
CME review article

This feature is supported in part by an educational grant from AstraZeneca LP

Taming chronic cough

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Objective: To review the available evidence on treating chronic cough to relay a thoughtful, evidence-based approach for the diagnosis and treatment of chronic cough.

Data Sources: MEDLINE, PubMed, EMBASE, and CINAHL were searched using the following keywords: *cough, asthma, gastroesophageal reflux, sinusitis, rhinitis (allergic, seasonal), postnasal drip, vocal cord dysfunction, lung disease (interstitial), bronchiectasis, and bronchoscopy.*

Study Selection: Studies were selected based on their relevance to the diagnosis and treatment of chronic cough. Because of a lack of randomized prospective studies, nonrandomized and retrospective studies were considered, with their strengths and limitations noted.

Results: Few randomized controlled trials have addressed the diagnosis and treatment of chronic cough. There are several prospective noncontrolled trials for adults with chronic cough that found a high percentage of cough resolution when using an approach that focused on the diagnosis and treatment of the most common causes: asthma, gastroesophageal reflux disease, and upper airway cough syndrome. Preliminary studies in children support an approach that distinguishes between a wet and dry cough, as well as an in-depth investigation of any specific symptoms that point to an underlying chronic illness.

Conclusion: Allergists, as experts in treating upper airway and lower airway disorders, are uniquely poised to diagnose and treat chronic cough.

Ann Allergy Asthma Immunol. 2007;98:305–313.

Off-label disclosure: Drs Rank, Kelkar, and Oppenheimer have indicated that this article does not include the discussion of unapproved/investigative use of a commercial product/device.

Financial disclosure: Drs Kelkar and Oppenheimer have indicated that in the last 12 months they have been on the Consultant/Speakers' Bureau for Merck, GSK, Astra-Zeneca, Schering, Pfizer, UCB, Abbott, Wyeth, Greer, and Aventis.

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INTRODUCTION

Chronic cough (lasting longer than 8 weeks in adults and 4 weeks in children) is a common (10% to 20% of adults) and debilitating ailment.¹ Cough has an important physiologic role in the human body's defense system, because it results in clearing of excess secretions and foreign bodies from the airway. However, in some patients cough may be excessive and unnecessary and may lead to a general deterioration in their quality of life.² Patients seek medical attention for their cough for a variety of reasons, chief among them is to receive reassurance that nothing is seriously wrong (Table 1).² A

more recent prospective survey study of patients with chronic cough found the most prevalent problems from a patient's perspective were frustration, irritability, anger, frequent physician visits and testing, and sleep disturbances.³

Vagus nerve fibers have been shown, in animal models, to terminate along the tracheobronchial tree.⁴ The subtype of vagus nerve fibers (C-fiber, rapidly adapting receptors, or other fiber type) and the relative contribution of vagus nerve fibers to provoking a cough response in the brainstem are areas of ongoing research.⁴ Following the anatomy of the vagus nerve offers a logical approach to explore the differential diagnosis of chronic cough. A diagnostic workup of chronic cough, termed the *anatomic, diagnostic protocol*, has been studied prospectively (not randomized or blinded) and offers a framework for many of the published diagnostic algorithms.⁵ By following this pathway, Irwin and colleagues⁵ have demonstrated successful treatment of chronic cough in 84% to 98% of patients. Other published results

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Received for publication November 27, 2006.

Received in revised form January 1, 2007.

Accepted for publication January 16, 2007.

Table 1. Reasons Patients Seek Care for Chronic Cough*

Reason	Patients, %
Needs reassurance nothing is serious	77
Concerned something is wrong	72
Frequent retching	56
Exhaustion	54
Others think something is wrong	53
Embarrassment	49
Self-consciousness	46
Difficulty speaking on the telephone	39
Hoarseness	39
Had to change lifestyle	36
Cannot sleep at night	34
Can no longer sing in church	31

* Adapted from French et al.²

from specialist cough clinics, most of which used a similar approach, note patient improvement of 68% to 98%, with 9 of 12 groups listing success rates of more than 90%.⁵⁻¹⁶

