Ask the *expert*

Eosinophilic esophagitis

Evan S. Dellon, MD, MPH

Ask the expert features questions submitted by members, with answers provided by ASGE physician experts. ASGE's Publications Committee identifies authors and topics for the column. In this issue, Evan S. Dellon, MD, MPH, responds to questions on eosinophilic esophagitis. Dr. Dellon is an assistant professor of Medicine at the Center for Esophageal Diseases and Swallowing and the Center for Gastrointestinal Biology and Disease, Division of Gastroenterology and Hepatology, Department of Medicine, University of North Carolina School of Medicine, Chapel Hill, N.C.

Disclosures: Dr. Dellon has disclosed relationships with AstraZeneca, Mertigage Pharma, Inc., Oncoscope, Inc., the National Institutes of Health, the American College of Gastroenterology, the American Gastroenterological Association Institute and the CURED Foundation.

1. Q: From a practical standpoint, how is eosinophilic esophagitis (EoE) diagnosed? Do you recommend a proton pump inhibitor (PPI) trial prior to performing an endoscopy with biopsies in a patient with suspected EoE? If so, what dose and duration of the PPI therapy do you recommend?

A: The most recent consensus guidelines for the diagnosis of EoE emphasize that EoE is a clinicopathologic entity and that symptoms and histologic findings must be considered together to make a diagnosis; no single finding in isolation is diagnostic.[1] In particular, to diagnose EoE, three criteria must be met: 1) symptoms of esophageal dysfunction (for example, dysphagia, food impaction, heartburn, chest pain and regurgitation); 2) a maximum eosinophil count of ≥15 eosinophils per high-power microscope field (eos/hpf), with few exceptions; and 3) eosinophilia limited to the esophagus, with exclusion of other possible causes of esophageal eosinophilia.

This last point is particularly important. The finding of eosinophilic infiltration of the esophageal mucosa on biopsy does not, in and of itself, make the diagnosis of EoE. There is a differential diagnosis for esophageal eosinophilia,[1] but the most common conditions that must be considered are gastroesophageal reflux disease (GERD) and proton-pump inhibitor (PPI)-responsive esophageal eosinophilia (PPI-REE).

GERD has been shown to cause esophageal eosinophilia presumably due to acid-mediated mucosal injury,[2] and even very high eosinophil counts alone do not distinguish EoE from GERD.[3,4] PPI-REE is a newly recognized clinical phenotype in which patients with clinical features of EoE and high levels of esophageal eosinophilia have a complete symptom and histologic response to treatment with PPI therapy alone. Such a response has been reported in at least 30 to 40 percent of patients with esophageal eosinophilia,[5-7] and preliminary in vitro data suggest that the mechanism may be an anti-inflammatory effect of PPIs, independent of their acid-suppressive action.[8]

With this background, a PPI trial is key to confirming the diagnosis of EoE, excluding PPI-REE, and assessing for the presence of GERD. While there are few data to support specific dosing regimens or specific drugs, the typical dose that is used in this setting is 20 to 40 mg of any of the available agents, administered twice daily for eight weeks.[1]

The timing of the PPI trial depends on the clinical situation. If the patient has had recurrent food impactions, severe dysphagia, weight loss or other alarm symptoms, then more urgent endoscopy is required, and the delay required for a PPI trial would not be clinically appropriate at the outset. A PPI trial would still be needed, however, to confirm a diagnosis of EoE should esophageal eosinophilia be found.

If the patient has chronic dysphagia and no alarm symptoms and there is a high suspicion of EoE, starting a PPI trial prior to the index endoscopy is reasonable, as it makes the diagnostic process more efficient since only one endoscopy is required. However, if there is chronic dysphagia and a lower suspicion of EoE, proceeding to esophagogastroduodenoscopy (EGD) in a PPI-naïve state may be preferential because a full spectrum of esophageal pathology can be observed.

2. Q: What is the natural history of untreated EoE in a young adult?

A: There are few high-quality data concerning the long-term natural history of EoE in young adults, as no large cohorts have been observed without treatment over years or decades. From smaller cohort studies, retrospective data and placebo arms of clinical trials, however, a number of conclusions about the natural history of EoE can be made.

