Cough is one of the most common conditions that pharmacists are asked to advise about. Coughs may have many causes, from the common cold to life-threatening illnesses such as cancer. It is important that pharmacists should make an informed judgement about when a patient’s cough can be self-managed with OTC medications or whether it requires referral to a doctor.

Cough is a reflex which protects the lungs from the inhalation of irritants and cleans the airways of an excess build-up of secretions and solid particles. It is initiated by stimulation of mucosal receptors located in the nasopharynx, trachea, larynx and bronchial tree. Stimuli are carried by cranial nerves IX (glossopharyngeal nerve) and X (vagus nerve) to a cough centre in the cerebral medulla. The reflex arc is completed by an outgoing message to contract the diaphragm and other respiratory muscles. A cough may be induced voluntarily or, to some extent, voluntarily inhibited.

 Causes and Symptoms

Cough may be characterised as:
- acute – lasting less than three weeks
- subacute – lasting three to eight weeks
- chronic – persisting beyond eight weeks.

Acute cough

The most common causes are viral upper respiratory tract infections. Other causes include acute bacterial sinusitis, exacerbation of chronic obstructive pulmonary disease (COPD), allergic rhinitis, environmental exposure and allergies. Rarely, a life-threatening illness may present primarily with an acute cough – e.g., pulmonary embolus, cardiogenic pulmonary oedema, pneumonia.

Viral cough typically presents with sudden onset, accompanied by fever and associated cold symptoms. The cough is usually non-productive or produces a small amount of clear or white sputum. Symptoms are often worse in the evening.

Allergic cough is often seasonal, non-productive and is accompanied by other symptoms such as sneezing, nasal discharge or blockage and itchy eyes and throat.

One of the less common causes of acute cough is croup (laryngotracheobronchitis). It usually occurs in infants and young children and is most commonly caused by parainfluenza viruses, respiratory syncytial viruses (RSVs) or influenza A and B viruses. The cough is usually preceded by cold symptoms and has a harsh, barking quality. It is often associated with difficulty in breathing and an inspiratory stridor (an abnormal high-pitched sound on breathing in).

A short, dry, painful cough is typical of the early stages of pneumonia and may be accompanied by a high temperature, malaise, breathlessness, chills, headaches and, occasionally, pleurisy. Although initially non-productive, the cough rapidly becomes productive, with red-stained sputum.
**Questions to ask**

- Duration of cough – is it acute or chronic?
- Smoking history – smokers are at higher risk for chronic and recurrent cough, which may eventually develop into chronic bronchitis and emphysema.
- Nature of cough – e.g., productive (chesty), non-productive (dry), tight.
- If productive, nature of sputum (see Practice Point 2).
- Age – with increasing age conditions such as bronchitis, pneumonia and carcinoma become more prevalent; if a child, see Practice Points 3 and 4.
- Onset of cough – a cough that is worse in the morning may suggest postnasal drip, bronchiectasis or chronic bronchitis; a cough that is worse at night may suggest pneumonia or asthma (especially in a child).
- Presence of other symptoms – e.g., wheeze, shortness of breath, chest pain, fever, sinus pain, nasal congestion.
- Medical history (e.g., asthma, GORD, heart problems) and current medications.

**When to refer**

- Duration longer than three weeks (however, postnasal drip and hayfever can last for more than three weeks and may not necessitate referral if successfully managed).
- Chest pain (possible cardiovascular cause)
- Cough that recurs on a regular basis
- Wheeze and/or shortness of breath (possible asthma)
- Sputum – thick, yellow or green (possible bronchiectasis or bronchitis); blood stained (possible lung cancer or TB); rust-coloured (possible pneumonia); frothy and pink/red (possible heart failure)
- Recurrent nocturnal cough (possible asthma)
- Pain on inspiration (possible pleurisy or pneumothorax)
- Ineffective cough medication
- Suspected adverse drug reaction
- Suspected whooping cough or croup.

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**Table 1. Differential diagnosis of cough**

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral infection (tracheitis or bronchitis)</td>
<td>Smoking</td>
</tr>
<tr>
<td>Mainly rhinoviruses; other agents include coronaviruses, coxsackieviruses, echoviruses, orthomyxoviruses (including influenza A and B), adenoviruses</td>
<td>Gastro-oesophageal reflux disease (GORD)</td>
</tr>
<tr>
<td>Bacterial infection (tracheitis or bronchitis)</td>
<td>Asthma</td>
</tr>
<tr>
<td>Strep. pneumoniae, H. influenzae, B. pertussis, Legionella spp., Moraxella catarrhalis, Chlamydia pneumoniae</td>
<td>Postnasal drip</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>Chronic rhinitis or sinusitis</td>
</tr>
<tr>
<td>Environmental pollutants</td>
<td>Smoke, allergens</td>
</tr>
<tr>
<td>Aspiration</td>
<td>Chronic pneumonia (especially tuberculosis and <em>Pneumocystis carinii</em>)</td>
</tr>
<tr>
<td>Foreign body</td>
<td>Cancer</td>
</tr>
<tr>
<td></td>
<td>Bronchial or lung</td>
</tr>
</tbody>
</table>