We searched the MEDLINE, PubMed, EMBASE, and CINAHL databases using the following keywords: *cough, asthma, gastroesophageal reflux, sinusitis, rhinitis (allergic, seasonal), postnasal drip, vocal cord dysfunction, lung disease (interstitial), bronchiectasis, and bronchoscopy*. Studies were selected for inclusion in this review based on their relevance to the diagnosis and treatment of chronic cough. Because of a lack of randomized prospective studies, non-randomized and retrospective studies were considered, with their strengths and limitations noted. Through our search, we found that 3 major organizations have published guidelines for the evaluation and treatment of chronic cough: the American College of Chest Physicians (ACCP),¹⁷ the British Thoracic Society (BTS),¹⁸ and the European Respiratory Society.¹⁹ In this article, we highlight the key points of these guidelines and the evidence supporting them, exploring both similarities and differences among them with emphasis on the role that the allergist can fill in the diagnosis and treatment of chronic cough. We place an emphasis on the 3 leading causes of chronic cough in adults, upper airway cough syndrome (UACS, also known as postnasal drip syndrome), asthma, and gastroesophageal reflux disease (GERD), and on important aspects of the diagnosis and treatment of chronic cough in children.

HISTORY

Performing a thorough history can be helpful in delineating the cause of chronic cough, although the character of the cough (wet, dry, bark, or honk), timing (nocturnal or with meals), or associated complications have not been found to be predictive of cough origin in adults.¹⁰ The description of the sputum quality is also generally not helpful in adult patients.⁹ Inquiring about typical symptoms consistent with asthma, GERD, or rhinitis may be helpful in beginning the workup. GERD is more likely associated with dyspepsia, heartburn, water brash, or hoarse voice; however, these symptoms may

be absent in up to 75% of the patients who are later found to have GERD-associated cough confirmed by testing or by response to treatment.²⁰ McGarvey and colleagues¹¹ published positive predictive values for specific symptoms: asthma symptoms (nocturnal cough precipitated by cold air, exercise, aerosols) had a positive predictive value of 56%, UACS symptoms (throat clearing, sensation of postnasal drip, nasal discharge, previous sinusitis) had a positive predictive value of 52%, and GERD symptoms (dyspepsia, postprandial cough) had a positive predictive value of 40%.

It is also crucial to carefully perform a medication history, noting with special interest any patient who has recently been using an angiotensin-converting enzyme (ACE) inhibitor. A smoking history is also important, as are lines of questioning exploring the patient's motivation and previous efforts to quit the habit. Cough that resolves with sleep had previously been believed to be psychogenic, although studies have shown that cough due to GERD and bronchitis is also less likely to occur at night.^{21,22} Irwin and Madison²³ suggest that psychosocial dysfunction must be considered a consequence rather than a cause of chronic cough. An occupational history is considered a crucial part of the history, and any suggestion of a culprit exposure should be followed up with a more detailed line of questioning.²⁴

Infectious exposures and a review of the health of close contacts may be helpful: cough paroxysms, posttussive emesis, and/or inspiratory whooping should prompt consideration of *Bordetella pertussis* infection.^{25,26} Pertussis was found to account for 21% of patients (with a persistent cough) in a cohort study.²⁷ In children, one should inquire about purulent and productive cough (careful search for bronchiectasis), growth or feeding difficulties, neurodevelopmental status (increased risk for aspiration), or history of recurrent pneumonia (immune deficiency).²⁸ It is also important to understand the parent's expectations and concerns regarding their child's cough.²⁸ For adult patients as well, attempting to understand how much the cough is bothering them (a minor nuisance vs leading to work absenteeism) can offer useful insight when considering how to proceed. Lastly, because many patients have been evaluated by one or multiple physicians for their problem, a thorough history should include a detailed account of previous testing, treatment (including attempts to gauge compliance), and response to prior intervention.

