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REVIEW

Chronic cough: State-of-the-art review

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Cough is the most common presenting complaint in adults seeking medical treatment in an ambulatory setting. Chronic cough (persisting greater than 3 weeks) can be associated with myriad diseases that may overlap multiple medical specialties. For this reason, a thorough assessment of the patient with chronic cough relies on a multidisciplinary approach and close cooperation between pulmonary medicine, gastroenterology, and otolaryngology. Despite this daunting task, success can be achieved in up to 90% of patients with chronic cough if a systematic and thorough approach is used. The purpose of this review is to summarize the state-of-the-art in the diagnosis and treatment of chronic cough for the practicing otolaryngologist.

Cough is the most common presenting complaint in adults seeking medical treatment in an ambulatory setting.[1] Although cough is generally caused by a brief, self-limiting illness, it can become a persistent symptom in some cases. The exact reason why cough causes so many patients to seek medical attention is unknown but may be related to fear of having a serious disease. Also, cough-related morbidity (sleep disturbance, syncope, and urinary incontinence in women) can cause the patient to schedule an appointment with their physician. Data from clinics specializing in chronic cough show a preponderance of female patients, and in fact women have been shown to have an intrinsically elevated cough response. In addition, both female patients with chronic cough and normal women controls have augmented inhalation cough challenge in clinical studies. Lastly, a higher frequency of angiotensin-converting enzyme (ACE) inhibitor–induced cough has been shown in women.[2]

The etiology of chronic cough (cough persisting for >3 weeks) is extensive and can be explained by the myriad afferent pathways involved in the cough reflex.[3] Because cough can arise from virtually anywhere the vagus travels, the full assessment of the patient with chronic cough relies on a multidisciplinary approach and close cooperation between pulmonary medicine, gastroenterology, and otolaryngology. Despite this daunting task, success can be achieved in up to 90% of patients with chronic cough if a systematic and thorough approach is used.[2]

BASIC SCIENCE: THE COUGH REFLEX ARC

The afferent or sensory branch of the cough reflex initiates the cough reflex arc. The sensory nerve fibers are distributed throughout the ciliated epithelial cells of the upper and lower airways from the pharynx to the terminal bronchioles. These receptors can be triggered by chemical and mechanical stimuli such as foreign bodies, irritant particles, fumes, and extrinsic pressure from masses. The greatest concentration of cough receptors are located in the larynx, carina, and at the bifurcation of medium- to large-sized bronchi. A summary of the location of all principal cough receptors is listed in Table 1.

In addition, "higher centers" in the central nervous system can act as afferent limbs "since cough can be voluntarily initiated, postponed, or suppressed" as pointed out by Irwin et al.[4] These afferent impulses (transmitted primarily via the vagus) converge on the "cough center" of the brain, located in the medulla. This diffuse region acts as the central command center, integrating impulses and coordinating the complicated expiratory muscle activity that makes up an effective cough. Efferent impulses leave the medulla and travel to the larynx/tracheobronchial tree (via the vagus) and the intercostal mus-

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Table 1
Location of cough receptors and associated sensory nerve

Region	Afferent nerve
Paranasal	Trigeminal (V)
Pharynx	Glossopharyngeal (IX)
Larynx/tracheobronchial tree*	Vagus (X)
External auditory canal/ tympanic membrane	Vagus (X)
Esophagus, stomach, pleura	Vagus (X)
Diaphragm, pericardium	Phrenic

*Greatest concentration of cough receptors.

cles, abdominal wall, diaphragm, and pelvic floor (via the phrenic and spinal motor nerves C3 through S2).[3]

BASIC SCIENCE: THE PHASES OF COUGH GENERATION

Inspiratory Phase

The initial stage of the cough reflex begins with a sudden deep inspiratory gasp that fills the lungs with air.

Compressive Phase

The second stage of the cough reflex is signaled by a tight, valve-like closure of the larynx at the glottic and supraglottic levels, with the false vocal cords providing the critical 1-way valve effect that prevents air egress. Contraction of the expiratory muscles (chest wall, diaphragm, abdomen, pelvic floor) in the face of a closed glottis creates a dramatic increase in airway pressure in the airways.

