

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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Chronic Cough and Gastroesophageal Reflux Disease



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G&H What is the most common cause of chronic cough?

DF Acute episodes of cough, often referred to as acute bronchitis, are among the most common conditions seen in medicine and are usually self-limited and related to upper respiratory tract infections. However, a distinction must be made between acute and chronic cough. The latter is significantly more complicated to treat, and its cause is often unknown. In many cases, chronic cough begins as one of several symptoms in an upper respiratory infection and persists. Patients experiencing chronic cough are often referred to pulmonologists; allergists; ear, nose, and throat doctors; and gastroenterologists, who each try to uncover the source, but a large portion of chronic cough remains unexplained, or idiopathic. There are pulmonary causes, particularly in patients who smoke or who have asthma or chronic obstructive pulmonary disease. Lately, there has been a push to try to advance gastroesophageal reflux disease (GERD) as the major cause, although the large majority of patients who are presumed to have GERD are found not to have clinical reflux on pH testing. While GERD has been shown to play a role in chronic cough, it is likely just a cofactor and not the main culprit in idiopathic chronic cough.

G&H Is there an association between chronic cough and nonacid or weakly acidic reflux?

DF There is possibly an association. It is very difficult to prove; therefore, many physicians recommend and use combined pH-impedance testing to try to determine whether nonacid reflux is involved. Presumably, any

irregular substance (eg, particulate or refluxate) that gets into the throat can act as an irritant and initiate coughing.

G&H Should treatment consist of therapies that control reflux instead of those that control acid?

DF The data on treatment are still not very clear. Reflux medication does help a subset of patients who have chronic cough; however, many patients with cough are given reflux medication empirically and do not improve, so it is hard to know if treating acid reflux that way is helpful.

My colleagues and I conducted a study evaluating definitive treatment of reflux for cough, in which patients with a primary symptom of chronic cough underwent gastric fundoplication. Abnormal preoperative impedance was not associated with postoperative improvement of cough symptoms. Instead, predictors of improvement were concomitant typical GERD symptoms of heartburn and regurgitation, and a positive capsule pH test. Patients with chronic cough combined with one or both cofactors tended to improve with the gastric fundoplication. These findings indicate that irregular impedance testing by itself is not very predictive of extraesophageal reflux and that patients who have cough without traditional GERD symptoms often do not improve with reflux medication or surgical treatment.

G&H How is GERD-related chronic cough differentiated from non-GERD-related chronic cough?

DF Differentiation, in my opinion, is more related to a thorough patient history and listening to the patient than

to any technologic device that is being used. Patients who present with classic GERD symptoms and cough tend to have GERD-related cough. Nighttime coughs or coughing after meals are signs associated with reflux-induced cough. Similarly, it is easier to point to GERD as a potential etiology when patients display a history of GERD, heartburn, or regurgitation. When patients deny having GERD, regurgitation, belching, or any other symptoms, the likelihood of them actually having acid reflux as a primary cause of their cough is small.

G&H What is the relationship between cough, GERD, and phonation?

DF This is an interesting question and one that I believe needs further attention. In my practice, patients often relate talking as a trigger for their chronic cough. The hypothesized mechanism for this is laryngeal, specifically vocal fold, hypersensitivity. To further evaluate this phenomenon, my colleagues and I conducted a blinded, cross-sectional study of 27 nonsmoking patients with chronic cough (>8 weeks refractory to maximum antireflux medication) to determine whether GERD was the cause of chronic cough. All patients underwent 24-hour acoustic recording synchronized with ambulatory pH-impedance monitoring, and cough, phonation, and pH-impedance events were recorded.

We then evaluated the temporal relationship between cough, GERD, and phonation using several statistical techniques and found that the actual trauma from coughing caused further coughs. We also found that *de novo* coughs would occur after patients spoke or experienced a minor reflux event, as defined by the pH-impedance testing. These findings are interesting because even minor reflux events were triggers for cough. More interesting, however, is that phonation or talking was a trigger for cough in a majority of the patients. Both findings implicate the larynx as a potential source for the sensitivity of the airway. The stimulation of the vocal folds by phonation and the minor irritation from GERD are both triggers for chronic cough patients.

G&H What treatment options are currently available to manage chronic cough?

DF If the cough is GERD-related, then treating the GERD with proton pump inhibitors (PPIs) is the most common approach. A 3-month empiric trial with either once- or twice-daily PPIs is generally advocated.

Pulmonary etiologies should be excluded to ensure that malignancy or intrinsic lung diseases are not the source of the cough. Evaluation for a contribution from GERD is also often performed. If these conditions are ruled out

and no other obvious cause is identified, an etiology that should be considered is laryngeal sensory neuropathy. The mechanism for this condition is upregulation of sensory nerves at the level of the larynx caused by repeated vocal fold trauma from the cough. To illustrate this further, the sound produced by the cough derives from the vocal folds striking each other. This repeated trauma results in sensitivity at the level of the vocal folds, which can be stimulated by changes in heat, talking, smells, and other usually benign physiologic tasks and exposures.

There are at least 3 treatment options available for laryngeal sensory neuropathy. The first and most conservative is improving the vocal hygiene by increasing water intake and reducing the viscosity of the upper airway mucus, which can act as a trigger. Patients also need to use sips of water to quench the foreign body–trigger sensation before the cough paroxysm starts. In essence, this breaks the cycle of cough begetting more cough. It is also helpful for these patients to use a humidifier or vaporizer to hydrate the upper and lower pulmonary tracts. Similarly, some patients assume they have postnasal drainage and are treated with drying medications such as decongestants and antihistamines, which can worsen symptoms. In fact, anything drying such as caffeine, alcohol, or even snoring at night can exacerbate the dryness of the throat and cough. Another simple consideration is avoidance of menthol cough drops, which are considered an obvious treatment for cough, but actually do not work for patients with chronic cough. Those cough suppressants contain a small amount of alcohol that create a drying effect in the throat, and the need to cough returns as soon as that drying effect disappears.