It is clear that EoE is a chronic disease and that symptoms frequently recur after treatment is stopped.[1, 9-12] Patients with dysphagia and esophageal strictures who undergo esophageal dilation can have a symptom response of more than one year, but symptoms of dysphagia also recur in this group.[13] For untreated patients, symptoms of dysphagia and esophageal eosinophilia tend to persist and spontaneous resolution of symptoms is rare, but to date, no cases have been reported to progress to hypereosinophilic syndrome, and no malignancies have been attributed to EoE.[14-17]

continued on page 2

 continued from page 1

It has been noted in several retrospective studies that children and adults have different clinical and endoscopic features when they present with EoE.[1, 4, 18-20] Clinical experience teaches that a child with EoE who presents with feeding intolerance, regurgitation and inflammatory changes on endoscopy (linear furrows, white plaques or exudates and decreased vascularity or pallor) may progress as an adult to dysphagia and fibrotic changes (a narrow-caliber esophagus with prominent rings or strictures) on endoscopy.

Furthermore, a recent abstract has suggested that the frequency of esophageal strictures increases with longer duration of disease.[21] Still, there are no prospective studies confirming these two observations. At present, more information is needed to identify predictors of disease severity and progression.

3. Q: What do you currently recommend for the initial treatment in patients with newly diagnosed EoE, and what should the treatment endpoints be?

A: For both children and adults, there are strong data supporting either topical glucocorticoid use or dietary elimination as first-line therapy for patients newly diagnosed with EoE. Which option is selected depends on the clinical picture, local expertise and patient preference. (Dietary elimination is discussed in question #5.)

With regard to topical glucocorticoids, both fluticasone and budesonide have been shown to be superior to placebo in studies of children and adults.[22-25] The recommended dose of fluticasone in children is 88 to 440 mcg, two to four times daily; in adults, 440 to 880 mcg twice daily. The doses of budesonide are 1 mg daily in children < 10 years of age and 2 mg daily in those 10 years and older.[1]

With both of these agents, an existing asthma preparation is modified to be swallowed rather than inhaled, and it is important to instruct patients in their use so that as much medication is deposited in the esophagus as possible.

There are currently no comparative studies of fluticasone and budesonide, but a recent trial comparing an oral viscous budesonide preparation to swallowed/nebulized budesonide suggests that greater esophageal medication deposition is achieved with the viscous solution.[26]

My general preference is to start with an eight-week course of a topical glucocorticoid agent. More recently, I have been using oral viscous budesonide because, even though the patient has to mix the preparation, it seems more intuitive to swallow the medication to coat the esophagus than to manipulate a multi-dose inhaler. Nevertheless, fluticasone is a perfectly acceptable first agent. I also discuss dietary elimination therapy as an effective option with all patients as well. If a motivated patient wants to avoid glucocorticoid therapy and start with dietary therapy, then I am happy to use this as a first-line approach.

The issue of treatment endpoints in EoE is controversial, and almost every study to date has used a different endpoint.[27] My overall treatment goal is to improve symptoms and reduce eosinophilic inflammation, while minimizing the impact of treatment on a patient's quality of life.

While I do not aim for a specific eosinophil cut-point as a target, I would like ideally to have the esophageal biopsies as close to normal as possible. However, if a patient's symptoms are improved but there is still a low level of esophageal eosinophilia, I do not escalate therapy.

4. Q: What are the current management recommendations for asymptomatic patients who are incidentally found to have EoE? Do we wait for such patients to become symptomatic, or should we be aggressive and treat them early so that they do not develop esophageal strictures? If so, what is the endpoint?

A: By definition, clinical symptoms of esophageal dysfunction are required for the diagnosis of EoE; however, it is possible to encounter endoscopic changes consistent with EoE (rings, felinization, linear furrows, etc.) during an endoscopy performed for other reasons, and biopsies can show esophageal eosinophilia in the absence of symptoms.

In patients such as these, there are several questions to address before considering therapy. First, could this be another eosinophilic GI disorder (for example, eosinophilic gastroenteritis or eosinophilic colitis) that could have caused the non-esophageal clinical symptoms that prompted the initial endoscopy? Second, does the patient have peripheral eosinophilia or other systemic reasons for esophageal eosinophilia?

Third, is the patient truly asymptomatic from the esophageal standpoint? Often, patients with EoE have made major dietary modifications to cope with swallowing difficulties, and they will not report dysphagia. Nevertheless, if they are asked about eating slowly, taking small bites of food, chewing foods until a mushy consistency is achieved,

continued on page 3

 continued from page 2

avoiding eating at restaurants or in social situations or drinking a lot of fluids with meals to help foods go down, subtle symptoms can be picked up. Additionally, in children with EoE, classic symptoms of dysphagia are not seen, and nausea, vomiting, regurgitation or heartburn attributed to reflux, or even abdominal pain can be the presenting symptoms.

