

COPD

— the disease and non-drug treatment

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Chronic obstructive pulmonary disease affects 900,000 people in the UK and is the only leading cause of death that is increasing in prevalence. This article outlines the epidemiology, pathophysiology, clinical features, natural history and non-drug treatment of the disease

Conceptual image of two halves of a man's face, representing the effects of smoking

Chronic obstructive pulmonary disease (COPD) is a chronic disease of the lungs characterised by expiratory airflow obstruction. Most commonly although not exclusively affecting smokers, COPD causes a progressive decline in lung function leading to increasing breathlessness, particularly on exertion. Individuals with COPD are frequently unable to perform activities of daily living because of exercise limitation and COPD is a common cause of disability among older people in this country and around the world.¹ In addition, the lives of many patients with COPD are regularly punctuated with exacerbations of their disease due to respiratory infections.

COPD is a major burden for patients, their carers and the wider community and presents a significant challenge for the pri-

mary care physician and respiratory specialist. With large numbers of smokers now emerging in developing countries as well, COPD is becoming a global problem impacting on health care systems worldwide. Although the impairment of lung function in COPD is irreversible, the situation is not all "doom and gloom" because drug therapies and non-pharmacological management, provided by a multidisciplinary team, benefit many patients. Current management strategies for COPD focus on controlling symptoms and achieving an optimal quality of life in this chronic disease.

Awareness of COPD as an important chronic disease in the developed and developing world has recently been increased by the publication of international guidelines for its diagnosis and management — "The global initiative for chronic obstructive lung disease (GOLD)".² UK guidelines for the management of COPD have also been published by the National Institute for Clinical Excellence (NICE)³. In this article we will describe the diagnosis, pathophysiology and clinical features of COPD and outline therapeutic approaches to its management.

— EPIDEMIOLOGY

The pathological changes of emphysema were first observed by Laennec in the 18th century⁴ but COPD was recognised as a clinical entity with the rise of cigarette smoking in the latter half of the 20th century. Approximately 900,000 people suffer with COPD in the UK, most presenting between the ages of 50 and 80. COPD is the leading cause of respiratory disability in the UK among older people.⁵ The prevalence of COPD is increasing in the developed and developing world in line with increases in tobacco consumption.¹ It is the fourth leading cause of death in the US, exceeded only by heart attacks, cancers and stroke.⁶ COPD is the only leading cause of death that is increasing in prevalence.¹

In the UK approximately 30,000 deaths per year are a result of COPD.³ Moreover, morbidity and disability from COPD is considerable. COPD is predominantly a disease of the elderly and it contributes to frailty and dependence in this population. Admissions for COPD occupy around one million bed days in England and Wales each year and overall costs to the NHS have been estimated at almost £1bn annually.

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Disability from COPD has wider economic costs with around 21 million working days lost to the disease in the UK annually.⁷

Most patients are smokers or ex-smokers. Other less common risk factors include inherited alpha-1-antitrypsin deficiency or occupational exposures such as coal dust. A link with socioeconomic status has been suggested but it is still not clear if this is a result of an increased exposure to risk factors.⁸

— PATHOPHYSIOLOGY OF COPD

COPD is characterised by progressive airflow obstruction; indeed this is a universal and defining feature of the disease. The NICE definition of COPD is given in Panel 1. However, COPD is an umbrella term encompassing a number of disease entities. These are distinct in their underlying pathophysiology but share a common link with cigarette smoking and cause airflow obstruction. Emphysema and chronic bronchitis are the most recognised subtypes of COPD. These usually co-exist in an individual but their contribution varies widely among patients. The airflow obstruction in COPD is not fully reversible but some patients do show reversibility to bronchodilator drugs or corticosteroids. In this respect there is some overlap with chronic asthma, where airflow obstruction may also become fixed. COPD is therefore a heterogeneous disease in its pathology, physiology and clinical manifestations. COPD develops in around 15 per cent of smokers and susceptibility to the disease is probably genetically determined.

