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REVIEW ARTICLE

A clinical review of chronic cough from a primary care perspective

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Algorithm

Abstract Chronic cough is a common problem for primary care physicians, with prevalence rates of up to 22%. The pathogenic triad of upper airway cough syndrome (UACS), asthma, and gastroesophageal reflux disease (GERD) are either solely or partly responsible for up to 95% of patients who present with chronic cough. The objectives of this article are to present a basic scientific overview of chronic cough and to provide a strategic and systematic management algorithm to primary care physicians to maximize efficacy and efficiency in the treatment of patients with chronic cough. An online PubMed search was initially used. Subsequently, evidence-based sources were referenced. These included the Cochrane Database of Systematic Reviews, Evidence-BasedMedicine.com, Medscape's Primary Care Practice Guidelines, and the National Guideline Clearinghouse. Articles reviewed had no timeline limitations and inclusion criteria included published textbooks, publications in professional medical journals, and national databases. Chest radiographs are indicated for all patients with chronic cough. Smoking and cough-inducing medications need to be addressed. Once these factors are eliminated, management strategies for UACS, asthma, nonasthmatic eosinophilic bronchitis, GERD, and laryngopharyngeal reflux are discussed. Treatment strategies include empiric treatment, definitive diagnostic testing, behavior modifications, and aggressive drug regimens. A strategic and systematic management approach needs to be used to ensure that the most accurate and most efficient diagnostic and therapeutic outcomes are achieved. The recommended step-wise treatment protocol for chronic cough is based on a combination of empiric, integrative, and additive therapeutic strategies.

Cough has been consistently ranked among the top five reasons for visits to medical professionals and was recently identified as the number-one symptomatic problem for hospital outpatient department visits.[1-4] It is probably safe to say that primary care physicians encounter patients with a symptom of cough on a weekly, if not daily, basis. Coughing for several days is undoubtedly bothersome for patients, but coughing on a regular basis for long periods of time can significantly impair the overall quality of life for anyone. Although the typical cough is short-lived and self-limiting, approximately 20% of patients could suffer for months or even years with persistent cough. The prevalence of chronic cough is significant and it was demonstrated that in an outpatient pulmonary practice, persistent cough could account for as much as 40% of the practice volume.[5]

This patient-oriented review article will provide a fundamental overview of chronic cough. Based on a review of medical literature, expert consensus, and published evidence-based clinical practice guidelines, a systematic primary care management alogrithm for chronic cough will be presented. The objectives of this article are to provide a strategy for primary care physicians to effectively and effi-

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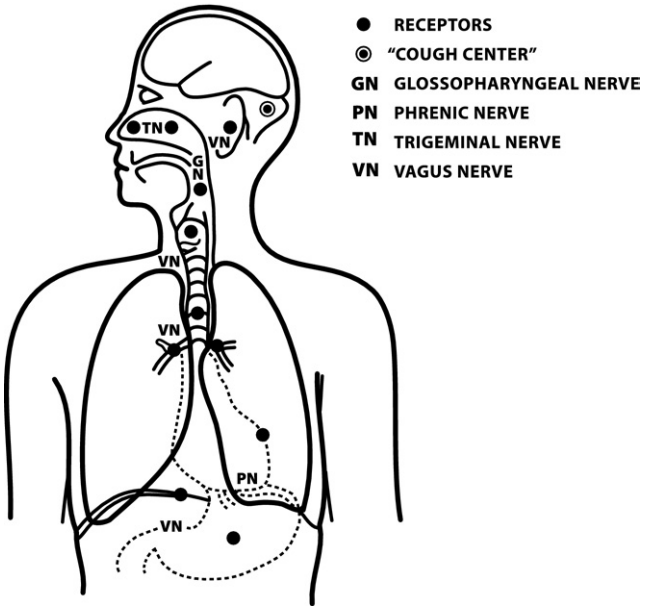

Figure 1 Schematic representation of the anatomy of the cough reflex. (Modified and reproduced with permission. Irwin RS, Rosen MJ, Braman SS: Cough. A comprehensive review. Arch Intern Med 137:1186-1191, 1977. © 1977, American Medical Association. All rights reserved.)

ciently treat patients with chronic cough and to recognize when a specialist referral is appropriate.

