and right heart catheterisation (particularly with exercise). Cardiopulmonary exercise testing may also provide some useful information in differentiating a predominantly cardiac vs respiratory cause of a patient's symptoms.

Given the potential for significant overlap in the aetiology of a patient's dyspnoea, ongoing clinical review and assessment for improvement following a specific treatment commencement is essential. Clinical review should assess whether symptoms have improved, whether further investigations are required and whether referral for management by multiple specialists is required (eg, sleep physician to manage obstructive sleep apnoea in a patient with HFpEF).

Case studies

Case study one

GARY, aged 25, presents with dyspnoea progressing over six months. He is now short of breath when walking with his mates, and has stopped working and playing sport. Gary has a history of childhood asthma.

Initial investigations show the following:

- FBC: Normal apart from polycythemic (haemoglobin = 187)
- Chest X-ray: Enlarged pulmonary arteries
- ECG: Right ventricular strain
- Spirometry and DLCO: Normal spirometry, severely reduced DLCO
- Echocardiogram: RVSP of 51mmHg and moderately dilated right ventricle, consistent with severe pulmonary hypertension

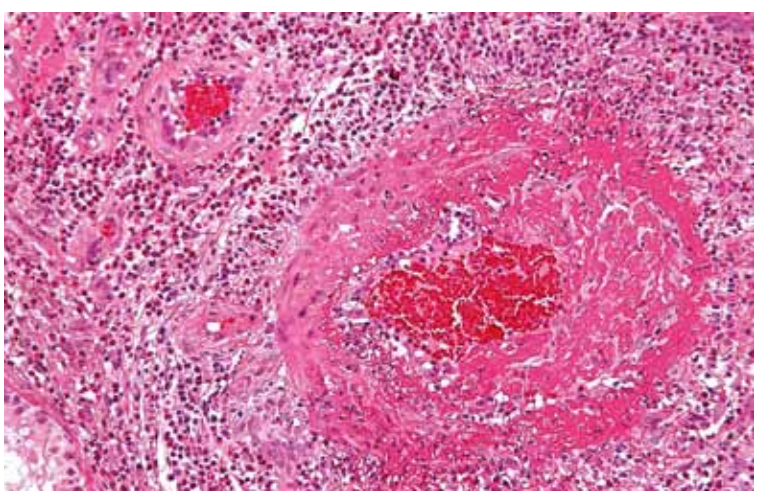
He is quickly referred to a respiratory physician, and diagnosis of idiopathic pulmonary arterial hypertension is confirmed at right heart catheterisation. After being started on appropriate treatment, Gary's breathlessness resolves, and he returns to work and to sport.

Despite the high likelihood of asthma (given his young age and past history), initial investigations led to the GP considering an alternative diagnosis. Rapid diagnosis and treatment result in prompt improvement in his symptoms.

Case study two

Janet, aged 56, presents complaining of breathlessness and wheeze over the past three months. She complains of nocturnal and early morning symptoms. Her initial investigations show the following:

- FBC: Normal haemoglobin, eosinophilia
- Chest X-ray: Patchy infiltrates in both lung fields
- ECG: Normal
- Spirometry and DLCO: Airflow limitation with significant bronchodilator response, normal DLCO.



High magnification micrograph of eosinophilic vasculitis consistent with Churg-Strauss syndrome.
Source: Nephron http://bit.ly/1FYzaul

An initial diagnosis of asthma is made, and Janet is commenced on combination ICS. On review one month later, her symptoms are no better. In light of the ongoing symptoms, an asthma action plan with a course of oral steroids is commenced and inhaler technique reviewed. At follow-up one month later, Janet's symptoms are ongoing, so she is referred to a respiratory physician.

Investigations confirm asthma plus Churg–Strauss syndrome, and she is commenced on therapy, with substantially improved symptoms, spirometry and eosinophilia. The anticipated response to therapy is not seen in this patient at review. Planned review and appropriate referral lead to appropriate therapy and clinical response.

Case study three

Simon, aged 55, presents with progressive breathlessness over a two-year period and no other symptoms. He is breathless getting dressed and showering.

