

Over-the-counter advice for coughs

About 48 million cases of acute cough occur annually in the UK and most will prompt patients to use over-the-counter medicines. In this article, **Sarah Marshall** gives an overview of coughs and factors that pharmacists should consider

A cough is a protective reflex invoked when something blocks or irritates the airway. It is a forced expulsive manoeuvre, usually against a closed glottis (the opening between the vocal cords), associated with a characteristic sound. Its purpose is to maintain normal breathing by removing mucus or noxious substances from the larynx, trachea and larger bronchi.

The reflex is complex but can be pictured in three phases:

- Receptors in the respiratory tract mucosa respond to chemical or mechanical stimuli and discharge impulses along cholinergic nerve fibres.
- These impulses are received by the cough centre(s) in the brain.
- The cough centre sends impulses along cholinergic nerve pathways, causing the diaphragm and abdominal and intercostal muscles to contract, resulting in the cough.

Coughing is a non-specific symptom that can be linked to over 100 conditions, ranging from minor and self-limiting to life-threatening. The sensitivity of the cough reflex can increase with infection, some diseases and the use of some drugs.

An acute cough (defined as one lasting less than three weeks) is the most common reason for patients to consult their GP — accounting for 12 million visits a year — and is often associated with an upper respiratory tract infection (URTI).

There are at least 200 viruses that can lead to such infections, resulting in hypersecretion of mucus by goblet cells and vasodilation and, therefore, nasal congestion, sneezing, nasal discharge, post-nasal drip (mucus drips from the post-nasal space and irritates the pharynx and trachea), which in turn lead to throat clearing and cough.

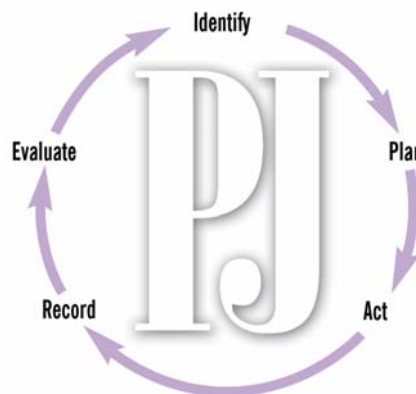
If a cough lasts more than eight weeks, it is described as chronic. Chronic coughs are typically dry or minimally productive (see below). Examples of common causes of chronic cough include adverse drug reactions, exposure to environmental aggravants and gastro-oesophageal reflux or upper airway disease.

Significant factors

In order to give appropriate advice on coughs, pharmacists need to consider factors such as the patient's age (see Panel 1, p86, for coughs in children), the duration, onset and nature of the cough, and the patient's medical history. For example, inhalation of a foreign body (most commonly seen in children) can cause cough with sudden onset.



In 2001, sales of liquid cough preparations in the UK grossed £96.5m — equivalent to the sale of at least 24 million bottles



Identify knowledge gaps

1. What is the purpose of menthol in products for cough?
2. What is croup?
3. What would be an appropriate alternative antihypertensive for a patient with cough caused by an angiotensin-converting enzyme inhibitor?

Before reading on, think about how this article may help you to do your job better. The Royal Pharmaceutical Society's areas of competence for pharmacists are listed in "Plan and record", (available at: www.rpsgb.org/education). This article relates to "common disease states" (see appendix 4 of "Plan and record").

Nature of the cough Useful questions about the nature of a cough include:

- Is the cough unproductive or productive?
- How does the cough sound?
- Does the cough vary in severity during the day or night?

Unproductive coughs can be described by patients as dry, tickly, tight or irritating. They are usually caused by a viral URTI but can also occur as result of a smoky environment, a dry atmosphere, air pollution or a change in temperature. They can also be a symptom of asthma, lung cancer, or an adverse drug reaction.

