



Managing Cough in Adults: Is there a Serious Underlying Cause?

A thorough history and physical examination, targeted investigations, adequate treatment trials and the option of combining therapeutic approaches are important components of an effective management plan in patients with acute and chronic cough. Serious underlying causes such as malignancy, pneumonia or congestive cardiac failure should be excluded.

Cough is a normal physiological reflex to remove secretion from and prevent inhalation of foreign material into the lungs. It is one of the most common reasons for patients to present in primary care and has significant social and economic impacts. It also affects patients' wellbeing and can significantly impair quality of life.¹⁻³ Cough can be difficult to manage and many evidence-based guidelines have been published⁴⁻⁸ with the American College of Chest Physicians recommending that clinicians use an empiric integrative diagnostic approach in adult patients presenting with cough.⁸ This article outlines a diagnostic approach to the management of cough in adults.

Mechanism of cough

The cough reflex is usually initiated by stimulation of afferent structures found in upper and lower airways, and the tympanic membrane and external auditory meatus. These structures respond to both chemical and mechanical stimuli and are innervated by the vagus nerve,⁹

which sends a signal to the 'cough centre' in the brain stem, with subsequent motor activation of expiratory muscle groups, including the diaphragm, larynx, pharynx and intercostals. However, cough can also be generated at a central nervous system level or voluntarily.

Cough categorisation

Cough can be categorised arbitrarily by time, with acute cough typically lasting less than three weeks, and chronic cough lasting more than eight weeks.^{7,10} Cough lasting between these periods can be defined as sub-acute cough and can be managed as chronic cough once post-infectious cough is excluded. Cough can

also be described as productive (>30mL of sputum per day)¹¹ or non-productive. Clinicians should also enquire about any particular trigger, and quantity and quality of sputum produced (including the presence of blood).

Acute cough

Recent onset cough is usually self-limiting and commonly caused by infections (especially viral) of the upper or lower respiratory tracts, including the common cold.¹² It affects healthy adults and those with chronic lung diseases. Clinically, it is important to determine through medical history and physical examination whether the acute cough is due to a non-life-threatening diagnosis such as infection, an exacerbation of a pre-existing condition (eg, asthma) or chronic obstructive pulmonary disease, or whether it is due to a more serious cause such as pulmonary embolism, congestive heart failure or pneumonia. Features such as coryzal symptoms, sputum and fever, or physical examination

Key points

- A detailed medical history and physical examination are important in managing patients with cough.
- Acute cough is defined as cough lasting less than three weeks and chronic cough as lasting more than eight weeks.
- Acute cough is commonly caused by infections (especially viral) of the respiratory tract.
- It is important to exclude serious illness as a cause of acute cough and to exclude a post-infectious cause in patients with sub-acute cough.
- A trial of cessation of medications that can cause cough is recommended.
- Chronic cough is strongly associated with smoking. Upper airway cough syndrome, asthma or gastro-oesophageal reflux diseases are the most likely causes of chronic cough in a healthy non-smoker.
- A combined therapeutic approach in sequential steps and referral of the patient to a specialist may be required in the management of chronic cough.

About the authors

Dr Benjamin Kwan MB BS, BSc(Med), FRACP is a respiratory and sleep medicine Staff Specialist and Network Director of Physician Training at St George and Sutherland Hospitals Network; and Conjoint Lecturer at The University of New South Wales, Australia.

Dr Chin Goh MB BS, BSc(Med) is a respiratory and sleep medicine Advanced Trainee (final year) at St George Hospital, Sydney, Australia.



Guidelines on cough

- Therapeutic Guidelines: Respiratory. Version 4, 2009⁴
- CICADA: Cough in children and adults: diagnosis and assessment.
- European Respiratory Society: ERS guidelines on the assessment of cough⁶
- British Thoracic Society: Recommendation for the management of cough in adults⁷
- American College of Chest Physicians: Diagnosis and management of cough executive summary⁸

findings such as upper airway inflammation and presence of crackles on auscultation may help determine the anatomical site of the infection (see the box).