A second treatment option is pharmacologic intervention. The medications used to treat laryngeal sensory neuropathy or airway hypersensitivity syndrome are similar to those used to treat neuropathy in other parts of the body. For instance, gabapentin, amitriptyline, pregabalin (Lyrica, Pfizer), and tramadol are often used and work fairly well. The correct medication for a particular person's condition needs to be considered carefully. It is often necessary to titrate doses until an effect is achieved.

A third less commonly discussed, although effective, approach is behavioral modification that involves working with speech language pathologists who are trained in cough suppression therapy. They are able to teach various techniques for managing that tickle in the throat that makes people want to cough. Other common treatment approaches exist, but are beyond the scope of this column.

G&H What role does surgery play in managing chronic cough?

DF Surgery should be considered a last resort for treatment. Circumstances in which surgery is helpful in

chronic cough are rare. The most discussed treatment for presumed GERD-related chronic cough that has been refractory to pharmacologic intervention is gastric fundoplication. I do not recommend this surgery to my patients, even in extreme cases, unless I am absolutely convinced that GERD is the culprit, which is difficult to prove. Patients whose cough readily responds to PPIs with objective evidence of GERD on pH-impedance testing could be considered candidates. Without objective evidence of GERD and/or concomitant symptoms of heartburn or regurgitation, the likelihood of a durable improvement from surgery is relatively small. I would argue that in the majority of cases, GERD is not the cause of chronic cough.

G&H Which diagnostic tests or cough monitoring systems are used to assess cough?

DF It must be emphasized that the most important diagnostic test is a careful patient history. Triggers for a patient's cough can be illuminating and can help direct diagnostic and treatment decisions. Clinicians must also recognize whether patients have pneumonia, asthma, or chronic obstructive pulmonary disease that could be causing the cough. Patients should undergo pulmonary function tests and further pulmonary evaluation as needed. All patients with refractory chronic cough should undergo flexible laryngoscopy to confirm that there are no lesions in their upper airway (eg, pharynx, larynx) that could be triggering their cough. If GERD is a suspected source, patients can either be placed on a PPI for 3 months or undergo an upper endoscopy with pH-impedance testing and considerations made for esophageal manometry.

In general, cough monitoring systems are usually not used in clinical practice. They are, however, extremely useful in the research realm because they provide objectivity and a good measure for improvement. These systems do have some limitations, though, including the issue of temporality. Some devices do not record every sound, and it can be challenging to digitally differentiate a throat clear from a cough or phonation. In the absence of this technology, this differentiation is often performed manually, which is time-consuming and tedious.

G&H What are the next steps of research in this area?

DF One of the most important steps is to use interdisciplinary partnerships to share new approaches to management, develop new hypotheses regarding mechanisms, and cross-pollinate across specialties. Sharing of ideas and opening a dialogue will advance research at a faster rate. Chronic cough is a condition that affects so many patients and is cared for by so many specialties that it is incumbent on clinicians to entertain and investigate new ideas regarding etiology and management.

There have been several long-term studies to examine the efficacy of acoustic cough monitoring devices; however, we need more studies evaluating other etiologies besides GERD. Most cough monitoring devices enumerate the number of coughs, but to investigate the cause of the cough, these devices need to have the ability to synchronize with objective diagnostic tests, such as impedance and pH testing, in order to examine the temporality of other physiologic aspects.

Dr Francis has no relevant conflicts of interest to disclose.

Suggested Reading

- Francis DO, Goutte M, Slaughter JC, et al. Traditional reflux parameters and not impedance monitoring predict outcome after fundoplication in extraesophageal reflux. *Laryngoscope*. 2011;121(9):1902-1909.
- Francis DO, Rymer JA, Slaughter JC, et al. High economic burden of caring for patients with suspected extraesophageal reflux. *Am J Gastroenterol*. 2013;108(6):905-911.
- Francis DO, Slaughter JC, Ates F, et al. Airway hypersensitivity, reflux, and phonation contribute to chronic cough [published ahead of print October 19, 2015]. *Clin Gastroenterol Hepatol*. doi:10.1016/j.cgh.2015.10.009.
- Gibson P, Wang G, McGarvey L, Vertigan AE, Altman KW, Birring SS. Treatment of unexplained chronic cough: CHEST Guideline and Expert Panel Report [published ahead of print October 1, 2015]. *Chest*. doi:10.1378/chest.15-1496.
- Lv HJ, Qiu ZM. Refractory chronic cough due to gastroesophageal reflux: definition, mechanism and management. *World J Methodol*. 2015;5(3):149-156.
- Pavić I, Čepin-Bogović J, Hojsak I. The relationship between gastroesophageal reflux and chronic unexplained cough in children [published ahead of print August 30, 2015]. *Clin Pediatr (Phila)*. doi:10.1177/0009922815603675.
- Sylvester DC, Karkos PD, Vaughan C, et al. Chronic cough, reflux, postnasal drip syndrome, and the otolaryngologist. *Int J Otolaryngol*. 2012;2012:564852.
- Xiao Y, Carlson D, Boris L, et al. The acoustic cough monitoring and manometric profile of cough and throat clearing. *Dis Esophagus*. 2014;27(1):5-12.