Productive ("chesty" or "loose") coughs produce sputum. Coloured sputum (eg, yellow or brown) can be a sign of a bacterial chest infection, such as bronchitis or pneumonia. Blood in the sputum can indicate tuberculosis or cancer. Some patients describe a "chesty but non-productive" cough, where there is congestion on the chest but no mucus is produced, and this should be treated as a productive rather than non-productive cough.

A bout of coughing in which a whooping sound is heard suggests pertussis (whooping cough). Patients who wheeze should be referred. Dry coughs in children that are

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Panel 1: Coughs in children

Coughs in children should be managed differently from those in adults because infections that cause minor symptoms in adults can lead to life threatening conditions, such as bronchiolitis, in children. Schoolchildren suffer between seven and 10 URTIs each year. More than 90 per cent of coughs in children are due to a respiratory tract infection such as a cold, croup, bronchitis, bronchiolitis, whooping cough or pneumonia.¹

Croup Croup (acute laryngotracheobronchitis) is a viral infection of the larynx and trachea leading to oedema and narrowing of the airway. It occurs mostly in children between six months and two years of age, but can present in any child under six years. The child wakes in the night with severe bouts of a barking cough. Breathing may be noisy on inspiration (stridor). Although symptoms usually lessen in the morning they can recur the following night. Other symptoms can include a runny nose, hoarseness and sore throat, fever, malaise, loss of appetite, and aches and pains. Although croup mostly follows a cold it can also arise spontaneously. Symptoms usually peak at between one and three days. A child should be referred if:

- Breathing becomes rapid or wheezy and inspiration is particularly noisy
- He or she is struggling to breathe and becomes restless, or is drooling and unable to swallow
- A fever persists despite giving paracetamol or ibuprofen and cooling the child down
- He or she turns pale or blue

Steam has traditionally been used to treat croup but the value of this has been questioned.² In addition, there is a risk of scalding. If breathing is noisy or difficult, parents should calm and reassure the child and sit him or her upright. Fever should be lowered and cool drinks given. Going briefly out into cool night air may be beneficial.

Whooping cough Whooping cough is caused by infection with *Bordetella pertussis*. Although its incidence is low as a result of immunisation programmes, it can still occur in children under five years of age and unimmunised adults. Mild cases can also occur in people who have been vaccinated. Initially the patient develops cold-like symptoms, followed a few days later by a cough. The cough occurs in violent bouts after which a "whoop" can be heard on inspiration as the patient struggles to inhale. Vomiting can also occur. Whooping cough requires treatment with antibiotics. The whoop can last for several months.

Bronchiolitis Bronchiolitis is inflammation of the small airways in the lungs, typically as a result of respiratory syncytial virus infection. It is commonest in infants under one year old. Symptoms include cough, low fever, rapid breathing, wheeze, apnoea and cyanosis.

When to refer In addition to the points listed in Panel 4, children should be referred if they:

- Are dribbling and cannot swallow (this can indicate epiglottitis, a rare but serious condition that can be difficult to differentiate from croup and that requires referral to hospital)
- Have persistent earache
- Have rapid breathing
- Are dehydrated
- Are drowsy

Given that most coughs are self-limiting, and the controversy surrounding cough medicines (see main text), it may be advisable only to recommend demulcent syrups for young children. However if a child has an irritating cough it may be appropriate to use a sedating antihistamine. As well as suppressing the cough the sedative effects will help the child sleep. However, children should not be given cough medicines containing sedative ingredients if they are having difficulty breathing. In addition, examination of the throat should not be attempted in children with stridor or breathing difficulties because it can lead to obstruction.



Oscar Burriel/SP/L

worse at night can indicate asthma, even if wheezing is not present. A cough that sounds like a harsh bark in children under six years suggests croup (see Panel 1).

