COPD has a number of diagnostic challenges. Here, the authors consider the process and look at the issues GPs might face.

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality in the UK and worldwide. It is one of the commonest respiratory conditions seen in primary care and is the second commonest cause of emergency hospital admissions in the UK. It is estimated that 4.7% of patients in a general practice will have clinically significant COPD. Currently there are 900,000 patients in the UK diagnosed, yet this may be the tip of the iceberg. It is likely a further two million people may have undiagnosed COPD in the UK. The costs to the NHS are substantial with estimated direct costs of over £800 million annually. With many patients still of working age, the cost to the economy is also great with over 24 million working days lost to the disease. The burden of symptoms and exacerbations on patients has a significant impact on quality of life and there were nearly 24,000 attributable deaths in 2010, making it the fourth biggest cause of years of life lost in the UK.

Patients at risk of COPD
The majority of patients with COPD are, or have been, smokers. It is estimated that tobacco exposure accounts for 80% of COPD, but other important causes include a patient’s occupation and exposure to indoor pollution from the use of biomass fuels such as wood and plant materials. Despite this, only 25% of smokers will develop COPD and it is not clear how to identify those most at risk. Studies of families and genetic linkage suggest that there is a predisposition to COPD in some people. Between 1 and 5% of patients diagnosed with COPD have a deficiency of the serum glycoprotein alpha-1 antitrypsin that results in an increased risk of developing COPD at an early age. Alpha-1 antitrypsin is a neutrophil elastase inhibitor. Deficiency of this protein results in increased damage to lung tissue as a result of inflammation induced by smoking. In severe deficiency, chronic liver disease may also occur. Consideration for testing should be given in patients who are diagnosed at a young age (<45 years), those with no clear risk factor, concomitant liver disease or a family history of alpha-1 antitrypsin deficiency.

Diagnosing COPD
There is no single diagnostic test for COPD and therefore diagnosis relies on clinical history, exposure to known risk factors and spirometric findings. COPD should be considered in any patient presenting with breathlessness, wheeze, cough or sputum production, particularly if they have appropriate risk factors.

Clinical features
The onset of symptoms is insidious and on reflection, patients may have been symptomatic for many years before diagnosis. Examination of past records often shows previous episodes of “winter bronchitis” or
chest infections. There is usually a steady decline in symptoms over time as lung function worsens. Breathlessness is usually the major symptom and tends to be persistent and progressive. It may be associated with wheeze or chest tightness. Cough may initially be intermittent or just associated with exacerbations and may variably be associated with sputum production. Although COPD symptoms are typically persistent, they may be punctuated by acute exacerbations where symptoms temporarily worsen and then recover, although not always back to baseline levels. Physical examination signs may be few and far between in early disease although complications and extrapulmonary manifestations, such as muscle wasting may occur early.

Red flag symptoms may indicate severe disease, complications or another underlying disease. These should prompt urgent investigation and referral as necessary. Haemoptysis may occur during respiratory infections, however COPD patients are at a higher risk of lung cancer and an urgent referral should be sought. Likewise marked weight loss or rapid decline may suggest an underlying malignancy and should be investigated. A list of symptoms requiring further consideration is listed in Table 1.

Factors to consider when diagnosing COPD

Alternative diagnoses
For the majority of patients, the diagnosis of COPD will be clear. Asthma is the main differential diagnosis and there are several features that may help distinguish between the two. Typically asthmatic patients have episodic breathlessness and cough, with a more marked diurnal variation and variability of symptoms between episodes. They are usually younger and may or may not have a smoking history of >10 pack years. There may be other features of atopy present such as eczema, allergic rhinitis and nasal polyps. They often demonstrate reversible airflow obstruction in response to inhaled bronchodilators. However, some patients with chronic asthma develop fixed airflow obstruction and persistent symptoms. In this case there is usually a clear history of poorly controlled asthma for many years before. In addition the two diseases may co-exist and some COPD patients will have an element of reversibility in airflow obstruction.

