The term chronic obstructive pulmonary disease (COPD) was first coined by William Briscoe in 1965.1 It is an umbrella term used to describe a group of airways diseases that are not fully reversible, are predominantly caused by smoking and affect patients over 35 years of age.2 COPD is a progressive, life-threatening condition that affects millions of people within the UK and worldwide. An understanding of the risk factors, symptoms and diagnostic measures are required to be able to manage this progressive disease effectively. Details of the pathophysiology of COPD can be found in Box 1 (p384).

COPD is often undiagnosed — it is estimated that only 900,000 out of three million people who have COPD in England have been diagnosed.3 Globally, COPD is currently the fourth leading cause of death and the World Health Organization estimates that, by 2030, COPD will become the third leading cause of death.4,5 In England and Wales, one person dies every 20 minutes as a result of COPD. It accounts for 1.4 million GP consultations and over 30,000 deaths in the UK each year. COPD is the second most common cause of emergency admissions to hospital and the fifth largest cause of readmissions into hospital.4 COPD results in over one million hospital bed days in England.4 In the UK, direct care costs associated with COPD amount to £3bn per year, and the overall cost is £6.6bn annually.6

Risk factors
The risk factors for COPD are not completely understood — epidemiological studies have identified associations rather than cause and effect relationships.

It is hypothesised that the risk of developing COPD is due to an interaction between “host factors” (such as genetics and gender) and “environmental factors” (such as smoking and occupational exposure).2,7

Smoking Tobacco smoke has been implicated in the development of chronic bronchitis and emphysema since the 1960s.8 Tobacco smoke has numerous pulmonary effects, which include the release of destructive proteolytic enzymes from inflammatory cells in the lung, oxidative stress and inactivation of α1-antitrypsin (see Box 1, p384).

Although it has been estimated that 15–20% of smokers develop COPD, recent evidence suggests that the actual proportion is 50%.9 The risk of COPD developing in smokers is dose related and is affected by the age at which smoking started and the total pack-years smoked:

Chronic obstructive pulmonary disease is an incurable condition affecting millions of people worldwide.
Environmental exposure to tobacco smoke is also associated with reduced lung function. Maternal smoking has been shown to affect lung development in utero and is linked with reduced lung function among offspring in adulthood.\(^{10,11}\) Passive smoking is also associated with reduced lung function, although this association is not as strong. The effect of smoking and smoking cessation on lung function is illustrated in Figure 1.

**Occupational dusts and chemicals** Occupational dusts and chemicals have been recognised as co-factors for developing COPD and there is a relationship between the degree of lung impairment and the intensity and duration of exposure. Examples of implicated substances include organic and inorganic dusts, chemicals and fumes.\(^{12,13}\) A survey involving almost 10,000 adult patients showed that occupational exposure caused 19.2% of COPD cases, with 31.1% having never smoked.\(^{14}\) This is consistent with American Thoracic Society estimates of occupational exposure accounting for 10–20% of all COPD cases.\(^{2,19}\)

**Indoor air pollution** The burning of open fires of wood, animal dung, coal and agricultural residues (eg, for cooking and heating) can lead to high levels of indoor air pollution in poorly ventilated dwellings. The global population at risk of this form of COPD is three billion, with women in parts of the Middle East, Africa and Asia at particular risk.\(^{15}\) This COPD risk factor currently causes 10–20% of all cases worldwide and results in two million deaths each year.\(^{17}\)

**Genetics** The best documented “host factor” for the development of COPD is the recessive, hereditary deficiency of \(\alpha\)-1-antitrypsin (Box 1, p384). Predominantly affecting people of northern European origin, \(\alpha\)-1-antitrypsin deficiency results in the early and accelerated development of panlobular emphysema in smokers and non-smokers, with the risk in smokers increasing exponentially.\(^{16}\) Worldwide, \(\alpha\)-1-antitrypsin deficiency accounts for only a small number COPD cases.\(^{1,14}\)

**Other risk factors** Other risk factors for the development of COPD include:

- Lung growth and development: a meta-analysis has shown a positive correlation between birth weight and forced expiratory volume in one second (FEV\(_1\)) (see “Diagnosis” below) in adulthood.\(^{18}\)
- Gender: the role of gender in the development of COPD is unclear, although some studies have suggested that women are more susceptible to the effects of tobacco smoke than men. Previous studies had shown a greater prevalence and mortality among men than women; however more recent studies show that in developed countries the prevalence is now similar, probably as a result of women living longer and their changing patterns of smoking.\(^{19}\)

**Symptoms**

COPD is characterised primarily by the presence of breathlessness, chronic cough and sputum production. However, the early stages of COPD are often asymptomatic and it is not until patients experience significant limitation that they seek medical advice.