Methods

An online PubMed search of "chronic cough" was initially used to identify articles to be reviewed. Subsequent search keywords included "diagnosis," "treatment," "management," and "evidence-based." The Cochrane Database of Systematic Reviews, Evidence-BasedMedicine.com, Medscape's Primary Care Practice Guidelines, and the National Guideline Clearinghouse sources were then referenced. The evidence-based source that was most consulted for this project was the National Guideline Clearinghouse (www.guidelines.gov). There were no timeline start or end limits for the searches. Inclusion criteria included published textbooks, publications in professional medical journals, and national databases.

Discussion

Basic science of cough. The major physiologic role of cough is to protect the airway as a primary defense mechanism against foreign bodies, airborne particles, organisms, food, and gastric content.[6] The anatomy of cough includes structures of the cardiopulmonary, gastrointestinal, and nervous systems. Cough appears to be initiated through a complex reflex arc of multiple cough receptors in various locations in the body. Cough receptors have been identified in the pharynx, trachea, larynx, bronchi, esophagus, stomach, diaphragm, and pericardium (Fig. 1). Activation of these cough receptors occur most commonly along the tracheobronchial tree, specifically in the larynx, carina, and the bifurcation of the bronchi, where the greatest concentration of cough receptors are located.[7] However, activation of cough receptors in any of the previously mentioned anatomical structures will also stimulate cough.

Table 1 Complications of cough

Rib fractures	Musculoskeletal pain
Annoyance	Laryngeal irritation and hoarseness
Insomnia	Excessive perspiration
Physical exhaustion	Urinary incontinence
Headache	Self-consciousness or worry
Dizziness	Negative social consequences
Somatic dysfunctions	

Two major types of cough receptors have been identified. The first type responds to chemical stimuli, both exogenous and endogenous. Endogenous chemicals may include gastric acid, histamine, bradykinin, and prostaglandins. The second type of receptors are responsive to mechanical stimuli such as direct physical contact or displacement, often caused by foreign materials. Although several additional subclassifications of sensory receptors have been postulated (eg, afferent pulmonary and bronchial C-fibers and A-fibers, rapidly adapting receptors, slowly adapting receptors) further neurophysiologic discussion on cough receptors would be beyond the scope of this article.[6]

The nervous system is ultimately responsible for the mechanism of cough, with three major nerves being responsible for triggering the cough reflex. These nerves are the trigeminal, glossopharyngeal, and vagus nerves. These cranial nerves supply all the afferent pathways from the cough receptors, with the vagus nerve playing the largest role through its pharyngeal, superior laryngeal, and pulmonary branches. Once the cough receptors are activated, afferent impulses are transmitted to the cough center of the brain, which is located in the medulla oblongata. The medulla then sends efferent impulses to the larynx and the tracheobronchial tree, also via the vagus nerve. Efferent impulses are also sent to the diaphragm, intercostals muscles, abdominal wall muscles, and pelvic floor muscles via the phrenic nerve and other spinal motor nerve branches. It is the muscular contractions of these muscles that produce the expelling forces of the cough.

Complications of cough. Although cough is primarily a protective function, sometimes it can cause very unpleasant consequences. A forceful cough could generate intrathoracic pressures of up to 300 mm Hg and expiratory velocities of 500 mph.[8,9] Although these pressures and velocities are responsible for the beneficial effects of clearing the airways, they are also responsible for many of the complications of cough (Table 1). These complications include rib fractures, exhaustion, headache, dizziness, musculoskeletal pain, and hoarseness. Other undesirable outcomes include difficulty sleeping, excessive perspiration, urinary inconti-

