

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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Allergy Testing in Patients With Eosinophilic Esophagitis



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G&H How is a diagnosis of eosinophilic esophagitis made?

SA Eosinophilic esophagitis (EoE) is a clinicopathologic diagnosis that is dependent upon 15 or more eosinophils per high-power field on a biopsy specimen viewed with hematoxylin and eosin stain at 400× microscopy. Certain symptoms may suggest EoE, but there is no single defining symptom or feature. Generally, a diagnosis of EoE can be made if the patient shows continued esophageal eosinophilia of 15 or more eosinophils per high-power field after an 8-week trial of high-dose proton pump inhibitors.

G&H Does EoE present differently between adult and pediatric patients?

SA Yes. The predominant symptom in adults is dysphagia, sometimes with concurrent strictures or food impaction. Adults may also present with concentric rings, which are fixed fibrotic rings in the esophagus (also known as trachealization of the esophagus or a feline esophagus), or a pale esophagus that is furrowed and contains plaques.

Symptoms in children differ according to the age of the patient. Young children often present with symptoms similar to gastroesophageal reflux disease, including regurgitation. Some young children may have trouble gaining weight or will fail to thrive due to vomiting or picky eating. School-aged children tend to complain of abdominal pain, which is nonspecific. In those cases, a clinician should try to elicit the symptoms of dysphagia by asking

questions about the length of time that food is chewed, how much liquid a patient drinks when chewing, and whether the patient appears to regurgitate food while eating. Adolescent-age patients typically experience difficulty swallowing, similar to adults. The findings of strictures, narrowing, and concentric rings are much less commonly seen in children. In general, this population tends to present with inflammatory features such as plaques, furrows, and pallor. However, an adult or pediatric patient may have a normal-appearing esophagus, in which case 15 or more eosinophils per high-power field are necessary in order to make a diagnosis.

G&H What is currently understood about the connection between foods and EoE?

SA It is clear that foods trigger EoE because of the data from elimination diets. What is unknown is whether the presence of immunoglobulin E (IgE) modulates how long a patient has EoE, if it has anything to do with the natural history of the disease, or if it can help in the prognosis of EoE. In that regard, food testing in allergic patients can be complicated, and not all tests will identify the correct food; an allergist has to know which test to perform and why. For example, removing certain foods (eg, milk or peanuts) from a patient's diet when he or she exhibits no clinical problems when eating yet has a reaction to a skin test and then reintroducing the food months or years after removal can break the patient's tolerance toward the food and cause the patient to manifest an allergic reaction to it (eg, hives, respiratory distress, hypotension).

G&H What are the common allergy tests that are performed to evaluate EoE?

SA Allergy testing is used to try to find triggers of EoE rather than to establish a diagnosis of the disease. The most common standardized, validated test that allergists use to evaluate EoE is skin-prick testing, in which a commercially made food or aeroallergen extract is dropped onto the skin of the patient and scratched through. This elicits an immediate hypersensitivity response because mast cells in the skin have IgE antibodies bound to them. The mast cells degranulate due to the antigen to which they have IgE, which causes hives to appear locally within 15 minutes. The disadvantage to IgE testing in the context of EoE is that hypersensitivity is not only IgE-mediated. In fact, it is unclear whether IgE plays a true pathogenic role in evaluating EoE. Whereas skin-prick testing is used to evaluate immediate hypersensitivity, EoE appears to be a delayed hypersensitivity.

The food patch test is based on the concept of delayed hypersensitivity. An allergist places fresh, single-ingredient foods (typically baby foods) into a metal chamber (Finn Chamber, SmartPractice) and tapes it to the back of the patient for 48 to 72 hours. The chamber is then removed and read immediately, with a second reading after 24 to 48 hours. Theoretically, this test evaluates the mechanism of EoE better than the skin-prick test because it determines delayed-type sensitivity. However, although patch testing is validated in the context of contact dermatitis and eczema, patch testing for foods is not validated in regard to EoE, nor are the extracts standardized.

Another commonly performed allergy test is serum testing, which determines the presence and level of IgE but not necessarily the function. Similar to skin-prick testing, serum testing looks for an IgE-mediated reaction and tests for immediate hypersensitivity; therefore, it does not find the trigger of EoE very well. However, this test is fairly sensitive because the scales have a wide range. It is also an enzyme-linked immunosorbent assay–based test and provides a color reaction if a patient has a specific IgE that binds to an antigen on a solid phase.

It is important to remember that with any type of IgE testing, even in the context of diseases for which it is validated and standardized, such as for immediate hypersensitivity, a positive IgE to food does not necessarily mean that that food is pathogenic for the disease state. For example, a patient who is allergic to peanuts but can eat almonds may have IgE to both peanut and almond, but only the peanut IgE causes a problem. Therefore, the negative predictive value of IgE testing, even considering anaphylaxis or immediate hypersensitivity, is much better than the positive predictive value.