Initial investigations show the following:

- FBC: Normal
- Chest X-ray: Reduced lung volumes and fibrosis
- ECG: Left ventricular hypertrophy
- Spirometry and DLCO: Not done initially
- Echocardiogram: Normal

A referral to a cardiologist is made because of the abnormal ECG, after

cont'd next page

References

1. Parshall MB, et al. An official American Thoracic Society statement: Update on the mechanisms, assessment and management of dyspnea. *American Journal of Respiratory and Critical Care Medicine* 2012; 185:435-52.
2. Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease, updated 2015: bit.ly/1pAvOWD
3. *Australian Asthma Handbook. Version 1.0*. National Asthma Council Australia, Melbourne, 2014: www.asthmahandbook.org.au
4. Travis WD, et al. An official American Thoracic Society/European Respiratory Society statement: Update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. *American Journal of Respiratory and Critical Care Medicine* 2013; 188:733-48.
5. Simonneau G, Gatzoulis MA, Adatia I, et al. Updated clinical classification of pulmonary hypertension. *Journal of the American College of Cardiology* 2013; 62:D34-41.
6. Strange G, et al. Pulmonary hypertension and breathlessness: Is it a combination we can ignore? *Internal Medicine Journal* 2014; 44:114-23.
7. Paulus WJ, et al. How to diagnose diastolic heart failure: A consensus statement on the diagnosis of heart failure with normal left ventricular ejection fraction by the Heart Failure and Echocardiography Associations of the European Society of Cardiology. *European Heart Journal 2007*; 28:2539-50.
8. Yancy CW, et al. 2013 ACCF/AHA guideline for the management of heart failure: A report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Journal of the American College of Cardiology* 2013; 62:e147-239.
9. Weber M, Hamm C. Role of B-type natriuretic peptide (BNP) and NT-proBNP in clinical routine. *Heart* 2006; 92:843-49.
10. Senni M, et al. New strategies for heart failure with preserved ejection fraction: The importance of targeted therapies for heart failure phenotypes. *European Heart Journal* 2014; 35:2797-815.
11. Vahanian A, Iung B. The new ESC/EACTS guidelines on the management of valvular heart disease. *Archives of Cardiovascular Diseases* 2012; 105:465-67.
12. Taylor J. The 2010 version of the ESC guidelines for the management of grown-up adult congenital heart disease are discussed by guidelines task force chairman H Baumgartner. *European Heart Journal* 2010; 31:2825-26.
13. Jankowska EA, et al. Iron deficiency and heart failure: Diagnostic dilemmas and therapeutic perspectives. *European Heart Journal* 2013; 34:816-29.
14. van Empel VP, Kaye DM. Integration of exercise evaluation into the algorithm for evaluation of patients with suspected heart failure with preserved ejection fraction. *International Journal of Cardiology* 2013; 168:716-22.

Further reading and online resources

Available on request from howtotreat@cirrusmedia.com.au

from previous page

which a coronary angiogram is performed. This shows moderate left circumflex and right coronary artery disease.

Simon undergoes two-vessel CABG to these lesions, unfortunately, without subsequent improvement in dyspnoea. Spirometry shows very severe restrictive deficit with significantly reduced DLCO post-CABG.

After referral to respiratory physicians, a CT chest is performed and the diagnosis of idiopathic pulmonary fibrosis is made. Simon is rapidly assessed for lung transplantation but unfortunately dies waiting for transplantation.

Silent myocardial ischaemia (ie, no chest pain) is a very unusual cause of progressive breathlessness. Other causes of breathlessness need to be considered and quickly investigated.

Case study four

Anne, aged 69, presents with dyspnoea walking to her letterbox. She has recently given up ballroom dancing as a result of symptomatic limitation. She has a past history of resistant hypertension (currently on four agents), polycystic kidney disease, osteoarthritis and one prior hospitalisation with pulmonary oedema.

On examination, Anne's BMI is 32 and she has a BP of 160/90, with mild peripheral oedema and clear lung fields.

