

Evidence-based Evaluation and Management of Chronic Cough



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KEYWORDS

- Chronic cough • Upper airway cough syndrome • Cough variant asthma
- Reflux disease • Nonasthmatic eosinophilic bronchitis
- Cough hypersensitivity syndrome

KEY POINTS

- Chronic cough is a common complaint in the outpatient setting.
- The evaluation of chronic cough is largely based on anatomic diagnostic protocols focused on the most common causes.
- The evidence supporting such protocols is limited and etiologic work-up can occasionally be extensive, costly, and low yield.
- Sequential empiric therapy for the most common causes of chronic cough has thus been recommended instead.
- Focus on the pathophysiologic mechanisms of chronic cough has recently led to the proposal that cough hypersensitivity syndrome is central in its pathogenesis.

INTRODUCTION

The cough reflex is a defense mechanism protecting the lungs from aspiration and also facilitating clearance of secretions, noxious substances, and foreign bodies from the airways.

Cough of any duration is the most common presenting symptom in the primary care setting. According to the National Ambulatory Medical Care Survey from 2010,¹ cough was the primary reason for an outpatient visit in more than 2% of cases. Cough negatively affects patients' quality of life²⁻⁴ and may also lead to severe complications, such as syncope, urine incontinence, rib fractures, pneumothorax, and lung herniation.

Acute cough, which is most commonly caused by a viral upper respiratory illness, typically resolves within 3 weeks. A recent systematic review found that the mean duration of acute cough reported in the literature was about 18 days, contrary to patients' expectation, which was 7 to 9 days.⁵

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Chronic cough lasts more than 8 weeks and it is self-reported by more than 10% of adults in the community.⁶ Chronic cough may last for several years; cause significant physical and psychological distress to the patients; and lead to multiple office visits, extensive testing, as well as referrals to specialists such as allergy, otolaryngology, and pulmonology.⁷

CAUSES OF CHRONIC COUGH

The most common causes of chronic cough include smoking and its long-term consequences, such as chronic obstructive pulmonary disease, angiotensin-converting enzyme (ACE) inhibitor use, upper airway cough syndrome (UACS), airway bronchospasm (asthma) and gastroesophageal reflux disease (GERD).

Angiotensin-converting Enzyme Inhibitors

ACE inhibitors may cause cough in 5% to 20% of patients who receive these medications.⁸ This adverse effect is not dose dependent, and may occur anytime during the course of treatment, typically a few days to several months after treatment is initiated. The mechanism behind ACE inhibitor-induced cough is thought to be the accumulation of bradykinin and other substances, which are metabolized by the ACE. ACE inhibitor-induced cough typically resolves within 1 to 4 weeks after discontinuing the ACE inhibitor.⁹ Angiotensin receptor blockers (ARBs) are less likely to cause cough compared with ACE inhibitors (rates seem to be similar to placebo) and may be used as an alternative when this side effect warrants discontinuation of the ACE inhibitor. In patients who are nonsmokers, not on treatment with an ACE inhibitor, and have normal chest radiographs, chronic cough is caused by UACS (most common), asthma (second most common), or GERD (third most common) in a large percentage of cases, which may exceed 90%.¹⁰ These conditions may coexist in the same patient and are frequently asymptomatic (silent) besides cough.

Upper Airway Cough Syndrome

UACS (also referred to as postnasal drip or rhinitis) can be caused by allergic rhinitis (seasonal or perennial), nonallergic rhinitis (vasomotor and nonallergic rhinitis with eosinophilia), rhinitis medicamentosa (rebound symptoms after prolonged use of decongestants), infection (chronic bacterial sinusitis), allergic fungal sinusitis, and anatomic abnormalities such as deviated septum. It is not known why some patients with chronic rhinitis or sinusitis go on to develop persistent cough and some do not. UACS can be silent (no symptoms besides cough) in up to 20% of cases.¹¹ Because of its chronicity it is likely that, over time, patients will become tolerant to other symptoms, which are not as bothersome as cough. The diagnosis of silent UACS can reliably be made only after patients show improvement with prescribed treatment, because there are no pathognomonic features on history, physical examination, and laboratory testing. Questions have thus been raised as to whether silent UACS is a separate entity or should instead be classified as chronic unexplained cough,¹² or even a form of cough hypersensitivity syndrome.

Asthma

Asthma is characterized by airway hyperresponsiveness, variable and reversible airway obstruction, and eosinophilic inflammation of the airways. As in patients with UACS, cough may be the only manifestation of the underlying disease process (cough variant asthma), and other symptoms commonly associated with asthma,

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