Most patients presenting with acute cough do not need any investigation. However, patients who are at risk or who present with more worrying symptoms will require a chest x-ray and other specific investigations. Although there is little evidence that various over-the-counter preparations have a specific pharmacological effect, many patients do report a clinical benefit. Dextromethorphan, menthol, sedative antihistamines, codeine and pholcodine have all been shown to suppress cough reflex in clinical studies using cough challenge methodologies. Codeine and pholcodine are opiates and have a greater side effect profile than dextromethorphan.⁷ The flowchart later in this article shows an example of a clinical pathway for managing acute cough. Some of the usual common causes of acute cough are described below.

Acute bronchitis

Acute infection of the larger airways in otherwise healthy patients is most often viral and does not require antibiotics. Use of a neuraminidase inhibitor such as oseltamivir within 48 hours of onset of symptoms can reduce the clinical course of an influenza infection by one day on average.¹³ In treating the common cold, a first-generation antihistamine together with a decongestant has been shown to reduce severity and hasten resolution of cough and postnasal drip whilst the NSAID naproxen also improves cough.^{12,14}

The incidence of infection caused by *Bordetella pertussis* (whooping cough) in adults has increased worldwide and should be considered if the cough is persistent and paroxysmal or accompanied by post-tussive emesis or inspiratory whoop.¹⁵ Investigation should include an early posterior nasopharyngeal swab for culture and/or polymerase chain reaction testing for *B. pertussis*. Recommended treatments include isolation for five days and use of macrolide antibiotics, which can achieve clinical benefit if given within the first week, whereas later treatment may minimise the spread of infection.¹⁶

Asthma and asthma-like syndromes

Asthma onset can occur late in adulthood in individuals with smoking history or preceding rhinitis.¹⁷ Patients with uncontrolled or poorly controlled asthma can present with acute cough, particularly after exposure to trigger factors, or spontaneously at night. Associated symptoms such as chest tightness, wheeze or dyspnoea and a history of asthma or atopy are helpful. Obstructive spirometry with significant bronchodilator reversibility is a typical finding, and most patients will have a positive bronchoprovocation test.

Management of asthma includes allergen avoidance, appropriate preventive and reliever bronchodilators, and management of exacerbation according to established guidelines (eg, the Global Initiative for Asthma guidelines).¹⁸ Initial treatment should include use of an inhaled corticosteroid and a β agonist, and a response should be expected within one week. Oral leukotriene inhibitors may also be effective in people with asthma-induced cough, and can be added if cough persists.¹⁹ Concurrently managing conditions that may co-exist and aggravate the cough, such as smoking, respiratory tract infection, gastro-oesophageal reflux disease (GORD) and rhinitis with postnasal drip, is also recommended.

Drug-induced cough

Although uncommon, certain medications can cause cough, and these should be excluded in patients with unexplained cough. A temporal relation between

Important history and examination findings not to be missed

History

- Recent respiratory infection
- Occupational factors
- Smoking history
- Prominent dyspnoea
- Haemoptysis
- Systemic features (eg, fever, weight loss)
- Dysphagia, aspiration, gastro-oesophageal reflux symptoms
- Medications (eg, angiotensin converting enzyme inhibitors)
- Prominent aggravating factor

Physical examination findings

- Crackles on auscultation
- Examination of ear, nose and throat for rhinosinusitis
- Spirometry, bronchodilator reversibility, bronchial provocation challenge

cough development and commencement of a new drug treatment may not always be evident. Important drugs to consider include angiotensin converting enzyme (ACE) inhibitors (up to 15% of patients taking this medication may develop cough), beta-blockers in patients with asthma, and aspirin. Drugs that can cause diffuse interstitial lung disease, such as amiodarone and methotrexate may also cause chronic cough. A trial without the potentially offending drug (including cigarette smoking) is the first step in the management of a patient with a suspected drug-induced cough.

Other causes

It is important to consider a foreign body as a cause of acute cough, especially in patients at risk of aspiration. Radio-opaque objects may be visible on plain x-ray; further imaging (eg, CT scan of the chest) or endoscopic procedures (eg, nasoendoscopy or bronchoscopy) may be needed for diagnosis and retrieval of the foreign body.