**Subacute cough (postinfectious cough)**

Airway inflammation may follow a respiratory tract infection and result in a persistent, non-productive cough lasting for up to eight weeks. This cough eventually resolves, but inhaled ipratropium, inhaled or oral corticosteroids or a centrally acting antitussive may be used to provide symptomatic relief. Subacute cough may also be due to bacterial sinusitis, pertussis or asthma.

**Chronic cough**

Chronic bronchitis, usually due to cigarette smoking, is thought to be the most common overall cause of chronic cough, but most smokers with cough do not seek medical attention. Patients with a chronic cough who smoke should be counselled and assisted with smoking cessation. The most common causes of chronic cough in non-smokers are postnasal drip, asthma and gastro-oesophageal reflux disease. Chronic cough may have two or more causes in up to 60% of patients.
Upper airway cough syndrome – UACS (also called postnasal drip syndrome) \(^{5,7,8}\)

This may be due to allergic or vasomotor rhinitis, chronic sinusitis, postinfectious rhinitis, rhinitis medicamentosa or pregnancy-associated rhinitis. It is characterised by a sinus or nasal discharge that flows back into the pharynx and irritates the vocal cords, leading to a cough. Patients will typically have frequent clearing of their throat during the day, complain of cough when laughing or talking for prolonged periods of time and may have exacerbation of their cough when they lie down.

Asthma \(^{2,6-12}\)

Cough is a symptom of asthma and often accompanies wheeze, chest tightness and shortness of breath. In ‘cough-variant asthma’, cough occurs alone in the absence of other symptoms. Cough-variant asthma, although rare, should be considered when a persistent cough is exacerbated by cold or exercise, or when the cough worsens at night. A recurrent night-time cough can indicate asthma, especially in children. The preferred method of diagnosis is spirometry before and after bronchodilator use.

Gastro-oesophageal reflux disease \(^{5,11,13}\)

Cough in GORD is triggered by reflux of acid into the distal oesophagus and stimulation of an oesophageo-tracheobronchial reflex. Cough is not dependent on aspiration into the larynx or tracheobronchial tree. Symptomatic heartburn occurs in only a minority of those affected and a symptom based diagnosis can be supplemented with an empiric two-week trial of double-dose proton pump inhibitor.

Drugs

**Angiotensin-converting Enzyme Inhibitors** – approximately 10-20% of patients receiving ACE inhibitors develop cough. This occurs more commonly in women. Angiotensin-converting enzyme metabolises pro-inflammatory mediators such as bradykinins and substance P. Use of an ACE inhibitor may result in increased levels of these mediators, causing an accumulation of prostaglandin E2, thus stimulating the cough reflex. Usually, cough onset occurs within one week of starting the medication, but it may occur up to a year later. The severity of the cough can vary from a mild tickle in the throat to a severe hacking, debilitating cough. When the drug is discontinued, the cough usually abates in one to four weeks, but it may persist for up to three months. There is no advantage in changing from one ACE inhibitor to another. There is evidence that inhaled sodium cromoglycate may be beneficial for the cough if the ACE inhibitor cannot be withdrawn. The risk of cough is lower with angiotensin receptor antagonists, occurring in 1.5-3% of patients (similar to placebo).

**Beta blockers** can also induce cough and/or wheezing in certain people. They should be avoided in patients with a history of asthma or with pre-existing airway hyper-responsiveness or airway obstruction.

Other causes of chronic cough include:

- **Adult pertussis** (whooping cough) may lead to prolonged cough, and should be considered as a cause if coughing bouts are very severe and protracted, and lead to vomiting. \(^{16}\)
- **Productive cough** is the most common presentation of tuberculosis (TB) and should always be considered in high-risk groups, including the elderly, alcoholics,
the immunosuppressed; and immigrants from countries with a high prevalence of TB.19

- Bronchiectasis is characterised by irreversible dilation and destruction of the bronchial walls, usually as a result of a bronchial infection, a tumour or an aspirated foreign body. Symptoms include a constant cough producing copious amounts of purulent green-yellow sputum which may be blood-stained; persistent moist, coarse crackles and, occasionally, clubbing of the fingers. The gold standard diagnostic test is a high-resolution computerised tomography (CT) scan of the chest.2,5,6,10