Expiratory Phase

Opening of the laryngeal sphincter initiates this phase, resulting in an explosive release of a high-pressure air column ("bechic blast"). The expiratory muscles continue to contract, maintaining the rapid air flow. The vocal cords, supraglottic structures, and posterior commissure vibrate, actively displacing secretions loose from the larynx. In addition (and more importantly), the cross-sectional area of the trachea is reduced significantly during this phase (by as much as 80%) and a powerful "tussive squeeze" is generated, clearing secretions from the tracheobronchial tree, via the high-velocity, turbulent airflow.[3]

CHRONIC COUGH: ETIOLOGY

The myriad etiologies attributed to chronic cough can make the task of arriving at a diagnosis appear quite daunting at first (Table 2). However, a systematic approach that emphasizes the 3 most common causes of chronic cough greatly simplifies the work up.

Table 2
Differential diagnosis for cough in an adult

- PND
  - Allergic rhinitis
  - Chronic sinusitis
- GERD/LPR
- Cough-variant asthma
- ACE Inhibitor medications
- Pertussis (whooping cough)
- Neurogenic
  - Traumatic vagal injury
  - Post-URI neuropathy
- Psychogenic
- Chronic aspiration
- Zenker's diverticulum
- Foreign body
  - Tracheobronchial tree
  - Laryngopharynx
  - Sinonasal
  - External auditory canal
- Chronic bronchitis
- Bronchiectasis
- Lung carcinoma
- Subglottic stenosis
- Tracheomalacia
- Tracheoesophageal fistula
- Tuberculosis
- Sarcoidosis
- Congestive heart failure

URI, upper-respiratory infection.

Postnasal drip (PND), cough-variant asthma, and gastroesophageal reflux disease (GERD) are the cause of chronic cough in 86% of adult patients. This percentage increases to over 99% when evaluating immunocompetent nonsmokers with normal chest x-ray findings and no history of ACE-inhibitor use (Table 3).[4] Therefore, in the vast majority of otherwise healthy adult patients who are referred for chronic cough, the diagnostic choices are limited. If allergy testing, sinus CT studies, and pulmonary function testing are normal, the etiology of chronic cough is almost invariably GERD related. In fact, the prevalence of GERD-associated cough may be as high as 40%.[5] This underscores the need for physicians to maintain a high index of suspicion for GERD when evaluating complaints of chronic cough. As pointed out by Irwin et al,[6] chronic cough can be the only

Table 3
Etiology of 99% of chronic cough cases found in healthy, nonsmoking adults (Immunocompetent, nonsmokers with normal chest x-ray not on ACE inhibitors)

1. PND (allergic rhinitis/chronic sinusitis)
2. Cough-variant asthma
3. GERD/LPR

symptom present in a GERD patient, and GERD-induced cough should be suspected even in the absence of heartburn or other gastrointestinal symptoms.

Pathophysiology of GERD-Associated Cough

GERD-associated cough has been postulated to occur by 2 mechanisms: (1) acid exposure in the distal esophagus stimulating an esophageal-tracheobronchial cough reflex via the vagus nerve and (2) microaspiration of esophageal contents into the laryngopharynx and tracheobronchial tree. The first mechanism occurs with traditional distal GERD, and the second mechanism is caused by extraesophageal GERD or laryngopharyngeal reflux (LPR). Experimental and clinical studies provide support for both mechanisms, so both distal and proximal reflux appear to play at least some role in chronic cough. A study by Irwin et al[7] using dual-channel pH monitoring showed a higher correlation of cough with distal esophageal acid exposure(28%) than proximal esophageal acid exposure (6%). In addition, Ing et al[8] showed that patients with GERD-induced cough had a significant increase in cough frequency with acid versus saline infusions into the distal esophagus. This acid-induced cough reflex arc could be blocked with esophageal lidocaine infusion.[8] These studies support the importance of a vagally medicated esophageal-tracheobronchial cough reflex. Another common finding in GERD-associated cough patients is ineffective esophageal motility and prolonged esophageal acid clearance. More extensive exposure of acid to the esophagus seems to support distal esophageal reflex mechanisms in cough production as well.[9] It is unlikely that esophageal acid exposure is the sole cause of cough, however. More recent evidence using dual-channel pH monitoring showed a significant number of patients with GERD-associated cough had proximal reflux disease in the absence of pathologic distal reflux disease. Schnatz et al[10] showed that 17% of patients whose pulmonary symptoms (cough and asthma) responded to antireflux therapy would not have been recognized as having abnormal reflux if the proximal pH probe data (eg, dual-channel pH monitoring) had not been performed. In addition, others have observed acid reflux events into the hypopharynx in 60% cough patients.[11] Bronchoscopies performed in patients with GERD-associated cough, however, have failed to show any evidence of acid-related tracheobronchial injury[6] so the exact mechanism of microaspiration and cough is not known.