In the absence of true symptoms, incidental esophageal eosinophilia is not EoE, and little is known about the natural history of this condition. It is also unknown whether treating the inflammation would prevent future symptoms or complications, and there are currently no recommendations for initiating treatment in this setting. In the scenario presented, I would follow the patient clinically — after all, something prompted that initial endoscopy — and I would monitor him or her for the development of esophageal symptoms.

5. Q: What is the role of an elimination diet for the treatment of EoE in adults?

A: Dietary elimination is a first-line treatment option for EoE in both adults and children. Data support three general approaches: targeted elimination based on allergy testing, an empiric six-food elimination diet (SFED) whereby wheat, dairy, eggs, soy, nuts and seafood are removed and use of an allergen-free elemental diet formula.[1, 28-32]

In children, elemental diets are nearly universally effective, and the vast majority also respond to a SFED. Data are more limited in adults but are emerging. Targeted elimination seems to be least effective, likely due to issues with food allergy testing itself (see question #6).[33] An elemental diet using a hypoallergenic formula of amino acids, corn syrup solids and medium chain triglycerides can be effective, but the formula options are unpalatable and the regimen difficult to comply with, so it is not a viable long-term treatment option in most circumstances.[34]

The most promising elimination diet is the SFED. This approach has recently been prospectively studied in adults, and approximately two thirds of subjects had a complete histologic response, and more than 90 percent had symptom improvement.[30]

Although effective, dietary therapy requires a multidisciplinary approach to optimize the treatment response. A team of allergists, dieticians or nutritionists and gastroenterologists must work together to provide the patient with sufficient information so that foods can be completely eliminated while adequate nutritional support is maintained during the elimination phase.

Patients also need to understand that an elimination diet is just the first phase and that food reintroduction is required to identify the actual triggers. This typically requires multiple endoscopic evaluations over at least four to six months, so a patient must be motivated to complete the process and understand the level of monitoring required. When done properly, however, this approach can obviate the need for pharmacologic therapy and provide a long-term and durable treatment option.

6. Q: Is there a role for food allergy testing in adult patients diagnosed with EoE?

A: The role of food allergy testing in EoE is controversial, primarily because it is not known whether the immunoglobulin E (IgE)-mediated food allergies detected on skin prick testing (the modality used most widely, in contrast to atopy patch testing) are applicable to triggers in EoE.[1] Data on adults show a poor correlation between allergy test results and the actual food trigger after food reintroduction;[30] however, data on children from expert centers suggest that a combination of skin prick and patch testing can identify the majority of allergen triggers.[32]

Currently, because of the high frequency of atopic disorders in patients with EoE, as well as the potential presence of IgE-mediated food allergies, it is recommended that patients with EoE have an evaluation with an allergist or immunologist. The decision to test for food allergies will depend, however, on the allergist's practice as well as whether dietary elimination therapy is a possibility. If a patient is not interested in dietary treatment with a targeted elimination approach, then there is not a strong reason to test for specific food allergies.

7. Q: After successful treatment for EoE, which strategy is best for preventing adverse outcomes?

A: For the majority of patients with EoE, once treatment is stopped symptoms will recur within one to two years or sooner.[10, 11, 13] Individual patients, however, will have a wide spectrum of symptoms, ranging from mild and intermittent dysphagia, to recurrent emergency department visits for food bolus impactions, to malnutrition from feeding intolerance in children.

The severity of symptoms, in combination with complications of EoE (esophageal strictures, food impaction, esophageal rupture or perforation) and patient preference, can be used to individualize a plan to prevent adverse

continued on page 4

 continued from page 3

outcomes. It might be reasonable to follow patients with mild symptoms, who have had a good treatment response, expectantly after just one treatment course and assess them periodically for recurrent symptoms.

For the majority of patients with more prominent symptoms or a prior complication, however, it is likely that some type of maintenance therapy will be required. To date, it is unknown whether the best approach is dietary restriction, ongoing use of topical glucocorticoids or repeat esophageal dilation. I discuss each of these options with patients and either decrease a topical glucocorticoid to the lowest effective dose or continue dietary elimination, if that is effective. In some cases, patients prefer intermittent esophageal dilation when they become symptomatic, and this is also a reasonable approach.

8. Q: A patient with EoE has no improvement in dysphagia with oral fluticasone or after Savary dilation to a maximum diameter of 13 mm. The patient is now on budesonide with minimal, if any, response. What should be the next step in treating this patient?