G&H Which dietary therapies are available to treat EoE?

SA There are several dietary therapies available to treat EoE. An elimination diet can be performed 2 ways: as a testing-based diet, which is usually a combination of skin-prick and food-patch testing, or as an empiric-elimination diet. Dr Jonathan Spergel and colleagues have found that the combination of prick and patch testing with empiric milk elimination can predict triggers to food 77% of the time. The prick/patch-based method tends to work better in children than in adults. However, patch testing can be fairly labor-intensive and requires the staff, time, and reagents necessary in order to place the patches on the patient, which can be a limiting factor for a private practitioner.

The empiric-elimination diet, also called the 6-food elimination diet, involves avoiding milk, eggs, soy, wheat, peanuts/tree nuts, and fish/shellfish. This approach works in approximately 50% to 70% of adults and children. Most adult patients prefer this therapy because it is much less labor-intensive than the prick/patch method. However, there is a paucity of data on whether the empiric-elimination diet works well when the number of foods is cut down to fewer than 6 categories. Data suggest that eliminating only milk, eggs, soy, and wheat works approximately 50% of the time, and that a milk-elimination diet in pediatric patients may be beneficial 60% to 70% of the time. More data on alternative elimination diets are needed.

The elemental formula therapy is built on amino acid–based formulas and is used less often than other dietary therapies. When patients (both adult and pediatric) are able to adhere to the diet, it works more than 90% of the time, usually in the range of 96% to 98%. The challenge is that the formulas are not very palatable and patients cannot eat anything else; therefore, most patients are not able to tolerate the diet long term. Additionally, the patient has to undergo repeat endoscopies every time a food group is added in order to find a diet that is safe, which can be hard on families; this is true for any elimination diet.

Component testing examines specific parts of an antigen for peanut, milk, and egg, but there is not enough literature to determine whether this method is helpful.

G&H How common are food allergies in patients with EoE?

SA It depends on the definition of food allergy and the age of the patient. If food allergy is defined as a food sensitization, approximately 70% of children and 50% to 60% of adults will have serum positivity or skin-prick-test positivity to a food. Food allergy defined in terms

of outcome—removing a problematic food to improve endoscopy results, histology, and quality of life—rather than testing is determined by the empiric-elimination diet. Data suggest that removing a food from a patient's diet will improve symptoms of EoE for approximately 50% to 70% of patients. In general, milk, eggs, soy, and wheat are the top 4 triggers, with milk and wheat as the top 2 allergies. Although peanuts, tree nuts, fish, and shellfish are common anaphylaxis triggers, they are not very common EoE triggers.

G&H What role do aeroallergens play in the diagnosis of EoE?

SA Aeroallergens seem to be less common triggers for EoE, but testing for them remains important, as literature shows that aspergillus or dust mites can drive eosinophils into the esophagus, and some patients have EoE during pollen season. Immunotherapy for aeroallergens has been demonstrated in case reports to improve EoE.

In general, allergic diseases play off of one another and are often triggered by one thing (for example, a baby who has a virus can flare his or her asthma and eczema at the same time). If a patient experiences worse EoE during the ragweed season on the East Coast, it may not be beneficial to obtain a biopsy if past biopsies have demonstrated EoE exacerbation during the pollen season. Similarly, the response to a dietary therapy could be hindered by the ragweed exposure. In addition, recent literature shows that pollen-allergic patients tend to have more eosinophils in the esophagus during the pollen season. It is important to consider the entire atopic person, not just the EoE.

G&H What are the priorities of research in this field?

SA One of the major priorities is to understand the different phenotypes of EoE. For instance, some patients may have more severe fibrosis or develop strictures quicker than

others, in which case a more aggressive intervention would be needed than in someone with a milder phenotype.

Another priority is finding alternative methods to survey the esophagus that are less invasive than endoscopy and general anesthesia, as those can be a burden to patients. Research is being conducted on string and sponge tests and transnasal endoscopy, but it would be very helpful to see if there can be any surrogate markers (such as blood or stool) for EoE.

Other areas of needed research include when, how, and for how long to treat patients with intermittent EoE exacerbations, how to know if EoE is flaring without having to do a biopsy every time, and the side effects of the treatments.

Dr Aceves is a co-inventor of oral viscous budesonide (patented by the University of California, San Diego and licensed by Shire Pharmaceuticals); has received funding from the National Institutes of Health, National Institute of Allergy and Infectious Diseases, National Center for Advancing Translational Sciences, and National Institute of Diabetes and Digestive and Kidney Diseases; and is a member of the medical advisory panel of the American Partnership for Eosinophilic Disorders.

Suggested Reading

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