Physical Findings of LPR

Physical findings frequently observed in patients with LPR include diffuse laryngeal edema and erythema, thick endolaryngeal mucous, laryngeal pseudosulcus, and posterior commissure hypertrophy, commonly referred to as pachydermia. Classically, posterior laryngeal changes, such as pachydermia, have been linked to LPR, but recent studies have shown that the entire larynx can undergo significant changes when exposed to gastric contents.[12] Belafsky et al[12] recently developed a validated 8-item clinical severity rating scale for LPR based on findings during fiberoptic laryngoscopy called the reflux finding score. The scale incorporates of variety of laryngeal inflammatory findings associated with LPR, including vocal fold and infraglottic edema (pseudosulcus), erythema, and posterior commisure hypertrophy.[12]

Diagnosis of GERD-Associated Cough

A high index of suspicion for GERD as the primary etiology of chronic cough must be maintained. It has been estimated the GERD may be clinically "silent" (ie, no heartburn) in as many as 75% of patients who are referred for chronic cough. Clues in the patient's history may include concomitant LPR symptoms such as throat clearing, hoarseness (especially in the morning), and globus sensation. In addition, the patient may relate worsening of the cough with substances that are known to decrease the lower esophageal sphincter tone such as caffeine, mints, chocolate, fatty foods, cigarettes, or alcohol.[5]

The diagnosis of LPR can be made using either empiric medical therapy with proton pump inhibitors (PPIs) or by means of dual-channel 24-hour pH monitoring.[13] If a patient with chronic cough is found to have signs of posterior laryngitis, pachydermia, and/or pseudosulcus[14] on laryngoscopy, it is reasonable to assume that reflux disease can be attributed to his/her cough. In these instances, empiric therapy with PPIs (eg, Esomeprazole, AstraZeneca, Wilmington, DE, 40 mg twice a day) and reflux precautions are reasonable.[13] One should be cautioned that chronic cough because of GERD is fairly slow to respond to antireflux therapy, taking 6 months or more to resolve.[2] A great deal of patience and encouragement may be required by the treating physician.

Another approach to the diagnosis of GERD-associated cough is to test suspected patients by way of 24-hour, dual-channel pH monitoring using a distal and proximal probe. Diagnosis of classic GERD based on the distal probe data is generally straight forward. A combination of several factors, including the percentage of time the pH drops below 4 in both the supine and upright positions and the number and duration of reflux episodes, is used to generate a DeMeester score. When the DeMeester score exceeds 14.72, the patient is considered to have significant GERD. These patients are at risk for esophageal erosion and subsequent sequelae and should be further evaluated by a gastroenterologist for endoscopy or other upper gastrointestinal workup.[15]

Using the proximal probe data to diagnose LPR is much more problematic than the relatively straightforward diagnostic criteria of GERD. There is no universal agreement as to what is considered "abnormal" proximal reflux. Some consider a single reflux episode into the laryngopharynx during a 24-hour period as abnormal; others require that reflux at the laryngopharynx occur $>1\%$ of the time during a 24-study period to be considered pathologic. There is also no standardized position for the proximal probe in relation to the upper esophageal sphincter (UES). Some place the probe above the UES in the pharynx, and others place the

probe at the UES or 1 to 4 cm below.[16] Until there is standardization of these factors, the diagnosis of LPR will continue to be controversial.

