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Eosinophilic Esophagitis: Historical perspective on an evolving disease

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Introduction

During the last 2 decades, a new disease, eosinophilic esophagitis (EoE) emerged as one of the leading causes of food impaction and dysphagia in adults and vague reflux-like symptoms in children. Early case series describing adult patients indicated that this disease possessed distinct features that differentiated it from gastroesophageal reflux disease (GERD). Following these early descriptions, a tide of reports provided a clearer symptom complex in children and adults that ultimately helped to define EoE as a clinicopathological condition characterized by symptoms of esophageal dysfunction and dense esophageal epithelial eosinophilia (> 15 eos/HPF). Clinical, basic and translational studies have provided a deeper understanding of this somewhat enigmatic disease that mechanistically is defined as an antigen driven condition limited to the esophagus. We will summarize many of the key historical features of EoE and provide a glimpse of potential future developments.

Initial descriptions of esophageal eosinophilia

While eosinophils reside in the majority of the gastrointestinal mucosae, they are not present in the normal esophageal epithelia. Initial reports of esophageal eosinophilia associated this histological finding with GERD^{1, 2}. How and why acid affected the esophageal epithelium in some, but not all patients still escapes our understanding but the association of GERD

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with esophageal eosinophilia held firm for a number of years. Interestingly, these early reports characterized eosinophilia as >1 eo/HPF and the size of the HPF were not standardized. In 1985, Lee et al reported eosinophilic infiltration in esophageal mucosal biopsy in 11 patients with average age of 14.6 years; these patients had reflux symptoms, and their eosinophil density was low ³. In retrospect these were probably patients with gastro-esophageal reflux disease (GERD).

GERD is not the only disease associated with esophageal eosinophilia

While GERD associated eosinophilia was thought to be the predominant cause of esophagitis for years, a number of case series began to report clinical features that were somewhat different than that associated with classic GERD. In 1978, Landres et al reported an isolated case of vigorous achalasia in a patient with marked smooth muscle hypertrophy and eosinophilic infiltration of esophagus ⁴. He concluded that this patient likely represented a variant of eosinophilic gastroenteritis, which predisposed to esophageal motor disorder. This case is unusual in that large numbers of eosinophils are uncommonly found in esophageal tissues affected by achalasia or other defined motor disorders. In 1981, Picus and Frank reported a case of 16 year old boy with progressive dysphagia for one and half years and dense esophageal eosinophilia ⁵. Endoscopic findings revealed multiple 1 mm nodular filling defects near a stricture and proximal dilation. Radiological studies showed luminal narrowing as well as wall rigidity and peripheral blood showed high circulating eosinophil count. Again, the authors assumed it was a variant of eosinophilic gastroenteritis. Following this, a series of case reports provided more details of patients who presented with dysphagia and esophageal eosinophilia some of who developed esophageal strictures ⁶⁻⁸.

Critical observations of new clinical disorder-Eosinophilic Esophagitis

In 1989, Attwood et al published an abstract in Gut, describing “Oesophageal Asthma – an episodic dysphagia with eosinophilic infiltrates” ⁹. These investigators compared a group of 15 adults who presented with dysphagia without esophageal obstruction and normal pH monitoring to a group of 100 adults with GERD as defined by increased acid exposure in the distal esophagus. Differences between the two groups were that the group without increased acid exposure was found to have significantly greater number of eosinophils than the group with GERD. The key finding of this case series was that it identified patients with dysphagia, with a range of severity up to complete bolus obstruction, presented with dense esophageal eosinophilia. In 1993, they published these key findings that described adults with dysphagia, normal pH monitoring and dense esophageal eosinophilia (>20 eos/HPF) and termed this *Esophageal Eosinophilia with dysphagia. A distinct clinicopathological syndrome* ¹⁰. Importantly, control patients with proven GERD had a mean of 3.3 eos/HPF in the esophageal epithelium. Endoscopic appearances using fiber optic technology likely limited descriptions of the full details now observed in this disease and may partially explain the fact that no endoscopic abnormalities were visualized in their series. Seven patients had food hypersensitivity, and all required advanced intervention (dilatation and / or steroids in one case) for resolution of symptoms.