Table 2 Causes of cough

	Common	Less common	Uncommon
Adults	UACS	LPR	Aspiration
	Asthma	NAEB	Bronchogenic
	GERD	Postinfectious process	Cancer
	Airborne irritants	Pulmonary edema	Pneumonia
	ACE inhibitors	Pulmonary embolus	Psychogenic cough
		Bronchiectasis	Sarcoidosis
			Zenker's diverticulum
Children	Asthma	Foreign body	Aspiration
	GERD		Cystic fibrosis
	Respiratory tract infections		Congenital abnormalities
			Environmental exposures
			Primary ciliary dyskinesia
			Psychogenic cough

Table 3 Medications that can cause cough

Classes of medications	Other specific medications
ACE inhibitors	Aripiprazole
Antihistamines	Cilostazol
Beta-blockers	Clopidogrel
Inhaled beta-agonists	Cromolyn
Inhaled anticholinergics	Cromolyn sodium
Inhaled corticosteroids	Eplerenone
	Etanercept
	Exemestane
	Ezetimibe
	Lamivudine
	Lamotrigine
	Montelukast
	Mycophenolate mofetil
	Nicotine nasal or inhaled
	Pravastatin
	Raloxifene
	Riluzole
	Risperidone
	Tacrolimus
	Tamsulosin
	Teriparatide
	Tiagabine
	Trastuzumab
	Zanamivir
	Zidovudine

nence, self-consciousness, and feelings of anxiety that "something is wrong."

Classification and causes of cough. Cough can be differentiated into three categories. Acute cough is defined as cough lasting less than three weeks. Subacute cough is defined as cough lasting three to eight weeks. And finally, chronic cough is defined as cough persisting beyond eight weeks.[10]

Cough can be caused by a multitude of reasons (Table 2). The category of chronic cough is usually associated with factors such as postnasal drip, gastroesophageal reflux disease (GERD), asthma, smoking, and medications (Table 3). It has been reported that angiotensin-converting enzyme (ACE) inhibitors cause cough in as much as 35% of patients treated with these agents (Table 4).[11] However, because of the general clinical awareness of this class of medication's adverse affects, ACE inhibitors do not seem to be a complicating factor in the management of chronic cough. ACE inhibitor–induced cough usually starts within the first week the medication is started and typically resolves within one to four days of discontinuation. Although the development of cough can be delayed for up to six months and sometimes can take up to three months to resolve, these responses to ACE inhibitors are, fortunately, very uncommon.[11,12]

Chronic cough. The prevalence of chronic cough is estimated to range from 14% to 23%.[13] It can be physically and socially debilitating for many patients, depending on its severity. These patients deserve empathy as well as a clear explanation of the potentially long process that may be required to completely treat this problem. Primary care physicians need a quick but comprehensive way to handle this chronic problem. Therefore, a logical and systematic approach needs to be undertaken.

The first logical question should be: What is the etiology of this patient's chronic cough? As seen in Table 2, there are many causes of cough. However, there are only a handful of causes that account for the vast majority of chronic cough. It has been reported that as much as 95% of patients with chronic cough can be attributed to four conditions. In studies of patients seen in tertiary pulmonary practices for chronic cough, 65% to 95% were diagnosed with postinfectious bronchial inflammation, postnasal drip, asthma, or GERD (Table 5). In many patients, however, a combination of these was present.[10,13-16] In one study, it was shown that a single cause was identified in only 38% of chronic cough cases, whereas two or more causes were felt to be responsible in 59% of the cases.[5] Prospective studies have shown that ACE inhibitors were responsible for chronic cough in only 0% to 3% of patients who presented for that particular problem.[5,16] If the factors of smoking and the use of ACE inhibitors were eliminated during the acquisition of the

Table 4 ACE inhibitors

Captopril	Lisinopril
Enalapril	Benazepril
Ramipril	Fosinopril
Quinapril	Zofenopril

Table 5 Most commonly diagnosed causes of chronic cough*

UACS	41%
Asthma	24%
GERD	21%
Bronchial inflammation	3%
Others	8%

*102 patients studied.[5]

patient's history, other studies have shown that three conditions account for the etiologic cause of chronic cough in 92% to 99% of immunocompetent patients who had normal chest radiographs.[14,16] These data were reinforced in another study that followed 78 chronic cough patients with the aforementioned criteria, and it demonstrated that 94% of these patients were diagnosed with at least one of the three conditions that the authors called the "pathogenic triad of chronic cough." These three conditions were upper airway cough syndrome (UACS), asthma, and GERD.[13]