PHYSICAL EXAMINATION

The physical examination in the evaluation of chronic cough should focus on the upper and lower airways. Features of allergic rhinoconjunctivitis (pale and swollen turbinates, prominent nasal crease, nasal polyps, allergic shiners, and Dennie-Morgan lines) will help the physician focus on allergy testing and treatment. Facial tenderness or swelling with a mucopurulent discharge from the nasal passageways can help lead to an evaluation and treatment of sinusitis. Purulent postnasal drip is suggestive of sinusitis. An erythematous or cobblestoned appearance of the posterior pharyngeal mucosa is neither sensitive nor specific for UACS.^{7,29} Club-

bing should prompt further testing for bronchiectasis or interstitial lung disease. Wheezing may favor a diagnosis of asthma but is not a sensitive or specific indicator. Examination features of GERD may include epigastric tenderness or an erythematous appearance of the vocal cords on direct laryngoscopy, although these features lack sensitivity in excluding GERD. Lastly, examination of tympanic membranes for embedded hairs, foreign objects, or wax impaction can help make the unusual diagnosis of Arnold nerve reflex cough.³⁰

CHRONIC COUGH WORKUP: INITIAL CONSIDERATIONS

Although a plethora of diagnostic options exist, the initial testing should rely heavily on guidance from the history and physical examination. In the ACCP guidelines for adult patients, a chest x-ray examination is recommended for all patients with chronic cough.¹⁷ Although a chest x-ray examination was found to be useful in determining the diagnosis in only 7% to 33% of patients,^{7,31} it is especially helpful because it rules out significant pulmonary parenchymal disease and thus allows the physician to begin to address the issue of reassurance in patients concerned about a serious illness. If a patient is taking an ACE inhibitor, use of the medication should be stopped (if possible) and the cough reassessed after 1 to 3 months. For tobacco smokers, patients should be counseled that the cough may initially worsen after smoking cessation but has been shown to improve in 90% of patients during a 5-year period.³² In nonsmokers with a normal chest x-ray examination result and no history of ACE inhibitor use, the ACCP, BTS, and European Respiratory Society guidelines recommend directing efforts toward the 3 leading causes: UACS, asthma, or GERD or a combination thereof.

UPPER AIRWAY COUGH SYNDROME

The afferent vagus nerve has fibers along the posterior pharynx. Thus, it should come as no surprise that UACS is one of the most commonly identified causes of chronic cough. The term *UACS* includes cough secondary to allergic rhinitis, nonallergic rhinitis, nonallergic rhinitis with eosinophilia, postinfectious rhinitis, bacterial sinusitis, allergic fungal sinusitis, abnormal anatomy causing rhinitis, chemical or occupational irritant rhinitis, rhinitis medicamentosa, and rhinitis of pregnancy. Both the BTS and ACCP guidelines recommend empiric treatment for UACS in the absence of a clear cause but differ on the initial choice of therapy. The data favoring initiating therapy with a first-generation antihistamine decongestant therapy approach include the successful resolution of cough symptoms in the original publication of the anatomic, diagnostic pathway.⁵ Further support for using a first-generation antihistamine decongestant preparation empirically for UACS comes from a prospective trial that demonstrated success in 39 of 45 patients with chronic cough.²⁹ On the other hand, the utility of topical steroids has been seen in a chronic cough cohort studied by Irwin and colleagues,⁷ in which they demonstrated a 98% success rate for the treatment

of allergic rhinitis— or nonallergic rhinitis—induced cough. O'Connell and colleagues⁸ found a 69% success rate, and McGarvey et al¹¹ found a 82% success rate with treatment of UACS-induced cough with use of topical corticosteroids.

Unfortunately, not enough evidence is available to state which empiric UACS treatment is most effective, thus reinforcing the need for a randomized prospective trial comparing these treatments. Despite the debate over the best initial empiric treatment, it is clear that making a more definitive diagnosis can lead to successful treatment recommendations. Further diagnostic workup to clarify the cause may include allergy testing, rhinolaryngoscopy, and sinus imaging. For allergic rhinitis, the recommended treatment is a combination of avoidance, nasal steroids, antihistamines, and allergen immunotherapy. Nonallergic rhinitis can be treated with nasal steroids, decongestants, anticholinergics, or antihistamine nasal spray. Other types of rhinitis are treated with avoidance of an inciting trigger. Sinusitis is treated initially with antibiotics (with or without oral corticosteroids) and often requires further medical treatment (and occasionally surgery) for those who develop recalcitrant chronic sinusitis.

