Chronic obstructive pulmonary disease (COPD) is a term used to describe a group of progressive airways diseases that are not fully reversible. COPD has no cure, but the goals of therapy are to:

- Relieve symptoms
- Prevent disease progression
- Improve exercise tolerance and health status
- Prevent and treat exacerbations and any complications
- Reduce mortality

Pharmacological therapy
Whether medicines are able to slow the progression of COPD remains controversial and inconclusive. Currently, inhaled medicines are the mainstay of treatment and are used to prevent and control symptoms, reduce the frequency and severity of exacerbations, improve health status and improve exercise tolerance. The response to inhaled pharmacological therapy should be assessed routinely and reviewed to ensure that patients achieve an optimal response.

The choice of medicine and inhaler device is dependent on a range of factors that include symptom severity, degree of airways obstruction (measured by spirometry), frequency and severity of exacerbations, and patient choice. It has been estimated that up to 50% of patients use their inhaler device incorrectly, thus the choice of device will also depend on an individual’s ability to use the device effectively. Training on inhaler technique is essential in ensuring that patients gain maximal benefits from treatment.

Bronchodilators
Bronchodilators are central to the management of COPD symptoms. Owing to the obstructive nature of COPD, bronchodilators offer little or no improvement in forced expiratory volume in one second (FEV1). However, they do reduce pulmonary hyperinflation, improve emptying of the lungs and improve exercise tolerance. They also improve airway smooth muscle tone and increase mucociliary clearance.

There are three classes of bronchodilators:

- Beta2 agonists
- Muscarinic antagonists (anticholinergics)
- Methylxanthines

Inhaled beta2 agonists and muscarinic antagonists are available in short- and long-acting forms, administered via a range of devices. Bronchodilators are also available in oral and nebulised forms, although these are associated with a slower onset of action and greater incidence of side effects, respectively.

Short-acting beta2 agonists
Short-acting beta2 agonists (SABAs), such as salbutamol and terbutaline, are the most commonly used bronchodilators for COPD. Stimulation of beta2 receptors relaxes airway smooth muscle, which increases cyclic adenosine monophosphate (cAMP) and produces bronchodilation.

SABAs have a rapid onset of action, working within minutes and lasting up to four hours, although, compared with asthma, the time to peak response is slower for patients with COPD.

The side effects of SABAs are pharmacologically predictable and dose dependent. Stimulation of atrial beta2 receptors can produce sinus tachycardia. Effects on skeletal beta2 receptors can result in fine muscle tremor, especially of the hands. SABAs increase the cellular uptake of potassium ions, which can result in hypokalaemia. Other side effects include hypoxaemia, restlessness and increased anxiety. However, SABAs are generally well tolerated and adverse effects are minimal when used at the recommended doses.

Long-acting beta2 agonists
Long-acting beta2 agonists (LABAs), such as salmeterol and formoterol, have similar bronchodilatory effects to the SABAs, but these effects last longer — about 12 hours with no loss of effectiveness overnight or with regular use in COPD patients.

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SUMMARY

Chronic obstructive pulmonary disease (COPD) has no cure. The goals of therapy include slowing disease progression, relieving symptoms, improving exercise tolerance and preventing and treating exacerbations.

Inhaled medicines are the primary treatment for COPD. Short-acting bronchodilators are used in mild disease. Adding long-acting bronchodilators and inhaled corticosteroids should be based on clinical guidelines and spirometry results. Smoking cessation is the most effective intervention for patients with COPD. Other therapies such as oxygen and pulmonary rehabilitation can also help improve outcomes in COPD.

Inhaled corticosteroids

The use of inhaled corticosteroids in COPD is controversial. Evidence suggests that monotherapy with inhaled corticosteroids offers no benefit and results in a greater incidence of non-fatal pneumonia and adverse effects compared with placebo.

Although inhaled corticosteroids are not licensed for use as monotherapy in COPD, it has been reported that 70% of COPD patients are prescribed these, reflecting the fact that many are inappropriately treated as asthmatics. Although there have been concerns raised regarding the incidence of osteoporosis and cataracts with inhaled corticosteroids, evidence indicates that this is related to the underlying COPD rather than corticosteroid use.

Inhaled combination therapy

Systematic reviews and randomised controlled trials have investigated the role of various combinations of inhaled therapies for COPD. A range of outcome measures have been studied including all-cause mortality, exacerbations, hospital admissions, decline in FEV₁, change in quality of life as assessed by the St George's Respiratory Questionnaire and adverse events.

Licensed combinations of LABA plus inhaled corticosteroid are available, eg, Seretide (salmeterol plus fluticasone propionate) and Symbicort (formoterol fumarate plus budesonide).

Triple therapy When triple inhaled therapy (with a LABA, an inhaled corticosteroid and a LAMA) has been compared with a LABA plus an inhaled corticosteroid or a LAMA alone, triple therapy was associated with a reduced...
risk of exacerbations and hospital admissions, and improved quality of life. No differences were found in all-cause mortality.