Accompanying symptoms Coughs associated with a respiratory tract infection are often accompanied by symptoms such as a blocked or runny nose, sore throat and catarrh, fever, aches and pain. Chest pain on deep inspiration or coughing can indicate pleurisy or pulmonary embolism (this may follow calf pain) but can simply be caused by strained intercostal muscles due to coughing, especially in patients with chronic cough. Shortness of breath can be a sign of serious conditions, such as chronic bronchitis, emphysema or heart failure and must be referred. Unexplained weight loss also implies serious disease.

Medical history and other medicines

Patients should be asked about other conditions, such as chronic bronchitis (a type of chronic obstructive pulmonary disease [COPD]) and heart disease. Chronic bronchitis is defined as production of sputum on most days for three consecutive months of the year for two successive years. People with chronic bronchitis are at a greater risk of chest infections and the use of cough suppressants may be harmful.

Chronic coughing can indicate a failing heart in those with a history of heart disease and, in people with asthma or COPD, increasing cough can indicate a worsening condition that requires hospital admission.

Gastro-oesophageal reflux disease can lead to coughing (sometimes cough may be the only symptom) and, according to the British Thoracic Society, failure to consider this as a cause is a common reason for treatment failure.

There are some drugs, such as angiotensin-converting enzyme inhibitors, that can cause chronic coughing (see Panel 2) whereas others can interact with ingredients in cough preparations (see Panel 3).

If there is a family history of eczema, asthma or hay fever, a child may be more prone to prolonged episodes of coughing as a result of a simple URTI.

Smoking About a third of long-term smokers develop a chronic cough. A change in the nature of a smoker's cough (eg, more productive or frequent, or a different sound) may suggest malignancy (see *PJ*, 28 October 2006, pp521-4). Smokers often accept cough and breathlessness as a side effect of smoking and failure to see a doctor early results in a poor prognosis for those with lung cancer. Cough is an opportunity to discuss smoking cessation.

Treatment

Most cases of cough seen in a pharmacy are as a result of a viral URTI and will resolve without treatment within a few days although many patients will want to use an over-the-counter medicine. Panel 4 summarises when patients should be referred to their GP, who

can take a detailed history and perform a physical examination (including percussion and auscultation) to exclude serious infection or disease. For patients in whom there is no reason to suspect a bacterial infection or underlying disease, however, it may be desirable either to suppress or to encourage coughing.

The ingredients in OTC cough preparations can be divided into four groups: cough suppressants, expectorants, demulcents and bronchodilators.

Cough suppressants Coughing can significantly impair quality of life; it can cause sleep disturbance, stress incontinence, chest pain and vomiting (especially in children). Cough suppressants can be used for short-term symptomatic relief of unproductive cough. They should not be used to treat a productive cough because mucus retained in the lungs can increase the risk of infection.

Opioid cough suppressants Codeine, pholcodine and dextromethorphan act centrally to suppress the cough reflex. Although all three may be effective, dextromethorphan and pholcodine have a lower risk of constipation and dependence developing. In addition, both pholcodine and codeine can cause drowsiness whereas dextromethorphan is non-sedating in most people. According to the British Thoracic Society, codeine and pholcodine have no greater efficacy than dextromethorphan.⁴

Opiates should be used with caution in people with asthma, hepatic or renal impairment or a history of drug abuse. At antitussive doses, opioids have no significant interactions with other drugs.⁵

Despite the availability of paediatric formulations of codeine and pholcodine linctuses, opiate cough suppressants are not generally recommended in children and should be avoided in those under one year.

Menthol Menthol by inhalation has been shown to suppress the cough reflex, but its effect is short lived. For an inhalation, hot (but not boiling) water should be used to reduce the risk of scalding and slow the release of volatile constituents. Aromatic vapour rubs are not recommended in babies under three months.

Sedating antihistamines Examples of sedating antihistamines used in products for cough are diphenhydramine, promethazine and triprolidine. Non-sedating antihistamines are less effective for cough. Sedating antihistamines suppress cough by reducing cholinergic transmission of impulses along the cough reflex. They are also useful for cough because they dry up nasal secretions that cause post-nasal drip. Their sedative effect may be valuable for treating nocturnal coughs especially if combined with an opiate cough suppressant.