Spirometry The measurement of airflow obstruction is necessary for the diagnosis of COPD and spirometry is a simple, non-invasive and reproducible technique. Subjects are asked to perform a forced expiratory manoeuvre (this involves blowing out as hard and fast possible into a sealed tube) and the volume of expired air is plotted against time. In COPD there is limitation to the flow of air during expiration and therefore the volume of air expired in the first second (the FEV₁) is reduced. The change in FEV₁ in response to bronchodilator drugs or steroids has been used to characterise airflow obstruction in COPD but this provides little additional diagnostic information and does not predict an individual's clinical response to therapy. These

measurements are therefore not recommended for routine clinical practice.

Emphysema Emphysema is a pathological process in which there is destruction of the terminal bronchioles and distal airspaces. This leads to loss of the alveolar surface area and therefore the impairment of gas exchange. The process often progresses to the development of larger redundant airspaces within the lung called bullae. Emphysema causes the destruction of the supporting tissue surrounding the small airways, which therefore tend to close during expiration when the pressure outside the airways rises. This results in airflow obstruction particularly affecting the small airways. The “purse lip” breathing often seen in patients with COPD is a protective manoeuvre that increases the pressure within the airways. This causes a reduction or a delay in the closure of these airways. In addition, the loss of elastic tissue in the lung causes the lungs to hyperinflate because the lungs are unable to resist the natural tendency of the rib cage to expand outwards. Hyperinflation is a particularly important cause of breathlessness in COPD because the diaphragm and other respiratory muscles have to work much harder to ventilate the lungs. Bronchodilator therapy may provide symptomatic relief for patients with emphysema by reducing hyperinflation even if there is no change in FEV₁. The reduction of hyperinflation is the principal aim of surgical techniques in the treatment of COPD such as lung volume reduction surgery or bullectomy.

Chronic bronchitis Chronic bronchitis refers to chronic mucus hypersecretion that frequently occurs in cigarette smokers. Mucus hypersecretion is caused by inflammation in the large airways (usually due to cigarette smoke) leading to proliferation of mucus producing cells in the respiratory epithelium. The result is a chronic productive cough and frequent respiratory infections. In COPD, this frequently persists even after smoking has stopped. Chronic bronchitis is part of an inflammatory process usually triggered by cigarette smoking that results in airflow obstruction due to remodelling and narrowing of the airways.

— CLINICAL FEATURES

The diagnosis of COPD relies on the combination of suggestive symptoms and signs together with the presence of airflow obstruction on spirometry. The following features are suggestive of COPD:

- Smoker or ex-smoker
- Older patient (>40 years old) and onset of symptoms in later life
- Chronic productive cough
- Breathlessness that is usually persistent and progressive

Panel 1: NICE definition of COPD

COPD is characterised by airflow obstruction. The airflow obstruction is usually progressive, not fully reversible and does not change markedly over several months. The disease is predominantly caused by smoking

Panel 2: The differences between COPD and asthma

Clinical features	COPD	Asthma
Smoker or ex-smoker	Nearly all	Possibly
Symptoms at under 65 years of age	Rare	Often
Chronic productive cough	Common	Uncommon
Breathlessness	Persistent and progressive	Variable
Night time waking with breathlessness or wheeze	Uncommon	Common
Significant diurnal or day-to-day variability of symptoms	Uncommon	Common

Confirmation of airflow obstruction on spirometry is required for the diagnosis of COPD ($FEV_1 < 80$ per cent predicted and FEV_1 /forced vital capacity ratio < 70 per cent).

Cough and sputum production is frequently the first symptom of COPD but many patients do not present until they are breathless. Because the lungs have a large reserve capacity, airflow obstruction may be advanced by this stage. Breathlessness is often progressive and associated with exacerbations with increased cough and sputum production. Clinical signs are not diagnostic but include hyperinflation, wheeze or quiet breath sounds. The finding of airflow obstruction is universal in COPD. The differentiation of COPD from chronic asthma can be difficult; indeed the two conditions show considerable overlap (Panel 2). For example, some COPD patients demonstrate eosinophilic airway inflammation, normally a characteristic of asthma.⁹

The chest X-ray is not diagnostic in COPD but is mandatory to exclude other diagnoses. High-resolution computed tomography (CT) scanning provides a detailed assessment of the degree of alveolar destruction in emphysema. This may be helpful if surgical intervention is contemplated or if the diagnosis is in doubt, but is not required for routine assessment of COPD.

