

Cough

Hosnieh Fathi

Alyn H Morice

Abstract

In primary care, cough is the presenting symptom of over half of new patient consultations. The majority of these presentations to primary care are due to acute cough, a benign self-limiting illness caused by a myriad of viral pathogens, such as rhinovirus, adenovirus and the recently discovered metapneumovirus. Chronic cough has only recently been recognized as a separate syndrome and is separate from the cough of chronic obstructive pulmonary disease. The physical and psychological impacts of chronic cough on quality of life, such as cough syncope and social isolation are well described in the literature. In the absence of any obvious chest disease, it has three main causes: gastric reflux, asthma syndromes (cough-variant asthma and eosinophilic bronchitis), and rhinitis (upper airways cough syndrome in the USA). However, the majority of 'difficult' chronic cough cases have a typical clinical history pointing to reflux as the most likely cause. For the treatment of chronic cough, the main aim is either tackling the cause or suppressing this symptom.

Keywords chronic cough; cough receptors; cough suppressant; reflux

The 'Cinderella' symptom

Cough is the commonest symptom for which patients consult a medical practitioner.¹ Despite its massive burden on healthcare resources, cough is often dismissed as an unimportant irritation rather than a symptom of major socioeconomic importance. There are no specific treatments for acute cough, but billions of pounds are spent worldwide in palliating the effects of the

viruses. Occasionally there are serious health consequences caused by specific acute viral infections such as influenza, when systemic symptoms predominate over the presenting cough. Cough can also be an alarming symptom of more serious conditions, such as lung cancer or pulmonary embolism, specifically when it is found in certain populations (such as smokers) or accompanied by haemoptysis. Chronic cough is common but poorly managed due to lack of appreciation of its aetiology.

Definition

Chronic cough, cough lasting more than eight weeks, is a common clinical presentation in the respiratory department. What is usually understood by the term 'chronic cough' is the symptom of cough in the absence of other obvious airway diseases. In this case, infectious causes are unlikely and the literature supports three common diagnoses: asthma, gastro-oesophageal reflux and rhinitis (postnasal drip syndrome).

Epidemiology

Chronic cough is reported in 3–40% of the population.^{2,3} For unknown reasons, women cough more than men, and smoking has a dose-related effect on productive cough.⁴ Other significant associations are environmental factors (such as industrial exposures), obesity, regurgitation and irritable bowel syndrome.

Previous surveys have tried to delineate the epidemiology of cough by using questionnaires such as the Medical Research Council (MRC) chronic bronchitis questionnaire, which details cough following COPD. Chronic cough, productive of little or no sputum, is a major presenting feature of cough to the growing number of cough clinics. We have recently conducted a study in Yorkshire looking at the incidence of chronic cough in a randomly selected population of 4000 patients. Cough was reported at a greater than weekly incidence by 12% of the population and was reported to disrupt daily living activities by 7%.⁵

Pathology

Cough is an expulsive expiration with a characteristic sound which serves as a protective reflex. The cough centre, in the brain stem, receives stimulation from vagal afferents. Stimulation of cough receptors, anywhere in the territory of the vagus nerve, with any noxious stimuli (e.g. inhaled foreign body, gastro-oesophageal reflux (GOR), or impacted ear wax), can lead to cough. Upregulation of these receptors (such as the capsaicin receptor (TRPV1)) heightens cough sensitivity and starts the cough bouts.⁶ Changes in atmospheric conditions (TRPV1 is also a temperature receptor), perfumes, acid from GOR, inflammatory mediators (such as bradykinin⁷), and ACE inhibitors⁸ can stimulate the activity of these receptors and start a paroxysm of cough. In patients prone to TH2 inflammation, eosinophilic infiltration of the airways may produce the asthmatic syndromes of cough predominant in asthma (without bronchoconstriction) and eosinophilic bronchitis (without bronchoconstriction and hyperresponsiveness).

Hosnieh Fathi MD MSc is a Clinical Research Fellow at Castle Hill Hospital, UK. She qualified from Tehran University of Medical Sciences, Iran. She has recently finished a MSc course in Health Services Research and Technology Assessment, University of Sheffield. Her research interests include chronic cough and reflux cough. Competing interests: none declared.

Alyn H Morice MD FRCP is Professor of Respiratory Medicine and Head of Cardiovascular and Respiratory Studies at Castle Hill Hospital, Cottingham, East Yorkshire, UK. Competing interests: none declared.