Where tuberculosis is prevalent in a community, patients who present with a cough plus associated systemic features



(such as weight loss, night sweats or cervical lymphadenopathy) and chest x-ray changes need to be investigated to exclude *Mycobacterium tuberculosis* infection.³ Early morning sputum samples should be taken to look for acid-fast bacilli. Referral to a specialised tuberculosis chest clinic is warranted in highly suspected individuals. Further investigations such as Mantoux skin test or QuantiFeron Gold and bronchoscopic investigation may then be arranged.

Another diagnosis that is important not to miss is malignancy. Suspicion should be raised in people who are heavy smokers and have alarming clinical features such as haemoptysis and weight loss (see the chronic cough section). Other more rare causes of acute cough include pneumothorax, pleural effusion, pulmonary embolism and heart failure.^{20,21}

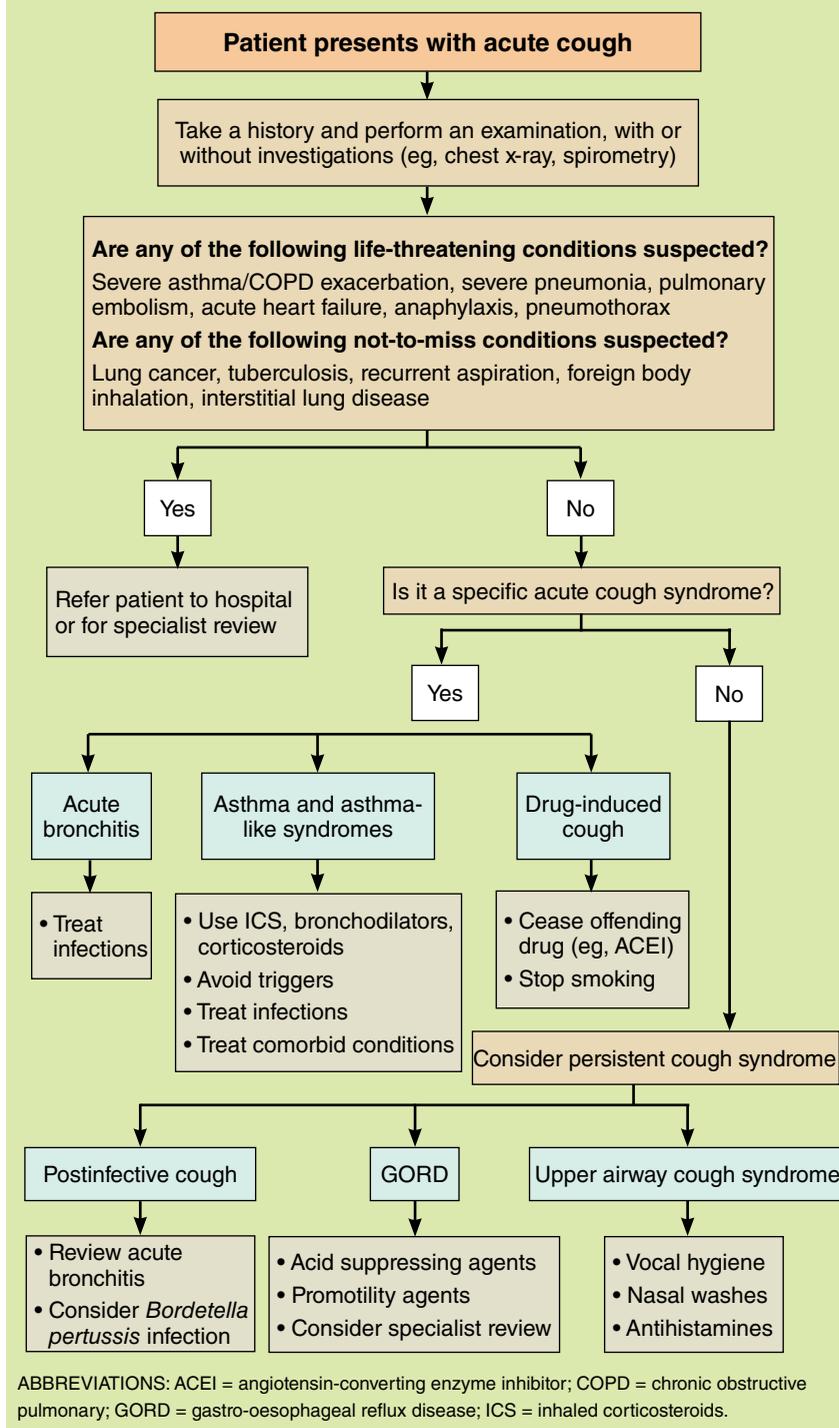
Sub-acute cough

There is currently little data regarding causes and treatment of sub-acute cough. Clinically, it is useful to determine if the cough is of a post-infectious nature. In such cases, probable reasons for lingering cough include persistent upper airway irritation, mucous accumulation, persistent postnasal drip or bronchial hyper-responsiveness. It is important to exclude infections such as tuberculosis or pertussis, and acute exacerbation of chronic respiratory diseases such as asthma or COPD. In non-infectious cases of sub-acute cough, the recommendation is to evaluate and manage the patient as presenting with chronic cough.

Chronic cough

The prevalence of chronic cough is strongly associated with smoking, with people who are current smokers having a two- to threefold greater prevalence than those who have never smoked.^{8,22} The prevalence rate increases with the number of cigarettes smoked and decreases significantly with smoking cessation. Other environmental and occupational factors, including particulates, certain home heating components (eg, wood stove, paraffin heater) and road traffic pollutants, may also need to be addressed. Several prospective studies have reported that the most likely causes

Suggested management pathway for patients with acute cough



of chronic cough in people who are non-smokers and who have no recent chest infection and a normal chest x-ray, include upper airway cough syndrome (includes postnasal drip syndrome), asthma and GORD. Furthermore, a