Although the "pathogenic triad of chronic cough" does indeed account for the majority of the cases of chronic cough, others studies implicate two other potentially significant causes for physicians to consider in their approach to patients with chronic cough. Therefore, it is noteworthy to report and discuss these two causes—nonasthmatic eosinophilic bronchitis (NAEB) and laryngopharyngeal reflux (LPR).[17-20]

Upper airway cough syndrome. Upper airway cough syndrome is the most common cause of chronic cough and is the new term coined by the American College of Chest Physicians in 2006 that replaces the originally British term of *postnasal drip syndrome*.

UACS encompasses almost every rhinosinus condition that has been linked to cause chronic cough (Table 6).[21] Because of the broad definition of UACS, it is by far the most common cause implicated in as much as 87% of patients with chronic cough.[22] The proposed pathophysiologic mechanism is the often unnoticeable and undetectable stimulation of the upper airway cough receptors by secretions from the nasal mucosa. Unfortunately, there are no pathognomonic findings of UACS and this is actually its hallmark. Studies show that even a thorough history and physical examination does not appear to significantly aid in the differential diagnosis process.[16,22,23] The diagnosis of UACS is made on the basis of response to therapy.[21] Therefore, the diagnostic and therapeutic approach to UACS is the empiric treatment with an antihistamine and a decongestant. If UACS is the causative factor, responses are typically seen within two weeks of initiating therapy, although sometimes cough resolution may take several months.[22]

Asthma and cough-variant asthma. Asthma is the second most common cause of chronic cough. Although we know that not every patient who wheezes is asthmatic, there is one thing that every asthmatic does do: cough. As a matter of fact, cough may be the only presenting symptom of asthma in as much as 57% of patients with the disease (cough-variant asthma).[10]

The pathophysiology of asthma is bronchial inflammation, with the consequent effects of airway hyper-responsiveness and bronchial constriction causing obstruction of expiratory airflow. The definitive and specific diagnosis of asthma can only be made with pulmonary function testing, specifically spirometry and the methacholine bronchoprovocation challenge test. Like other chronic diseases, all attempts should be made to acquire a definitive diagnosis first. The mainstay of treatment of asthma (whether it is of the cough variant or not) is the combination of corticosteroids, beta-2 agonists, and, more recently, leukotriene receptor antagonists. An additive stepwise approach should be taken to ensure maximal efficacy with the least amount of medications possible. Typically, a good response is seen within one week, although complete cough resolution may take up to eight weeks.[22]

Gastroesophageal reflux disease. Gastroesophageal reflux disease is the third most common cause of chronic cough. The typical symptoms of GERD are heartburn, regurgitation, and difficulty swallowing. However, cough is also a common symptom and was shown in one study to be the sole presenting symptom in 43% of the patients diagnosed with GERD.[5] It is believed that reflux of gastroesophageal acid stimulates the cough receptors in the esophagus and triggers the cough reflex through the afferent fibers of the vagus nerve.[24] The pathophysiology of GERD is not definitively known, but an abnormal lower esophageal sphincter pressure and increased reflux during transient lower esophageal sphincter relaxations are believed to be key etiologic factors.[25]

Table 6 Inclusive illnesses of UACS

- Allergic rhinitis and allergic rhinosinusitis
- Nonallergic rhinitis
  - Infectious
  - Rhinosinusitis
  - Rhinopharyngitis
  - Postinfectious rhinitis
  - Rhinitis medicamentosa
  - Rhinitis caused by anatomic abnormalities
  - Rhinitis caused by physical irritants
  - Rhinitis caused by chemical irritants
  - Rhinitis of pregnancy
  - Nonallergic rhinitis with eosinophilia (NARES)
  - Vasomotor rhinitis
    - Odors
    - Alcohol
    - Emotional
    - Temperature changes
    - Barometric pressure changes

