



Managing cough in adults

Is there a serious underlying cause?

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 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 postinfectious cause in patients with subacute 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 disease are the most likely causes of chronic cough in a healthy nonsmoker.
- A combined therapeutic approach in sequential steps and referral of the patient to a specialist may be required in the management of chronic cough.

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A thorough history and physical examination, as well as 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' well being and can significantly impair quality of life.¹⁻³

Cough can be difficult to manage and many evidence-based guidelines have been published (see the box on page 40),⁴⁻⁸ 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, as well as 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

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GUIDELINES ON COUGH

- *Therapeutic Guidelines: Respiratory*, Version 4, 2009⁴
- CICADA: Cough in children and adults: diagnosis and assessment. Australian cough guideline summary statement⁵
- 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

‘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 arbitrarily categorised 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 subacute cough and can be managed as chronic cough once postinfectious cough is excluded. Cough can also be described as productive (>30 mL of sputum per day)¹¹ or nonproductive. Clinicians should also enquire about any particular trigger, as well as quantity and quality of sputum (including presence of blood) produced.

Acute cough

Recent onset cough is usually self-limiting and commonly caused by infections (especially viral) of the upper or lower respiratory tracts (common cold).¹² It affects both 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 (e.g. 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 findings such as upper airway inflammation and presence of crackles on auscultation may help determine the anatomical site of the infection (see the box on this page).

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 compared with dextromethorphan.⁷ The flowchart on page 41 is 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

IMPORTANT HISTORY AND EXAMINATION FINDINGS NOT TO BE MISSED

History

- Recent respiratory infection
- Occupational factors
- Smoking history
- Prominent dyspnoea
- Haemoptysis
- Systemic features (e.g. fever, weight loss)
- Dysphagia, aspiration, gastro-oesophageal reflux symptoms
- Medications (e.g. 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

resolution of cough and postnasal drip whereas 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 spread of infection.¹⁶

Asthma and asthma-like syndromes

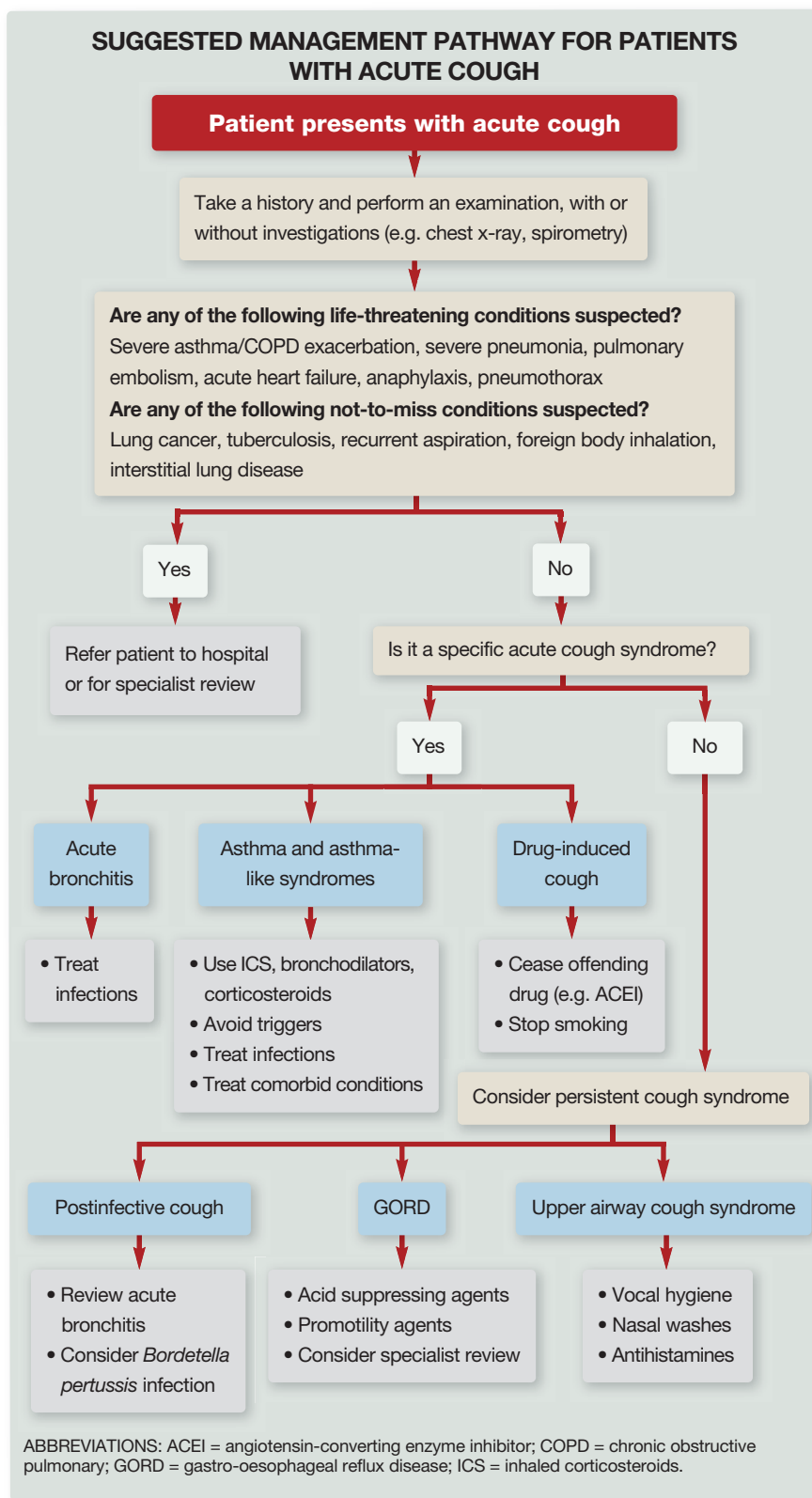
Asthma onset can be late in adulthood in individuals with smoking history or

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 (e.g. 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 It is also recommended to concurrently manage 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.