combination of two or more of these conditions is responsible for up to a third of cases.²³⁻²⁵ Other important conditions causing chronic cough include bronchiectasis, ACE inhibitor-related cough, diffuse parenchymal lung disease



and psychogenic cough. When no clear cause is found, the preferred term 'unexplained cough' is used. No clear cause is found in up to 20% of cases in carefully investigated case series, but probably even more in clinical practice.²¹

In managing a patient with chronic cough in primary practice, it is important to take a detailed history, including current and previous occupation, domestic environment, dust/chemical exposure and presence of pets, and perform a physical examination. A chest x-ray and spirometry should also be performed. If an obstructive pattern is observed, a pre- and post-short-acting β_2 -agonist effect on forced expiratory volume in one second (FEV₁) should be measured.

There is currently no evidence linking the cough duration to a particular cause, nor ongoing viral infection to persistent cough. There is also a poor diagnostic sensitivity and specificity relating to cough characteristics.²⁶ However, cough reflex sensitivity may be enhanced by viral infection, ACE inhibitors, GORD and asthma.^{24,27,28} Any associated alarming features warrant immediate attention. These features include a significant smoking history (more than 20 pack years), haemoptysis, new onset hoarseness, prominent dyspnoea (nocturnal or resting), systemic features (eg, fever, weight loss, night sweats), complicated gastro-oesophageal symptoms (eg, anaemia, overt bleeding, dysphagia), feeding troubles or recurrent pneumonia.⁵ Abnormal respiratory clinical findings or radiographic changes also merit further investigation.

Systematically addressing the following specific common conditions may aid in the management of chronic cough. However, if there is failure of empirical treatment or targeted investigations are normal, the patient should be referred to a specialist. An approach to the diagnosis and management of chronic cough is shown in the flowchart.

Upper airways disease

Clinical features of nasal inflammation (blockage, rhinorrhoea, itchiness) with conjunctivitis may suggest allergic rhinitis, especially in atopic individuals. Skin prick testing may assist in identifying common allergens. Treatment of cough in this setting involves management of allergic rhinitis according to cur-

rent guidelines,¹⁵ primarily with topical nasal corticosteroids. Antihistamines, decongestants, allergen avoidance and immune-therapy may also play a role.

