Cough

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Abstract

Cough is the most common reason why patients seek medical attention. Acute cough caused by viral upper respiratory tract infection is usually self-limiting and seldom requires investigation. In contrast, chronic cough is challenging to manage as it often remains unexplained despite thorough investigation. Cough reflex hypersensitivity is a key abnormality in patients with cough, and the term 'cough hypersensitivity syndrome' (CHS) has recently been proposed to emphasize this. The evaluation of patients with CHS includes identifying reversible cough hypersensitivity, minimizing aggravating factors and giving non-specific antitussive therapy.

Keywords Acute cough; chronic cough; cough; cough hypersensitivity syndrome; cough reflex; cough reflex hypersensitivity

Key points

- Prevalence of cough in the community is as high as 33%
- Heightened cough reflex sensitivity is a key underlying mechanism of cough
- It is important to identify corticosteroid-responsive cough
- Non-specific antitussive therapies include gabapentin, pregabalin, opioids and speech and language therapy or cough suppression physiotherapy

Introduction

Cough is a defence mechanism that protects the airways from aspiration and clears secretions. It is often described as an inspiratory effort followed by a forced expiration against a transiently closed glottis, which results in a rapid expulsion of air. An impaired cough reflex is seen in patients with neuromuscular disease and after stroke, and can lead to an increased risk of aspiration and pulmonary infection. In contrast, a heightened cough reflex is a typical finding in patients with chronic cough.

Cough is the most common reason patients seek a medical consultation. The prevalence of cough in the community is estimated at 9–33%, and the economic cost to society is substantial; more than £100 million is spent on antitussive drugs every year in the UK.[1] Although most of this relates to acute cough caused by viral upper respiratory tract infection, chronic cough (cough lasting >8 weeks) is also common, accounting for 10% of respiratory outpatient clinic referrals.[2] It is associated with significant physical and psychological morbidity; syncope, urinary incontinence, chest pain, sleep disturbance, relationship difficulties, social embarrassment and depression are just some of the adverse consequences.

Chronic cough is challenging to manage as many cases remain unexplained even after detailed investigation. This has led to proposals for a greater focus on the key underlying mechanism – heightened cough reflex sensitivity. The name 'cough hypersensitivity syndrome' (CHS), has been advocated by the European Respiratory Society for this condition. CHS has been defined as a disorder characterized by 'a troublesome cough triggered by low levels of thermal, mechanical or chemical exposure'.[3,4] This review will focus on the evaluation and assessment of patients with cough, with particular emphasis on chronic cough.

Upper respiratory tract infection-associated cough

Viral upper respiratory tract infection is by far the most common cause of acute cough (duration less than 2 weeks). Acute cough is associated with transient heightened cough reflex sensitivity and usually does not require assessment or therapy. There is little high-quality evidence to support the efficacy of antitussive drugs. The reasons are multifactorial; inefficacy of medications, the use of unvalidated outcome measures and the difficulty of determining the clinical significance of findings from studies are important limitations. The best evidence for antitussive therapy supports the use of honey and vapour rubs containing camphorated oils for children, and the opioid-like, *N*-methyl-D-aspartate receptor antagonist dextromethorphan for adults. The demulcent effects of syrups, hypersalivation associated with the sugary taste of many medications and the commonly used ingredient menthol are all likely to have antitussive effects.

In some patients, the cough persists and is often referred to as post-infectious, post-viral or subacute cough. The prevalence of post-infectious cough is unclear, but it is common and challenging to treat in primary care. It is also associated with cough reflex hypersensitivity. Most patients with post-infectious cough do not require investigation. Pertussis is emerging as an important cause in adults – up to 25% of cases of post-infectious cough. The most important differential diagnosis for subacute cough is asthma. Antitussive drugs, bronchodilators and inhaled corticosteroids are often prescribed to treat subacute cough. There is limited evidence for their efficacy; the most encouraging data available are for inhaled corticosteroids.