Problems also arise with "negative" test results because the sensitivity of dual-channel pH probes for picking up LPR has been reported to be as low as 75% to 80%. In other words, a negative pH probe does not necessarily rule out LPR. The reason for this phenomenon appears to be because of the intermittent nature of LPR. Richter and Hicks[17] have shown how the intermittent nature of LPR can cause problems with the reproducibility of pH studies. A small series of patients with LPR and positive pH probes underwent retesting with a repeat dual-channel pH probe, and only 55% had abnormal proximal reflux (LPR) on retesting.[17]

Although this method is scientifically more rigorous than empiric therapy, pH probe monitoring is not foolproof. In cases in which evidence of LPR is absent on laryngoscopy (lack of posterior laryngitis or pseudosulcus), pH probe testing should be strongly considered. GERD-associated cough can occur exclusively via distal esophageal acid exposure, as previously stated; therefore, LPR-associated laryngeal signs may be absent. If it is determined that pH probe testing is necessary, the referring physician should ensure that the person administering the test instructs the patient to log in all episodes of cough during the test period so that cough and reflux events can be correlated. Evidence of pathologic reflux disease by either the distal or proximal pH probe data warrants treatment of the patient with PPIs and reflux precautions as outlined previously. Caution must be observed in interpreting pH probe data. A "negative" study for reflux disease should be examined carefully to see if there is a correlation between reflux events and the patient's cough. If a strong correlation exists between reflux events and the onset of cough, this may be considered pathological reflux disease, even if all other parameters indicate an otherwise "negative" test.[2,6]

Medical Treatment of GERD-Associated Cough

Medical treatment for chronic cough because of GERD should consist of PPI administration until symptoms resolve or are under control and should continue for an additional 3 months thereafter.[18] This regimen requires patience and patient reassurance because it takes an average of 5.5 months for the cough to disappear.[19] After completing the described treatment course, the medications may be gradually discontinued. Because GERD is a chronic intermittent disease, cough may return if treatment is stopped so episodic or long-term therapy may be indicated.

PPIs work by blocking the terminal step in acid secretion through the inhibition of H+, K+ adenosine triphosphatase enzyme of the gastric parietal cell. This results in potent suppression of gastric acid secretion but rarely causes complete achlorhydria. PPIs have been deemed safe to use by a Food and Drug Administration Gastrointestinal Drugs Advisory Committee[20] and appear to have no ill effects for up to 8 years of continuous use. In terms of the appropriate dosage of PPIs, there is almost universal agreement that twice-a-day dosing in necessary for extraesophageal reflux disease. Taking the PPI 30 to 60 minutes before meals (ie, before breakfast and dinner) is an extremely important point to emphasize to the patient because this significantly improves efficacy. The possibility of patient noncompliance is an important consideration in the case of a "therapeutic failure"; studies have shown that only half of patients treated for LPR take their medications as prescribed.[21]

It is not unusual for patients with GERD-associated cough to require more aggressive medical therapy with antireflux medications. Doubling the dose of PPIs (eg, Esomeprazole 80 mg twice a day) and the addition of a nighttime H2-blocker (ranitidine 300 mg) to cover for suspected nocturnal acid breakthrough may be necessary. Nocturnal acid breakthrough is related to a high nocturnal histamine concentration in subjects taking PPIs and seems to be respond better to H2 blockers than PPIs.[22]

Surgical Treatment of GERD-Associated Cough

Surgical treatment also plays a role in the treatment of patients with GERD-associated cough who either fail medical therapy or who require lifetime medical treatment to control their cough. A number of recent studies show that antireflux surgery (typically laparoscopic Nissen fundoplication) controls classic GERD symptoms (heartburn) in most cases, but atypical symptoms (cough, hoarseness) do not seem to respond as well. There is no identifying criterion that distinguishes which patients with reflux-related cough will respond to surgical treatment, but showing a temporal correlation between cough and reflux events seems to be important. This correlation can be shown by carefully reviewing the pH probe tracing, as previously described. In patients with strong temporal correlation between cough and reflux events, the success of Nissen fundoplication surgery can be greater than 80%. On the other hand, patients with poor esophageal body motility tend to have a higher complication rate (dysphagia) and lower success rate after fundoplication and may not be good surgical candidates.[23] Some investigators have suggested that patients who fail medical therapy for their extraesophageal reflux disease are poor surgical candidates,[21] but others believe that surgical success can be achieved in these patients if they are carefully selected.[23]