Other conditions presenting with breathlessness can usually be identified from findings on spirometry and chest X-ray or other investigations such as echocardiography, CT scanning and detailed lung function testing (see Panel 3, p363).

THE STAGING OF COPD

As well as confirming the diagnosis of COPD, spirometry gives a measure of the severity of airflow obstruction. Simple staging systems are used to categorise the severity of COPD according to the reduc-

tion in FEV_1 . The NICE guidelines suggest the following:

- Mild airflow obstruction
 FEV_1 50–80 per cent predicted
- Moderate airflow obstruction
 FEV_1 30–49 per cent predicted
- Severe airflow obstruction
 $FEV_1 < 30$ per cent predicted

This method of staging is of value in providing information about the degree of lung function impairment and is an indicator of prognosis. However, it is of limited value in predicting symptoms such as breathlessness. Patients with severe airflow obstruction may have relatively few symptoms and vice versa. Other methods of assessing the impact of COPD are of additional use. For example, symptoms of breathlessness can be quantified using the Medical Research Council (MRC) classification (see Panel 4, p363).¹⁰ Other disease variables such as nutritional status and exercise capacity have a significant impact on prognosis and symptoms and can be used to estimate the severity of the disease. More recently attempts to increase the sophistication of the assessment of COPD severity have combined other disease indices such as nutritional status, exercise capacity and dyspnoea.¹¹

NATURAL HISTORY OF COPD

The natural history and secondary consequences of COPD include an increase in infections, weight loss, anxiety and depression, in addition to the respiratory symptoms.

Progression of airflow obstruction

Normally FEV_1 declines with age. In smokers who are susceptible to COPD this decline is accelerated.¹² In those who stop smoking, this decline slows to that expected in a non-smoker. The inevitable

consequence of the decline in lung function below a critical level is the development of worsening breathlessness and respiratory failure. Even after smoking has stopped, other consequences of the disease such as recurrent exacerbations may contribute to further decreases in lung function.¹³

Respiratory failure The onset of respiratory failure is an ominous sign in COPD. The relentless decline in lung function in COPD eventually results in impaired gas exchange leading to systemic hypoxaemia (low concentration of oxygen in arterial blood). This has a number of consequences, most importantly pulmonary arterial hypertension and right ventricular hypertrophy. Some patients also develop carbon dioxide retention (hypercapnia) because the normal ventilatory response to carbon dioxide becomes blunted. These patients are at risk of dangerous hypoventilation if given uncontrolled supplemental oxygen (see below). Hypercapnia and hypoxia also have effects on the kidneys causing activation of the renin-angiotensin system. This leads to salt and water retention and oedema formation. This syndrome is called cor pulmonale.

Exacerbations Patients with COPD are susceptible to respiratory infections and in some patients this is a frequent problem particularly in the winter months. Infections may be viral, but bacterial infections such as *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* are also common. Recurrent exacerbations can result in accelerated decline in lung function and have an impact on breathlessness because of prolonged bouts of inactivity. COPD exacerbations are a frequent cause of admission to hospital and are a major burden to health care services.

Weight loss Some patients with COPD lose weight substantially and suffer cachexia (a lack of nutrition and wasting seen in chronic diseases).¹⁴ Significant weight loss is a poor prognostic indicator independent of the severity of airflow obstruction. Loss of both fat and muscle mass contributes to weight loss in COPD. Detailed assessments of body composition can allow estimation of the relative loss of fat and muscle tissue. A number of factors contribute to weight loss in COPD. In those most severely affected, a systemic inflammatory response has been implicated.¹⁵ There is accumulating evidence that skeletal muscle wasting dysfunction is an important feature of COPD.¹⁶ Muscle weakness and fatigue is common in COPD and makes a contribution to exercise limitation and disability. In many patients this is a result of years of inactivity leading to deconditioning. Other disease factors such as systemic

inflammation and hypoxia can also contribute.