ASTHMA

The theoretical connection between chronic cough and bronchial inflammation is presumed to be the vagal innervation along the bronchial tree. Chronic cough may be the only manifestation of asthma, the so-called cough-variant asthma. Spirometry with prebronchodilator and postbronchodilator response is believed to be an important component of the workup for the diagnosis of asthma. If pulmonary function test results are normal, methacholine challenge is useful to rule out asthma given its high negative predictive value in symptomatic patients (100% in 4 separate studies).^{7,9,29,33} Regardless of the methacholine challenge results, the definitive diagnosis of cough variant asthma is only made after cough improves or resolves after antiasthma therapy.³⁴

Therapy can be with either an inhaled or systemic corticosteroid. No data are available that have compared the 2 initial treatment approaches. The BTS cites expert opinion as the basis for stating that cough is unlikely to be due to eosinophilic airway inflammation if there is no response to treatment with prednisolone with 30 mg/d for 2 weeks.¹⁸ A randomized controlled trial of 13 patients (8 refractory to inhaled β -agonist and 5 to inhaled corticosteroid) found significant improvement of cough sensitivity to capsaicin after 14 days of zafirlukast treatment.³⁵ This study supports the BTS recommendation to consider adding leukotriene modifiers rather than long-acting β -agonists in step-up therapy for patients with cough variant asthma.¹⁸ Larger studies, however, are needed to clarify the role of leukotriene modifiers in cough variant asthma.

NONASTHMATIC EOSINOPHILIC BRONCHITIS

Nonasthmatic eosinophilic bronchitis was first described in 1989 when a small group of patients with corticosteroid-responsive chronic cough were found to have normal lung

function test results, normal methacholine challenge results, and an increase in sputum eosinophils.³⁶ Another study demonstrated that 12 of 91 patients evaluated for chronic cough had nonasthmatic eosinophilic bronchitis and that all 12 of the patients responded to inhaled budesonide, 800 $\mu\text{g}/\text{d}$.⁶ A follow-up study of patients with nonasthmatic eosinophilic bronchitis demonstrated that budesonide, 400 $\mu\text{g}/\text{d}$, decreased sputum eosinophils in tandem with decreasing cough.³⁷ The BTS guideline relies on a failed response to systemic steroids to rule out nonasthmatic eosinophilic bronchitis, whereas sputum induction or bronchial wash fluid for eosinophil collection are emphasized by the ACCP guidelines.³⁸ Clearly, the choice between testing and empiric treatment will depend on the individual physician's diagnostic resources.

GASTROESOPHAGEAL REFLUX DISEASE

Chronic cough can also be caused by GERD via irritation of the vagus nerve. The vagus nerve has fibers thought to be sensitive to acid or nonacid volume reflux and fibers that may sense the direct irritant effects of refluxed acid on the larynx and trachea.^{20,39,40} Diagnosing GERD as the cause of chronic cough is challenging because none of our currently available tests for GERD-related cough are highly predictive of a response to acid suppression medical therapy. Normal upper endoscopy does not exclude reflux as the cause of a chronic cough. Although pH probe studies, barium esophagrams, and impedance studies may be helpful, both the ACCP and BTS guidelines suggest first trying empiric treatment with twice daily proton pump inhibition (PPI) along with other antireflux therapy (dietary changes, smoking cessation, limiting alcohol, elevation of sleeping position, weight loss, sleep apnea evaluation, and prokinetic agents if necessary) for 3 months.⁴¹

The utility of adding prokinetic therapy was demonstrated in a study that examined 56 patients with GERD-related cough: 24 patients responded to PPIs alone with an additional 18 patients only responding after the addition of a prokinetic agent.⁴² This same study lends further support to the recommendation of empirically treating GERD-related cough before testing, because 44 of 56 patients with chronic cough were successfully treated without the need for pH probe testing.⁴³ A prospective study undertaken to examine patients with a positive pH test result and their response to twice daily PPIs found that only 35% of the patients with positive pH test results demonstrated improvement in their chronic cough with PPIs.⁴³ This recalcitrance may be attributable to severe GERD refractory to medical treatment or continued symptoms that result from nonacid refluxate causing cough. In those who do not respond to empiric therapy, further investigation of GERD with studies such as a pH probe or impedance testing with the aid of a gastroenterologist is indicated. Antireflux surgery should be considered if the patient has continued symptoms and objective evidence of reflux while receiving maximal medical therapy, although evidence to support the efficacy of this approach is limited.