Among COPD patients with an FEV$_1$ of <50%, the use of a LABA plus an inhaled corticosteroid or a LAMA alone were found to be the most cost-effective therapies. Nonetheless, as exacerbation rates increased, so did the cost-effectiveness of triple therapy. The updated National Institute for Health and Clinical Excellence guideline therefore recommends the use of triple therapy for patients who have been using a combination of LABA plus inhaled corticosteroid or a LAMA alone and remain breathless or have persistent exacerbations.

**Staging**

NICE has updated its treatment algorithm for inhaled therapies (see Figure 1). The guidance suggests that patients should be initiated on a SABA or a SAMA. If they remain breathless or have exacerbations then, depending on their FEV$_1$, they should be optimised according to the following:

- If FEV$_1$ ≥50% of predicted value, use either a LABA or LAMA
- If FEV$_1$ <50% of predicted value, use either a LAMA or a combination of LABA plus inhaled corticosteroid

Irrespective of baseline FEV$_1$, if patients continue to have persistent exacerbations or breathlessness they will eventually require triple inhaled therapy.

**Smoking cessation**

The single most effective intervention for COPD patients, in terms of both clinical and cost-effectiveness, is smoking cessation. Stopping smoking can slow the rate of decline of FEV$_1$, and thus the progression of COPD, and can reduce mortality substantially. Smoking cessation in early, mild COPD reduces the decline of lung function, but it has little effect on lung function in advanced disease. All COPD patients still smoking should be encouraged to stop at every opportunity, irrespective of age.

An up-to-date smoking history, including smoking pack years, should be documented for all patients with COPD. For calculation of smoking pack years, see p383 of the accompanying article.

Various medicines are available to help patients quit smoking, including bupropion, varenicline and a range of nicotine replacement therapies (such as gums, patches and inhalators). Unless contraindicated these should be offered as part of a support programme to optimise the chances of quitting.

**Oral corticosteroids**

Maintenance use of oral corticosteroids is not usually recommended for COPD. However, for some patients with advanced COPD, it may not be possible to withdraw oral corticosteroids after an exacerbation. In these instances, the corticosteroid dose should be kept as low as possible and the patient should be monitored for development of osteoporosis and given appropriate prophylaxis. All patients over the age of 65 years should be given prophylaxis against osteoporosis (eg, with bisphosphonates).

**Mucolytics**

Purulent sputum is common in COPD — the use of mucolytics, such as carbocisteine, erdosteine and N-acetylcysteine, can reduce sputum viscosity and so aid expectoration.
**Other therapies for COPD**

**Oxygen** Hypoxia can occur in severe COPD, which can result in cor pulmonale. If left untreated, this has a poor prognosis with a five-year survival of less than 50%. Long-term oxygen therapy is indicated for:

- Stable patients with a partial pressure of oxygen (PaO₂) of less than 7.3kPa
- Patients with a PaO₂ of 7.3–8kPa with an additional risk factor (such as polycythaemia, nocturnal hypoaxaemia, peripheral oedema or pulmonary hypertension)

To obtain maximal benefits from oxygen therapy, patients should receive oxygen for at least 15 hours per day, with greater benefits seen for patients on oxygen for 20 hours per day. These patients should be reviewed annually by practitioners familiar with long-term oxygen therapy and the review should include pulse oximetry.

**Vaccinations** Pneumococcal vaccination and annual influenza vaccination are recommended for all patients with a chronic respiratory disease such as COPD. These reduce rates of hospital admission and risk of death from pneumonia and influenza.

**Pulmonary rehabilitation** As COPD progresses, worsening dyspnoea makes physical activity and exercise increasingly difficult. This becomes a vicious cycle that can lead to social isolation and worsening of symptoms. Pulmonary rehabilitation is a multidisciplinary programme that is individually designed and tailored to optimise a patient’s physical and social performance and autonomy. It can offer statistically significant and clinically meaningful improvements in quality of life, exercise capacity and dyspnoea and has been shown to be a cost-effective intervention. The National Institute for Health and Clinical Excellence recommends that pulmonary rehabilitation should be available for all COPD patients who have had a recent hospital admission for an acute exacerbation, or who consider themselves functionally disabled by COPD and have a Medical Research Council dyspnoea score of 3 or above (see accompanying article, p384).

**Surgery** Surgical options are available for patients with very severe COPD. Dyspnoea can be improved by bullectomy (ie, the removal of bullae — thin-walled, air-filled spaces in the lungs) or lung volume reduction surgery (ie, the removal of areas of poorly functioning lung). The latter, and lung transplantation, are only considered for patients with advanced disease despite maximal medical therapy.

Systematic reviews and randomised controlled trials have shown that, when compared with placebo, mucolytics significantly reduce the frequency of exacerbations and increase the number of patients who remain exacerbation free. They have also been shown to increase FEV₁, predicted FEV₁ and peak expiratory flow rate when compared with placebo (with no difference in adverse effects). However, they do not reduce rates of hospital admission or increase quality of life.

