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## CLINICAL VIGNETTE

# Wheezing Secondary to Gastroesophageal Reflux Disease (GERD)

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### Introduction

Gastroesophageal Reflux Disease (GERD) is reflux of gastric contents into the esophagus due to relaxation of the lower esophageal sphincter, resulting in bothersome symptoms and or complications, typically pyrosis (heartburn), regurgitation, and dysphagia. However, there are also many extra-esophageal manifestations of GERD including pulmonary, cardiac, and ear, nose, and throat disorders, which can present without the typical symptoms. These include chest discomfort, abdominal pain, postnasal drip, coughing, wheezing, bronchitis, and pneumonia.<sup>1</sup> GERD is common reason for a visit to a primary care physician's office. Thus it is important to recognize extra-esophageal manifestations of GERD. The following is an account of a pulmonary manifestation of GERD: wheezing.

### Case Report

The patient is a 40-year-old obese, Hispanic female with history of pre-diabetes who presented to establish care. She described a "crackling" sound in her throat since 2005 after an episode of bronchitis. She only noticed it when lying down on her right side. She also felt a lump in her throat, intermittently over a period of several years that resolves when sitting up. She denied any other symptoms and has no history of asthma, allergies, or tobacco use. She saw a Pulmonologist at which time a chest x-ray and spirometry were normal and thus was referred to an Otolaryngologist (ENT). Prior to her appointment with ENT, she established care with me and complained of upper respiratory tract infection (URTI) symptoms. At that time, expiratory wheezing was appreciated only in the right upper lung field, which is where she normally heard the crackling sounds. The diagnosis was unclear but thought to be possibly secondary to postnasal drip syndrome, reactive airway disease, acute bronchitis, or new onset asthma. She was started on an albuterol inhaler and referred for a formal Pulmonary Function Test (PFT). Shortly after, she saw ENT and was found to have symmetric hypertrophy of bilateral lingual tonsils and moderate to severe chronic GERD on laryngoscopy. She was already taking omeprazole as needed (which had not been shared previously); ENT recommended daily omeprazole, along with follow up in 2 months. At her follow up with me, she stated that after 2 weeks of daily PPI use, the crackling sensation resolved, and she reduced the dose to only once per week with food. The albuterol inhaler did not help with the wheezing. PFTs showed

mild decrease in diffusion capacity, mild restrictive defect, and no airflow obstruction. Given she was asymptomatic, no further treatment was recommended and did not follow up with ENT. Patient has since been lost to follow up.

### Discussion

GERD affects one-third of the population monthly with ten percent complaining of daily or weekly symptoms. GERD is due to the inappropriate relaxation of the lower esophageal sphincter (LES), resulting in gastric contents refluxing upward and damaging the esophagus. The exact etiology of GERD is unclear, but multiple factors can lead to LES relaxation including: alcohol, tobacco, obesity, poor posture, certain medications (e.g., calcium channel blockers, theophyllines, nitrates, antihistamines, etc.), certain foods or beverages (fatty or fried foods, chocolate, garlic, onion, caffeine, mint, and anything acidic or spicy), large meals before bedtime, hiatal hernias, diabetes, pregnancy, and rapid weight gain.<sup>1</sup>

As noted previously, the most common symptoms are heartburn, regurgitation, and dysphagia. However, extra-esophageal manifestations exist, and for this case, will focus particularly on pulmonary symptoms, specifically GERD-related asthma. GERD triggers pulmonary symptoms and those with pulmonary symptoms are more likely to have GERD, although results may vary given differences in the definition of GERD and differences in objective measures of reflux.<sup>1,2,3</sup> The most common of the pulmonary diseases are chronic cough ("reflux cough syndrome") and bronchial asthma ("reflux asthma syndrome").<sup>1</sup> Approximately 10 to 40 percent of chronic cough can be caused by GERD, especially if experiencing nocturnal reflux.<sup>1</sup> Approximately 30 to 80 percent of asthmatics have GERD, and approximately twenty percent have intermittent bronchospasms.<sup>1,2</sup> Other pulmonary conditions include chronic bronchitis, bronchiectasis, pulmonary aspiration, interstitial pulmonary fibrosis (IPF), chronic obstructive pulmonary disease (COPD), and obstructive sleep apnea (OSA). Thus identifying those with GERD as a trigger is important.<sup>1,2</sup>