Bronchiectasis is a condition where airways become thickened, inflamed and enlarged. The most prominent symptom is cough productive of large volumes of purulent sputum. Patients often have repeated infections and bacterial colonisation of sputum. It may be confused with COPD in the early stages but it can also co-exist with COPD. Further investigation in secondary care is usually required to identify the cause, including sputum analysis, immune system function and computed tomography of the chest.

Complications of COPD are common in the late stages of the disease and should be referred to secondary care for further investigation and management.

Co-morbid conditions and complications
COPD is a multisystem disease and has effects beyond the lungs. Symptoms of anxiety and depression are common in COPD, affecting approximately 40% of patients, and should be sought when seeing patients. Weight loss and muscle wasting are also common in advanced disease and should prompt consideration of dietetic and physiotherapy input. There is an increased risk of cardiovascular disease which is in part related to exposure to smoking but also the systemic inflammatory effects of COPD itself.

Complications of COPD are common in the late stages of the disease and should be referred to secondary care for further investigation and management. Pulmonary hypertension may manifest itself as cor pulmonale (right sided heart failure). Peripheral limb swelling, raised jugular venous pressure and cyanosis should all raise the suspicion of this and should be investigated by echocardiography initially. Respiratory failure occurs when the blood oxygen levels are below 8kPa and is more likely in severe disease or patients with evidence of cyanosis. Type II respiratory failure refers to hypoxaemia and hypercapnoea which may manifest itself as excessive drowsiness and headaches.

Grading severity
There are several strategies for grading severity of COPD. The most widespread method is based on the severity of airflow obstruction based on the percentage predicted forced expiratory volume in one second (FEV₁) (Table 2). Patients with severe or very severe disease are generally more symptomatic and at risk of complications. They should be considered for secondary care referral where treatments including oxygen, lung volume reduction or palliative care can be considered. However, FEV₁ does not necessarily correlate well with a patient’s symptoms or survival. Assessments of breathlessness using the modified
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Precautions: Should not be used to treat asthma or for relief of acute episodes of bronchospasm, i.e. rescue therapy. May cause paradoxical bronchospasm. Re-evaluation of the treatment regimen should be conducted if there is a change in COPD intensity. Use with caution in patients with a myocardial infarction during the previous 6 months, unstable angina, newly diagnosed arrhythmia within the previous 3 months, or hospitalisation within the previous 12 months for heart failure functional classes III and IV as per the “New York Heart Association”.

Consistent with its anticholinergic activity, dry mouth has been observed and may in the long term be associated with dental caries. Also, use with caution in patients with symptomatic prostatic hyperplasia or bladder-neck obstruction or with narrow-angle glaucoma. Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine. Interactions: Although co-administration with other anticholinergic-containing medicinal products is not recommended and has not been studied, no clinical evidence of interactions when taking the therapeutic dose has been observed.

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Medical Research Council grading (Table 3) and exercise tolerance using a six-minute walk test are helpful. Combined with BMI and percent predicted FEV₁, they contribute to the BODE index, which enables an estimation of survival (BMI, Degree of Obstruction, Dyspnoea, Exercise tolerance).

**Investigations in primary care**

**Spirometry**

The spirometric criterion for diagnosing airflow obstruction is a ratio of FEV₁ to forced vital capacity (FVC) of <0.70. Table 2 lists the spirometric criteria for diagnosing and grading COPD. The patient’s age, height and sex is required to calculate the percentage predicted, which is usually calculated automatically by the spirometer. It is important to note that in older patients an FEV₁/FVC ratio of less than 0.7 may be normal. COPD should only be diagnosed where there are also symptoms and risk factors present. In COPD, spirometry should be measured following administration of a bronchodilator. Formal reversibility testing is not required unless there is a suspicion of asthma. Basic spirometry can be undertaken by any healthcare worker trained to do so and should comply with ATS/ERS guidance. Equipment should be regularly calibrated and serviced according to the manufacturer’s guidelines. Provided there are no contraindications to undertaking spirometry (Table 4), all patients should perform reproducible expiratory manoeuvres to maximal ability that allows an accurate FEV₁ and FVC to be obtained. While the patient may be seated or standing, it is important to record which position they are in and all subsequent attempts repeated in the same way. It is recommended that patients wear a nose clip to occlude the nostrils. Reasons for failure in this case are incomplete effort, double blows and failure to exhale for as long as needed to accurately ascertain an FVC. The time-volume curve should plateau for at least one second before the test is terminated. In patients with very severe COPD, forced expiratory times may exceed 30 seconds and hence encouragement to continue the blow until they feel they have exhaled fully. The flow volume loop should be examined for any evidence of artefact. Figure 2 demonstrates a normal and an obstructive flow-volume loop. Figure 3 demonstrates a variety of common problems that can be identified by examination of the flow-volume loop. It is important to obtain three repeatable results and the ATS/ERS guidelines set out the criteria for acceptability.