Clinical approach

In patients with asthmatic cough and rhinitis, diagnosis and treatment are broadly similar to that in the established guidelines. However, the consistency of three main causes of chronic cough has been recently challenged. The majority of chronic cough patients presenting to secondary care have a very similar clinical history and it has been suggested that the failure to diagnose non-acidic reflux as the underlying cause of the majority of 'difficult' chronic cough underlies the poor assessment of this symptom.

Medical history

The key to understanding chronic cough is the clinical history coupled with an understanding of the potential aetiology. All cough guidelines recommend stopping ACE inhibitors in patients with chronic cough, this is because as mentioned above, they sensitize the cough reflex, making previously sub-clinical disease symptomatic. Those dealing with patients with chronic cough have become increasingly aware of the atypical presentation of reflux disease in the form of chronic cough. However, knowledge of the pathophysiology of reflux empowers the clinician to ask specific questions pointing at the diagnosis in favour of this condition (Table 1).

The crural diaphragm normally holds the gastro-oesophageal junction in a J shape. Reflux can occur in prolonged talking (on the telephone), laughing and singing, when diaphragm fails to maintain this shape. The pharyngo-gastric reflex causes opening of the lower oesophageal sphincter during swallowing. Certain

foods, in particular, trigger this reflex (toast or biscuits). Similarly, postprandial reflux, occurring approximately ten minutes after a meal, is a characteristic feature of reflux cough. Metallic taste in the mouth and aphonia are other features. Finally, there is characteristic diurnal variation with the cough diminishing at night, as the lower oesophageal sphincter closes. On waking, the patient is usually free from cough. It occurs as they get out of the bed. Cough on rising is a characteristic feature which occurs as they reach the bathroom, or, indeed, as they regain the upright posture. In taking the clinical history of a patient with chronic cough, it is a mysterious symptom until these specific questions are asked.

Investigation

A chest X-ray is usually sufficient to differentiate those with primary respiratory illness from the majority without. Occasionally bronchiectasis and other rarer syndromes, such as cystic fibrosis, may be the underlying cause, but CT scan has a relatively low yield in those presenting with an apparently idiopathic cough. Ventricular obliteration, a laryngoscopy finding, is highly characteristic for GOR in reflux cough (Figure 1). Manometry and pH studies can also be useful if deciding whether fundoplication should be offered.

Treatment

The European Respiratory Society (ERS) and British Thoracic Society (BTS) guidelines endorse therapeutic trials. The treatments

Key questions in history indicating the reflux origin of the cough

Hoarseness or a problem with your voice?
 Clearing your throat?
 Excess mucus in the throat, or drip down the back of your nose?
 Retching or vomiting when you cough?
 Cough on first lying down or bending over?
 Chest tightness or wheeze when coughing?
 Heartburn, indigestion, stomach acid coming up (or do you take medications for this)?
 A tickle in your throat, or a lump in your throat?
 Cough with eating (during or straight after meals)?
 Cough with certain foods?
 Cough when you get out of bed in the morning?
 Cough brought on by singing or speaking (for example, on the telephone)?
 Coughing during the day rather than night?
 A strange taste in your mouth?

Table 1

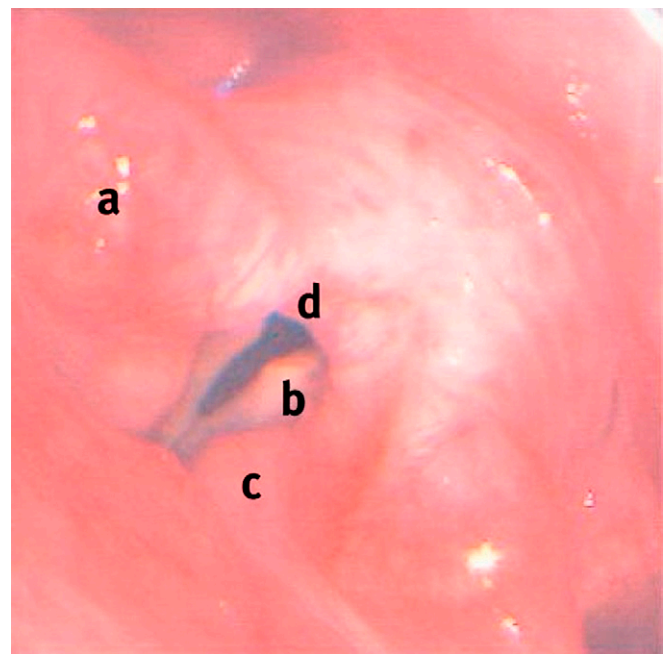


Figure 1 Typical reflux variations in laryngoscopy. **a** Arythenoid erythema. **b** Vocal cord oedema. **c** Ventricular obliteration. **d** Posterior commissure hypertrophy.