**Breathlessness** For patients, breathlessness (dyspnoea) is often the most concerning early symptom of COPD. It is persistent and progressive, and is usually worse with physical exertion. As the disease progresses, breathlessness becomes more problematic, even with minimal exertion or at rest.

The Medical Research Council dyspnoea scale (see Box 2, p384), can be used to establish the extent of a patient’s exertional breathlessness and can help to predict mortality in COPD.\(^{20}\) In addition to defining the degree of dyspnoea-related disability associated with COPD, the MRC dyspnoea scale can also be used to determine at

\[
\text{Total pack years} = \frac{\text{Number of cigarettes smoked per day} \times \text{number of years smoked}}{20}
\]
DEGREE OF BREATHLESSNESS RELATED TO ACTIVITIES

Too breathless to leave the house, or breathless when stops for breath after walking about 100 metres or after a walk slower than contemporaries on level ground because not troubled by breathlessness except on strenuous exercise. Short of breath when hurrying or walking up a slight hill.

Box 1: COPD pathophysiology

Chronic obstructive pulmonary disease (COPD) is an umbrella term for a group of chronic respiratory diseases, including emphysema and chronic bronchitis.

Emphysema. Emphysema is a pathological process that involves the progressive and destructive enlargement of the bronchioles, alveolar ducts and alveolar sacs. This leads to loss of surfaces available for gas exchange and a loss of elastic recoil in the small airways. Elastic recoil is essential for maintaining the force of expiration — its loss in emphysema can result in airways collapse, especially during expiration, which in turn leads to increased thoracic gas volume and hyperinflation in the lungs.

There are two main types of emphysema: centrilobular and panacinar. Centrilobular emphysema is the most common form, characterised by the destruction of bronchioles, alveolar ducts and alveoli, and is more common in the upper lobes of lungs in cigarette smokers and coal miners. Panacinar emphysema is less common and is associated with deficiency of α1-antitrypsin — a protease inhibitor that protects against lung damage. It is thought that the presence of oestrogen, which stimulates the synthesis of protease inhibitors such as α1-antitrypsin, confers protection in women.

Chronic bronchitis. Chronic bronchitis is defined as the presence of cough and sputum production for at least three months in each of two consecutive years. It is an inflammatory process that occurs in the bronchi in response to inhaled irritants, usually due to cigarette smoking. This results in the accumulation and hypersecretion of mucous-secreting glands in the bronchial tree. Viral and bacterial infections can cause worsening of symptoms and exacerbations. Common bacterial infections can be caused by pathogens such as Streptococcus pneumoniae, Moraxella catarrhalis and Haemophilus influenzae.

In advanced COPD, the impairment of gas diffusion can lead to hypoxaemia (low oxygen), hypercapnia (increased carbon dioxide) and pulmonary hypertension, with resultant vascular remodelling, increased right-ventricular pressure and subsequent right-ventricular failure, known as cor pulmonale. Peripheral oedema in cor pulmonale is mediated by the physiological changes that occur following hypoxaemia and hypercapnia. These include activation of the renin-angiotensin system, salt and water retention and a reduction in renal blood flow.

Although patients with emphysema experience greater dyspnoea than patients with bronchitis, they are better able to preserve gas exchange (because, unlike bronchitis, the ventilation-to-perfusion ratio is maintained) and thus are less likely to develop cor pulmonale and polycythaemia (increased red blood cells) at an early stage.

Box 2: Medical Research Council dyspnoea scale27

<table>
<thead>
<tr>
<th>GRADE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Not troubled by breathlessness except on strenuous exercise</td>
</tr>
<tr>
<td>2</td>
<td>Short of breath when hurrying or walking up a slight hill</td>
</tr>
<tr>
<td>3</td>
<td>Walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath when walking at own pace</td>
</tr>
<tr>
<td>4</td>
<td>Stops for breath after walking about 100 metres or after a few minutes on level ground</td>
</tr>
<tr>
<td>5</td>
<td>Too breathless to leave the house, or breathless when dressing or undressing</td>
</tr>
</tbody>
</table>

which stage pulmonary rehabilitation would be cost-effective and indicated (see p393 of accompanying article). Pulmonary rehabilitation is indicated for patients admitted to hospital following a COPD exacerbation or for patients with an MRC score of 3 or higher.