Cough-Variant Asthma: Diagnosis and Treatment

Asthma is a respiratory disease that involves variable airflow obstruction because of inflammatory factors. The principle symptoms of asthma are shortness of breath and wheezing as a general rule, but in patients with cough-variant asthma (CVA), these cardinal signs of asthma are often absent. Most clinical criteria for establishing a diag-

nosis of asthma use (at least in part) spirometry (PFT) data. Criteria include either (1) a decrease in forced expiratory volume in 1 second from baseline of at least 20% after inhalation of methacholine or (2) an increase in forced expiratory volume in 1 second of at least 15% above baseline after inhalation of a bronchodilator (albuterol). However, these strict PFT criteria may exclude some patients with CVA who may not have demonstrable airflow obstruction on spirometry.[2] Some investigators use a trial of an inhaled corticosteroid (ie, pulmicort, AstraZeneca, Willmington, DE) for 4 to 8 weeks to empirically treat CVA in the absence of confirmatory spirometry data. They note that there is often a delayed response in the resolution of CVA, which may take several months.[2] Recent studies have also shown that leukotriene inhibitors such as zafirlukast (Accolate, AstraZeneca, Wilmington, DE) can be effective in patients with CVA.[24] Further complicating this diagnosis of CVA is the emergence of a previously unrecognized etiology of chronic cough, referred to as "eosinophilic bronchitis," which is characterized by airway eosinophilia without bronchial hyperresponsiveness. This condition shares similarities to CVA because both show eosinophilic sputum and improvement with inhaled corticosteroids. Obviously, the diagnosis of CVA is the purview of the treating pulmonologist, but otolaryngologists should be aware of the differing viewpoints in the diagnosis and treatment of this condition.[2]

PND (Rhinosinusits and Allergic Rhinitis)

Unlike GERD and CVA, the association of chronic cough with upper-airway disease (allergic rhinitis/sinusitis) is imprecise and based more on empiric observations than actual scientific evidence. Many series published in the US literature on chronic cough report that PND syndrome is one of the most common causes of chronic cough. However, this term tends to be a "wastebasket" symptom complex that lacks objective findings and can be linked to multiple, disparate disease processes including reflux disease, allergic rhinitis, and chronic sinusitis. Interestingly, PND may be a uniquely American invention; a large telephone survey of cold symptomatology found that over 50% of subjects contacted in the United States associated a cold with PND, whereas virtually no respondents from India or Latin America admitted to the symptom.[2]

PND as a "cause" of cough has been advanced by clinicians who have observed that combinations of antihistamines and decongestants are often effective in the management of patients with chronic cough. Irwin[19] points out that the older sedating antihistamines such as brompheniramine maleate and azatadine maleate tend to be more effective than the newer nonsedating antihistamines, perhaps because of these greater anticholinergic properties. Most of these patients diagnosed with PND probably had clinical allergic rhinitis or sinusitis, although it is not clear from the study protocol. More importantly, the response to antihistamines in PND patients may just represent a generalized reduction in lower-respiratory inflammation because H1 antagonists have been successfully used to treat "atopic cough." In fact, Grossman[25] has introduced the concept of "one airway, one disease," in which the upper and lower airways are viewed as a continuum of inflammation involving 1 airway that may have a common origin for the underlying pathological disease.

Another disease process that may cause PND-associated cough is sinusitis. Holinger and Sanders[3] have shown that sinusitis is the second most common diagnosis in children with chronic cough between the ages of 6 and 16. The actual contribution of chronic sinusitis to adult chronic cough is unknown, but clinical practice supports that it plays a role in some cases. A CT scan of the paranasal sinuses is the best test to show the presence of disease.

ACE Inhibitor–Induced Cough

The association of a dry nonproductive cough in patients taking ACE inhibitors is well established. It is commonly reported that up to one third of patients on ACE inhibitors can develop cough; the actual incidence is probably closer to 10%.[26] ACE inhibitor–induced cough can occur within a few weeks of starting therapy, but it is not unusual for the cough to develop after several months or even years of treatment. For that reason, one should always discontinue the ACE inhibitor in the event of cough no matter how long the patient has been taking the medication. If the cough is caused by the agent, symptoms should resolve or markedly improve within 4 weeks. Replacement with another ACE inhibitor should not be attempted because the cough will recur in almost all cases. Angiotensin II Inhibitors (losartan potassium) are a good alternative because cough does not seem to be a significant side effect with this class of antihypertensives.[19] In situations in which the patient's medical condition is such that ACE inhibitors cannot be discontinued (such as severe congestive heart failure), adjuvant treatments for patients cough can be used. Recent studies have shown that cromolyn sodium (Nasalcrom, Roxane, Columbus, OH) and hydrochlorothiazide can ameliorate ACE inhibitor–induced cough.[26]