Patients with chronic rhinosinusitis who experience mucopurulent nasal discharge, sinus pain, anosmia and headaches may also be burdened by chronic cough. Management includes nasal saline irrigation and intranasal corticosteroid therapy for at least four weeks, with oral antibiotics cover for the same period.²⁹ Use of oral corticosteroids for a short duration is indicated if there is associated nasal polyposis. If the above medical therapy fails, a CT scan of the sinuses should be arranged for diagnosis and/or surgical planning, with subsequent referral of the patient to an ear, nose and throat specialist.

Vocal chord dysfunction

Patients with vocal chord dysfunction experience stridor and dysphonia due to episodic, uncontrollable narrowing of the cords during inspiration, with associated dyspnoea and cough occasionally. Direct laryngoscopy and flattening of the inspiratory flow-volume loop on spirometry can support the diagnosis. Acute interventions of vocal cord paradoxical movement sometimes involve continuous positive airway pressure and, rarely, tracheostomy. Successful longer-term treatment reported involves voice therapy and psychological counselling.³⁰ Apart from reassurance, irritant avoidance and supportive care, these patients are perhaps best managed in consultation with an experienced speech pathologist. Optimising medical treatment of comorbidities such as asthma is also crucial. Vocal chord dysfunction often leads to a misdiagnosis of asthma and subsequent overtreatment with inhaled corticosteroids; however, the two may coexist.

Nonasthmatic eosinophilic bronchitis

Nonasthmatic eosinophilic bronchitis is an increasingly recognised cause of chronic cough, usually with minimal sputum production. However, induced sputum in these patients demonstrates increased eosinophil counts. Typically, the patient has no airflow limitation on spirometry and no bronchial hyper-reactivity on bronchial challenge test. These

results suggest active airway inflammation in the absence of airway hyper-responsiveness. Treatment with inhaled corticosteroids should alleviate the cough within four weeks of therapy.³¹⁻³⁴

Chronic lung diseases

Patients with chronic lung diseases often have persistent cough, with excessive sputum production seen in those with conditions such as chronic bronchitis and bronchiectasis. Chronic obstructive pulmonary disease (COPD) is characterised by airflow obstruction and is usually progressive, with enhanced chronic airway inflammation to noxious particles. The clinical diagnosis should be suspected in patients with dyspnoea, chronic cough or sputum production, and exposure to risk factors (eg, tobacco smoke, pollution, burning of biomass fuels). Assessment and management of patients with COPD should be guided by established guidelines (eg, Global Initiative for Chronic Obstructive Lung Disease guidelines).³⁵

Bronchiectasis shares many clinical features with COPD. Clinical diagnosis can be established by chronic daily cough with viscid sputum production and a high-resolution CT scan of the chest demonstrating bronchial thickening and luminal dilatation. This could be due to a congenital condition, such as cystic fibrosis, ciliary dyskinesia or immunodeficiency, or acquired through recurrent or significant airway insults, such as childhood infections, foreign body aspiration or connective tissue disease. Treatment aims at controlling infection and improving bronchial hygiene. Referral of the patient to a respiratory physician, with support from a multidisciplinary team (including a physiotherapist and pulmonary rehabilitation), is recommended.

Asthma

Asthma is a common cause of chronic cough and should be considered once upper airway cough syndrome has been evaluated. Medical history is not reliable to exclude the diagnosis and the bronchoprovocation test, which has a high negative predictive value and a positive predictive value of 60% to 88%,^{22,36} is often needed.³⁷ Most patients will respond to treatment, including inhaled



corticosteroids and β -agonists within one week, but complete resolution may take eight weeks or more. If cough persists, a 5-day to 10-day trial of oral corticosteroids may be required (see the sec-