**Pulse oximetry**

Pulse oximetry cannot be used in the diagnosis of COPD. It is useful in obtaining a baseline measurement in stable patients in order to determine those that may require oxygen therapy and for future comparison during exacerbations. The use of pulse oximetry should be undertaken to assess the need for referral.

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**TABLE 3: MRC DYSPNOEA SCALE**

<table>
<thead>
<tr>
<th>MRC Breathlessness score</th>
<th>Degree of breathlessness related to activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not troubled by breathlessness except during strenuous exercise</td>
</tr>
<tr>
<td>2</td>
<td>Short of breath hurrying on the level or walking up a slight incline</td>
</tr>
<tr>
<td>3</td>
<td>Walks slower than most people on the level and stops after one mile or at 15 minutes</td>
</tr>
<tr>
<td>4</td>
<td>Stops for breath after 100 yards or a few minutes on level ground</td>
</tr>
<tr>
<td>5</td>
<td>Too breathless to leave the house, or breathless when dressing</td>
</tr>
</tbody>
</table>

**TABLE 4: INDICATIONS AND CONTRAINDICATIONS TO SPIROMETRY**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive smoking history</td>
<td>Pneumothorax</td>
</tr>
<tr>
<td>Dyspnoea, wheeze, cough</td>
<td>Haemoptysis of unknown origin</td>
</tr>
<tr>
<td>Increasing age</td>
<td>Unstable cardiovascular status (within 1 month of MI or PE)</td>
</tr>
<tr>
<td>Breathless on exertion</td>
<td>Uncontrolled hypertension</td>
</tr>
<tr>
<td>History of recurrent “chest infection”</td>
<td>History of haemorrhagic cerebrovascular accident</td>
</tr>
<tr>
<td>Monitoring patients with established diagnosis</td>
<td>Recent thoracic, abdominal or eye surgery (or current evidence if raised intraocular pressure or unstable aneurysm)</td>
</tr>
</tbody>
</table>
for oxygen therapy in cases where oxygen saturations are ≤ 92% or there is evidence of cyanosis, cor pulmonale and in all patients with an FEV₁ < 50% predicted.

**Imaging**

NICE guidance recommends a chest radiograph following a diagnosis of COPD. They aid little in the diagnosis of COPD but may detect other abnormalities which change treatment practice in 14% of cases. It is more useful where there is diagnostic uncertainty or suspicion of complications. However it is not sufficiently sensitive or specific to exclude other diagnoses and therefore referral to secondary care and consideration of computed tomography of the chest may be required.

**Management in primary care**

**Smoking cessation**

The first goal of treatment should be smoking cessation. This is the only intervention that has been shown to slow the decline in lung function and is the single most effective and cost-effective treatment for COPD. Smoking cessation is most effective when counselling is combined with pharmacotherapy. Quit rates can be increased by up to 70%, although the majority of patients will not quit at the first attempt. Pharmacotherapy options include nicotine replacement, bupropion or varenicline, and the choice should take into account patient preference, previous quit attempts and presence of co-morbidities including cardiovascular disease and depression.

