

Chronic cough

a guide to evaluation and management

A chronic persistent cough can be exhausting for the patient and a real challenge for the doctor. With a systematic approach to dealing with the problem, the chances of effecting a satisfactory therapeutic outcome are very good.



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Oh no! That patient of mine with chronic cough is still no better. What am I going to do? Be honest, you must have patients in your practice who evoke this response. Cough is one of the most common complaints for which patients seek medical attention. Its prevalence depends on smoking and other environmental factors: rates of between 5 and 40% have been reported for the general population and up to 23% for nonsmoking adults.

This article outlines the assessment of adult patients who present with chronic cough, including the requirement for a chest x-ray as a minimum investigation. The presentation and management of important causes in patients with a normal x-ray are then discussed; serious underlying diseases causing abnormalities on x-ray will not be covered in detail. The approach to diagnosis and treatment presented here is summarised in the flowchart on page 18.

What is chronic cough?

There are two main categories of cough: acute and chronic. For this article, chronic cough is defined to be cough persisting for more than three weeks and usually for more than eight weeks. Various definitions occur in the literature, but the one used here enables use of most of the information obtained from studies of chronic cough.

Evaluation

If a careful assessment is performed, a cause can be determined for more than 90% of cases of chronic cough. In most cases, this symptom in a non-smoker who is not taking drugs that may cause cough and who has a normal chest x-ray (i.e. no abnormality or inconsequential minimal old stable scarring) will be due to one of three problems:

- postnasal discharge
- bronchial asthma
- occult gastro-oesophageal reflux.

IN SUMMARY

- The most effective management is specific therapy directed at the underlying cause, which results in a positive response in more than 80% of patients. Therefore, a careful assessment to identify the cause of chronic cough is important.
- A chest x-ray should be taken early in the clinical investigation of chronic cough.
- The three most common causes of chronic cough when chest x-rays are normal are postnasal discharge, bronchial asthma and occult gastro-oesophageal reflux.
- Remember that cough may be the sole manifestation of occult reflux or asthma.
- Causes of chronic cough can coexist. If one cause seems likely, this should be treated; if multiple causes seem likely and important, treatment should be directed at each.
- Referral to a thoracic physician should be considered if the patient's x-ray is abnormal, if the x-ray is normal but there is no response to first line therapy over three to four weeks, or if serious symptoms exist (e.g. haemoptysis).

The prevalence of causes of chronic cough in patients who have a normal chest x-ray are listed in the Table. Note that up to 20% of cases have multiple causes.

The complications of cough often lead patients to seek medical attention. The most common ones are subjective perceptions of exhaustion and self-consciousness, interference with sleep, hoarse voice, musculoskeletal pain, urinary stress incontinence, abdominal hernias, cough syncope and even rib fractures.

History

A detailed history is essential when assessing a patient with chronic cough. Aspects that need to be considered are discussed in the box on page 20.

It is important to remember that more than one possible cause may be present. For example, a patient who has been taking ACE inhibitors for months or years may develop cough due to occult gastro-oesophageal reflux or postviral bronchial hyper-reactivity. In such situations, the history is critically important.

Physical examination

At least a basic examination of the upper respiratory tract (including the nasal passages and oropharynx) is necessary, and can be performed in any GP's office. Always feel for supraclavicular lymphadenopathy because this may be the only sign of underlying lung cancer.

Examine the chest carefully, looking particularly for crackles that may suggest bronchiectasis or interstitial lung disease and for evidence of pleural effusion, bronchial breathing, polyphonic wheezing or a localised fixed wheeze. Is there any evidence of left ventricular or right ventricular failure? Look for clubbing (which may be suggestive of interstitial lung disease, for example) and for obstruction of the superior vena cava or gynaecomastia that might indicate lung cancer.