In 1994, Straumann et al described a series of 10 patients with acute recurrent dysphagia seen over a 4-year period, who showed discrete endoscopic changes, and high concentrations of epithelial esophageal eosinophils, who improved following systemic steroid and antihistamine treatment¹¹. From this series it was clear that the endoscopic findings including rings, white exudates and furrows were variably expressed since some patient's esophageal mucosae appeared relatively normal. He termed this *Idiopathic Eosinophilic Esophagitis*.

Taken together, these 2 reports from 2 different continents, described key clinical findings observed in adults with dysphagia who had dense mucosal eosinophilia that was limited to the esophagus who did not have GERD. Importantly, endoscopic findings were variable, leading to the necessity of procuring endoscopic pinch biopsy to make the diagnosis. Since this practice was not widespread, because of the lack of diagnostic utility, larger recognition of this newfound disease remained somewhat limited.

These two series, published by a gastroenterologist in private practice, Dr. Straumann and a surgeon, Dr. Attwood formed the beginnings their quest to define key clinical features and therapeutic approaches over the next 20 years.

Increasing awareness of EoE in pediatric gastroenterology community

With the emergence of improved sedation practices in the early 1990's, pediatric gastroenterologists began to perform fiber optic endoscopy with increased frequency. Coincident with this increased use, came the recognition that histological evidence of inflammation could be present despite an endoscopically normal appearing mucosa¹². This observation lead to the practice of procuring mucosal samples as a standard of care practice for children undergoing endoscopic assessment of symptoms, a key difference from adult practice.

During this time, an increasing number of children were observed to have symptoms that persisted despite anti-acid blockade. Children ranging in age from toddlers to teenagers presented with a wide range of symptoms including vomiting, regurgitation, feeding problems and abdominal pain that were unresponsive to H2 receptor antagonists or proton pump inhibitors (PPIs), and who, at the time of endoscopy, were found to have dense mucosal eosinophilia limited to the esophagus¹³⁻²⁰. Associated clinical features observed in these patients included a male predominance, radiologic evidence of strictures, endoscopic findings of white exudates, edema and rings. Consistent with the initial reports in adults, some children seemed to experience a high degree of concomitant atopic diseases including food allergy, eczema and asthma.

Eosinophilic Esophagitis may be a food allergic disease

With the increasing clinical descriptions, lack of therapeutic approaches, and potential allergic mechanism underlying this disease, Kelly et al took a novel approach in 1995¹³. They provided a detailed description of 10 children who experienced vomiting and abdominal pain, dense esophageal eosinophilia >20 / HPF and lack of response to either acid blockade or fundoplication (n=2), who responded clinically and histologically to an amino

acid based formula. Strict use of the formula lead to normalization of the esophagus and when allergenic food was added back into the diet, symptoms and esophageal eosinophilia returned. This study set the stage for a number of future studies that have examined the allergic diathesis and mechanisms of EoE. In this regard, development of therapeutic regimens included removing the six most common food allergens and instituting a diet based on the removal of foods based on food allergy testing ^{21, 22}. In addition, the global concept of EoE being a chronic disease was initiated since patients relapsed once foods were added back into the diet.

Alternative approaches to treat EoE

Because of difficulties adhering to diet restriction and the impact of steroids in other eosinophilic diseases, investigators took two different approaches. In 1998, Liacouras et al demonstrated that patients with EoE responded clinically and histologically to prednisone but that symptoms recurred when the medication was stopped ¹⁶. In the same year, Faubion et al adapted a novel approach to provide topical steroids to the esophageal mucosa ¹⁵. They hypothesized that steroid sprayed from the metered dose inhaler used for asthma, could be delivered by the saliva to the esophageal mucosa leading to an anti-inflammatory response. In their series of 4 patients, they found that this delivery mechanism was effective in relieving symptoms and when examined, diminished esophageal eosinophilia. Subsequent studies using a variety of different preparations in adults and children have shown this approach to significantly decrease symptoms and mucosal eosinophilia ^{23–40}. Other approaches toward modulating the immune system to treat EoE include leukotriene antagonist as described by Attwood et al, antibody based approaches to block IL-5 and a CRTH2 antagonist ^{41–46}.

With the increasing identification of fixed narrowings in patients with EoE, dilatation has been very helpful in EoE management. Some early reports of perforation risk were perhaps overstated and may have been accounted for by the use of rigid esophagoscopy and bougie dilatation ⁴⁷. However, the increased use of flexible endoscopic approaches with either balloon or bougie have been shown to provide safe outcomes with a risk of perforation at < 1% per procedure, a similar risk as with dilatation of peptic stricture ^{48–50}.