GERD is also a diagnosis that is not simple to definitively confirm with a specified lab test or a procedure. A prospective study in 2005 explored the comparison of endoscopy with biopsy, radionuclide scintigraphy, the comparison of barium swallow with fluoroscopy, 24-h esophageal pH monitoring, and the omeperazole challenge test to see which one diagnostic test would yield the highest sensitivity and specificity in the diagnosis of GERD. The results did show that 24-h pH monitoring had the best combination of sensitivity (77.7%) and specificity (92%) and was thus determined to be the single best test to diagnose GERD. However, it was also noted that the sensitivity of 77.7% of this test was disappointingly lower than the level that is usually desired for a gold standard.[26] Therefore, because of a suboptimal gold standard test and significant patient inconvenience, the recommendation is to withhold diagnostic testing and initiate empiric therapy for the initial management of GERD. Dietary and lifestyle modifications are a major part of this therapy and include limiting fat intake; avoiding caffeine, chocolate, mints, citrus products, alcohol, and smoking; and limiting vigorous exercise that increases intraabdominal pressure.[27] Empiric acid suppression drug therapy for GERD should be initiated with proton pump inhibitors. This class of medication is believed to be more effective than traditional H-2 receptor antagonists according to the American Gastroenterological Association Medical Position Statement on the Management of Gastroesophageal Reflux Disease.[28] Depending on patient compliance, resolution of chronic cough can be seen in as little as two weeks. However, at least a six- to eight-week trial of aggressive medical therapy is often needed.[29]

Laryngopharyngeal reflux. Laryngopharyngeal reflux appears to be a subtype of GERD and can be present in a significant number of patients with chronic cough.[27] One study shows that 62% of patients with LPR suffered from chronic cough.[20]

LPR is often referred to as "silent GERD" because, although the pathophysiology is similar to GERD, LPR does not present with the classic symptoms of heartburn or dyspepsia. It is believed that microaspiration of esophageal contents, such as gastric acid and pepsin, into the laryngopharynx and tracheobronchial tree, is what triggers the cough.[24]

LPR is most likely the result of a problem involving the upper esophageal sphincter, whereas traditional GERD involves the lower esophageal sphincter. This can explain why symptoms occur commonly in the upright position and are aggravated by any physical activity that increases intrathoracic pressure (eg, bending over, Valsalva maneuver). Further, the symptom of heartburn is rarely present, even in the recumbent position.

In a well-cited article by Koufman, chronic cough[30] was found to be the second most common symptom of laryngopharyngeal reflux, with "hoarseness" (71%) ranking number one and globus sensation (47%) ranking number three.[31]

The management of LPR is essentially the same as the treatment protocol for GERD. A proton pump inhibitor taken twice daily and diet/lifestyle modifications are the mainstay, but, unfortunately, LPR does not respond as quickly to treatment compared with GERD. Studies show that symptom resolution of LPR often takes several months.[30,32]

Nonasthmatic eosinophilic bronchitis. Nonasthmatic eosinophilic bronchitis (NAEB) may not be as prevalent as UACS, asthma, or GERD/LPR as a cause of chronic cough, but its discussion here is significant because it is included in the algorithmic approach to chronic cough, which will be discussed in the next section.

Nonasthmatic eosinophilic bronchitis has been implicated as an etiology of chronic cough in 13% to 33% of patients.[13,19,33-35] Several studies have reported that NAEB occurs in 10% to 30% of patients referred to a specialist with an isolated chronic cough.[17-19]