- Heart failure – often the first symptoms experienced are nocturnal dyspnoea and shortness of breath. This may progress to a productive cough with frothy, pink to red sputum.6,9

- Carcinoma of the lung – cough is the presenting complaint of about a quarter of patients with lung cancer and develops subsequently in up to 90% of cases. It should be suspected in smokers who develop a marked change in the character of their cough. The cough usually produces small quantities of sputum, which may be blood-streaked. Associated symptoms may include dyspnoea, weigh loss, fatigue and clubbing of the fingers. Controlling the cough may be an important part of the patient’s palliative care.6,10

- Interstitial lung disease – e.g., sarcoidosis, cytotoxic or radiotherapy-induced alveolitis, idiopathic pulmonary fibrosis, may present with a chronic cough.7,10

- Psychogenic cough occurs less frequently in adults than in children. Many patients with this condition do not cough during sleep, are not awakened by cough, and generally do not cough during enjoyable distractions. In adolescents, psychogenic cough may present as an explosive, bark-like or honking cough. A diagnosis of psychogenic cough should be made only after all other possibilities have been eliminated. Removal of stress factors, behaviour modification therapy, and short-term use of antitussives may be beneficial.5,10

- Eosinophilic bronchitis has recently been reported as a cause of chronic cough in 10-20% of patients. Patients with eosinophilic bronchitis have normal spirometry results and respond to inhaled and systemic corticosteroids.9

### Treatment

The pharmacist will generally be called on to treat acute coughs, as patients with chronic coughs should be referred to a doctor so that the underlying disorder can be identified and treated. A Cochrane review found that there is no good evidence for or against the effectiveness of OTC medicines in acute cough. In acute cough due to the common cold, a combination first-generation antihistamine/decongestant may be given for symptomatic relief.5,6,16

### Antitussives (cough suppressants)8-10,16-20

Centrally acting antitussives are opiate derivatives and inhibit or suppress the cough reflex by depressing the medullary cough centre.

- **Dextromethorphan** is generally non-sedating, does not depress respiration in usual doses and has few side effects. It has a low potential for abuse; however, there have been rare reports of mania following abuse and consumption of very large quantities and this should be borne in mind if regular purchases are made. It may contribute to the serotonin syndrome and should not be taken in combination with other serotonergic drugs (e.g., antidepressants, tramadol, ‘triptans’). It should not be used with, or within 14 days of, a MAOI.

- **Codeine, dihydrocodeine and pholcodine** may induce drowsiness and may enhance the effects of CNS depressants. Pholcodine is less likely to cause constipation and respiratory depression and is also less likely to produce dependence. Unlike codeine and dihydrocodeine, pholcodine has little or no analgesic action.

Until evidence to the contrary becomes available, antitussives have a limited role in the treatment of acute non-productive cough. However, if a cough suppressant is deemed necessary, dextromethorphan is probably the antitussive of choice because of low incidence of CNS effects and less risk of dependence. Cough suppressants should not be used in productive coughs and should be avoided in asthma, COPD and respiratory failure as they may mask worsening symptoms.5,10,14,17

### Expectorants8-10,17-20

Expectorants are thought to help expel bronchial secretions from the respiratory tract by decreasing their viscosity, thus facilitating

### Relevant fact cards

Below is a list of fact cards relevant to the topic of this month’s inPhARmation. PSC suggests pharmacists and their staff familiarise themselves with these cards and use them while counselling customers.

- **Coughs**
- **Smoking series**
- **Children’s cold & flu**
- **Asthma series**
- **Colds & flu**
- **Hayfever**
- **Sinus problems**
- **Heartburn & indigestion**
their removal by ciliary action and coughing. By increasing respiratory tract secretions they may exert a demulcent (soothing) action on the mucosal lining. The clinical use of expectorants is controversial as their efficacy is still in doubt, and more objective experimental data is required. Adequate hydration is the single most important measure that can be taken to encourage expectoration.

Guaifenesin is the most commonly used expectorant in OTC cough remedies. It is the only substance that has been approved for use as an expectorant by the FDA, although some trials have shown it to be ineffective. It is generally well tolerated, with nausea and vomiting being the most common adverse effects. Urinary calculi composed of a calcium salt of a metabolite of guaifenesin have been reported in patients consuming large quantities of guaifenesin-containing preparations.

Ammonium salts and senega are also included as expectorants in some cough mixtures. Ammonium salts are contraindicated in hepatic and renal impairment. Large doses may cause nausea and vomiting, and ammonium chloride produces a transient diuresis and acidosis. Some cough mixtures contain both an antitussive and an expectorant; the use of such combinations is illogical and should not be recommended.