LARYNGOPHARYNGEAL REFLUX

Laryngopharyngeal reflux has increasingly been recognized as a distinct entity from GERD and has been reported in up to 10% of patients who presented to otolaryngology clinics.⁴⁴ Laryngopharyngeal reflux suggests specific irritation of the laryngopharyngeal region, as opposed to GERD, where reflux of acid or nonacid stomach contents irritates the esophagus. Based on survey data, persistent cough is present in 97% of patients with laryngopharyngeal reflux, along with other symptoms, including throat clearing (98%), globus pharyngeus (95%), and hoarseness (97%).⁴⁵ A suggested algorithm for assessing and managing laryngopharyngeal reflux has been proposed, which includes an initial reflux symptom index and a reflux finding score based on laryngoscopy.⁴⁶ After a preliminary diagnosis of laryngopharyngeal reflux, suggested therapy includes a 3-month trial period with PPI and lifestyle and dietary modification. A randomized controlled trial of omeprazole vs placebo demonstrated a significant improvement in hoarseness and throat clearing in the treatment group but only a nonsignificant trend of improvement for cough.⁴⁷ If no significant improvement is seen, it is recommended that patients undergo further diagnostic workup, which may include multichannel impedance and pH monitoring.⁴⁶

OTHER NOTABLE CAUSES OF CHRONIC COUGH

Many other explanations for chronic cough exist and are presented in Table 2. A few diagnoses merit further description: vocal cord dysfunction, unexplained cough (also labeled idiopathic or psychogenic), and interstitial lung disease. Vocal cord dysfunction leading to cough can be difficult to diagnose and can also confound the diagnosis of asthma. It is important to consider vocal cord dysfunction as a possible cause of chronic cough and to perform the necessary testing to confirm the diagnosis (direct laryngoscopy during a provoked episode of cough or breathlessness).⁴⁸ Although many patients with chronic cough have undiagnosed conditions because of a failure to consider and adequately treat the common and uncommon causes, a distinct population of patients with idiopathic cough has been suggested by McGarvey.⁴⁹ This argument is supported by the similarities of patients with undiagnosed cough: most of these patients are middle-aged women with a triggering viral upper respiratory tract infection. Interstitial lung disease should be considered when there are clues to suggest interstitial pulmonary fibrosis, sarcoidosis, or hypersensitivity pneumonitis. It is important to remember that patients with interstitial lung disease may have a normal chest x-ray film up to 10% of the time. A chest computed tomogram (CT) is thus the next recommended testing option for diagnostic confirmation.⁵⁰ In addition, 50% of patients with known interstitial lung disease were found to have alternative explanations for their chronic cough, which serves to further emphasize the importance of considering multiple concomitant cough origins.⁵¹

Table 2. Causes and Treatment of Chronic Cough*

Cause	Treatment
UACS	Treat specific cause if found, otherwise empiric treatment with intranasal steroid or first-generation antihistamine or decongestant
GERD	Treat empirically with medical antireflux therapy; further testing if no improvement (such as pH probe test, esophagram, or manometry)
Asthma	Test with borometry ± bronchoprovocation if necessary; otherwise treat empirically with ICSs and leukotriene modifiers or systemic steroids
NAEB	Test for sputum eosinophils if available, treat with ICSs
ACE-I cough	Discontinue use of ACE-Is and monitor for improvement for 3 months
Occupational cough	Modification of exposure to the inciting factors
Suppurative airway disease	Diagnosed bronchoscopically and treated with long-term antibiotics
Lung tumors	Suspicion remains despite normal chest x-ray examination result and chest CT: proceed with bronchoscopy
Aspiration	Swallow evaluation and treatment based on findings
Tic cough	Refer to psychiatry department
Arnold nerve	Remove irritant from tympanic membrane
Unexplained cough	Empiric antitussive medicines

Abbreviations: ACE-I, angiotensin-converting enzyme inhibitor; CT, computed tomography; GERD, gastrointestinal reflux disease; ICSs, inhaled corticosteroids; NAEB, nonasthmatic eosinophilic bronchitis; UACS, upper airway cough syndrome.

* In patients with normal chest x-ray examination results and a history of no smoking.