The pathophysiology of NAEB is bronchial irritation characterized by eosinophilic infiltration of the bronchial tree. It is differentiated from asthma because there is no airway hyper-responsiveness and spirometry tests are normal.[10] It is also differentiated from classic bronchitis by the presence of active eosinophils in the airway epithelium, which manifests in sputum cytology. Laboratory evaluation of lower airway sputum can rule out this disease if less than 3% of eosinophils are seen in the sputum sample.[17] The drawback of this diagnostic technique is that accurate interpretation of results depend on the visualization of cells from lower respiratory tract secretions with minimal contamination from saliva. In other words, the test is completely dependent on the quality of the sputum sample. Unfortunately, many patients are not able to spontaneously produce lower airway sputum and must undergo a relatively arduous process of inhaling nebulized hypertonic saline and voluntary coughing to induce an acceptable sample of sputum. Another method to rule out NAEB is the failure of symptom improvement with the use of inhaled corticosteroids because this disease is so highly responsive to this class of medication. A study conducted by Brightling et al shows a definitive improvement of cough scores along with a greater than 4 fold reduction in sputum eosinophilia after a four-week trial of patients using an inhaled corticosteroid.[36] Based on the data of this study, patients should see noticeable improvement of cough within two weeks of inhaled corticosteroid treatment.

Management strategy for chronic cough. The management of chronic cough can be frustrating for both the patient and the clinician because several months may be needed to achieve the desired outcome of complete cough resolution. A systematic strategy to most effectively diagnose and treat chronic cough based on evidence from medical literature and accepted clinical guidelines will now be presented and discussed (Fig. 2).