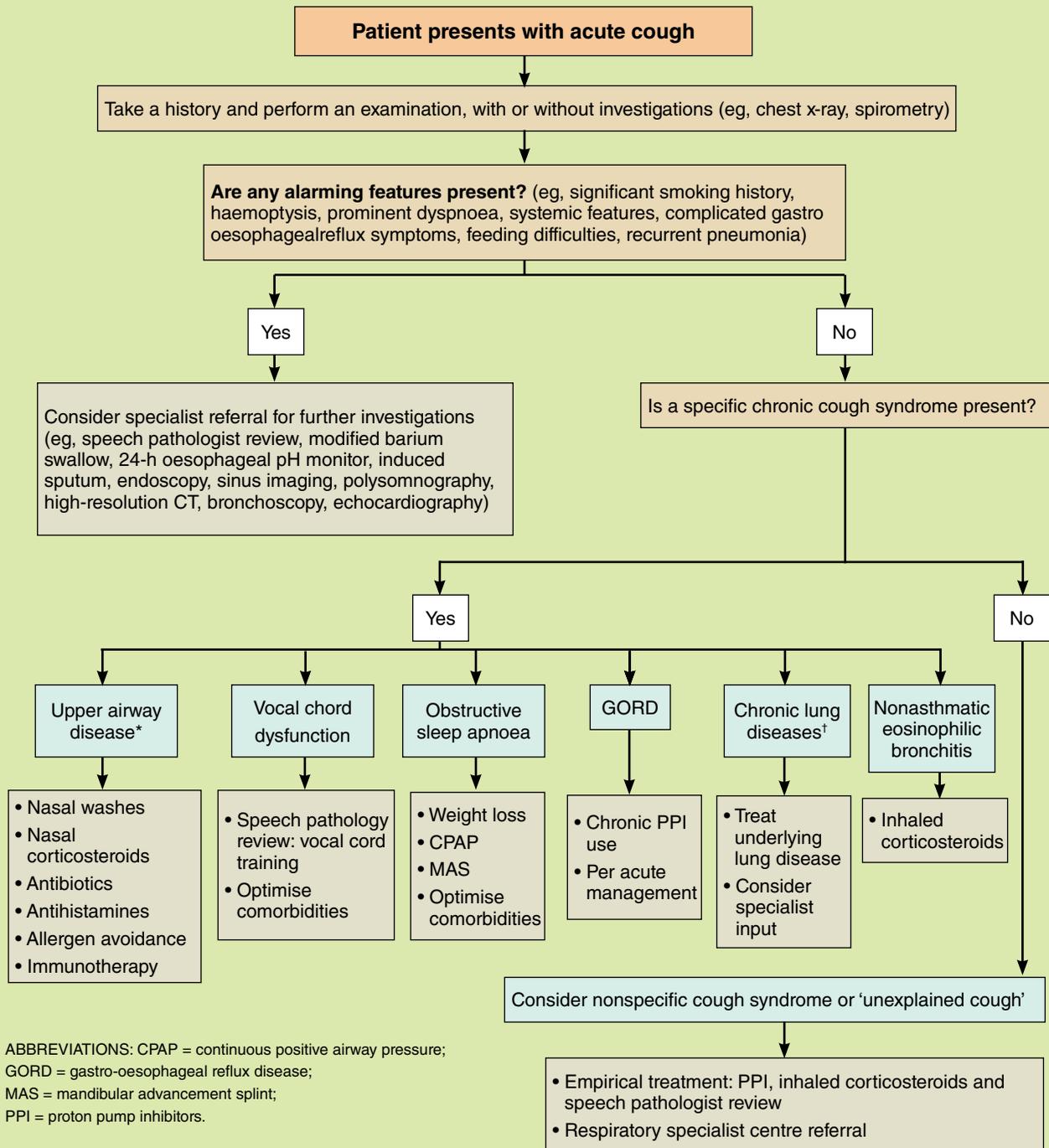
tion on asthma under the acute cough heading).