Investigations

All adults with a chronic cough sufficient to cause them to consult a doctor should have a chest x-ray as a minimum investigation because the cough may be a symptom of serious underlying disease. Examples include:

- pulmonary malignancy (including bronchogenic carcinoma and mesothelioma)

Gastro-oesophageal reflux as a cause of chronic cough

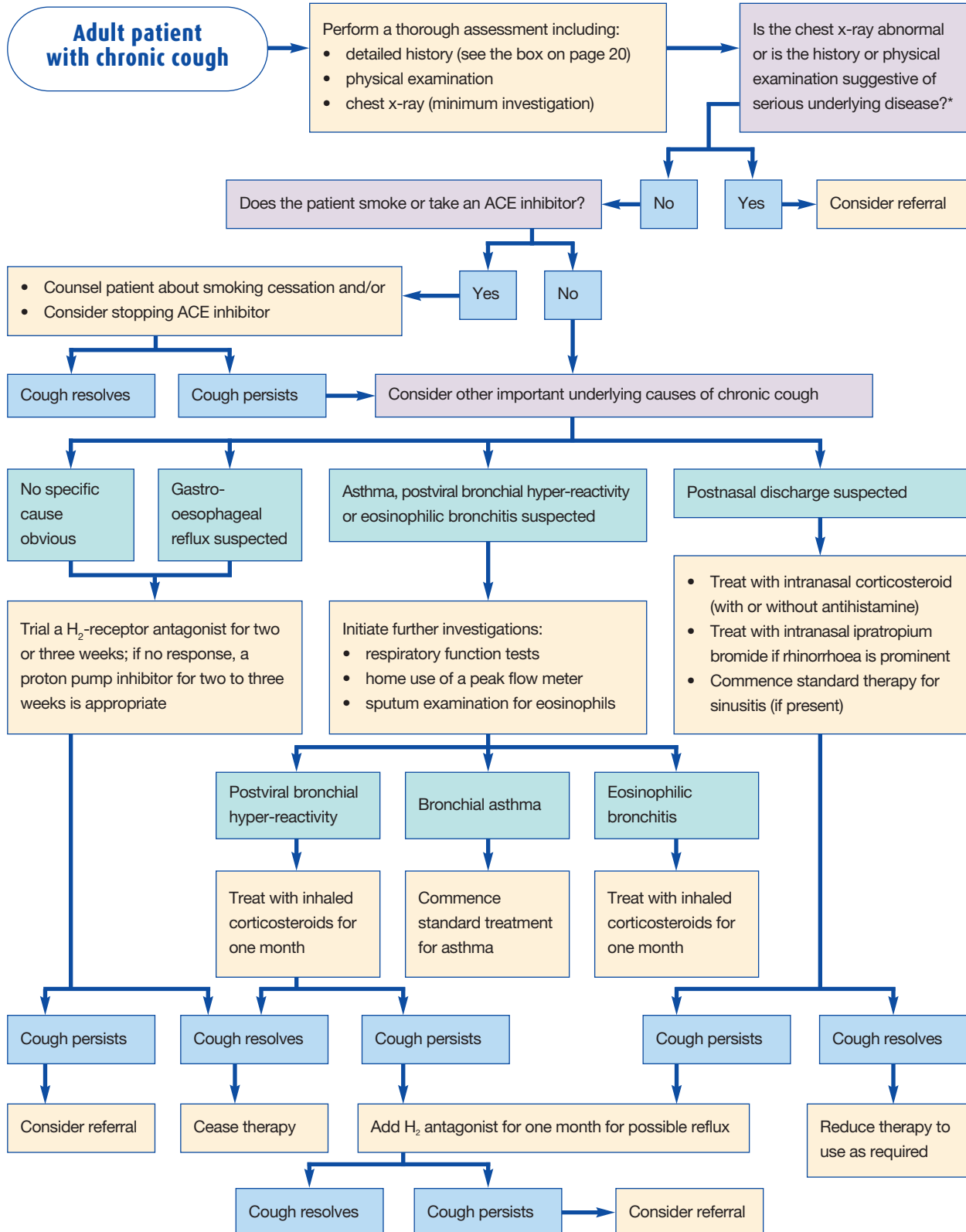
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A common cause of chronic cough is gastro-oesophageal reflux that is otherwise asymptomatic. A complex reflex arc is initiated by sensory input from irritant receptors in the distal oesophagus reacting to the acid, leading to orchestrated neuromuscular output managed by the cough centre. A vicious cycle may be established, in which the reflux produces cough and the cough leads to further reflux.