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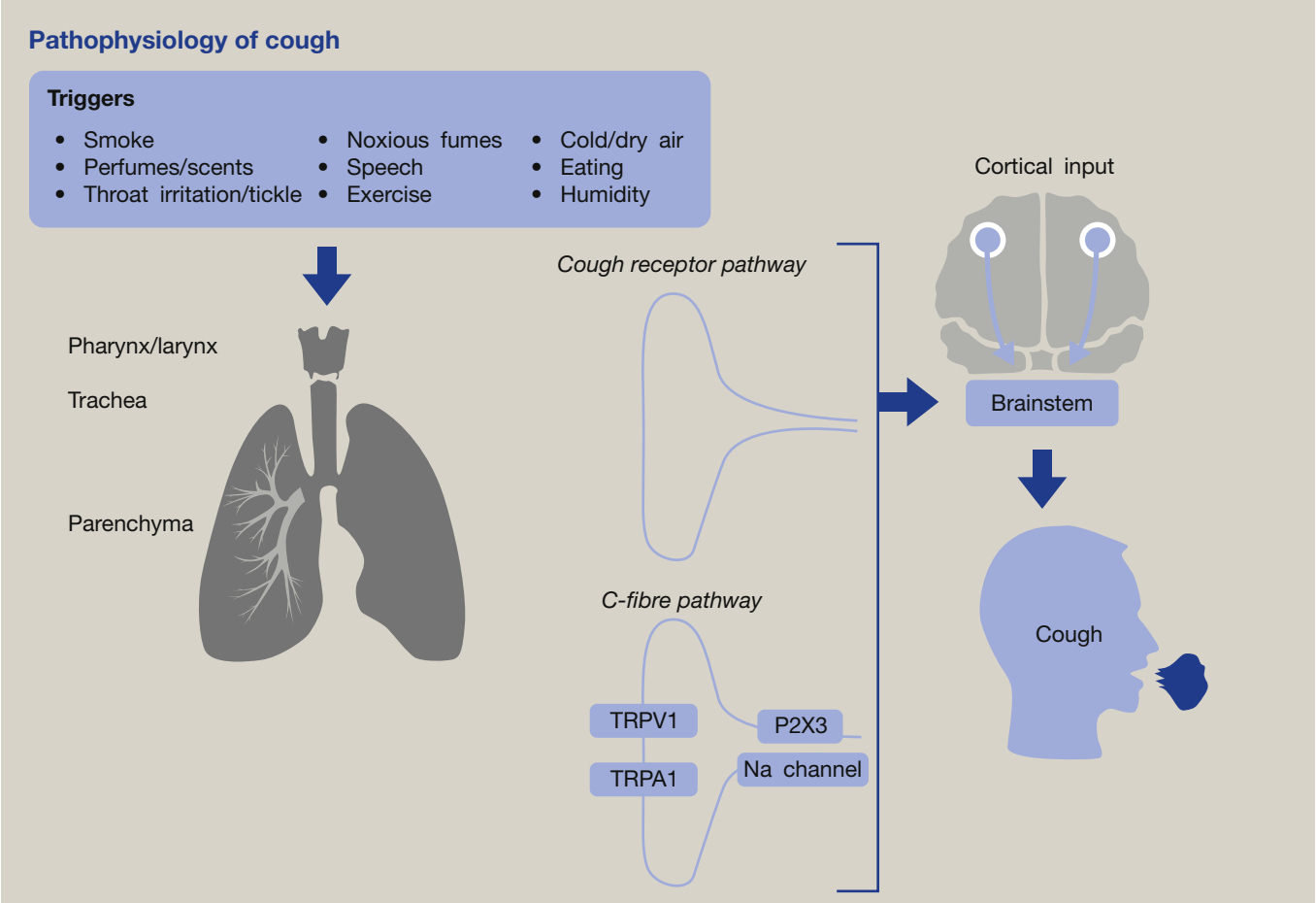
Pathophysiology

Cough receptors, found throughout the airways and lung parenchyma, are activated by a wide range of triggers (Figure 1).[5] Many patients report laryngeal paraesthesia such as a tickle in the throat, suggesting afferent sensory nerve hypersensitization. The brainstem coordinates inputs from peripheral afferent nerves and central regulatory cortical fibres and then activates the motor pathway of the cough reflex. Cough reflex hypersensitivity is assessed with cough challenge tests, using tussive agents such as capsaicin, but they do not reliably discriminate those with cough from healthy individuals and are of limited clinical value. Cough reflex hypersensitivity is transient or reversible when associated with infection, eosinophilic airway inflammation and angiotensin-converting enzyme (ACE) inhibitor drug therapy, but in most patients with unexplained chronic cough it is persistent.[3] The mechanism of sensitization of the cough reflex is poorly understood and deserves further study. There is a clinical need to develop pharmacological therapy that can down-regulate cough reflex sensitivity to physiological levels. The goal of therapy should be cough reduction or control, rather than total suppression.

Evaluation and management of chronic cough (Figure 2)

Initial assessment: the initial assessment involves history, examination, spirometry and a chest X-ray. A careful history will identify potential causes and aggravating factors. This should focus on symptoms of cough reflex hypersensitivity such as an irritation or tickling sensation in the throat, triggers, respiratory symptoms other than cough, smoking status, medication use (particularly ACE inhibitors), aggravators of cough such as gastro-oesophageal reflux (GOR) and rhinitis, and adverse effects on quality of life such as urinary incontinence. The presence of haemoptysis, weight loss and fever should prompt rapid evaluation to exclude malignancy and infection. Examination, spirometry and chest X-ray are recommended to identify the wide range of bronchopulmonary disorders that could present with cough; the assessment of these is reviewed elsewhere.



TRPV1, transient receptor potential vanilloid 1; TRPA1, Transient receptor potential ankyrin 1; P2X3; Na channel, sodium channel.

Sensory neuronal model of cough. Nociceptor C-fibres in the airway mucosal surface are sensitive to chemical stimuli including irritants such as capsaicin and inflammatory mediators such as bradykinins. Another sensory pathway consists of a group of afferent nerves situated beneath the epithelium of extrapulmonary large airways. These nerves are known as *cough receptors* and are chemically insensitive but responsive to mechanical or punctate stimuli (e.g. inhaled particulate matter)

Figure 1