A: This is a complex situation, and there are many potential reasons that must be investigated to explain an apparent non-response to topical glucocorticoids or dilation. The first possibility is that the patient was not taking the swallowed glucocorticoid medication regularly or was taking it inappropriately. The second possibility is that the medication dose was too low. It is not uncommon to encounter patients who are thought to have glucocorticoid-refractory EoE but who were treated with doses that were only a quarter of the usual starting dose (see question #3).

The third possibility is that there is superimposed Candidal esophagitis complicating the topical glucocorticoid therapy and causing persistent symptoms of dysphagia; this has been reported in up to 15 to 30 percent of EoE patients treated with these agents.[23, 25, 26] The fourth possibility is that the topical glucocorticoids have successfully treated the esophageal eosinophilic inflammation, but the esophagus remains narrow in caliber or there is still a stricture causing dysphagia; dilation to 13 mm may not be adequate in this patient.

The fifth possibility is that there is a superimposed motility disorder. Esophageal dysmotility and esophageal longitudinal muscle dysfunction have been reported in a subset of patients with EoE,[35-37] and the esophagus is also less compliant in EoE patients.[38]

The sixth possibility is that there is persistent eosinophilic infiltration of the esophagus that is contributing to ongoing symptoms, and the patient is truly not responsive to topical glucocorticoids used at an appropriate dose. In a patient like this, I would repeat an upper endoscopy after at least six to eight weeks of treatment with 2 mg of budesonide per day, assess for Candida, repeat esophageal dilation and take biopsies from the distal and proximal esophagus.

If there is no inflammation, repeated dilation is needed and esophageal manometry should be considered. If there is ongoing inflammation, I would discontinue glucocorticoids and start dietary elimination therapy, most likely with a SFED. I would also consider an allergy consultation to assess for other atopic diseases and the possible role of environmental aeroallergens, given that in some patients environmental allergens, rather than food allergies, appear to trigger EoE.[39, 40]

9. Q: Is there any difference in the efficacy of intranasal fluticasone compared with a fluticasone metered-dose inhaler (MDI) for the treatment of EoE?

A: No one has examined this issue, but it would make a good clinical trial! My preference is to use a fluticasone MDI for treatment of EoE because there is far more experience with this approach in the literature than with any other. The intranasal formulation of fluticasone should theoretically be effective if sufficient doses can be delivered to the esophagus.

It is important to realize that each actuation of the intranasal formulation dispenses only 50 mcg of fluticasone, compared with 220 mcg for the MDI. Therefore, to achieve an equivalent daily starting dose (880 mcg twice daily), more than 30 actuations of the intranasal dispenser are needed, compared with eight puffs from the MDI. Moreover, the dose of glucocorticoid must not be dispensed intranasally but should be directly swallowed. For these reasons, I think the MDI is preferable.

continued on page 5

 continued from page 4

10. Q: Is a follow-up endoscopy necessary in EoE if a patient has responded to therapy and is relatively asymptomatic?

A: My practice is to obtain a follow-up endoscopic examination in all patients after their initial course of therapy. In certain cases, if a patient is completely asymptomatic and is opposed to proceeding with another endoscopy, I will respect his or her preference.

Because a number of clinical trials have suggested that clinical symptoms and endoscopic response do not necessarily correlate,[23, 26, 27, 41, 42] however, I think confirming at least once that there is a histologic response that matches the clinical improvement is important. In particular, this approach allows titration of maintenance medications or restarting therapies in the future without necessarily repeating an endoscopy at that time.

The information presented in Ask the expert *reflects the opinions of the author and does not represent the position of ASGE. ASGE expressly disclaims any warranties or guarantees, expressed or implied, and is not liable for damages of any kind in connection with the material, information, or procedures set forth.*

ADDITIONAL RESOURCES

- "**ASGE Guideline on Esophageal dilation**," developed by the ASGE Standards of Practice Committee.
- "**Testing for refractory gastroesophageal reflux disease**," by Akpinar Zehrai, MD, Elif Saritas Yuksel, MD and Michael F. Vaezi, MD, PhD, MSc (Epi) From the quarterly, clinical e-newsletter, *ASGE Leading Edge*, Vol. 2, No. 2, Aug. 22, 2012.