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- interstitial lung disease
 - tuberculosis
 - pulmonary vasculitis or pulmonary thromboembolism
 - bronchiectasis (seen in patients with cystic fibrosis, for example)
 - pulmonary hypertension
 - cardiac failure.
- In the majority of patients, a chest x-ray will be the only investigation required. However, a patient should promptly be referred for further

Chronic cough: a guide to diagnosis and treatment



* See the section 'Evaluation' beginning on page 16 for a discussion of serious underlying diseases causing chronic cough.

investigations if the x-ray is abnormal or if underlying disease is suggested by the history or findings on examination, such as haemoptysis, clubbing, pleural effusion (see Figure 1) or consolidation. Further investigations may include a thoracic CT scan or paranasal sinus x-rays and CT scan. If either postviral bronchial hyper-reactivity or asthma is suspected, detailed respiratory function tests may be indicated, with or without use of a peak flow meter at home. In some patients, useful investigations may include skin prick tests for atopy or 24-hour oesophageal pH monitoring (see the box on page 23).

For GPs who do not have access to complex respiratory function tests, simple spirometry before and after using a bronchodilator will show if variable airway obstruction is present. Home use of a peak flow meter will show variability suggesting bronchial asthma.

Important causes of chronic cough

If one is systematic in dealing with the problem of chronic cough then the chances of effecting a satisfactory therapeutic outcome are very good. The presentation and management of important causes that can be managed in general practice are discussed below in patients who have a normal chest x-ray.

Remember that a presentation of chronic cough is an excellent opportunity to counsel patients regarding smoking. Agents to assist smoking cessation may be considered – examples include bupropion (Zyban SR) and nicotine patches (NicabateCQ, Nicorette Patch).

ACE inhibitors

Presentation

Cough induced by ACE inhibitors occurs in 10 to 20% of individuals taking these drugs and is more common in women. It usually commences within six weeks of initiating therapy and can take six weeks or longer to remit after cessation. The cough is often worse on first lying

Table. Causes of chronic cough in patients with a normal chest x-ray

Causes*	Prevalence (%)
Bronchial asthma and/or postinfective bronchial hyper-responsiveness	33
Postnasal discharge	28
Chronic bronchitis (mainly in smokers)	12
Symptomatic gastro-oesophageal reflux	10
Otherwise asymptomatic gastro-oesophageal reflux (often postviral)	25
Other causes (examples include psychogenic cough, tracheomalacia, ACE inhibitor therapy, foreign body, pertussis infection, eosinophilic bronchitis)	10
* Multiple causes occur in up to 20% of cases.	

down in bed at night and is usually non-productive.

Management

If an ACE inhibitor was commenced within the last two to three months, ceasing the medication would be reasonable. However, if a patient has been taking an ACE inhibitor for many months or years without cough the medication is almost certainly not relevant to the current problem.

If ACE inhibitor therapy is to be ceased, diuretics and calcium channel blockers are suitable substitutes for treating hypertension; beta blocking agents should not be used at this stage because the patient may have occult asthma. A trial of inhaled sodium cromoglycate (Intal, Intal Forte) or nedocromil (Tilade) may be useful if the cough is very troublesome.

Postviral bronchial hyper-reactivity

Presentation

Some patients who do not normally have chronic lung disease may develop a period of airway hyper-reactivity after a respiratory infection that causes the cough to persist long after the infection has resolved. The cough of postviral bronchial hyper-reactivity is associated with other features of airway irritability (that is, precipitated

by laughing, talking, cold air, exertion, etc). It may be productive and might be waking the patient at night. Dyspnoea and wheeze are not features.

Many cases settle over weeks or months, but patients may develop a prolonged cough of similar duration after a respiratory infection in the future. Other patients occasionally go on to develop frank asthma.

Management

If postviral bronchial hyper-reactivity is suggested, detailed lung function tests are appropriate, including spirometry, lung volumes and a methacholine bronchial



Figure 1. Chest x-ray showing shadowing at the right base in a patient presenting with chronic cough. Further investigation is essential in such a case.

provocation test (or similar). These tests can be performed in any major respiratory function laboratory attached to a tertiary hospital or arranged through a respiratory physician. Patients show heightened bronchial hyper-reactivity, but no significant airflow limitation.