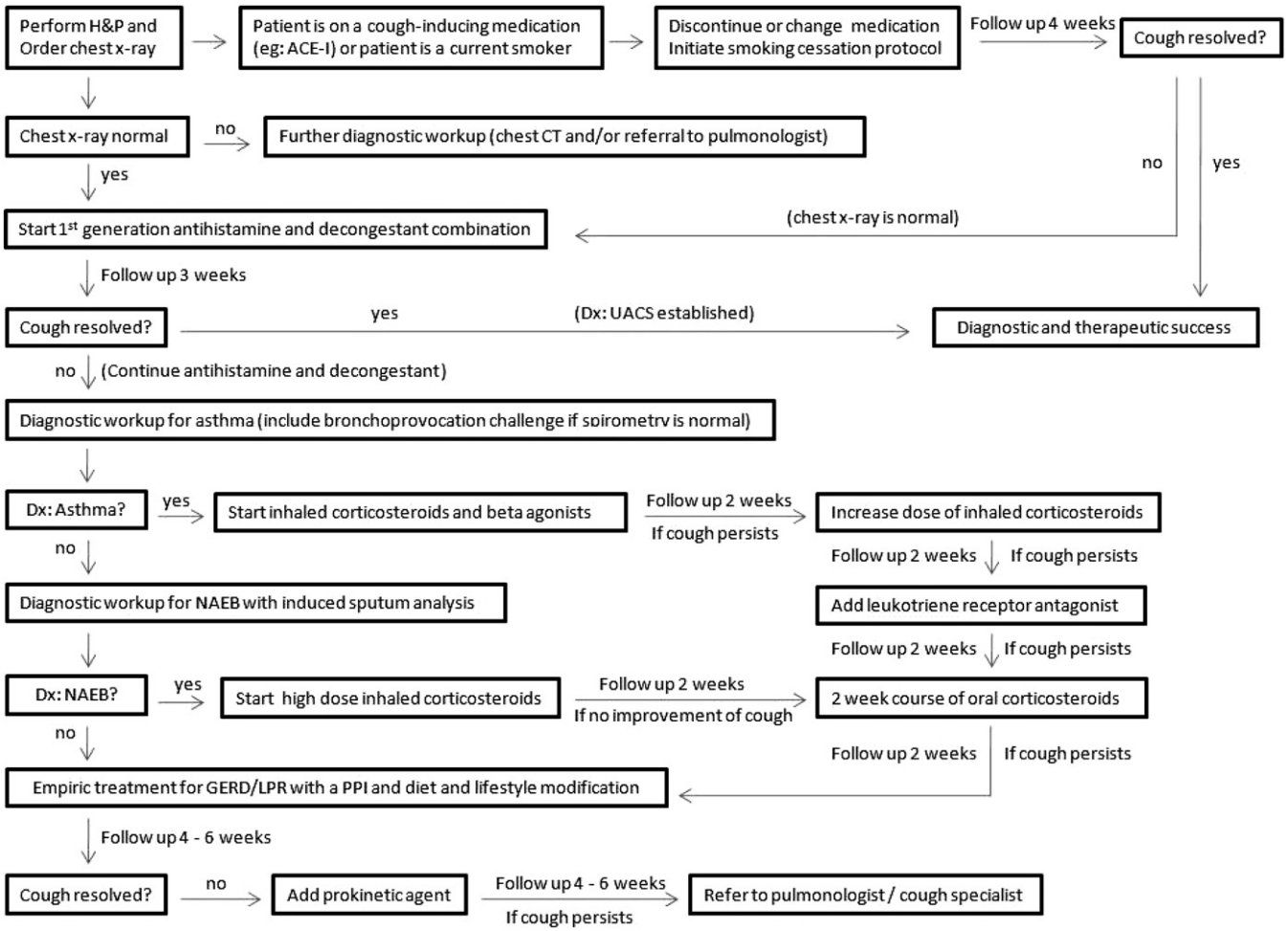

Figure 2 Management strategy for chronic cough. *ACE-I*, angiotensin-converting enzyme inhibitor; *UACS*, upper airway cough syndrome; *NAEB*, nonasthmatic eosinophilic bronchitis; *GERD*, gastroesophageal reflux disease; *LPR*, laryngoesophageal reflux; *PPI*, proton pump inhibitor.

Nearly every published study and clinical guidelines regarding chronic cough specifically relate to immunocompetent patients with normal radiographs who do not take an ACE inhibitor and do not smoke. Therefore, it is most logical that these factors be addressed first. The first step should be for the patient to be evaluated with a chest radiograph. This is especially important if the patient's history is significant for smoking because diagnostic consideration for bronchogenic carcinoma as well as chronic obstructive pulmonary disease should not be overlooked. An abnormal chest radiograph obviously warrants further studies, which could include computed tomography scans of the chest, bronchoscopy, needle biopsy, and sputum studies.

It would be ideal if the chest radiography could be obtained and intrepreted in the office in the same visit. However, it is most likely that in today's primary care setting, a chest radiograph would be obtained at another location, with results arriving at a later time. In the meantime, if the patient is a smoker, a smoking cessation plan should be implemented. If the patient is currently taking an ACE inhibitor or another cough-inducing medication, the medication should be discontinued immediately if possible and replaced with another class of medication as clinically appropriate. Discontinuation of the offending medication (specifically ACE inhibitors) should demonstrate resolution of the cough within four weeks.[21] If coughing persists, patient monitoring for up to three months has been suggested, but no specific temporal strategy has been strongly recommended in the literature.

If smoking and cough-inducing medications have been appropriately addressed and if the chest radiograph is unremarkable, a logical and systematic approach to the most common causes of chronic cough should be taken next, keeping in mind that more than one cause may be present. This recommended approach should yield the highest success rate in achieving cough resolution.[37]

Upper airway cough syndrome has been established as the most common cause and should therefore be addressed first. The recommendation is to initiate empiric therapy with both an antihistamine and a decongestant. The combination of dexbrompheniramine plus pseudoephedrine has been suggested.[10] However, chlorphenamine and phenylephrine is another option. First-generation H1 antihistamines are recommended because the nonsedating second-generation

Table 7 Systematic medication strategy for chronic cough in patients diagnosed with asthma

1. Inhaled corticosteroid plus short-acting inhaled B2 agonist
If no improvement of cough in 2 weeks, then:
2. Increase dosage of inhaled corticosteroid
If no improvement of cough in 2 weeks, then:
3. Add leukotriene receptor antagonist
If no improvement of cough in 2 weeks, then:
4. Two-week course of oral corticosteroids

H1 antihistamines do not seem to be as effective in cases of nonallergic rhinitis.[38]

If there is no resolution of the cough in three weeks, it is recommended that the antihistamine and decongestant be continued while diagnostic workup for asthma is undertaken. This is to prevent any confounding factors if asthma is ruled in because it maintains treatment coverage should multiple causes be responsible for the patient's chronic cough. The definitive diagnostic approach of asthma is to have the patient undergo a methacholine bronchoprovocation inhalation challenge test and measure reversible airflow obstrucion via spirometry. This diagnostic method is extremely accurate in the diagnosis of asthma as demonstrated by a negative predictive value of 100% in one study[23] and a positive predictive value of 100% in another.[39] If pulmonary studies cannot be performed, then empiric treatment with inhaled beta-agonists and inhaled corticosteroids is acceptable. However, it is important to note that improvement of cough with the empiric drug therapy cannot rule out asthma because NAEB is also responsive to treatment with inhaled corticosteroids.

