

# ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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## Pulmonary Disease and Reflux

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**G&H** Could you describe the pathophysiologic link between the esophagus and the pulmonary system and how it relates esophageal acid to asthma?

**SH** The pathophysiologic link between the esophagus and the lungs begins during organogenesis. The lungs develop as an outpocketing of the esophagus and are linked through autonomic innervation with the vagus nerve.

There are several basic pathophysiologic mechanisms by which esophageal acid exposure could affect asthma. First is a vagally mediated reflex between the esophagus and the lung. Another possible mechanism involves an axonal reflex, where the vagus nerve and central nervous system components are bypassed altogether. There is a direct neural connection between the esophagus and the lung, in which nitric oxide-containing neurons are activated, as shown in a guinea pig model. There is also a mechanism where the lung is primed with esophageal acid, which, when the asthmatic patient is exposed to another trigger like cat dander, causes an exaggerated response. This is commonly known as airway hyperreactivity. Finally, there is the possibility of microaspiration, in which tiny amounts of esophageal acid get into the upper airway, possibly the larynx and/or bronchi, causing significant respiratory responses. All of these pathophysiologic mechanisms result in neuroinflammation, leading to bronchoconstriction.

**G&H** How do these links manifest with esophageal exposure to acid?

**SH** Pathophysiologic experiments in animal models and in humans, where acid is instilled into the esophagus, show that acid causes respiratory responses, including increases

in airway resistance and decreases in peak expiratory flow rates—markers of bronchoconstriction. The vagus nerve and microaspiration are often both active.

In addition, asthma patients report that their respiratory symptoms are temporally associated with their reflux symptoms. When esophageal pH is monitored and acid is present in the distal esophagus, patients often experience wheezing, shortness of breath, or cough. All of these findings support the hypothesis that the esophagus and lung interact.

**G&H** Does this link have an effect on patients with asthma and reflux?

**SH** Yes. Asthma is an inflammatory disease. Therefore, to directly link asthma and esophageal reflux there needs to be evidence of inflammation. Currently, the best evidence of this link has been found in a guinea pig model, where esophageal acid causes the release of neuroinflammatory mediators, including tachykinins and substance P, in the lung.

**G&H** Is there evidence of similar links in other pulmonary diseases?

**SH** Yes. Reflux is the second most common cause of chronic cough, and the vagus nerve has an active role in this pathophysiologic mechanism as well. Reflux therapy improves or eliminates cough in these patients. The impact of reflux on other pulmonary diseases is not as well studied. For instance, patients with chronic obstructive pulmonary disease (COPD) or interstitial lung disease have an increased reflux prevalence compared to normal controls. Whether reflux plays a pathophysiologic role in other lung diseases is yet to be determined.

**G&H** Should asthma patients with increased esophageal acid exposure be treated for reflux?

**SH** Yes. These patients should be treated with at least a short-term 3-month empiric trial of acid suppressive therapy. Asthma is a heterogeneous disease with hundreds of triggers. Gastroesophageal reflux (GER) is just one of them. If a patient has reflux symptoms, it is important to determine whether treatment of their reflux improves

their asthma. In my experience, reflux therapy helps in selected asthmatic patients but not in all.

Just as one asthmatic patient may have an asthmatic reaction to cat dander whereas another does not, the same holds true for acid reflux. A significant number of asthmatics have reflux but whether reflux is a trigger of their asthma is very difficult to assess. There is no specific diagnostic test available at this time that identifies those asthmatics with GER-triggered asthma whose asthma improves with antireflux therapy. Currently, the best way to identify these patients is to do an empiric trial of medical reflux therapy and see if their asthma improves. Approximately 70% of all asthmatics have reflux symptoms. These patients should begin a 3-month empiric trial of proton-pump inhibitor (PPI) therapy, preferably twice daily, to fully control acid. Asthmatics who should be targeted for empiric PPI therapy include those with steroid-dependent asthma, regurgitation, severe asthma, nighttime asthma symptoms, and those requiring long-acting inhaled beta-agonists and/or more than one controller medicine for their asthma.

#### **G&H** How can GER be identified as a possible asthma trigger in patients with no active reflux symptoms?

**SH** One method is the use of esophageal pH testing; however, this is not always practical. To complicate the diagnostic picture even more, recent studies utilizing esophageal pH testing show that approximately 65% of asthmatics with documented GER have no GER symptoms—thus their reflux is clinically “silent.” Again, I would potentially begin an empiric trial on asthmatics who have the characteristics outlined above.

#### **G&H** Should a patient with suspected GER-triggered asthma be referred to a gastroenterologist for treatment?

**SH** It is unrealistic for gastroenterologists to see every GER-triggered asthma patient in the clinical setting. These patients for the most part present to their internal medicine doctors, their primary care practitioners, pulmonologists, and allergists. These physicians may refer the patient to a gastroenterologist.

Patients who fail an empiric PPI trial are more likely to be referred to a gastroenterologist. The question at this point is whether to perform an esophageal pH test while the patient is on medical therapy (ie, to see if acid is controlled) or to take them off reflux therapy for at least a week, then test to see if they have actual reflux at all. My recommendation would be to study the patient while on PPI therapy to be sure adequate acid control has been

achieved. Although this does not rule out nonacid reflux, proof of acid control would show that the acid is not playing a significant role in their difficult-to-control asthma.

If, at this point, pH testing reveals that the acid is not controlled, and their reflux persists despite high-dose PPI therapy with lifestyle/diet modifications, then the patient should be referred for gastroenterologic care as they may have severe reflux or complicated GER.

#### **G&H** What role do you see for the gastroenterologist in the care of these patients?

**SH** The role of the gastroenterologist is to help other physicians decide whether reflux is present and, if so, to determine whether it is adequately treated. Patients who present with significant long-term reflux symptoms where there is concern regarding Barrett esophagus or other complications of GER should also be referred. Asthmatics considering fundoplication should also be referred to a gastroenterologist. These patients need a careful examination, including esophageal motility testing, to help decide whether surgery is really a good option.

#### **G&H** When is fundoplication considered the best option in asthma patients?

**SH** The best candidates for fundoplication are asthmatic patients who have asthma improvement with reflux therapy, who desire fundoplication. I would be reluctant to send medical nonresponders to surgery. With that caveat, there are isolated case reports of patients who continue to have chronic persistent cough related to reflux, despite medical control of their esophageal acid exposure. Fundoplication improved their cough. In a smaller subset of subjects, esophageal impedance has been used to check for nonacid reflux, which is present in some of these patients before surgery. All patients contemplating fundoplication should also be evaluated by a gastroenterologist to determine whether they are good surgical candidates.

#### **Suggested Reading**

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