The pathophysiological link between GERD and asthma is not clear, but there are multiple theories (Figure 1).<sup>1</sup>

The esophageal and bronchial tree embryonically originated from the foregut.<sup>2</sup> Asthmatics may develop reflux secondary to three proposed theories. Firstly, pulmonary hyperinflation causes diaphragmatic dysfunction. Secondly, bronchoconstriction increases negative pleural pressure, affecting the pressure gradient between the thorax and abdominal cavity, or it may be that bronchoconstriction is a normal response to acid exposure, but asthmatics recover more slowly.<sup>1,2</sup> Lastly, bronchodilators may decrease LES pressure, aggravating reflux.<sup>1</sup>

On the other hand, GERD may trigger asthma via acid stimulation of the vagus nerve resulting in bronchial hyperresponsiveness, supported by the high rate of hiatal hernias in idiopathic pulmonary fibrosis (IPF), severe asthma, and the fact that GER is present in 63% of children with chronic asthma and recurrent pneumonias. Other mechanisms include irritation of sensitive airways and micro aspiration of gastric contents.<sup>1,2,4</sup> Both are interrelated given nociceptors in the airways and esophagus react similarly, resulting in asthma-like symptoms in GERD patients. Also, an acidic pH occurs with bronchoconstriction during GERD in asthmatic patients.<sup>1</sup>

GERD-related asthma should be considered in the differential diagnosis when a patient presents with a nocturnal cough, asthma that is exacerbated by large meals or alcohol, or asthma symptoms worse in the supine position. It should also be considered with adult onset of asthma, which is non-responsive to bronchodilators and steroids, or is associated with reflux prior to an asthma attack.<sup>1</sup>

Diagnosis and Treatment of GERD-related conditions are seen in Figure 2.

pH monitoring is the gold standard as it can correlate episodes of reflux with pulmonary symptoms. Sensitivity may increase with impedance monitoring; however, GERD and respiratory symptoms can coexist casually; thus it is most useful if the onset of respiratory symptoms coincides with an episode of reflux.<sup>1,2</sup> However, if the results are normal and there is still high suspicion, further evaluation by barium esophography, endoscopy, gastroesophageal scintigraphy, H pylori testing, and manometry can be considered.<sup>1</sup> However, the utility of barium esophography depends on the age and severity.<sup>2</sup> Endoscopy is not necessary if there are asthma and GERD symptoms but no alarm signs, such as dysphagia, odynophagia, weight loss, and anemia. Some experts state that an endoscopy should be performed if on long-term PPIs, especially if over the age of 50 and with greater than 10 years of symptoms, to screen for Barrett's esophagus.<sup>5</sup> Manometry has shown that the number of respiratory symptoms correlated well with prevalence of a motility abnormality, and the best surgical results occurred in those with normal motility.<sup>2</sup> However if all studies except for pH monitoring are normal, manometry is not recommended given low sensitivity and specificity.<sup>5</sup>

Treatment begins with lifestyle changes, followed by medication if no improvement in symptoms.<sup>1</sup> Medical therapy may improve symptoms but not necessarily pulmonary function.<sup>2</sup> Early studies show that if a patient has asthma but no GERD symptoms, a PPI may result in improvement of asthma symptoms. However, later controlled studies refute this theory.<sup>4,6</sup>

If GERD symptoms are present, a three month trial of twice per day PPI is recommended and respiratory symptoms and peak expiratory flow rates should be monitored. BID dosing is widely used despite not being supported by strong evidence.<sup>1,7</sup> PPIs are more effective than H2Bs.<sup>7</sup>

If there is improvement, one can continue PPIs for life but decreased to daily dosing, if possible. If GERD symptoms, but not asthma symptoms, improve, one can continue therapy per normal GERD guidelines.<sup>1,8</sup> If the trial is unsuccessful, this may mean that a patient's asthma is not triggered by GERD or that the GERD is not well-controlled, and a 24-hour esophageal pH testing while on a PPI should be considered to evaluate if there is proper acid suppression.<sup>1,9</sup>

If asthma is difficult to control with or without nocturnal symptoms and the patient does not have GERD, consider 24-hour esophageal pH testing off of treatment to determine if there is silent GERD.<sup>1</sup>