References

1. Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: Updated consensus recommendations for children and adults. J Allergy Clin Immunol 2011;128:3-20.e6.
2. Spechler SJ, Genta RM, Souza RF. Thoughts on the complex relationship between gastroesophageal reflux disease and eosinophilic esophagitis. Am J Gastroenterol 2007;102:1301-6.
3. Rodrigo S, Abboud G, Oh D, et al. High intraepithelial eosinophil counts in esophageal squamous epithelium are not specific for eosinophilic esophagitis in adults. Am J Gastroenterol 2008; 103:435-42.
4. Dellon ES, Gibbs WB, Fritchie KJ, et al. Clinical, endoscopic, and histologic findings distinguish eosinophilic esophagitis from gastroesophageal reflux disease. Clin Gastroenterol Hepatol 2009;7:1305-1313.
5. Ngo P, Furuta GT, Antonioli DA, et al. Eosinophils in the esophagus--peptic or allergic eosinophilic esophagitis? Case series of three patients with esophageal eosinophilia. Am J Gastroenterol 2006;101:1666-70.
6. Sayej WN, Patel R, Baker RD, et al. Treatment With High-dose Proton Pump Inhibitors Helps Distinguish Eosinophilic Esophagitis From Noneosinophilic Esophagitis. J Pediatr Gastroenterol Nutr 2009;49:393-9.
7. Molina-Infante J, Ferrando-Lamana L, Ripoll C, et al. Esophageal Eosinophilic Infiltration Responds to Proton Pump Inhibition in Most Adults. Clin Gastroenterol Hepatol 2011;9:110-7.
8. Cheng E, Zhang X, Huo X, et al. Omeprazole blocks eotaxin-3 expression by oesophageal squamous cells from patients with eosinophilic oesophagitis and GORD. Gut 2012.
9. Liacouras CA, Wenner WJ, Brown K, et al. Primary eosinophilic esophagitis in children: successful treatment with oral corticosteroids. J Pediatr Gastroenterol Nutr 1998;26:380-5.
10. Helou EF, Simonson J, Arora AS. 3-Yr-Follow-Up of Topical Corticosteroid Treatment for Eosinophilic Esophagitis in Adults. Am J Gastroenterol 2008; 103:2194-9.
11. Straumann A, Conus S, Degen L, et al. Long-term budesonide maintenance treatment is partially effective for patients with eosinophilic esophagitis. Clin Gastroenterol Hepatol 2011; 9:400-9 e1.
12. Straumann A. The natural history and complications of eosinophilic esophagitis. Thorac Surg Clin 2011;21:575-87.
13. Schoepfer AM, Gonsalves N, Bussmann C, et al. Esophageal dilation in eosinophilic esophagitis: effectiveness, safety, and impact on the underlying inflammation. Am J Gastroenterol 2010;105:1062-70.
14. DeBrosse CW, Franciosi JP, King EC, et al. Long-term outcomes in pediatric-onset esophageal eosinophilia. J Allergy Clin Immunol 2011;128:132-8.