Chronic cough. Chronic cough is one of the earliest symptoms of COPD. Cough can be productive or unproductive and initially occurs intermittently, becoming more frequent as the disease progresses. Unlike breathlessness, chronic cough usually occurs at the earliest stage of COPD and is often discounted by patients as a sign of ageing or lack of physical fitness.

Sputum. Regular production of sputum in three or more months over two consecutive years defines the presence of chronic bronchitis. However, sputum purulence in COPD patients varies considerably (in terms of quantity and colour, which may depend on the underlying causes of COPD) and is difficult to evaluate accurately due to differing patient habits with sputum (some patients will swallow rather than expectorate). A change in colour or volume of sputum may signify the early signs of an exacerbation of COPD.

Other symptoms. Wheeze and chest tightness can occur at any stage of COPD, but usually occurs in severe COPD. More frequent “winter colds” or “winter bronchitis” and fatigue are also common among those with COPD.

Diagnosis. A diagnosis of COPD should be considered in patients over the age of 35 years who have a risk factor such as smoking and who display one or more of the symptoms described above. The diagnosis should take into account the patient's medical history and previous exposure to risk factors for the disease. Airflow obstruction can be measured accurately using spirometry, and this should be performed at the time of diagnosis, with specific reference to the following measures: FEV1: volume of air that the patient is able to expel in the first second (expressed in litres and as a percentage of the predicted value) Forced vital capacity (FVC): total volume of air that the patient can forcibly exhale in one breath (expressed in litres and as a percentage of the predicted value) FEV1/FVC: the ratio of FEV1 to FVC

A post-bronchodilator FEV1/FVC ratio <0.7 confirms the presence of COPD. If the FEV1 is ≥80% of predicted, a diagnosis of COPD should only be made in the presence of other respiratory symptoms such as breathlessness or chronic cough.
Similarities with asthma  COPD and asthma may have some overlapping symptoms but can be distinguished based on the patient’s history, exposure to risk factors and spirometry results. Box 3 shows the clinical features differentiating COPD and asthma. It is worth noting that, in patients with chronic asthma, the distinction with COPD is sometimes difficult to make and it is assumed that asthma and COPD can co-exist in such patients.

Reversibility testing  If COPD diagnosis is in doubt, reversibility testing can help to distinguish the presence of COPD or another underlying respiratory disease such as asthma. Since COPD is characterised by airflow obstruction that is not fully reversible, reversibility testing using an inhaled bronchodilator (eg, salbutamol) can be used to distinguish between COPD and asthma. Minor degrees of reversibility have no prognostic value, but a marked post-bronchodilator response greater than 400ml suggests the presence of asthma.

Severity  The severity of COPD can be classified according to the patient’s FEV1 compared with predicted values (see below). However, it should be borne in mind that severity based on FEV1 may not always correspond to the degree of symptom control and exacerbation rates.

Disease severity is an indicator of prognosis. The five-year survival of patients with mild COPD is 78% for men and 72% for women. This reduces to 30% and 24%, respectively, for patients with severe disease.

Unsurprisingly, the economic impact of COPD also correlates with severity, with the annual cost for a patient with mild COPD estimated at £120 compared with over £3,000 for a patient with severe COPD.

According to the National Institute for Health and Clinical Excellence and the Global Initiative for Chronic Obstructive Lung Disease, patients with a post-bronchodilator FEV1/FVC ratio below 0.7 can be classified as follows:

- FEV1 ≥80%: stage 1 (mild)
- FEV1 50–79%: stage 2 (moderate)
- FEV1 30–49%: stage 3 (severe)
- FEV1 <30%: stage 4 (very severe)

Some studies have found that an index known as “BODE” is a better predictor of exacerbations, hospital admission and mortality than FEV1. BODE is an acronym for:

- Body mass index
- Obstruction (degree of airway obstruction): measured as a percentage of predicted FEV1
- Dyspnoea: measured using a modified MRC dyspnoea scale
- Exercise tolerance: measured with a six-minute walk test

The BODE index is a 10-point scoring system, with a higher score corresponding with a higher likelihood for poor patient outcomes. (Box 4 shows how points on the BODE index are allocated.) The updated NICE guidelines suggest that the BODE index should be used to assess the prognosis of all patients. The BODE index can be modified to a “BOD” index if there is difficulty carrying out an exercise tolerance test.

The severity of COPD will also guide treatment (see accompanying article, p390).
References