Common therapeutic steps used in chronic cough

Drug	Mode of action	Side effects	Contraindications	Regime
Omeprazole or Lansoprazole	Proton pump inhibitor (PPI)	Gastrointestinal (GI) disturbances, headache, dizziness	No contraindication, but should be used with caution in pregnancy, breastfeeding and liver diseases	Omeprazole (20 mg b.d.) or lansoprazole (30 mg b.d.) Oral, choose among PPIs and start initially (at least 2 months)
Ranitidine	H ₂ -receptor antagonists	GI disturbances, altered liver function tests, headache, dizziness	No contraindication, but should be used with caution in pregnancy, breastfeeding and renal impairment	300 mg o.d. oral, added to PPIs to suppress nocturnal acid
Metoclopramide	Dopamine receptor antagonist	Extra-pyramidal effects (especially in children and young adults), Hyperprolactinaemia, tardive dyskinesia, drowsiness, restlessness, depression	GI obstruction, perforation or haemorrhage, 3–4 days after GI surgery, phaeochromocytoma, breastfeeding	10 mg t.d.s. oral. Try for 1 month
Domperidone	Dopamine receptor antagonist	GI disturbances, Galactorrhea, rarely extra-pyramidal effects	Prolactinoma, hepatic impairment, pregnancy	10 mg t.d.s. oral. Try for 1 month
Morphine (slow released morphine sulphate)	Cough suppressant	Nausea and vomiting, constipation, drowsiness	Acute respiratory depression, acute alcoholism	5 mg b.d up to 10 mg b.d. oral. To be tried for 2 months
Disofrol ¹	Cough suppressant (putative TRPV1 antagonist)	Palpitation, drowsiness	Cardiovascular disease	1 tablet b.d. for a month, oral
Baclofen	GABA agonist (increasing lower oesophageal sphincter tone)	Drowsiness, muscular hypotonia, urinary disturbances, confusion, depression	Peptic ulcer	5 mg t.d.s. up to 10 mg t.d.s. oral for 2 months
Erythromycin	Motilin antagonist	GI disturbances	Porphyria, hepatic impairment, should be used with caution in pregnancy, breastfeeding and liver diseases	250 mg b.d. oral, 1 month

¹Disofrol is recommended in American College of Chest Physicians (ACCP) guidelines.

Table 2

either tackle the specific cause of cough or suppress it. [Table 2](#) demonstrates the steps in treatment. ◆

REFERENCES

- Morice AH. Epidemiology of cough. *Pulm Pharmacol Ther* 2002; **15**: 253–59.
- Fuller RW, Jackson DM. Physiology and treatment of cough. *Thorax* 1990; **45**: 425–30.
- Cullinan P. Persistent cough and sputum: prevalence and clinical characteristics in south east England. *Respir Med* 1992; **86**: 143–49.
- Janson C, Chinn S, Jarvis D, Burney P. Determinants of cough in young adults participating in the European Community Respiratory Health Survey. *Eur Respir J* 2001; **18**: 647–54.
- Ford AC, Forman D, Moayyedi P, Morice AH. Cough in the community: a cross sectional survey and the relationship to gastrointestinal symptoms. *Thorax* 2006; **61**: 975–79.
- Groneberg DA, Niimi A, Dinh QT, et al. Increased expression of transient receptor potential vanilloid-1 in airway nerves of chronic cough. *Am J Respir Crit Care Med* 2004; **170**: 1276–80.
- Ricciardolo FL, Rado V, Fabbri LM, Sterk PJ, Di Maria GU, Geppetti P. Bronchoconstriction induced by citric acid inhalation in guinea pigs: role of tachykinins, bradykinin, and nitric oxide. *Am J Respir Crit Care Med* 1999; **159**: 557–62.
- Morice AH, Lawry R, Brown MJ, et al. Angiotensin converting enzyme and cough reflex. *Lancet* 1987; **2**: 1116–18.

FURTHER READING

ERS, BTS and ACCP guidelines
Morice AH. Chronic cough: diagnosis, treatment and psychological consequences. *Breathe* 2006; **3**: 164–74.