Bordetella Pertussis (Whooping Cough)

The reemergence of pertussis (whooping cough) over the past decade has placed this disease back in the differential diagnosis of adult chronic cough. Children in the United States are for the most part protected by immunization; however, their immunity appears to wane after 12 years. The number of recognized cases in the United States has grown over the past 25 years, and in 2001 the Centers for Disease Control and Prevention reported over 8,000 cases. Pertussis begins as a nonspecific upper-respiratory infection with rhinorrhea, throat irritation, PND, and throat clearing. These symptoms typically last 2 weeks. After these symptoms fade, severe fits of coughing occur, often culminating in the whooping inspiratory noise that gives the disease its popular name. These paroxysms of cough are frequently severe enough that the patient may drop to his/her knees and

occasionally vomit. The coughing spells typically last 2 to 4 weeks but may persist for months in some cases. In patients with an unusually persistent cough after pertussis infection, the culprit may in fact be unchecked reflux disease. It appears that severe cough can, in some cases, lead to vagal reflex mechanisms and pressure/mechanical factors that promote the development of reflux disease.[19]

The diagnosis of pertussis is somewhat problematic because of the difficulty of culturing the organism, *Bordetella pertussis*. In the early disease stage, a direct test with culture or polymerase chain reaction from a nasopharyngeal swab specimen should be used. In later stages of the disease (when the patient is most likely to seek treatment), serology for pertussis toxin is the best choice. A single serum value of pertussis toxin >2 standard deviations above healthy controls is considered diagnostic.[27]

The key to managing pertussis is to prevent its spread to others. Prophylaxis with a macrolide antibiotic (or trimethoprim-sulfamethoxazole, if allergic) should be given to household contacts. This is especially true for unvaccinated infants because pertussis in small infants may be very severe. The use of antibiotics does not seem to change the natural course of the disease once the characteristic cough has developed, however. Codeine can be helpful in the symptomatic treatment of these patients.[19]

Neurologic

Postviral vagal neuropathy is a potential cause of chronic cough when other possibilities have been ruled out. Recent evidence supports the concept that some patients may have sustained vagal injury as a result of a viral infection. Many of these patients will have an antecedent upper-respiratory infection before the onset of cough. As a result, they may develop airway hyperresponsiveness that persists long after the resolution of the upper-respiratory infection. The hypersensitivity may be caused by a decrease in the cough threshold in response to irritative stimuli. These patients may be more susceptible to chemical or mechanical stimulation (ie, reflux, perfumes, chemical odors). The principles of treatment for this condition involve treating or avoiding any irritative stimuli such as allergies or reflux disease. Antitussive medication such as dextromethorphan or codeine may be beneficial. For recalcitrant cases, tramadol appears to be an effective medication.[28]

Sensory neuropathy because of surgical trauma or viral illness can lead to sudden-onset cough, laryngospasm, and/or throat clearing. The neuropathy can be confirmed using laryngeal electromyography as shown in 20 of 28 patients in a recent series reported by Lee and Woo.[29] Effective symptomatic relief of cough can be achieved in the majority of these patients using gabapentin at 100 to 900 mg/d in divided doses.

Chronic Aspiration

Cough that is associated with meals should trigger the physician to consider chronic aspiration as an etiology. Because of the associated risk of developing aspiration pneumonia (particularly in the elderly and otherwise infirm population), any indication of aspiration-associated cough should be investigated further.

The workup of aspiration can include either MBS or FEESST. MBS is usually performed and interpreted by a speech pathologist in conjunction with a radiologist. The test involves feeding radio-opaque boluses of varying food or liquid consistencies to patients while observing the bolus movement via x-ray. Entry of food or liquid below the glottic level indicates aspiration.