MULTIPLE CONCOMITANT COUGH ORIGINS

Chronic cough is frequently due to multiple causes; French and colleagues² found in their patients with chronic cough that 7% had a single cause, 53% had 2 causes, 36% had 3 causes, and 4% had 4 or more causes. This challenging aspect of treating chronic cough has spawned a key concept in management of chronic cough: if a therapy is at all effective, it is important to continue that therapy while adding a therapy directed toward the next potential trigger. For example, we would not recommend stopping a partially effective antireflux treatment when deciding to add empiric treatment for UACS.

APPROACH TO TREATING CHRONIC COUGH IN CHILDREN

Children with chronic cough are different enough from adult patients that a separate algorithm for children has been proposed in the 2006 ACCP guidelines.²⁸ The definition of chronic cough in pediatrics is different; for children, a cough lasting longer than 4 weeks is defined as chronic cough. Similar to the adult guidelines, one should search thoroughly for clues that point to an underlying origin in children (Table 3).^{28,52} The 3 most common causes of adult cough (UACS, GERD, and asthma) are less commonly encountered in children.^{53,54} A prospective study of a cohort with the average age of 2.6 years found protracted bacterial bronchitis to be the most common explanation for chronic cough and that asthma, GERD, and UACS comprised less than 10% of the diagnoses.⁵⁴ Another study suggests that asthma is rarely the cause of an isolated chronic cough in children (in those with no wheezing or abnormalities on their spirometry) based on a randomized trial that demonstrated salbutamol or beclomethasone had no significant effect on cough frequency or severity.⁵⁵ Unfortunately, however, this evidence is not strong enough to discount asthma as a possible cause of chronic

Table 3. Clues to Making a Specific Diagnosis of Chronic Cough in Children*

Clue	Findings
Abnormal lung examination result	Wheezing (asthma, tracheomalacia), crackles (parenchymal disease)
Purulent cough	Bronchiectasis, cystic fibrosis
Digital clubbing	Suppurative lung disease
Developmental delay	Aspiration
Failure to thrive	Serious systemic illness

* Modified from Chang and Glomb.²⁸

cough, especially considering that 2 other prospective studies examining chronic cough in children have both found asthma to be the most common cause.^{56,57}

If a careful history, physical examination, chest x-ray examination, and spirometry (in an able child) do not lead to a diagnosis and treatment plan, then an approach that distinguishes between dry and wet cough may prove helpful. The utility of distinguishing between dry and wet cough is based on a study that demonstrated an association between the description of cough and bronchoscopic secretion findings.⁵⁸ The ACCP guidelines suggest that children with dry cough receive inhaled steroids for empiric treatment of asthma, whereas those with wet cough receive consideration for a trial of antibiotics for presumed protracted bacterial bronchitis.²⁸ The data supporting the decision to treat wet cough with antibiotics rest largely on the prospective, uncontrolled trial demonstrating improvement in cough after a 2-week course of amoxicillin-clavulanic acid.⁵⁴ A Cochrane review concluded that although antibiotics for prolonged, moist cough may be beneficial, the evidence of their utility is limited by study design and quality.⁵⁹

Better evidence exists that treating sinusitis with antibiotics is effective in reducing cough, although it is unclear how

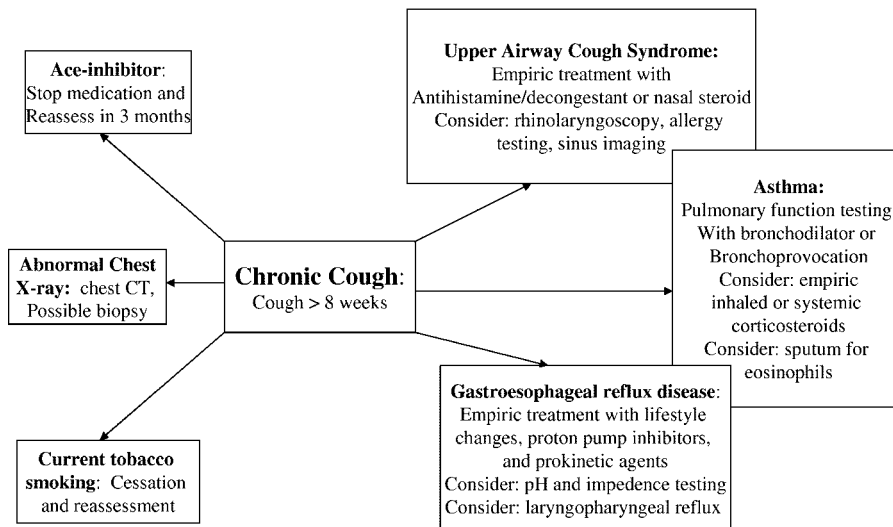


Figure 1. Simplified adult chronic cough algorithm. ACE indicates angiotensin-converting enzyme; CT, computed tomography.