Side effects include dry mouth, urine retention, constipation and blurred vision. Sedating antihistamines should be avoided in men with an enlarged prostate and people with glaucoma, and should be used with caution in the elderly.

Expectorants For productive coughs, expectorants are used to facilitate the expulsion of bronchial secretions. Low doses of emetics, including guaifenesin, ammonium chloride, ipecacuanha and squill, are classed as expectorants in cough preparations (but see below).

According to the US Food and Drug Administration, the dose of guaifenesin required to produce expectoration is 200mg three times a day.⁵

Other strategies to manage productive coughs include hydrating the airways and reducing the viscosity of mucus by drinking plenty of fluid or using steam inhalations.

Panel 2: ACE inhibitors³

Drugs that most frequently causes coughs are angiotensin-converting enzyme inhibitors. Onset is variable; a non-productive persistent cough can develop within a few hours of taking the first tablet or can appear after several months. ACE degrades bradykinin and substance P and, if it is inhibited, these inflammatory mediators accumulate in the upper respiratory tract, triggering cough.

If a cough suspected of being caused by an ACE inhibitor does not abate within four weeks, it may be necessary to discontinue therapy. Because all ACE inhibitors can potentially cause cough and this is not dose-dependent, therapy should be switched to a different class of drug, such as angiotensin-2 receptor antagonists which have similar properties to ACE inhibitors but do not affect bradykinin. After therapy is stopped, an ACE inhibitor-induced cough typically takes up to four weeks to resolve but can linger for up to three months.

Panel 3: Examples of possible interactions

OTC product	Interaction
Antihistamines	Anxiolytics, hypnotics and alcohol can enhance sedative and central nervous system depressant effects Phenothiazines and antimuscarinics can enhance anticholinergic effects (eg, blurred vision, dry mouth, urine retention, constipation) Monoamine oxidase inhibitors, and tricyclic and related antidepressants, can increase anticholinergic and sedative effects
Sympathomimetics	Antihypertensive therapy: antihypertensive effect can be reduced MAOIs (including moclobemide): hypertensive crisis is possible Tricyclic antidepressants and beta blockers: hypertension possible
Theophylline	Cimetidine, macrolides, quinolone antibiotics, fluconazole, fluvoxamine, St John's wort and calcium channel blockers can increase the risk of theophylline toxicity

Panel 4: When to refer

A patient should be referred if:

- A cough has lasted three weeks or more without improvement (earlier referral of children should be considered)
- He or she has general malaise, persisting sweats or fever
- Sputum is discoloured or bloodstained (green sputum is common in viral infections and may not warrant referral)
- He or she has chest pain, difficulty breathing, shortness of breath or wheeze
- Whooping cough is suspected
- The cough is recurrent and nocturnal
- An adverse drug reaction is suspected
- He or she has experienced unexplained weight loss
- Infections pose a serious risk (eg, patients with chronic respiratory conditions, heart disease, diabetes or immunosuppression, and the elderly)
- Gastro-oesophageal reflux disease is the suspected cause of the cough
- He or she has a smoker's cough that has changed in nature

Panel 5: Advice to patients with cough due to URTI*

- Most short-term coughs are caused by viruses so antibiotics will not help
- Paracetamol or ibuprofen can ease aches and fevers
- Increase fluid intake (hot honey and lemon can be soothing)
- Extra pillows can aid sleep (for children try raising the head of the cot or bed by 10cm)
- Steam or menthol inhalations can help
- Cough should resolve but can last for up to four weeks
- Stop smoking (and keep a child with cough away from smoke)
- See a doctor if . . . (see Panel 4)

* Patient information sheets designed for primary care are available from Prodigy (www.prodigy.nhs.uk) and the British Thoracic Society (www.brit-thoracic.org.uk)

Demulcents Demulcents include simple linctus and products containing ingredients such as honey and lemon, syrup or glycerol. They are thought to coat the pharyngeal mucosa, soothing inflammation and reducing irritation, and can be used to treat both productive and non-productive coughs. Demulcents can be safely taken by most patients, including pregnant women and children, although their high sugar content should be noted. Paediatric and sugar-free versions are available. Cough lozenges can also help soothe dry irritating coughs, but should not be given to children under three years of age because of the risk of choking.

