

# ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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## Approach to Diagnosis of Eosinophilic Esophagitis

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### G&H Are there standardized criteria for diagnosing eosinophilic esophagitis?

**ESD** Two sets of consensus guidelines for diagnosis of eosinophilic esophagitis (EoE) have been published; the first set was published in 2007, and an updated set was published this year. The updated guidelines provide a conceptual definition of EoE as a chronic immune-mediated disorder with symptoms of esophageal dysfunction and an esophageal mucosal eosinophilic infiltrate. There is an emphasis that EoE is a clinicopathologic condition; in other words, no one specific clinical or pathologic finding can be used by itself for diagnosis.

The first step in diagnosing EoE is to characterize the patient's symptoms. In adults, these symptoms typically include dysphagia, food impaction, and, occasionally, heartburn or chest pain; less common symptoms include abdominal pain, nausea, and vomiting. When asking about dysphagia, it is also important to ask about dietary modification, food avoidance, and other adaptive eating behaviors. The symptoms of EoE in children differ from those in adults; these symptoms are more nonspecific and may include feeding difficulties, failure to thrive, abdominal pain, regurgitation, nausea, and vomiting.

The next step is to perform an endoscopy to evaluate the symptoms and obtain esophageal biopsies in order to demonstrate infiltration of eosinophils in the esophageal epithelium. Currently, at least 15 eosinophils in at least

1 high-power microscopy field are needed to consider the diagnosis of EoE, and other histopathologic findings, such as eosinophilic microabscesses or fibrosis of the lamina propria, should also be considered.

The final step is to make sure that the esophageal eosinophilia is not explained by another condition, such as gastroesophageal reflux disease (GERD), eosinophilic gastroenteritis, Crohn's disease, achalasia, connective tissue disorders, parasitic infections, hypereosinophilic syndrome, or drug hypersensitivity. There is still controversy regarding how to exclude or separate reflux from EoE. Many physicians believe that when a patient has symptoms and biopsy findings suggestive of EoE, a trial of proton pump inhibitor (PPI) therapy (twice-daily dosing for at least 8 weeks) should be administered to see if the patient improves. A formal diagnosis of EoE is typically given only if the patient has persistent symptoms and esophageal eosinophilia after the PPI trial. However, the updated guidelines recognize a subgroup of patients who may clinically appear to have EoE and not reflux but who experience a complete symptomatic and histologic response to PPI therapy. This new category has been called PPI-responsive esophageal eosinophilia. This is an active area of research and debate, as little is currently known regarding the features of these patients.

### G&H How accurate are these diagnostic criteria?

**ESD** These guidelines are primarily based on expert opinion, so it is difficult to know how accurate they are. There has not yet been a population-based study prospectively validating these guidelines.

### G&H Is establishing a diagnosis of EoE difficult?

**ESD** If the guidelines are followed, a clear diagnosis of EoE can be made in the majority of cases. For example, a young adult with prior dysphagia, who presents to the emergency room with an acute food impaction and

is found to have typical endoscopic findings, and who has more than 15 eosinophils per high-power field on esophageal biopsy after a PPI trial, clearly has EoE. However, in a proportion of patients, it is challenging to tease apart whether they have EoE or GERD, EoE and superimposed GERD, or something else. In children, establishing the diagnosis may be more difficult because the symptoms are more nonspecific.

### **G&H** Why is it important to differentiate EoE from GERD?

**ESD** Differentiating EoE from GERD is important in order to provide the correct information to the patient, to provide some information about prognosis and disease course, and to select the appropriate treatment. This does not mean that an EoE patient cannot have GERD at the same time; many patients have both conditions simultaneously. However, if treatment with topical steroids or a restrictive elimination diet is being considered, it is particularly important to ensure that the diagnosis is correct by following the diagnostic steps outlined above.

### **G&H** Should family history be considered when establishing the diagnosis of EoE?

**ESD** Increasing data suggest that EoE has a genetic component, but the disease likely requires a combination of genetic and environmental factors. There are many families in whom siblings, a parent and child, or several generations have this condition. I often ask patients about their family history, not only because a positive family history could increase their chances of having the condition, but because sometimes patients do not view symptoms to be abnormal if everyone in their family also has these symptoms.

### **G&H** How can physicians determine whether an esophageal foreign body impaction is caused by EoE?

**ESD** Several studies have examined this issue, and EoE is now felt to be the cause of esophageal foreign body impaction in over 50% of patients who present to the emergency room. When a patient undergoes an urgent or emergent endoscopy to clear an esophageal food bolus, the endoscopist should also assess the esophagus, obtain biopsies, and conduct a clinical history to determine whether EoE is a diagnostic consideration.