FEESST is typically performed and interpreted by an otolaryngologist, often in combination with a speech pathologist. The test uses a specially designed endoscope that is passed transnasally. After proper placement of the endoscope, sensory testing is performed by delivering a calibrated pulse of air to the laryngeal mucosa. Sensory threshold levels are determined by watching for the laryngeal adductor response, which indicates the pulse was sensed. After determining the sensory threshold bilaterally, food and liquid boluses are fed to the subject, and the progress of the boluses is observed via the endoscope. Similar to MBS, different consistencies of food and liquid are used.

Both these testing methods can effectively diagnose aspiration. More importantly, the use of either of these tests in combination with dietary adjustments based on the results has shown the ability to reduce the number of aspiration pneumonias over a period of a year.

There are some important differences between these tests, however. FEESST provides better visualization of the anatomy of the larynx and pharynx. It is also likely more sensitive to trace aspiration.[30] FEESST also provides sensory information, which may be important when evaluating stroke patients.

MBS provides information regarding the upper esophageal sphincter and esophagus, areas in which FEESST does not visualize. This may be particularly helpful when evaluating conditions such as Zenker's diverticulum and tracheoesophageal fistula, which may also present with chronic cough.

Treatment of chronic cough caused by aspiration usually starts with dietary adjustments. Modifications in the diet are guided by findings on MBS or FEESST. Additional swallowing therapy under the guidance of a speech and language pathologist is often prescribed to improve or strengthen the swallow reflex as well. Finally, selected surgical procedures (eg, injection augmentation of the vocal fold(s) and medialization laryngoplasty) may be recommended in certain instances.

Additional Pulmonary Conditions

Various pulmonary and cardiac conditions can also be responsible for chronic cough and are listed in Table 2. Of these, chronic bronchitis is fairly common.[31] Typically, chronic bronchitis occurs in response to chronic smoking.[32] The pathophysiology of chonic bronchitis involves the loss of ciliated cells and an increase of goblet cells in the epi-

thelium. Cough usually appears in the second or third decade after initiating smoking and progressively worsens over time. Initial treatment involves smoking cessation, which may or may not improve symptoms immediately. Antibiotics have proven useful for acute exacerbations.[31]

Eosinic bronchitis is an inflammatory condition that affects the lungs and may be responsible for many cases of chronic cough, which otherwise elude proper diagnosis. The hallmark of this condition is the presence of sputum eosinophilia on spontaneous or induced sputum samples.[33] Patients typically present with chronic cough that does not respond to therapy for postnasal drip or LPR and typically have a negative methacholine challenge test. Patients with EB typically respond well to inhaled corticosteroids but may occasionally need systemic steroids.[34]

Sarcoidosis is a multisystem disorder of unknown etiology that affects the lungs in 90% of individuals.[35] In these individuals, one of the most common symptoms is chronic cough.[36,37] Sarcoidosis is often detected on chest x-ray but is usually confirmed by a finding of noncaseating granulomas on pathology. Systemic corticosteroids are the primarily treatment modality, but methotrexate and other cytotoxic agents have been used with some success as well.[35]

Bronchogenic carcinoma can often present initially with chronic cough. It is particularly important in smokers to screen for this disease because it is highly lethal, accounting for almost 28% of all cancer deaths.[38] Unfortunately, by the time initial diagnosis is made, many patients have widespread disease, and prognosis is extremely poor. A high index of suspicion can lead to earlier detection and possibly improve outcome.

The previously mentioned conditions, although not as common as LPR, cough-variant asthma, and PND in causing chronic cough, should be ruled out in all but the most obvious cases. A simple chest x-ray is often enough to diagnose such conditions as sarcoidosis and should be done routinely in these patients to screen for bronchogenic carcinoma.

Psychogenic Cough

The majority of psychogenic cough cases occur in children and adolescent patients; however, adult patients can develop nonorganic cough as well. It goes without saying that psychogenic cough is a diagnosis of exclusion. All of the previously mentioned etiologies must be exhaustively evaluated and treated before coming to the conclusion that the patient's cough is nonorganic. There is a well-known epidemiological association between chronic cough and anxiety[39]; however, it is unclear whether psychological distress is a cause or an effect of the chronic cough.

In cases in which psychogenic cough is suspected, a variety of interventions should be explored including psychotherapy, relaxation technique, breathing exercises, and speech therapy. Often, a combination of psychiatric treatment and referral to an experienced speech and language pathologist is required.[40,41]

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