Initial investigations show the following:

- FBC: Normal
- Chest X-ray: Mildly increased vascular markings
- ECG: Left ventricular hypertrophy
- Spirometry and DLCO: FEV_1 and forced vital capacity at lower limits of normal for age, DLCO is reduced

Anne has risk factors for diastolic dysfunction, but there is no clear diagnosis, so a CT chest and echocardiogram are requested.

The CT chest reveals minor interstitial fluid markings and enlargement of pulmonary arteries, and the echocardiogram shows normal left ventricular systolic function (LVEF ~55%) with biatrial enlargement. There is diastolic dysfunction (E/E' of 24) and moderate pulmonary hypertension (RVSP of 49mmHg), suggesting the presence of pulmonary hypertension secondary to diastolic dysfunction.

A referral is made to a local cardiologist with an interest in pulmonary hypertension and heart failure.

Following a cardiology review, Anne undergoes right heart catheterisation and a nuclear stress myocardial perfusion scan, which together confirm pulmonary hypertension secondary to diastolic dysfunction and HFpEF for medical management.

Medical therapy of oral frusemide and hydralazine are added, with improved blood pressure control. Anne commences a cardiac rehabilitation exercise program and is referred to a dietitian regarding weight-loss strategies. A sleep study is also performed to assess for underlying obstructive sleep apnoea.

Following these measures, Anne has a reasonable degree of symptomatic improvement and is able to return to ballroom dancing.

HFpEF is a common problem in older patients with multiple comorbidities. Although no specific therapies are presently available, risk factor modification and careful use of other heart failure therapies can significantly improve symptoms.

Case study five

Nigel, aged 77, presents with progressive dyspnoea over 6-8 months, with symptoms on climbing stairs, while shopping and when playing with his grandchildren.

He has a past medical history of hypertension (managed on perindopril 5mg daily) and hyperlipidaemia (on atorvastatin 20mg daily).

Significant findings on physical examination include mild bibasal crepitations on auscultation of lung fields, an ejection systolic murmur that radiates to his carotid arteries and a soft second heart sound.

Investigations demonstrate the following:

- FBC: Normal
- Chest X-ray: Increased cardiothoracic ratio and small bilateral pleural effusions
- ECG: Sinus rhythm, left ventricular hypertrophy
- Spirometry: Within normal limits, DLCO not done

Nigel is commenced on diuretic therapy as empiric treatment for heart failure while awaiting an urgent echo. He is reviewed one week later, and some mild improvement in dyspnoea is noted.

An echocardiogram reveals moderate left ventricular hypertrophy, normal systolic function and severe aortic stenosis.

The patient is referred to a cardiologist for assessment and undergoes workup for surgical aortic valve replacement.

Three months following cardiac surgery, Nigel has made an excellent functional recovery.

Initial empiric therapy while awaiting rapid further evaluation leads to an excellent outcome.

Conclusion

DYSPNOEA has a broad differential, and a directed history is essential to guide efficient and appropriate investigation. Initial investigations should include FBC, chest X-ray, ECG, spirometry and DLCO.

Specific therapies should be trialled after a provisional diagnosis has been made but keeping in mind the mantra 'treat and review' so that, if there has been inadequate treatment response, other differentials are considered and specialist referrals made.

An adequate response should include resolution of asthma symptoms by six months, reduced wheeze and dyspnoea in patients with COPD by three months, some reduction in dyspnoea within 1-2 weeks in patients with heart failure and resolution of dyspnoea as anaemia is corrected by one month.

If these goals are not met, then referral for specialist review is needed so that the diagnosis can be confirmed and up-titration of therapy performed.

In the future, there may be a role for 'breathlessness' clinics and multidisciplinary teams to expedite the workup of complex multifactorial dyspnoea.

How to Treat Quiz

Chronic breathlessnesss
— 31 July 2015

INSTRUCTIONS

Complete this quiz online and fill in the GP evaluation form to earn 2 CPD or PDP points.
We no longer accept quizzes by post or fax.