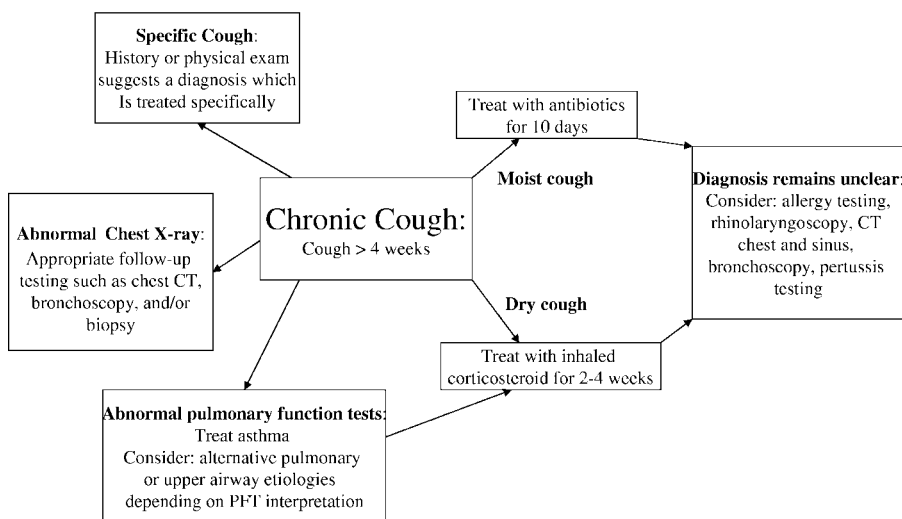


Figure 2. Simplified pediatric chronic cough algorithm. CT indicates computed tomography; PFT, pulmonary function testing.

often sinusitis causes chronic cough in children.⁶⁰ Although sinus CT is an important tool for the diagnosis of sinusitis, the results must be interpreted cautiously given that many asymptomatic patients have abnormal sinus CTs (approximately 50%).⁶¹ If there is no improvement with either inhaled steroid or antibiotics, then a more in-depth workup should ensue that includes a chest CT to look for bronchiectasis (and if present, a workup for immunodeficiency and cystic fibrosis), an evaluation for aspiration, infectious workup including tuberculosis testing, rhinolaryngoscopy to evaluate sinus disease, cardiac testing, and possibly bronchoscopy. Every effort in the workup of chronic cough in children should be directed toward identifying an underlying cause, especially in children

younger than 6 months. Empiric antitussive treatment is not favored by some based on data from acute cough studies that found no benefit and potential harmful effects.^{62,63}

ANTITUSSIVES, PROTUSSIVES, AND OTHER COUGH TREATMENTS

Although the data in children point against the use of antitussives and protussives, their use in adults may be helpful in some instances.^{62,63} Examples of antitussives include benzonatate, levodropropizine, moguisteine, codeine, and dextromethorphan, whereas protussives include hypertonic saline solution or amiloride. Randomized trials have demonstrated the antitussive efficacy of dextromethorphan, codeine, and

ipratropium bromide for chronic bronchitis, whereas protussive therapy has not been well studied.⁶⁴ Current ACCP guidelines are limited to recommending codeine for chronic cough and ipratropium bromide for chronic bronchitis.⁶⁵

Breathing exercises for “habit” or unexplained cough have been shown to be beneficial in one small study.⁶⁶ There are other empiric therapies that may prove helpful, such as amitriptyline, gabapentin, baclofen, and nebulized lidocaine treatments. Although these therapies have not been well studied, they may be considered in those patients refractory to all other treatments.

COST-EFFECTIVENESS OF VARIOUS APPROACHES TO COUGH EVALUATION

A study examined the cost-effectiveness of various intervention schemes involving UACS, asthma, and GERD in the treatment of chronic cough.⁶⁷ The optimal strategy to treat chronic cough for the patient who values cost savings is to treat each condition sequentially beginning with UACS. This strategy, unfortunately, leads to a longer time to cough resolution. A preferred strategy for the patient who places higher value on cough resolution would involve testing for all 3 conditions and treating them simultaneously.