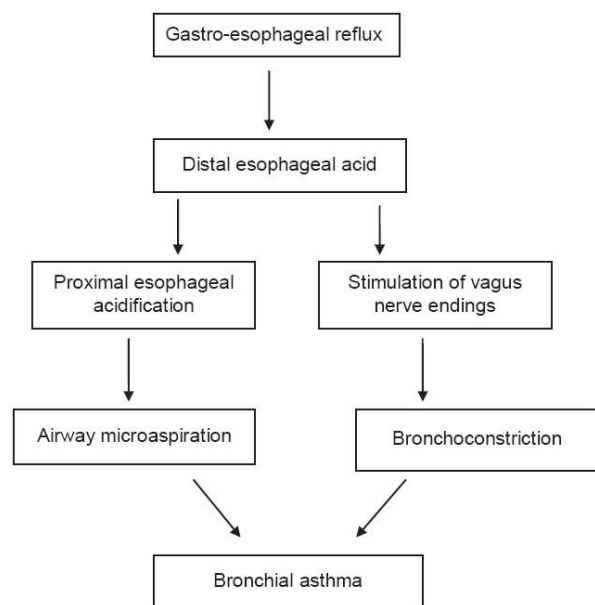
If medical therapy fails, surgery is another option. However, it mostly improves symptoms but will not improve pulmonary function. There are many flaws in the surgical studies, and 62% will still require medical treatment after surgery.<sup>1,2,9,10</sup> Overall, studies of H2B versus surgery show mixed results, but maximum PPI dosing is shown to be equivalent to surgery and can improve approximately 75% of symptoms in asthmatics with associated GERD.

## Conclusion

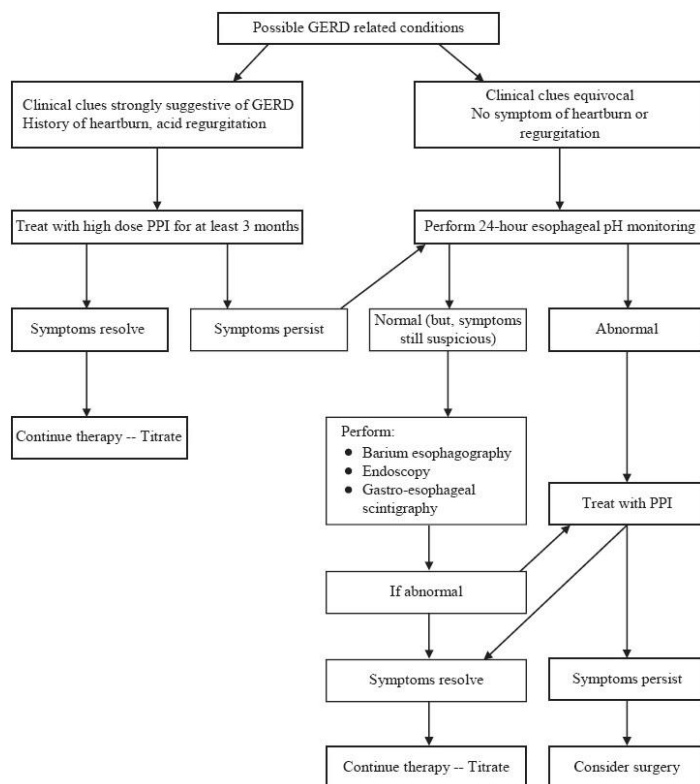
Given the high prevalence of GERD in the population and the diminished quality of life and other consequences if left untreated, it is important to recognize its extra-esophageal manifestations, especially pulmonary including wheezing, cough, bronchitis, pneumonia, pulmonary aspiration, idiopathic pulmonary fibrosis, COPD, and sleep apnea. If GERD can be treated, it is possible to prevent such complications or prevent exacerbation of underlying conditions. The link between GERD and asthma is still unclear, thus more research involving the direction of causation would be of benefit. Until this association is clearer, GERD should be in differential diagnosis when a patient presents with persistent pulmonary symptoms despite optimal medical therapy, and a trial of PPI should be considered.

## Figures

**Figure 1.** Pathophysiology of the GERD-Asthma Link.<sup>1</sup>



**Figure 2.** Algorithm for diagnosis of GERD-related conditions.<sup>1</sup>



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