Obstructive sleep apnoea

Obstructive sleep apnoea is character-

ised by symptoms of snoring, observed apnoeic episodes during sleep (with or without nocturnal awakenings) and daytime hyper-somnolence. Overnight polysomnography remains the standard for

Suggested management pathway for patients with chronic cough



ABBREVIATIONS: CPAP = continuous positive airway pressure; GORD = gastro-oesophageal reflux disease; MAS = mandibular advancement splint; PPI = proton pump inhibitors.

* Upper airway diseases include allergic rhinitis, chronic rhinosinusitis.

† Chronic lung diseases include airway abnormalities (eg, bronchomalacia), asthma, bronchiectasis, chronic bronchitis, chronic obstructive pulmonary disease, cystic fibrosis.



diagnosis. Management includes weight loss advice, nasal continuous positive airway pressure and mandibular splinting devices, depending on severity.

Gastro-oesophageal reflux disease

Up to a third of patients with GORD may experience chronic cough,³⁸ suggested by association of cough with meals, worsening on supine/stooping posture or the presence of dyspepsia. Reflux-associated cough may also affect patients without noticeable gastro-oesophageal symptoms. The most useful test for GORD is 24-hour ambulatory oesophageal pH monitoring. However, it is not routine to put patients through such a test. Anti-reflux treatment reduces cough reflex sensitivity in affected patients so a trial of acid suppressants may be warranted without investigation. Proton pump inhibitors with or without pro-kinetic agent cover, for at least eight weeks, are recommended.^{7,29} However, if the cough persists, acid suppressants should be discontinued after the recommended trial period.

Unexplained cough

Occasionally, cough persists despite addressing the acute and chronic causes described above. Some authors recommend a trial of empirical treatment with inhaled corticosteroids, proton pump inhibitors and speech pathologist review.²² Referral of the patient to a respiratory specialist may also assist, especially if conditions such as refractory asthma and eosinophilic bronchitis are suspected.

Conclusion

Cough is one of the most common causes of patients presenting to primary care physicians, and can be challenging from a diagnostic and therapeutic viewpoint. Chronic cough can be disabling and may have a significant cost burden. Viral upper respiratory tract infections are the most common cause of an acute cough and are usually self-limiting. Smoking is the most common cause of chronic cough, whereas asthma, GORD and upper airway cough syndrome are the most common causes in non-smokers.

An effective management plan is important in the evaluation and treatment of cough. Clinicians should take a thorough history and perform a physical examination, targeting investigations, providing adequate treatment trials and canvassing the option of combining therapeutic approaches. It is important to determine early whether a serious underlying cause such as malignancy, pneumonia or congestive cardiac failure is present. In difficult or undiagnosed cases, clinicians should refer the patient to a specialist with an interest in chronic cough management.

References are available on request.

Subscription Form



Subscribe NOW to receive EVERY ISSUE of Modern Medicine. Access 55 clinical CPD points and 10 ethics CPD points per year.

NON SUBSCRIBERS ONLY RECEIVE OCCASIONAL ISSUES.

Please complete this form in block letters, select your subscription option and, along with your payment, return to Modern Medicine, PO Box 84622, Greenside, 2034. Tel: 083-325-8947, Fax: 086-293-7289. e-mail: veronica@modernmedia.co.za

SUBSCRIPTION OPTIONS (PLEASE TICK)

12 Month subscription	R440,00	<input type="checkbox"/>
24 Month subscription	R770,00	<input type="checkbox"/>
36 Month subscription	R990,00	<input type="checkbox"/>

Full name:

Medical registration: MP.....

Year of qualification:

Postal address:

..... Code:

Tel: (.....)..... Fax: (.....).....

e-mail:

PLEASE SELECT YOUR PREFERRED PAYMENT OPTION

- Cheque – Enclosed, made payable to MODERN MEDICINE. Please post together with this completed form to the above address.
- Direct deposit – Fax this form together with a copy of your proof of payment to 086-293-7289.

Bankers	First National Bank
Branch Code	254905
Account Name	MODERN MEDICINE
Account Number	62365011809

NOTE: THE ABOVE PRICES ARE FOR SOUTH AFRICA ONLY. INTERNATIONAL RATES AVAILABLE ON REQUEST.