Anxiety and depression Anxiety and depression are frequently overlooked in COPD.¹⁷ Patients may become socially isolated and dependent because of limitations to mobility. Frequent hospital admission and distressing, frightening symptoms may also take a psychological toll on COPD sufferers. Depression can also exacerbate weight loss and cause sleep disturbance.

— STABLE COPD

Treatment for COPD is principally aimed at palliating symptoms and improving quality of life. Only smoking cessation and long-term oxygen therapy in patients who have chronic hypoxaemia have been shown to improve the prognosis.

In common with many chronic diseases a co-ordinated multidisciplinary approach including respiratory physicians, nurses, pharmacists, physiotherapists, occupational therapists and respiratory technicians is of benefit in maximising independence and improving physical and social functioning in COPD.

Drug therapy A number of inhaled and systemic drug therapies are available in COPD. Details of drug therapy are given in the accompanying article (p367–76). While drug therapy is effective, symptom control for most patients is at best partial and there remains a significant unmet need for therapy in COPD.

Oxygen Supplemental oxygen is of benefit to many patients, particularly those with respiratory failure. Oxygen therapy is delivered in a number of different ways depending on the clinical situation. Currently, oxygen is prescribed in primary care by general practitioners. This will change in 2005 when responsibility will be taken over by respiratory departments in secondary care.

Extended periods of hypoxia causes renal and cardiac damage and this can be prevented by long-term oxygen therapy (LTOT). This form of therapy involves the provision of continuous oxygen for most of the day. Patients whose arterial oxygen tension is consistently below 7.3 kPa should be offered LTOT. Patients are advised to use oxygen for at least 16 hours per day and this requires the provision of an oxygen concentrator in the home. This recommendation is based on large clinical trials demonstrating improvement in survival when used in this fashion.¹⁸ The time spent on oxygen needs to be balanced against loss of independence and reduction in activity as a consequence of being “tied” to a concentrator.

Oxygen is frequently provided in cylinders for patients to use “as required” (short

Panel 3: Differential diagnosis of COPD

- Asthma
- Bronchiectasis (an abnormal stretching and enlarging of the respiratory passages caused by mucus blockage)
- Pulmonary fibrosis
- Pulmonary embolism
- Lung cancer
- Chronic heart failure
- Anaemia

burst oxygen). Many patients request this and report benefit although scientific evidence for its efficacy is lacking.

Exercise performance is enhanced by oxygen in those who are hypoxic or desaturate (experience low oxygen saturation) during exercise.¹⁹ Portable oxygen systems are likely to benefit these patients by improving physical activity and independence. In the UK portable oxygen cylinders are available but these are heavy and inconvenient to carry. Lightweight liquid oxygen systems are available in some countries and, it is hoped, will become available here in the future.

Surgery Patients with emphysema may benefit from lung volume reduction surgery (LVRS) to remove non-functioning lung tissue. The aim is to reduce hyperinflation and therefore breathlessness. Rigorous pre-operative screening is required to determine suitability and in practice only a minority of patients with COPD are candidates for surgery. The main criterion for LVRS is the presence of emphysema in a heterogeneous distribution (usually upper lobe disease) with target areas of non-functioning lung that are suitable for resection. A recent large trial of LVRS in the US has shown benefits for patients with anatomically suitable disease, particularly those with poorer exercise capacity.²⁰ Patients with large bullae may also benefit from bullectomy. The physiological principles of this type of surgery are similar to LVRS.

Transplantation Transplantation is an option for patients with advanced disease. Lack of donor organs is the main limiting factor for provision of transplantation.