More clinical experiences and prospective research studies continue to emphasize the chronic nature of EoE, in that when treatments are stopped, symptoms and inflammation return.

Wider acceptance of EoE and increasing frequency of diagnosis

Following these publications there was a nearly logarithmic rise in publications focussing on this new entity EoE. Within these bodies of works, reports surfaced that documented EoE as a disease occurring primarily in Caucasian males with an overall incidence of 1 in 10,000⁵¹. From 2003–2007, works began to focus defining the clinical phenotype of EoE. Symptoms in children included vomiting, abdominal pain and feeding difficulties and adults were characterized by the stereotypical features of food impaction, dysphagia and in some circumstances, chest pain ^{22, 27, 52–68}. Endoscopic patterns of linear furrows, circular ridges and more defined rings (trachealisation), the presence of white micro abscesses and the

complication of severe strictures in some, were all manifestations of EoE ^{27, 52, 63, 69–79}. Retrospective studies detailing experiences with diet elimination, topical steroids and other treatments emerged ^{21, 22, 24–26, 28, 42, 47, 78, 80–84}. Overall a growing acceptance of a “new” disease became manifest and patient diagnoses and treatments ensued.

Development of Consensus Recommendations for Diagnosis and Treatment

Despite this increased recognition, several problems emerged that stymied not only clinical care, but an emerging research interest in this disease ⁸⁵. How many eosinophils were required to make the diagnosis? What is the size of diagnostic HPF? What symptoms are necessary to diagnose a patient with EoE? Most problematic was determining the criteria necessary to make a diagnosis of EoE. To address this, the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition held the First International Gastrointestinal Eosinophil Research Symposium in Orlando Florida in 2006. This meeting represented the culmination of a multi-disciplinary team of expert’s yearlong work to develop diagnostic recommendations and treatment approaches. The following year the First Consensus Recommendations were published that was founded on both expert clinical experience as well as the published literature, works that consisted primarily of case series and retrospective analyses ⁸⁶. A multi-disciplinary team of physician / clinical scientists determined that EoE was a clinico-pathological disease that required symptoms characterizing esophageal dysfunction and dense esophageal eosinophilia (>15 eos/HPF). Alternative causes for eosinophilia need to be ruled out and other parts of the gastrointestinal tract were normal. This publication provided strong support for the efforts of the advocacy organization, the American Partnership for Eosinophilic Disorders (APFED.org) to spearhead efforts in 2008, fifteen years after the first case series was published, to obtain approval for the ICD-9 classification (530.13) for EoE. Since then, three more guidelines have been published, each with new and improved recommendations that continue to be based on not only expert opinion but even more so now on prospective studies ^{87–89}. In this time frame the original acronym EE, was changed to EoE, to avoid confusion with the previous use of EE to describe erosive esophagitis. Taken together, these guidelines provide a basis for both clinical care and research studies.

Defining EoE phenotypes

With increased clinical experiences, the clinical diversity of EoE continues to undergo definition. For instance, EoE is likely the most common cause of food impaction in adults and children ^{58, 90–99}. A range of features characterize luminal narrowings associated with EoE including isolated esophageal strictures and rings, long segment narrowings and crepe paper esophagus. Although rare, esophageal perforation can occur as a result of dilation and also as a spontaneous event. In fact, EoE is now the commonest cause of spontaneous perforation of the esophagus, although it is usually a partial perforation, and treated differently to the original complete disruption originally described by Boorhaave ^{65, 100–102}. In addition, clinical phenotypes related to therapeutic responses have been identified. For instance, patients with an FK506-binding protein 5 (FKBP51) genotype are steroid

responsive thus pointing to a future role for molecular techniques to define personalized medicine ³².

Histological conundrums-What is Proton Pump Inhibitor Responsive Esophageal Eosinophilia?

One of the more confounding clinical problems that have arisen relates to determining whether the primary driver of esophageal eosinophilia is related to peptic or allergic etiologies. To address this, clinicians have either treated patients with high dose PPIs or performed pH monitoring of the distal esophagus ¹⁰³. These practices have uncovered a group of patients with symptoms of esophageal dysfunction, dense esophageal eosinophilia and normal pH monitoring that respond clinically and histologically to PPIs. For instance, Molina-Infante et al identified a large number of patients not thought to have GERD who responded to PPI therapy ^{104, 105}. Cheng et al provide a potential mechanism for this finding in studies in which omeprazole was shown to down regulate EoE related cytokines including IL-4, IL-13 and eotaxin-3 signalling in esophageal epithelial cells thru a STAT6 dependent process ^{106, 107}. Whether this represents undocumented GERD or an alternative action of PPIs related to its potential anti-inflammatory effect is not yet certain. Further studies defining the molecular features of EoE may lend further insights into this clinical finding.