Drug-induced cough

Although uncommon, certain medications can cause cough, and this should be excluded in patients with unexplained cough. A temporal relation between 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), β -blockers in patients with asthma, and aspirin. Drugs that can cause diffuse interstitial lung disease, such as amiodarone, bleomycin, methotrexate and nitrofurantoin, may also cause chronic cough. A trial off 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 (e.g. CT scan of the chest) or endoscopic procedures (e.g. nasoendoscopy or bronchoscopy) may be needed for diagnosis and retrieval of the foreign body.

In travellers or immigrants from countries where tuberculosis is prevalent and who present with a cough plus associated systemic features (such as weight loss, night sweats or cervical lymphadenopathy) and chest x-ray changes, *Mycobacterium tuberculosis* infection will need to be excluded.³ Early morning sputum samples should be carried out 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 rarer causes of acute cough include pneumothorax, pleural effusion, pulmonary embolism and heart failure.^{20,21}

Subacute cough

Currently there is little data regarding causes and treatment of subacute cough. Clinically it is useful to determine if the cough is of a postinfectious 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 noninfectious cases of subacute 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 three-fold greater prevalence compared with 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 (e.g. wood stove, kerosene heater) and road traffic pollutants, may also need to be addressed. Several prospective studies have reported that the most likely causes of chronic cough in people who are nonsmokers 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 make 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 of 'unexplained cough' is used. No clear cause is found in up to 20% of cases in carefully investigated case series, but probably 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 1 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 (e.g. fever, weight loss, night sweats), complicated gastro-oesophageal symptoms (e.g. 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 on page 44.

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 current guidelines,¹⁵ primarily with topical nasal corticosteroids. Antihistamines, decongestants, allergen avoidance and immunotherapy 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, intranasal corticosteroid therapy for at least four weeks, with oral antibiotics cover for the same period.²⁹ Use

SUGGESTED MANAGEMENT PATHWAY FOR PATIENTS WITH CHRONIC COUGH

Patient presents with chronic cough

Take a history and perform an examination, with or without investigations (e.g. chest x-ray, spirometry)

Are any alarming features present? (e.g. significant smoking history, haemoptysis, prominent dyspnoea, systemic features, complicated gastro-oesophageal reflux symptoms, feeding difficulties, recurrent pneumonia)

Yes

Consider specialist referral for further investigations (e.g. speech pathologist review, modified barium swallow, 24-h oesophageal pH monitor, induced sputum, endoscopy, sinus imaging, polysomnography, high-resolution CT, bronchoscopy, echocardiography)

No

Is a specific chronic cough syndrome present?

Yes

No

Upper airway disease*

- Nasal washes
- Nasal corticosteroids
- Antibiotics
- Antihistamines
- Allergen avoidance
- Immunotherapy

Vocal cord dysfunction

- Speech pathology review: vocal cord training
- Optimise comorbidities

Obstructive sleep apnoea

- Weight loss
- CPAP
- MAS
- Optimise comorbidities

GORD

- Chronic PPI use
- Per acute management

Chronic lung diseases†

- Treat underlying lung disease
- Consider specialist input

Nonasthmatic eosinophilic bronchitis

- Inhaled corticosteroids

Consider nonspecific cough syndrome or 'unexplained cough'

- Empirical treatment: PPI, inhaled corticosteroids and speech pathologist review
- Respiratory specialist centre referral

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 (e.g. bronchomalacia), asthma, bronchiectasis, chronic bronchitis, chronic obstructive pulmonary disease, cystic fibrosis.

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 cord dysfunction

Patients with vocal cord 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 cord 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 (e.g. tobacco smoke, pollution, burning of biomass fuels). Assessment and management of patients with COPD should be guided by established guidelines (e.g. 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 of 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 up to eight weeks or more. If cough persists, a 5- to 10-day trial of oral corticosteroids may be required (see the section on asthma under the acute cough heading).

Obstructive sleep apnoea

Obstructive sleep apnoea is characterised by symptoms of snoring, observed apnoeic episodes during sleep (with or without nocturnal awakenings) and daytime hypersomnolence. Overnight polysomnography remains the standard for 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. Antireflux treatment reduces cough reflex sensitivity in affected patients. Proton pump inhibitors, with or without prokinetic 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. A trial of empirical treatment with inhaled corticosteroids, proton pump inhibitors and speech pathologist review are recommended by some authors.²² Referral of the patient to a respiratory specialist centre 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 presentations to primary care physicians, and can be challenging from a diagnostic and therapeutic viewpoint. Chronic cough can be disabling and places a significant cost burden on our health system. 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; with asthma, GORD and upper airway cough syndrome being the most common causes in nonsmokers.

An effective management plan is important in the evaluation and treatment of cough. Clinicians should take a

thorough history and perform a physical examination, as well as 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 specialist with an interest in chronic cough management. **MT**

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References are included in the pdf version of this article available at www.medicinetoday.com.au.

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