continued on page 6

References continued from page 5

15. Straumann A, Spichtin HP, Grize L, et al. Natural history of primary eosinophilic esophagitis: a follow-up of 30 adult patients for up to 11.5 years. Gastroenterology 2003;125:1660-9.
16. Assa'ad AH, Putnam PE, Collins MH, et al. Pediatric patients with eosinophilic esophagitis: an 8-year follow-up. J Allergy Clin Immunol 2007;119:731-8.
17. Spergel JM, Brown-Whitehorn TF, Beausoleil JL, et al. 14 years of eosinophilic esophagitis: clinical features and prognosis. J Pediatr Gastroenterol Nutr 2009;48:30-6.
18. Noel RJ, Putnam PE, Rothenberg ME. Eosinophilic esophagitis. N Engl J Med 2004;351:940-1.
19. Furuta GT, Liacouras CA, Collins MH, et al. Eosinophilic esophagitis in children and adults: a systematic review and consensus recommendations for diagnosis and treatment. Gastroenterology 2007;133:1342-63.
20. Dellon ES, Aderoju A, Woosley JT, et al. Variability in diagnostic criteria for eosinophilic esophagitis: A systematic review. Am J Gastroenterol 2007;102:2300-13.
21. Schoepfer A, Safroneeva E, Bussmann C, et al. Fixed rings and strictures in eosinophilic esophagitis develop due to continuing inflammation over time. Gastroenterology 2012;142 (Suppl 2):AB 1032.
22. Konikoff MR, Noel RJ, Blanchard C, et al. A randomized, double-blind, placebo-controlled trial of fluticasone propionate for pediatric eosinophilic esophagitis. Gastroenterology 2006;131:1381-91.
23. Alexander JA, Jung KW, Arora AS, et al. Swallowed Fluticasone Improves Histologic but Not Symptomatic Responses of Adults with Eosinophilic Esophagitis. Clin Gastroenterol Hepatol 2012;10:742-9.e1.
24. Dohil R, Newbury R, Fox L, et al. Oral Viscous Budesonide Is Effective in Children With Eosinophilic Esophagitis in a Randomized, Placebo-controlled Trial. Gastroenterology 2010;139:418-29.
25. Straumann A, Conus S, Degen L, et al. Budesonide is effective in adolescent and adult patients with active eosinophilic esophagitis. Gastroenterology 2010;139:1526-37, 1537 e1.
26. Dellon ES, Sheikh A, Speck O, et al. Viscous Topical is More Effective than Nebulized Steroid Therapy for Patients with Eosinophilic Esophagitis. Gastroenterology 2012;143:321-324.e1.
27. Hirano I. Therapeutic End Points in Eosinophilic Esophagitis: Is Elimination of Esophageal Eosinophils Enough? Clin Gastroenterol Hepatol 2012;10:750-2.
28. Markowitz JE, Spergel JM, Ruchelli E, et al. Elemental diet is an effective treatment for eosinophilic esophagitis in children and adolescents. Am J Gastroenterol 2003;98:777-82.
29. Kagalwalla AF, Sentongo TA, Ritz S, et al. Effect of Six-Food Elimination Diet on Clinical and Histologic Outcomes in Eosinophilic Esophagitis. Clin Gastroenterol Hepatol 2006;4:1097-1102.
30. Gonsalves N, Yang GY, Doerfler B, et al. Elimination Diet Effectively Treats Eosinophilic Esophagitis in Adults; Food Reintroduction Identifies Causative Factors. Gastroenterology 2012;142.
31. Henderson CJ, Abonia JP, King EC, et al. Comparative dietary therapy effectiveness in remission of pediatric eosinophilic esophagitis. J Allergy Clin Immunol 2012;129:1570-8.
32. Spergel JM, Brown-Whitehorn TF, Cianferoni A, et al. Identification of causative foods in children with eosinophilic esophagitis treated with an elimination diet. J Allergy Clin Immunol 2012;130:461-467 e5.
33. Molina-Infante J, Martin-Noguerol E, Alvarado-Arenas M, et al. Selective elimination diet based on skin testing has suboptimal efficacy for adult eosinophilic esophagitis. J Allergy Clin Immunol 2012.
34. Peterson K, Clayton F, Vinson LA, et al. Utility of an Elemental Diet in Adult Eosinophilic Esophagitis. Gastroenterology 2011; 140 (Suppl 1):AB 1080.
35. Korsapati HR, Babaei A, Bhargava V, et al. Dysfunction of the Longitudinal Muscles of the Esophagus in Eosinophilic Esophagitis. Gut 2009;58:1056-62.
36. Nurko S, Rosen R, Furuta GT. Esophageal Dysmotility in Children With Eosinophilic Esophagitis: A Study Using Prolonged Esophageal Manometry. Am J Gastroenterol 2009;104:3050-7.
37. Roman S, Hirano I, Kwiatek MA, et al. Manometric features of eosinophilic esophagitis in esophageal pressure topography. Neurogastroenterol Motil 2011;23:208-14, e111.
38. Kwiatek MA, Hirano I, Kahrilas PJ, et al. Mechanical properties of the esophagus in eosinophilic esophagitis. Gastroenterology 2011; 140:82-90.
39. Fogg MI, Ruchelli E, Spergel JM. Pollen and eosinophilic esophagitis. J Allergy Clin Immunol 2003;112:796-7.
40. Moawad FJ, Veerappan GR, Lake JM, et al. Correlation between eosinophilic oesophagitis and aeroallergens. Aliment Pharmacol Ther 2010;31:509-15.
41. Gupta SK, Collins MH, Lewis JD, et al. Efficacy and Safety of Oral Budesonide Suspension (OBS) in Pediatric Subjects With Eosinophilic Esophagitis (EoE): Results From the Double-Blind, Placebo-Controlled PEER Study Gastroenterology 2011;140 (Suppl 1):S179.
42. Spergel JM, Rothenberg ME, Collins MH, et al. Reslizumab in children and adolescents with eosinophilic esophagitis: Results of a double-blind, randomized, placebo-controlled trial. J Allergy Clin Immunol 2012;129::456-63, 463.e1-3.