If the cough is troublesome, treatment with inhaled corticosteroids for one month is indicated and will usually settle the cough – examples include budesonide (Pulmicort, 200 to 400 µg twice daily), fluticasone (Flixotide, 250 to 500 µg twice daily) and beclomethasone

(Qvar, 100 to 200 µg twice daily). Treatment should be repeated if the cough recurs after subsequent respiratory infection, provided that other serious underlying disease has been excluded as the cause of that episode.

Important aspects of history taking

- Does the patient smoke? A history of smoking may suggest chronic bronchitis or lung cancer.
- How did the cough begin? Postviral airway hyper-reactivity and occult reflux are the two main possibilities if the patient had a respiratory infection that improved but left a persistent cough.
- Has the patient had episodes of chronic persistent cough interspersed with periods of normality lasting months or years? If so, bronchial asthma, postviral reactivity or occult reflux should be suspected.
- Are there triggers to the cough? Asthma and postviral bronchial hyper-reactivity are suggested if the cough is triggered by talking, laughing, cold air, exertion, passive smoke and pressure pack sprays.
- Is the cough troublesome in bed at night? Generally speaking, this feature points to asthma.
- Is the cough productive and, if so, is the sputum purulent? Frequent daily purulent sputum is suggestive of chronic bronchitis (in a smoker), bronchiectasis (which may be present even if the chest x-ray is normal), or chronic suppurative postnasal discharge.
- Is there haemoptysis? This is always a serious symptom, and can point to bronchiectasis, lung cancer or a foreign body.
- Does the patient have pain associated with the cough to suggest pleural involvement? This may occur in mesothelioma, for example.
- Is there dyspnoea, with or without wheeze? If so, asthma, chronic bronchitis or a pleural effusion is suggested.
- Has the patient had weight loss or night sweats? Both of these features suggest a serious underlying disease such as lung cancer or tuberculosis.
- Has there been any relief from the cough by trying an inhaled bronchodilator? Sometimes a patient who has a family member with asthma will have tried the relative's bronchodilator. A positive response is suggestive of asthma.
- Has the patient been taking an angiotensin receptor antagonist or ACE inhibitor? Note that the newer angiotensin receptor antagonists can cause cough, but considerably less often than the ACE inhibitors.
- Has there been whooping cough in the family or symptoms to suggest it?
- Are symptoms present to suggest postnasal discharge or recurrent paranasal sinusitis? Find out if the patient has had nasal polyps or nasal surgery in the past. Frequently clearing the throat would suggest a postnasal discharge.
- Does the patient suffer from heartburn? This symptom may suggest gastro-oesophageal reflux as a cause.
- What is the patient's occupation? Fumes, dust or paints in the workplace may be causing bronchial asthma, with cough being the first manifestation.

Occult bronchial asthma

Presentation

Chronic cough may be the only symptom of asthma, but a careful history may elicit associated wheeze or mild dyspnoea. Features of airway irritability may be present, and the cough may be troublesome in bed at night. The patient may have a history of atopic disease, such as allergic rhinitis, or of improvement with use of an inhaled bronchodilator. A family history of asthma may be present.

Management

If asthma is suspected, detailed respiratory function tests are indicated, including a methacholine bronchial provocation test (or similar), together with home use of a peak flow meter. Standard treatment for asthma should be commenced if the diagnosis is confirmed.

Postnasal discharge

Presentation

Cough due to postnasal discharge can occur in association with allergic or vasomotor rhinitis. Accompanying symptoms of sneezing, nasal obstruction and nasal itching may be present, and recurrent paranasal sinusitis is possible. Patients are sometimes aware of the discharge but might not link it to their cough. The cough may or may not follow a viral respiratory infection.

Management

If postnasal discharge is suspected (either as the sole cause or as a contributing factor), intranasal corticosteroids with or without a nonsedating antihistamine will usually control the symptoms. An example of an appropriate regimen may be budesonide ([Budamax Aqueous Nasal Spray

64 µg, Rhinocort Aqueous Nasal Spray 64 µg], one or two puffs to each nostril once daily for two to three weeks and then as required), with or without oral fexofenadine ([Telfast], 120 mg at night for a few nights and then as required). Intranasal ipratropium bromide (Atrovent Nasal) can be tried if rhinorrhoea is prominent. Skin prick tests for allergies may be useful for targeting methods to minimise environmental exposure.