If the methacholine bronchoprovocation test is positive and shows variable airflow obstruction or airway hyperresponsiveness, the diagnosis of asthma is definitively made and NAEB can be definitively ruled out. Appropriate multidrug treatment for asthma should now be implemented (Table 7). If cough does not resolve in eight weeks, further diagnostic workup should be pursued to look for other causes. If coughing does resolve, discontinuation of the antihistamine/decongestant is warranted and the patient should be monitored for return of cough.

A normal methacholine bronchoprovocation test, however, effectively rules out all forms of asthma and the next step is taken. Although GERD is the third most common cause of chronic cough, NAEB should be considered next, according to the most recent Evidence-Based Clinical Practice Guidelines from the American College of Chest Physicians.[37] This is a logical recommendation mainly because of the relative ease of definitively diagnosising NAEB. Although diagnostic confirmation via cough resolution with empiric inhaled corticosteroid may be acceptable, acquiring a definitve diagnosis with induced sputum analysis should be pursued first if possible. The first-line treatment strategy for NAEB should be to identify causal allergens or occupational sensitizers and to remove the exposure. Medical treatment is inhaled corticosteroids. Inhaled budesonide of 400 μg twice daily was shown to result in significant improvement of cough severity and frequency within four weeks.[36] If there is minimal to no improvement with the inhaled corticosteroids after two weeks, a course of oral corticosteroids should be tried for two weeks before the next diagnostic consideration is attempted.

GERD and LPR are the final diseases that are addressed in the management alogrithm of chronic cough. These two conditions can be managed concomitantly because the treatment plan is essentially identical. It is interesting to note that the management recommendation at this point is a little different from the previous management steps. Before definitive diagnostic testing is attempted, empiric treatment is actually the recommendation. This may be partly because of the expensive, time-consuming, and relatively invasive nature of 24-hour pH esophageal monitoring, but the predominant reasons appear to lie in the complexity of attaining appropriate testing conditions and in the difficulty in interpreting the results as they correlate with cough.[27,40]

Empiric treatment for chronic cough caused by GERD/LPR is dietary/lifestyle modifications and acid suppression therapy with medication. Proton pump inhibitors (Table 8) are favored over H2 antagonists because of their longer-acting effects of acid suppression.[28] The addition of a prokinetic agent may also be started either initially or later if there is minimal or no response. If cough is not resolved within one to three months and the patient's chronic cough remains undiagnosed after all of the above efforts, referral to a cough specialist or a pulmonologist is indicated.

Summary of chronic cough

Chronic cough is a common problem that many physicians must deal with. Prevalence rates of as high as 22% have been suggested in the United States.[41] In one trial, the pathogenic triad of UACS, asthma, and GERD was determined to be either solely or partly responsible for more than 99% of chronic cough in immunocompetent patients who have the following three characteristics: nonsmoker, not currently taking an ACE inhibitor, and have a normal chest radiograph.[16]

A systematic, evidence-based approach should be used to ensure that the most efficient and most effective diagnostic and therapeutic outcomes are achieved. The recommended treatment protocol for chronic cough is based on a combi-

Table 8 Proton pump inhibitors

Omeprazole
Lansoprazole
Rabeprazole
Pantoprazole
Esomeprazole

nation of empiric, integrative, and additive therapeutic strategies.

The primary care physician should refer the patient to a cough specialist or pulmonologist if symptom resolution does not occur after an earnest attempt to follow the clinical guidelines presented in this article.

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