Pulmonary rehabilitation Many patients with COPD avoid exercise and physical activity because of breathlessness. This may lead to a vicious cycle of increasing social isolation and inactivity leading to worsening symptoms. This cycle can be interrupted by a programme of exercise reconditioning called pulmonary rehabilitation, a multidisciplinary intervention aimed at maximising physical and social

Panel 4: The MRC breathlessness scale

1. Occurs on strenuous exercise only
2. Occurs while hurrying or on slight hill
3. Needs to stop for breath at own pace or walk slower than other people of similar age
4. Only able to walk 100 yards or few minutes on flat
5. Unable to leave house or breathless while dressing

functioning for patients with chronic lung diseases. Exercise training is the core component of pulmonary rehabilitation but most programmes also provide a programme of education on the disease and its treatment. Most programmes in the UK provide six to 12 weeks of outpatient exercise training. This usually comprises supervised exercise at hospital two or three times weekly together with unsupervised home exercise. Pulmonary rehabilitation has been shown in well conducted clinical trials to improve exercise capacity and quality of life and reduce breathlessness.²¹ There are also benefits in use of health care services.²² Despite these benefits, provision of pulmonary rehabilitation in the UK is patchy. Providing universal access to pulmonary rehabilitation is a key recommendation of the NICE guidelines.

Diet and nutrition Under-nourishment is a poor prognostic indicator in COPD. It is unclear whether sustained and significant increases in body weight can be achieved by nutritional supplementation.²³ Nutritional supplements may be ineffective because of a reduction in normal food intake. It is likely that such an intervention will be more effective if combined with an anabolic stimulus such as exercise.²⁴ Currently it is recommended that patients be provided with dietary advice and calorie supplements if appropriate.

— EXACERBATIONS OF COPD

Exacerbations of COPD are a major problem for patients and health care providers. Patients with less severe exacerbations can be treated at home but many require hospital admission. Exacerbations may herald acute respiratory failure in previously stable patients.

Treatment for exacerbations includes drug therapy, oxygen and ventilatory support if needed. More recently it has been recognised that treatment for many patients admitted to hospital could be administered at home if adequate nursing care were to be provided. Many hospitals in the UK have facilities for early discharge

and community support to reduce hospital admission and length of stay for COPD exacerbations. A number of studies have demonstrated that this is a safe and effective approach.²⁵

Drug therapy Acute exacerbations of COPD require the administration of bronchodilators, corticosteroids and antibiotics.

Respiratory failure Acute respiratory failure is common during exacerbations of COPD. This commonly presents with acute hypercapnia and acidosis and has a high mortality. Standard treatment for COPD exacerbations should be instituted together with oxygen. In patients with pre-existing hypercapnic respiratory failure ("acute on chronic" respiratory failure) care is needed with oxygen therapy because high flow oxygen can result in worsening hypercapnia and lead to coma. In this situation, oxygen administration should be controlled and blood gas tensions monitored.

Ventilatory support If standard medical treatment together with oxygen fails to bring about improvement, patients with hypercapnia and acidosis may benefit from ventilatory support. There is now strong evidence that this can be provided non-invasively through a tight fitting nasal or face mask.²⁶ Non-invasive ventilation can prevent intubation and mechanical ventilation. This significantly reduces the risk of ventilator associated pneumonia and reduces length of hospital stay. Moreover, non-invasive ventilation can be safely provided on the respiratory ward by appropriately trained nursing or technical staff.²⁷

Non-invasive ventilation (NIV) may not be possible in some situations (for example where the patients has a reduced conscious level or following respiratory arrest) and in those situations, or when NIV has failed, mechanical ventilation is required. Judgements about the desirability of mechanical ventilation in end-stage COPD remain controversial. In practice this requires careful discussion of the likely outcome in terms of survival and quality of life with the patient and his or her family.

CONCLUSIONS

COPD is a common chronic disease and an important cause of disability among older people. While lung damage is irreversible in COPD, symptoms can be improved in the condition by combined treatment that includes physical therapies such as pulmonary rehabilitation as well as drug treatment. A multi-professional approach that seeks to maintain the independence of COPD sufferers is a critical component of successful management of this debilitating disease.

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