The difficulty in this situation is that any foreign body in the esophagus can cause nonspecific eosinophilia from local tissue injury. Therefore, biopsies should be obtained from several different locations, including areas away from the site of food impaction (after the impac-

tion is cleared). If biopsies are positive for esophageal eosinophilia, the patient should be placed on a high-dose PPI trial and then undergo a follow-up endoscopy. On follow-up examination, the endoscopist can determine whether dilation is required to treat a critical stricture or ring, and he or she can obtain biopsies (while the patient is on high-dose PPI therapy, as is currently recommended in the consensus guidelines) to reassess for esophageal eosinophilia.

### **G&H** Does allergy testing play a role in establishing the diagnosis of EoE?

**ESD** Knowing a patient's atopic history—including asthma, atopic dermatitis, seasonal allergies, allergic rhinitis, or food allergies—can be helpful because allergic diseases are increased in patients with EoE. However, allergy testing does not play a role in establishing the diagnosis of this condition. While the role of allergy testing in EoE is still fairly controversial, it can be helpful for directing treatment. For example, many children undergo allergy testing immediately after being diagnosed to see whether there are allergens that can be eliminated from their diet or environment. In adult patients, the role of the allergist is less well defined. Many gastroenterologists reserve allergy testing in adults until after the patient has been treated with a topical steroid or for cases in which the patient does not respond to standard medical treatment.

### **G&H** What endoscopic findings indicate the presence of EoE?

**ESD** Classic endoscopic findings of EoE include esophageal rings, linear furrows that track up and down the esophagus, and white plaques or exudates (which are thought to be eosinophilic microabscesses). In addition, the esophagus can have decreased vasculature, can appear pale and congested, and can have a narrow caliber. The esophagus may be so narrow that simply passing an endoscope can tear the mucosa or cause a mucosal rent, a phenomenon called crepe paper mucosa. While these signs are thought to be common, in 10–20% of cases the findings are either very subtle or the esophagus is normal. Demonstrating the presence of endoscopic signs is not currently required in the diagnostic criteria, but if such signs are present, they help to support the diagnosis.

During endoscopy, the diagnosis of EoE cannot be made unless esophageal biopsies are obtained. To increase the sensitivity of diagnosis, a total of at least 5 biopsies should be taken from several levels of the esophagus (distal, mid, and proximal). In EoE, esophageal eosinophilia can be patchy, so the diagnosis may be missed if only a few biopsies are taken from the same area.

### G&H Are new technologies such as narrow-band imaging more effective at detecting endoscopic findings associated with EoE?

**ESD** Several studies have examined the use of narrow-band imaging (NBI) in EoE. Based on clinical experience, the hypothesis was that NBI would highlight the endoscopic findings of EoE. In one study that my colleagues and I conducted, however, there was no increased diagnostic yield between white-light endoscopy and NBI. Therefore, NBI may help on a case-by-case basis, but there are currently few data supporting its widespread use.

### G&H Has cost-effectiveness been examined in the diagnostic algorithm for EoE?

**ESD** Diagnosing EoE can be cumbersome because there is no single test that patients can undergo. Typically, if a patient undergoes an endoscopy for dysphagia and there is no clear cause, it makes sense to biopsy the esophagus to evaluate for EoE. One study reported that approximately 15% of patients with dysphagia who underwent endoscopy had EoE, which is a fairly high proportion. The yield of biopsies may be quite a bit lower for patients with other symptoms (eg, noncardiac chest pain or refractory GERD), so it may not be cost-effective to obtain biopsies in these settings. A recent study examined the cost-effectiveness of obtaining biopsies in all patients with refractory GERD who present for endoscopy and found that it was cost-effective to do so only if the prevalence of EoE in that setting exceeded 8%.

### G&H What do you foresee in terms of future diagnostic strategies?

**ESD** I foresee a shift toward tissue biomarkers and, possibly, blood tests for diagnosis of EoE. Several publications have looked at different biopsy staining techniques to highlight eosinophils and demonstrate

eosinophil activation (by looking at specific eosinophil granules that are released), and other studies have quantified elevated levels of inflammatory cytokines in the esophageal mucosa. There have also been studies looking at ancillary cell types (eg, mast cells) that could help to distinguish EoE from GERD. All of these studies hold promise for streamlining the diagnostic process, although these methods still need to be prospectively validated.

Another area currently being investigated is gene transcription analysis. The set of genes transcribed in EoE has been described in pediatric patients, and there is a clear signal of upregulated and downregulated genes. Researchers are currently in the process of validating this technique as a diagnostic test.

### Suggested Reading

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