**Pharmacological management**

The mainstay involves the use of inhaler therapies. Short acting beta-agonists (SABA) or short acting antimuscarinic antagonists (SAMA) are the initial empirical treatment for the relief of breathlessness and exercise limitation. The progression from short acting preparations should be made in stages if symptoms are uncontrolled or patients continue to suffer exacerbations. In those patients with an FEV₁ > 50% predicted choose a long acting beta-agonist (LABA) or a long acting muscarinic antagonist (LAMA) and if still breathless after a trial of treatment move to a LABA with an inhaled corticosteroid (ICS) combination alone. The addition of a LAMA can then be made on the basis of ongoing symptom burden. Where the FEV₁ < 50% predicted a trial of LABA+ICS or LAMA should be initiated first, with ongoing symptoms the therapy that was not given first would then be added in. Combination inhaler therapy remains the most widely used and provides the greatest symptomatic relief and a reduction in exacerbation frequency. The suitability of the device to deliver treatment is crucial.
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should be assessed as hand-held inhalers are not well used by all. Consideration in these groups should be given to spacer devices and nebulisers.  

**Pulmonary rehabilitation** (PR) is an extremely successful intervention to improve exercise capacity, muscle strength and quality of life. Pulmonary rehabilitation (PR) is an extremely successful intervention to improve exercise capacity, muscle strength and quality of life. 

PR programmes should be locally available and tailored to the individual patient. The programme is designed to be progressive in nature, including both aerobic and resistive exercise accompanied by a structured educational programme. COPD patients with self-reported exercise limitation (MRC dyspnoea score 3-5) should be considered for enrolment, and those with a lesser degree of limitation (MRC dyspnoea score 2) but considered functionally limited may also gain significant benefit. Evidence also exists for the value of early pulmonary rehabilitation following hospitalisation for an acute exacerbation. PR programmes should be of a minimum duration of six weeks, and include a minimum of two supervised exercise sessions and one unsupervised but prescribed session weekly. Following completion of the course patients should be provided with an individual written plan to encourage ongoing maintenance. For patients showing evidence of loss of functional status, particularly if more than one year has elapsed from attendance, there is recognised value in considering repeat PR. 

**Oxygen therapy** Hypoxaemia is a frequent complication of COPD and oxygen therapy has been shown to confer a survival benefit in appropriately selected hypoxaemic patients when given for a minimum period of 15 hours per day. Assessment should include arterial or capillary blood gas sampling on at least two occasions, separated by a minimum of three weeks, and those with a PaO2 <7.3kPa (or <8kPa in the presence of nocturnal hypoxaemia, secondary polycythaemia, peripheral oedema or pulmonary hypertension) may qualify for the provision of long-term oxygen therapy. Patients may frequently demonstrate worsening hypoxaemia during an intercurrent exacerbation and thus should be formally assessed after at least five weeks of clinical stability to avoid inappropriate long-term prescribing. Ambulatory oxygen therapy refers to the provision of oxygen delivered when the patient is engaged in physical activity. This is clearly important for patients who require oxygen at rest. However, some patients who do not require long-term oxygen therapy may experience significant exertional desaturation (of the order greater than 4% drop in arterial saturation to ≤90%) that limits physical activity. This does not indicate a prerequisite for ambulatory oxygen therapy but patients demonstrating both improved exercise capacity and quality of life with oxygen usage following a formal assessment should engage in a discussion about its acceptance and usage. Pulmonary rehabilitation provides an ideal opportunity for this exchange. It is important to note that oxygen is not an effective therapy for dyspnoea in the absence of hypoxaemia, thus the use of short-term oxygen therapy should be discouraged in this case and more effective therapies pursued. 

**Guidelines and referral criteria** NICE guidance on COPD was updated in 2010. It provides a comprehensive overview of diagnosis and management of COPD. Patients with severe disease (FEV1 <50%), an uncertain diagnosis, atypical features or suspicion of complications and co-existing pathologies should be referred to secondary care for evaluation. In addition, those patients where the degree of breathlessness seems out of proportion to spirometric abnormalities or there are recurrent exacerbations should also be referred. 

**References** For full references please visit www.bjfm.co.uk