Due to the inconsistent evidence for benefits of mucolytics, the updated NICE guideline recommends that they should be considered for patients with a chronic cough and productive sputum, but should only be continued if there is symptomatic improvement. The guideline also recommends that mucolytics should not be used routinely to prevent exacerbations in patients with stable COPD.

**Self-management and rescue medicines**

Self-management plans have been successfully used for many years in patients with asthma. In COPD, they are designed to allow patients to adapt their lifestyles and acquire skills to successfully identify the first signs of an exacerbation and respond appropriately.

NICE recommends that patients who are at risk of exacerbations should be given a self-management plan that encourages them to respond promptly to the symptoms of an exacerbation by:

- Starting oral corticosteroid therapy if their increased breathlessness interferes with their activities of daily living (unless contraindicated)
- Starting antibiotic therapy if their sputum is purulent
- Adjusting their bronchodilator therapy to control their symptoms

Patients should be given a course of antibiotic and corticosteroid tablets to keep at home for use as part of a self-management strategy, although evidence to support such strategies in COPD is lacking.

There are various national projects looking to assess the usefulness of self-management plans and “rescue” medicines. One such project is being undertaken by an NHS “health innovation and excellence cluster”, which is carrying out a pilot across north-east London, north-central London and Essex to assess the impact of these interventions on hospital admissions due to COPD exacerbations.

**New treatments**

**Roflumilast** Roflumilast is an oral phosphodiesterase-4 inhibitor that is administered once daily. It is licensed for add-on treatment to bronchodilator therapy in patients with severe COPD (FEV₁ <50% predicted) who have chronic bronchitis and a history of frequent exacerbations.

The side effects of roflumilast include weight loss, diarrhoea, nausea and an increased risk of psychiatric disorders such as insomnia, anxiety, nervousness and depression. The Scottish Medicines Consortium recently rejected the use of roflumilast because the economic analysis submitted by the manufacturer was deemed to be insufficient. A NICE technology appraisal is expected to be issued in 2011.

**Indacaterol** Indacaterol is a LABA that is administered once daily and is licensed for use in moderate-to-severe COPD.

There are limited data comparing indacaterol with existing long-acting bronchodilators and advantages in clinical efficacy appear marginal. At a recent meeting of the American College of Chest Physicians in Vancouver, Canada, results of a head-to-head study comparing...
indacaterol with tiotropium were presented. Indacaterol was shown to be non-inferior to tiotropium in improving lung function. No NICE appraisal is currently scheduled for indacaterol, but the SMC has approved its use in Scotland.46

References

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COPD

Lifelong Learning questions are available to complete in an online module on the Clinical Pharmacist section of PJ Online — accessible via www.clinicalpharmacist.com.

To complete the module, you will need to log in to the site. If you are a new visitor, it is simple to register as a user (free to all members of the Royal Pharmaceutical Society).

Questions
This month’s Lifelong Learning questions are based on the CLINICAL FOCUS articles on chronic obstructive pulmonary disease, which were commissioned from independent authors.

Answers from October’s module

Eating disorders

1 (a) F, (b) T, (c) F, (d) F, (e) T
2 (a) T, (b) F, (c) T, (d) T, (e) T
3 (a) T, (b) F, (c) F, (d) T, (e) F
4 (a) T, (b) F, (c) F, (d) T, (e) T
5 (a) F, (b) T, (c) T, (d) F, (e) T
6 (a) T, (b) F, (c) F, (d) F, (e) T
7 (a) F, (b) F, (c) T, (d) T, (e) T
8 (a) T, (b) T, (c) F, (d) T, (e) F
9 (a) F, (b) T, (c) T, (d) F, (e) T
10 (a) T, (b) F, (c) F, (d) T, (e) T

The information in the Box (below) is there to help you identify knowledge gaps and undertake continuing professional development. This online module will close on 1 February 2011.

Answers

When you have completed the online module, your answers will be submitted for marking and Clinical Pharmacist will send you a certificate and your results by email within two weeks of the module closing. Please do not hesitate to contact us if you have technical problems with the module. E: clinicalpharmacist@pharmj.org.uk

How to undertake continuing professional development

Our CLINICAL FOCUS articles and the online Lifelong Learning modules can help you plan your CPD and record the benefits of the activity at www.uptodate.org.uk.

Reflect on your gaps in knowledge

- What are the main causes of chronic obstructive pulmonary disease (COPD) and how is the condition diagnosed?
- What are the usual goals of COPD treatment and what therapeutic options are available?
- What lifestyle changes can be recommended for patients?

Act to enhance your practice

- Read the CLINICAL FOCUS articles in this issue (pp382–94)
- Test your knowledge by completing the questions at www.clinicalpharmacist.com
- Evaluate the activity
  - What have you learnt?
  - How has it added value to your practice?
  - What will you do now and how will this be achieved?

- Consider making this activity one of your nine CPD entries this year

The questions in this Lifelong Learning module have been approved by the Royal Pharmaceutical Society using an independent reviewer as a resource to support your professional development.