The mark required to obtain points is 80%. Please note that some questions have more than one correct answer.

GO ONLINE TO COMPLETE THE QUIZ

www.australiandoctor.com.au/education/how-to-treat

1. Which TWO are common causes of dyspnoea?
a) Asthma
b) Ischaemic heart disease
c) Anaemia
d) Type 2 diabetes

2. Which THREE are uncommon causes of dyspnoea?
a) Interstitial lung disease
b) Arrhythmia
c) Overlap syndrome
d) Valvular heart disease

3. Which THREE are red flags for early specialist referral?
a) Haemoptysis
b) Fatigue
c) Peripheral oedema
d) Syncope

4. Which TWO statements regarding COPD are correct?
a) The majority of heavy smokers develop severe COPD.
b) COPD is a common cause of breathlessness.
c) The diagnosis should be made on the basis of a history.
d) The diagnosis should be made on the basis of a history plus airflow limitation on spirometry.

5. Which THREE statements regarding the reasons for lack of improvement in asthma symptoms after one month on treatment are correct?
a) The interval is not long enough, and improvement can be expected in the first two months after initiation of therapy.
b) The diagnosis is not correct.
c) They are not taking therapy.
d) There are comorbidities that need identifying and treating.

6. Which TWO statements regarding heart failure are correct?
a) Heart failure is defined as a complex clinical syndrome characterised by structural and/or functional cardiac disorders that lead to impairment of the ability of the ventricles to fill or eject blood.
b) Dyspnoea is not the cause of breathlessness if the ejection fraction on an echo is greater than 55%.
c) Ischaemia is an uncommon cause of HFrEF.
d) Valvular heart disease is an uncommon cause of HFrEF.

7. Which TWO statements regarding valvular disease are correct?
a) Chest X-ray followed by CT scan of the chest are the appropriate investigations to assess the aetiology of a murmur and the severity of the associated valvular pathology.
b) Degenerative or calcific valvular defects are much more common in the older population.
c) Infective endocarditis can be safely managed by a GP.
d) Younger patients with valvular lesions are much more likely to have a primary valvular abnormality.

8. Which THREE statements regarding congenital heart disease are correct?
a) Patients who had a congenital defect repaired are often at risk of late complications from their diagnosis.
b) Undiagnosed atrial septal defect or patent ductus arteriosus may present later in life with dyspnoea.
c) Adult patients with congenital heart disease should be referred to the nearest expert centre for review by a team with experience in this area.
d) Up to 80% of patients with congenital heart disease are lost to cardiology follow-up during the transition from childhood clinics to adulthood.

9. Which THREE may be presenting symptoms of an arrhythmia?
a) Palpitations
b) Dyspnoea
c) Diaphoresis
d) Syncope

10. Which TWO statements regarding other causes of breathlessness are correct?
a) Iron repletion in those with deficiency can improve cognitive, symptomatic and exercise performance.
b) Obese people report dyspnoea as frequently as age-and-smoking-matched non-obese controls.
c) Obstructive airways disease is rarely associated with ischaemic heart disease.
d) Dyspnoea may be present in those with significant lower-limb osteoarthritis that limits their exercise capacity.

CPD QUIZ UPDATE

The RACGP requires that a brief GP evaluation form be completed with every quiz to obtain category 2 CPD or PDP points for the 2014-16 triennium. You can complete this online along with the quiz at **www.australiandoctor.com.au.** Because this is a requirement, we are no longer able to accept the quiz by post or fax. However, we have included the quiz questions here for those who like to prepare the answers before completing the quiz online.

Australian Doctor Education

HOW TO TREAT Editor: **Dr Claire Berman**
Email: **claire.berman@cirrusmedia.com.au**

NEXT WEEK

Next week's HTT uses case studies and expert commentary to highlight the issues facing rural health practitioners and their patients in terms of access to healthcare. The authors are **Associate Professor Mark Arnold**, Associate Dean and Head of the School of Rural Health, Sydney Medical School, University of Sydney and Professor David Tiller AO, visiting professor of medicine, School of Rural Health, University of Sydney.