FUTURE DIRECTIONS IN CHRONIC COUGH

Newer noninvasive techniques hold the potential to improve our ability to diagnose the underlying causes of chronic cough. Exhaled nitric oxide, a noninvasive measurement shown to correlate with airway inflammation, may offer an alternative or supplement to the currently available asthma diagnostics.⁶⁸ A preliminary study by Chatkin et al⁶⁹ demonstrated that elevated exhaled nitric oxide levels correlate with those patients with chronic cough who have a positive methacholine challenge test result. In an effort to more easily diagnose GERD-associated cough, the portable Aeriflux testing system was developed to measure the acidity of exhaled breath performed both during coughing spells and during asymptomatic periods and may prove useful in the diagnostic evaluation of cough. In addition to the development of more sensitive and specific tools for determining the cause of chronic cough, more evidence is strongly needed in both adults and children to clarify our treatment algorithms.

CONCLUSIONS

Chronic cough is one of the leading causes of consultation with a physician. It is a concerning and frustrating symptom for patients, many of whom have already experienced failed previous intervention. An approach using the anatomic, diagnostic protocol that emphasizes the sites of the vagus afferent nerve endings will lead to successful resolution of the cough for most patients. UACS, asthma, and GERD are the 3 most common causes (in adults) and require careful workup and treatment for those patients who have no obvious cause of the cough (Fig 1). Chronic cough in children should be approached differently than in adults (Fig 2). When one considers the leading cause(s) of chronic cough, it is clear

that allergists should be pivotal in the evaluation and treatment of this condition.

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Objectives: After reading this article, participants should be able to demonstrate an increased understanding of their knowledge of allergy/asthma/immunology clinical treatment and how this new information can be applied to their own practices.

Participants: This program is designed for physicians who are involved in providing patient care and who wish to advance their current knowledge in the field of allergy/asthma/immunology.

Credits: ACAAI designates each Annals CME Review Article for a maximum of 2 category 1 credits toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the activity. The American College of Allergy, Asthma and Immunology is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

CME Examination

1–5, Rank MA, Kelkar P, Oppenheimer JJ. 2007;98:305–313.

CME Test Questions

1. Which of the following is considered to be important in the initial diagnostic workup of all patients with chronic cough?
 - a. allergy testing
 - b. chest x-ray examination
 - c. bronchoscopy
 - d. sinus computed tomography (CT)
 - e. rhinolaryngoscopy
2. Physical examination can be helpful in the workup for chronic cough by
 - a. helping to exclude asthma
 - b. helping to exclude sinusitis
 - c. helping to exclude upper airway cough syndrome (UACS)
 - d. discovering an embedded hair on the tympanic membrane
 - e. helping to exclude gastrointestinal reflux disease (GERD)
3. Chronic cough in children differs from that encountered in adults in that
 - a. it is defined as lasting more than 12 weeks
 - b. it almost is exclusively caused by UACS, asthma, or GERD
 - c. a positive sinus CT has a high positive predictive value for diagnosis of acute bacterial sinusitis
 - d. it can be divided into categories of dry and moist cough for purposes of empiric treatment
 - e. chest radiograph is not necessary or helpful
4. The anatomic, diagnostic protocol for chronic cough evaluation
 - a. is based on the innervation pattern of the vagus nerve to help diagnose and treat chronic cough
 - b. is also used for acute cough
 - c. is used to achieve resolution of cough in 40% to 60% of patients
 - d. relies on the character and timing of the cough
 - e. is based on randomized controlled trials demonstrating superiority over other chronic cough protocols.
5. All of the following correlations are true EXCEPT
 - a. angiotensin-converting enzyme inhibitors: chronic cough that generally resolves 3 months after discontinued use of the medication
 - b. cigarette smokers: chronic cough immediately resolves after tobacco cessation
 - c. interstitial lung disease: a normal chest x-ray examination result cannot exclude this condition
 - d. unexplained cough: a rare cause of chronic cough
 - e. laryngopharyngeal reflux: is treated with proton pump inhibitor

Answers on page 348.