Demulcents such as glycerine, simple linctus, lemon and honey, soothe and coat the pharynx. They are inexpensive, have a pleasant taste and are particularly suitable for children and pregnant women because of their lack of active ingredients (although their effectiveness may be largely due to a placebo effect).²⁹,³¹

Other ingredients which may be found in cough medicines include:

- **Bromhexine**, a mucolytic which enhances the transport of mucus by reducing its viscosity and by activating the ciliated epithelium. Mucolytic therapy may reduce the frequency and duration of exacerbations in some patients with chronic bronchitis or COPD. Bromhexine may increase the concentration of concurrently-administered antibiotics in bronchial secretions and lung tissue. Mucolytics may disrupt the gastric mucosal barrier and should be used cautiously in patients with a history of peptic ulcer disease.¹⁰,¹₉,²₀

- **Antihistamines** – e.g., diphenhydramine, chlorpheniramine and promethazine – are thought to act through an anticholinergic-like drying action on the mucous membranes and they have the potential to form viscid mucus plugs by their drying action. The non-sedating antihistamines are less effective because of their less pronounced anticholinergic actions. Due to their drying effect, antihistamines may counteract the effect of expectorants and the combination should be avoided.⁸,⁹,¹⁷

- **Decongestants** such as phenylephrine and pseudoephedrine may be useful if the patient has nasal congestion in addition to a cough, but should otherwise be avoided. They may cause cardiovascular and CNS stimulation and are contraindicated in hypertension, hyperthyroidism, coronary heart disease, diabetes and with concurrent MAOIs.¹⁷,²¹

**References**

5. Diagnosis and Management of Cough, American College of Chest Physicians Evidence-Based Clinical Practice Guidelines; CHEST 2006; 129(1S-2S). www.chestjournal.org
Facts Behind The Fact Card – assessment
For Pharmacy Self Care members only

Questions  Select one correct answer from each of the following questions.

Answers due 30 June 2006

Please answer the following multiple choice questions using the information in Facts Behind the Fact Card and Practice Points. This activity is recognised under the PSA CPD & PI Program. ONE credit point will be awarded to pharmacists with five out of six answers correct.

To receive your credit remove the answer card provided. Complete the contact details section and your answers and fax the card to 02 6285 2869.

1. Acute coughs:
   a) require referral to a doctor, as they are usually an indication of a potentially serious underlying condition;
   b) are commonly caused by smoking;
   c) are often a symptom of a viral respiratory infection and may be symptomatically treated but will usually resolve without treatment;
   d) may be defined as coughs lasting for less than eight weeks.

2. When considering the possible cause of a cough:
   a) Asthma should only be suspected if the cough is accompanied by wheeze or tight chest
   b) A patient whose cough responds to inhaled corticosteroids but whose spirometry results do not indicate asthma may have eosinophilic bronchitis.
   c) A cough producing frothy pink-coloured sputum may be indicative of bronchiectasis.
   d) Gastro-oesophageal reflux should only be considered if the cough is accompanied by symptoms of heartburn

3. A lady comes into the pharmacy and asks for something to treat a dry cough, which she has had for about two weeks. The most appropriate response would be:
   a) Sell her a bottle of Robitussin DX.
   b) Advise her to go and see her doctor.
   c) Ask her if she has any other symptoms.
   d) Ask her if she smokes.

4. A lady comes into the pharmacy and asks for medicine for her three-year-old son who has been kept awake by a dry cough at night for the last week. What would be the most appropriate response?
   a) Ask her if her son has any cold symptoms.
   b) Sell her a bottle of Dimetapp DM Elixir.
   c) Advise her to take her son to the doctor.
   d) Ask her if there is any family history of asthma, eczema or hayfever.

5. Regarding treatment for cough:
   a) Taking large quantities of expectorant cough mixture containing guaifenesin may put a patient at risk of developing kidney stones.
   b) It has been scientifically established that cough suppressants are the treatment of choice for a dry cough.
   c) Cough mixtures containing alcohol are useful to give children at night to help them sleep.
   d) Dextromethorphan is the only centrally-acting antitussive that has no potential for abuse.

6. A middle-aged man comes into the pharmacy and asks for medicine for his cough. On questioning him you ascertain that it is a chesty cough that has been present for about four weeks and that he does not smoke. What would be the most appropriate response?
   a) Ask him if he has had a cold recently.
   b) Advise him to go and see his doctor.
   c) Sell him a bottle of Vicks Cough Syrup for Chesty Coughs.
   d) Ask him if he takes any other medications.