Occasionally, response to the above-mentioned measures is poor in patients with nonallergic rhinitis. In such cases, the older antihistamines may be useful, with or without decongestants. Acute sinusitis needs to be treated along standard lines.

Occult gastro-oesophageal reflux

Presentation

A frequent cause of chronic persistent cough is gastro-oesophageal reflux that is otherwise asymptomatic. The usual scenario is a patient who had developed a respiratory infection of the upper or lower tract, with cough persisting well after the infection resolved. The cough results in transient impairment of lower oesophageal sphincter tone, which allows reflux into the lower oesophagus (see Figure 2). A vicious cycle is thus established, in which the cough produces reflux and the reflux produces further coughing. Such a cough may persist for months or years following the respiratory infection, and the infection may have been forgotten by the patient.

The cough that is caused by otherwise asymptomatic reflux is usually nonproductive and rarely troublesome in bed at night (the lower oesophageal sphincter is more competent in the recumbent position). The features of cough in this setting contrast with those of the cough that may occur with well known symptomatic reflux with or without hiatus hernia.

Management

If a patient's features are of occult gastro-oesophageal reflux or all other causes

have been excluded, treatment for reflux should be trialled for at least one month without further investigations for reflux. Start with a H₂-receptor antagonist for two

to three weeks, such as ranitidine (150 mg twice daily), famotidine (Amfamox, Pepcid, Pepcidine; 20 to 40 mg twice daily) or nizatidine (Tazac). For patients who do

24-hour ambulatory oesophageal pH monitoring

If gastro-oesophageal reflux is suspected, 24-hour ambulatory oesophageal pH monitoring may be indicated (Figures A and B). The investigation is a sensitive test of oesophageal reflux and will show whether cough is temporally related to the reflux.



Figure A. Nasaloryngoscopy followed by an oesophageal pH probe insertion.

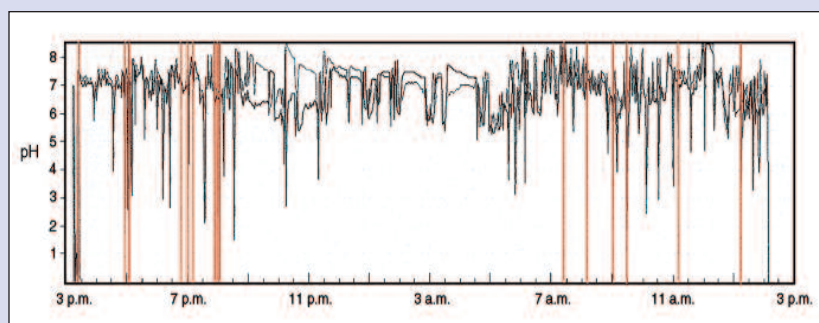


Figure B. A tracing from 24-hour ambulatory oesophageal pH monitoring, recorded with a probe in the lower oesophagus. The red lines represent episodes of cough; the black trace shows oesophageal pH. The result shows that many coughs are temporally associated with decreases in pH, and is consistent with a diagnosis of cough due to oesophageal reflux. Note that fewer decreases in pH occur in bed at night and that no coughing occurs during this period.

not respond, a proton pump inhibitor, such as omeprazole (Acimax, Losec, Maxor), lansoprazole (Zoton), rabeprazole (Pariet) or pantoprazole (Somac, 20 mg at night), is appropriate for a further two to three weeks. Between 80 and 85% of patients will have a marked improvement, and further investigation should be undertaken only if such improvement does not occur (24-hour ambulatory oesophageal pH monitoring is ideal, whereas a barium swallow and meal have little or no place in this setting).

In patients with chronic persistent cough unexplained by a systematic approach, a trial of antireflux therapy is appropriate even if no other symptoms of reflux are present. Chronic cough due to occult reflux may take two to three months to begin to improve and up to six months to disappear completely. Nonetheless, if the cough has not improved within four to six weeks then referral for further investigation is indicated. Endoscopy of the upper gastrointestinal tract may be indicated if the results of 24-hour pH monitoring are markedly abnormal. Antireflux surgery (fundoplication) is occasionally required for very troublesome cough proven by 24-hour ambulatory oesophageal pH monitoring that is not responsive to proton pump inhibitors in high doses.

