

# ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

Section Editor: Joel E. Richter, MD

---

## Eosinophilic Esophagitis

David A. Katzka, MD  
Associate Professor of Medicine  
University of Pennsylvania

**G&H** What is the typical presentation of eosinophilic esophagitis? Do children and adults present differently?

**DK** There is some overlap in the presentation of children and adults, but also major differences. In children, the most common manifestations are nausea and vomiting, as well as heartburn. In adults, the most common manifestations are long-term intermittent dysphagia to solids and sometimes heartburn.

**G&H** How is the diagnosis of eosinophilic esophagitis made?

**DK** A diagnosis is typically made on the basis of biopsy. However, there are classic demographic and endoscopic presentations that almost always indicate eosinophilic esophagitis. An adult with a history of food impaction or chronic solid food dysphagia with concurrent allergic illnesses, possibly including a history of asthma, a history of multiple food allergies, and a strong family history of food allergies, most likely has eosinophilic esophagitis. This diagnosis is even more certain when the individual is male and Caucasian, particularly those in the range of 15–40 years old. Endoscopically we see mucosal furrowing most commonly as well as esophageal rings and strictures of variable location and length and “white specks” which represent gross eosinophilic abscesses.

**G&H** Does eosinophilic esophagitis have a hereditary connection?

**DK** Yes. It is not uncommon for two or even three members of a family to have eosinophilic esophagitis. The series of patients that our group has studied includes six families in which at least two first-degree relatives had eosinophilic esophagitis. Other studies have also sup-

ported a strong family history of allergies in these patients. A study by Dr. Mark Rothenberg has suggested that there may be an autosomal dominant inheritance with variable penetrance for individuals with eosinophilic esophagitis. Patients in general have a strong personal history of multiple allergies such as asthma and atopic dermatitis in addition to eosinophilic esophagitis. This too suggests a genetic predisposition.

**G&H** Are pediatric and adult eosinophilic esophagitis usually connected?

**DK** We do not yet know if the adult form of eosinophilic esophagitis is a progression of pediatric disease. It is generally thought that most allergies are conditions that begin at birth, but we don't know if the disease that occurs in children is different from the disease that occurs in adults. Because we often see this disease as a continuum from childhood through adulthood with many similar features as regards pathology, demographics, and response to therapy, we assume they are the same. Then again, the different symptomatic and endoscopic presentations of adults and children and the inability to explain why adults do not present with symptoms until sometimes much later on in life without childhood symptoms is baffling.

**G&H** Why does this condition lead to dysphagia?

**DK** Most likely, dysphagia results from chronic inflammation. This inflammation leads to fibrosis and scarring, and subsequent ring formation or frank strictures in the esophagus. Although the inflammation can be treated, the strictures or rings of scar tissue are usually transmural (as shown by endoscopic ultrasound) and therefore not reversible, leading to persistent dysphagia. On the other hand, we know that treating the acute inflammatory response, even in the presence of persistent stricture formation, will improve the dysphagia.

**G&H** Why does the allergic reaction underlying this condition involve eosinophils?

**DK** The eosinophil is central to the allergic response. In eosinophilic esophagitis, mucosal exposure to an antigen results in increased numbers of antigen-presenting cells.

This leads to increased T cells, mast cells, interleukin-5, and tumor necrosis factor- $\alpha$ , which stimulate eotaxin to attract eosinophils.

**G&H** Are there studies ongoing to better identify the underlying cause of eosinophilic esophagitis?

**DK** Yes. Several laboratories are exploring the exact cellular response that occurs with allergies, in humans and in animal models. However, we are still a long way from knowing exactly how allergies occur and how conditions such as eosinophilic esophagitis develop as a response.

**G&H** What are the first therapeutic steps following diagnosis?

**DK** The cornerstone of therapy for eosinophilic esophagitis is identifying the allergens. All diagnosed patients undergo skin and blood testing for various food and airborne allergens. After allergy testing, the therapeutic approach differs for adults and children. Most adults are given a steroid preparation, typically fluticasone propionate, an inhaled steroid medication. For children, the most common approach is to prescribe a so-called elemental diet, composed of basic foodstuffs devoid of all allergens, with concomitant use of a nasogastric tube, which patients can generally use at home on their own.

**G&H** Why is an elemental diet not prescribed for adults?

**DK** One of the reasons why adults are generally not prescribed an elemental diet is acceptance. It is difficult for patients, many of whom are in their teenage and young adult years, to follow an elemental diet for days, weeks, months, or even years, and to use a nasogastric tube. Another reason why the elemental diet is not used more commonly is that often the underlying allergy is composed of not just one or two foods but six or more. Following a restricted diet can be difficult, if not impossible, when so many foods must be eliminated. Also, there is often not an exact correspondence between the results of allergy testing and the findings in the esophagus. Some patients with eosinophilic esophagitis may have a completely negative allergy tests. Others may avoid foods to which they have shown an allergy but still have the disease.

**G&H** What are the most common allergies that cause eosinophilic esophagitis?

**DK** The most common foods that are associated with allergic responses are milk, eggs, soy, corn, wheat, chicken, and nuts. Other common allergy foods are pork, fish, oats, turkey, apples, pineapple, and green beans. Patients

presenting with eosinophilic esophagitis would be tested for allergies to all of these foods.