Bronchodilators Bronchodilators include sympathomimetics and theophylline. They are included in cough preparations to relieve airway congestion.

Sympathomimetics Pseudoephedrine and ephedrine are included in cough and cold preparations for their nasal decongestant effects but also for their relaxant action on bronchial smooth muscle (via β_2 adrenoceptors). An expectorant combined with a sympathomimetic can be used to treat productive coughs. Pseudoephedrine and ephedrine can stimulate the central nervous system, resulting in sleeplessness if taken at night. Oral sympathomimetics should be avoided by patients with diabetes, heart disease, hypertension, glaucoma or hyperthyroidism (raised levels of thyroid hormone increases adrenoceptor sensitivity, and hence puts patients with hyperthyroidism at more risk of cardiac effects if sympathomimetics are used).

Theophylline The bronchodilator theophylline acts via cyclic adenosine monophosphate. However, there are limitations to its use because of numerous drug interactions. Care should be taken not to combine it with prescribed theophylline because it has a narrow therapeutic index. The amount of theophylline in OTC preparations may be subtherapeutic⁶ but adverse effects include gastrointestinal irritation, nausea, tachycardia, palpitations, central nervous system stimulation, insomnia and headache. Theophylline should be used with caution in the elderly, those with liver or cardiac disease, hypertension, hyperthyroidism, peptic ulcer, epilepsy or fever, and during pregnancy or while breast-feeding.

Action: practice points

Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist's CPD portfolio.

1. Cascade the information in this article to your health care staff.
2. Think about the ingredients in your cough remedies. Which product would you recommend first? Discuss your reasoning with colleagues.
3. How familiar are you with the ingredients of cough preparations? For example, could you tell a customer where squill or ipecacuanha come from and what else they have been used for?

Evaluate

For your work to be presented as CPD, you need to evaluate your reading and any other activities. Answer the following questions: What have you learnt? How has it added value to your practice? (Have you applied this learning or had any feedback?) What will you do now and how will this be achieved?

Are cough medicines effective?

A Cochrane review of OTC cough preparations for adults and children concluded that there was no strong evidence for or against their efficacy.⁷ However, although many of the trials conducted have been of poor quality — making it difficult to draw firm conclusions — the authors noted that most preparations appeared safe, with a low incidence of minor adverse effects.

Debated issues include the rationale behind some cough preparations: for example, some expectorants are based on the flawed theory that low doses of emetics promote expectoration. In addition, although most products now contain logical combinations of ingredients (eg, a sympathomimetic with an expectorant or cough suppressant), a few still contain irrational combinations (eg, expectorants with suppressants).

Preparations may also contain subtherapeutic doses of active ingredients. The response to dextromethorphan is dose dependent and maximum cough suppression occurs with 60mg⁴ but the recommended dose of many products is 7.5mg or 15mg. However, pharmacists should not advise patients to take more than the dose recommended.

Carefully designed large trials are needed to provide more evidence of the value of cough preparations. Nevertheless, patients often consider cough preparations beneficial. The British National Formulary acknowledges that some preparations may have a useful placebo function, but points out that a simple home remedy such as honey and lemon may be just as helpful. If a pharmacist considers it appropriate to recommend one of the numerous cough preparations available, the product should be selected based on the patient's symptoms and any combination of ingredients should be rational.

Panel 5 lists additional advice pharmacists can give.

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