Eosinophilic bronchitis

Presentation

A presentation has been described that does not conform to any of the above diagnoses. Patients are typically middle-aged adults with a dry cough or cough productive of small amounts of viscid sputum in the mornings. Most are non-smokers without wheezing or dyspnoea or any signs or lung function evidence of airflow limitation; bronchial reactivity is normal.

These patients do not have asthma or postviral bronchial hyper-reactivity, and reflux does not appear to be associated with the condition. However, examina-

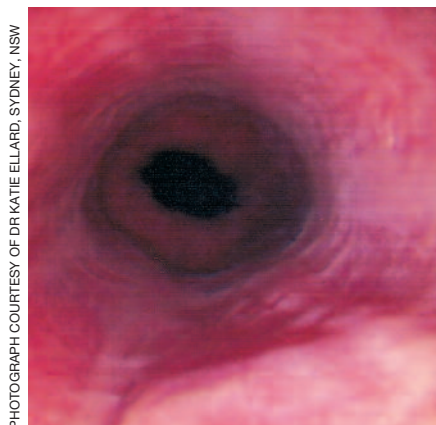


Figure 2. Mild reflux oesophagitis associated with a sliding hiatus hernia.

tion of the sputum (spontaneous or induced) shows that more than 3% of nonsquamous cells are eosinophils. This condition, known as eosinophilic bronchitis, was the cause of cough in 13.2% of cases of chronic cough in one series.¹

Management

If eosinophilic bronchitis is suspected on the history and examination, sputum should be examined for eosinophils. Lung function tests are normal. Inhaled corticosteroids should be trialled for one month if the diagnosis is confirmed.

Nonspecific cough suppression

The best way of managing chronic cough is by treating the underlying cause which will, in most cases, abolish the cough. While waiting for the treatment to work, however, the cough can be very distressing and require therapy aimed at suppressing the symptom. Most so-called cough suppressants are ineffective, but patients may find the following measures helpful.

Inhalations of water vapour

Some patients find inhaling hot water vapour very useful. A bowl of hot water (but not boiling water) is placed on a table, and the patient sits facing over it with a towel covering his or her head and

the bowl. The therapy can be continued, two or three times a day, until the underlying condition responds to specific treatment. Note that water vapour inhalations should not be used for children.

Nebulised ipratropium bromide

Ipratropium suppresses cough irritant receptors in the airways and can be helpful before bed, particularly if the cough is troublesome during sleep. Patients can hire a pump and use 500 to 1000 µg of nebulised ipratropium bromide. This treatment can be continued until the cough starts to respond to appropriately targeted therapy but is, unfortunately, expensive.

OTC medications

Some patients find a linctus of pholcodine useful (Actuss, Duro-Tuss, Linctus Tussinol, Logicin Cough Suppressant). Cepacol Cough and Sore Throat Lozenges may also be helpful.

Nedocromil

The evidence suggesting that nedocromil metered dose inhalers are useful for nonspecific cough management is not convincing. Nedocromil may have a place in bronchial asthma if cough is troublesome or in ACE inhibitor induced cough.

Referral

As a rule, both rural and urban GPs should be able to manage most patients with chronic persistent cough who have a normal chest x-ray. Referral to a thoracic physician should be considered if a patient has an abnormal chest x-ray because further investigation is mandatory. In addition, referral may be appropriate for a patient with a normal chest x-ray who does not respond to initial treatment.

Concluding comments

In the past, chronic cough has often been managed by prescribing a hotch potch of cough suppressants rather than

by directing treatment to the underlying cause. However, the most effective management of cough is specific therapy, which will benefit more than 80% of patients who do not have an abnormality on chest x-ray. Therefore, a careful assessment to identify the cause of the cough is important.

In the majority of cases, cessation of smoking or of ACE inhibitor therapy (if appropriate) and treatment directed at postviral bronchial hyper-reactivity, occult bronchial asthma, postnasal discharge or occult gastro-oesophageal reflux is likely to be successful. Referral should be considered if the patient's x-ray is abnormal or there is no response to first line therapy over a period of three to four weeks. **MT**

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Further reading

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