**G&H** What are the different options for steroid therapy?

**DK** Steroids can be administered in either an inhaled form or in a systemic preparation, such as prednisone. Inhaled steroids avoid the side effects associated with systemic prednisone. However, systemic prednisone is associated with a higher likelihood of a longer remission. At our clinic we tend to use inhaled steroids, and this seems to be the most common approach in general.

The challenge with inhaled steroids is that the relapse rate is quite high. Although some patients do go into remission for up to a year after therapy with inhaled steroids, many do not. Upon remission, some patients may continue to receive inhaled steroids, possibly indefinitely, perhaps in combination with newer medications, such as montelukast sodium (Singulair, Merck).

**G&H** Are new agents being evaluating for the treatment of eosinophilic esophagitis?

**DK** Yes. Mepolizumab (GlaxoSmithKline) is an interleukin-5 inhibitor that blocks some of the inflammatory response mediated by eosinophils. This agent has been used in other disorders, such as eosinophilic gastroenteritis, a similar condition, and has been found to be beneficial. However, there are no data yet in eosinophilic esophagitis. Phase I trials are currently in the planning stages.

**G&H** How are patients monitored during and following treatment?

**DK** Currently, the only available method for monitoring patients is endoscopy. In most adults, the allergic reaction is silent, unlike food allergies that result in hives, for example. Patients with eosinophilic esophagitis have been having small allergic reactions for years, and at the time of their diagnosis recurrent inflammation has already led to the development of rings and scar tissue. Serial endoscopy is the only way to clearly determine the progress of these patients.

It is not known how often patients should be monitored. Some investigators monitor patients once per year, and some monitor patients every 2–3 months. On the one hand, subjecting young people to endoscopies every 8 weeks seems extreme; but on the other hand, if monitoring less frequently means that the disease might go untreated, leading to stricture formation and irreversible damage to the esophagus, then endoscopies should be done often.

**G&H** What is the presentation of eosinophilic esophagitis in its most severe form, and can it be treated at that stage?

**DK** In adults, the most severe form of eosinophilic esophagitis is a small-caliber esophagus, in which the entire esophagus has strictured and narrowed. At this stage, the esophagus cannot be restored to normal due to the presence of scar tissue. Patients can be treated with aggressive therapy in order to prevent progression. The esophagus can also be dilated, but the risk associated with dilation is much higher at this stage because the lining of the esophagus is much more fragile, resulting in a higher chance of tear.

**G&H** How important is it to differentiate between eosinophilic esophagitis and gastroesophageal reflux disease?

**DK** In the past, many patients with eosinophilic esophagitis were diagnosed as having reflux disease and reflux strictures. Differentiating between these conditions is important since treatments are different. However, there may be some overlap between eosinophilic esophagitis and gastroesophageal reflux disease. It may be that separating patients into absolute categories is not the most effective approach. I have several patients that I am treating for both conditions.

A related issue is the need to establish exact criteria for eosinophilic esophagitis. Generally, the condition is defined by the number of eosinophils in a high-powered

field. However, there is no consensus on what that number should be. Stricter criteria need to be established for defining this disease. Such efforts are underway. Until then, most investigators are using anywhere from 18 to 25 eosinophils per high-powered field as their criterion.

## Suggested Reading

Straumann A, Berlinger C. Eosinophilic esophagitis: the endoscopist's enigma. *Gastrointest Endosc.* 2006;63:13-15.

Noel RJ, Putnam RE, Rothenberg ME. Eosinophilic esophagitis. *N Engl J Med.* 2004;351:940-941.

Potter JW, Saeian K, Staff D, et al. Eosinophilic esophagitis in adults: an emerging problem with unique esophageal features. *Gastrointest Endosc.* 2004;59:355-361.

Straumann A, Spichtin HP, Grize L, Bucher KA, Beglinger C, Simon HU. Natural history of primary eosinophilic esophagitis: a follow-up of 30 adult patients for up to 11.5 years. *Gastroenterology.* 2003;125:1660-1669.

Teitelbaum JE. Natural history of primary eosinophilic esophagitis: a follow up of 30 adult patients for up to 11.5 years. *J Ped Gastroenterol Nutr.* 2004;38:358-359.

Kaplan M, Mutlu EA, Jakate S, et al. Endoscopy in eosinophilic esophagitis: "feline" esophagus and perforation risk. *Clin Gastroenterol Hepatol.* 2003;1:433-437.

Mishra A, Rothenberg ME. Intratracheal IL-13 induces eosinophilic esophagitis by an IL-5, eotaxin-1, and STAT6-dependent mechanism. *Gastroenterology.* 2003;125:1419-1427.

Croese J, Fairley SK, Masson JW, et al. Clinical and endoscopic features of eosinophilic esophagitis in adults. *Gastrointest Endosc.* 2003;58:516-522.

Markowitz JE, Spergel JM, Ruchelli E, Liacouras CA. Elemental diet is an effective treatment for eosinophilic esophagitis in children and adolescents. *Am J Gastroenterol.* 2003;98:777-782.

Fujiwara H, Morita A, Kobayashi H, et al. Infiltrating eosinophils and eotaxin: their association with idiopathic eosinophilic esophagitis. *Ann Allergy Asthma Immunol.* 2002;89:429-432.