Understanding of chronicity

Following these initial case series very little progress was apparent in the literature until the detailed description of the chronic nature and natural history of EoE. Straumann et al described the longest follow-up of 30 adults with EoE (22 men, mean age, 40.6 years; range, 16–71 years) ¹⁰⁸. The presenting symptom was almost exclusively dysphagia with food impaction, and diagnosis was delayed an average of 4.6 years (range, 0–17 year). During the follow up period of 1.4 –11.5 years, 23% of patients reported increasing dysphagia, and 36.7 %reported stable symptoms. No change in endoscopic features was identified in 6 of 7 patients in whom a subepithelial component could be analysed, but an increase in fibrosis and thickening was documented. Follow up studies by the same group demonstrated that delay in diagnosis increased risk for stricture formation ¹⁰⁹.

Molecular techniques advance care and pathogenetic understanding

In 2006, Blanchard reported the seminal finding that EoE was defined by a uniquely conserved gene-expression profile that included overexpression of eotaxin-3¹¹⁰. Works from this group and others has defined a number of gene profiles for children and adults with EoE that have identified novel therapeutic targets. In addition, murine models and *ex vivo* systems continue to dissect pathogenetic pathways, in particular, those associated with IL-5, IL-13 and Thymic Stromal Lymphopoeitin (TSLP) ^{111–119}. Most recently, Wen et al described a novel molecular testing that provides diagnostic platform for patients with EoE in a rapid and objective manner using mucosal biopsies ¹²⁰. These approaches will likely pave the way for future diagnostic and therapeutic approaches leading to a more personalized approach to care.

Future concerns and directions

Expanding diagnostic criteria beyond a number

Whereas eosinophil counts remains the gold standard biomarker for diagnosis and primary endpoints, few diseases are characterized by one cell's number alone. Problems associated with this approach are lack of standardization of HPF size, location of biopsy, limited size of biopsy sample compared to the total surface area of the esophagus, variability in enumeration techniques and broad range of eosinophilia associated with peptic and allergic inflammation^{121–123}. In this regard, future studies that determine endoscopic, histological or molecular features that further define EoE are critical.

Challenges in monitoring disease activity

Assessment of disease activity is complicated by three factors. First, symptoms do not always reflect esophageal inflammation¹²⁴. Second, measurement of esophageal inflammation requires endoscopy and biopsy. Third, measurement of esophageal function, as it relates to EoE, has not been standardized. Each of these areas is undergoing study and rapid progress has been made during the last few years. A number of minimally invasive tools (Esophageal String Test, Esophageal Sponge) that would avoid endoscopy and sedation are undergoing development^{125, 126}. Functional tests such as the endoflip show great potential in identifying critical features of clinically significant fibrosis and remodelling^{127–129}. This last concern is critical since our current understanding of this disease has been developed based on events described within the esophageal epithelia as documented by mucosal pinch biopsies. In fact, this snapshot, may only reveal part of the story in that the inflammation, characterized by not only eosinophils, but also T cells, B cells, mast cells, basophils, fibroblasts and endothelia, may lead to remodelling that impacts deeper layers of the esophageal wall.

The clinical impact of this concern relates to the adult symptoms of dysphagia, food bolus obstruction and chest pain. The term regurgitation is sometimes used but it is usually only of the swallowed fluids above the obstructed esophagus and in taking a history from patients it is useful to try and distinguish the type of regurgitation in EoE (swallowed fluids) versus the type of regurgitation seen in GERD (acid reflux from the stomach). Also the use of the term vomiting in EoE usually refers to the efforts the patients make to wrretch to move the blocked food bolus – often trying to bring it up into the pharynx. This is not vomiting in the normal sense and is best describes as retching. When talking with patients it is useful to distinguish the vomiting they might suffer when the stomach empties itself through the esophagus in contrast to the retching and heaving that occurs from a food bolus obstruction in the esophagus. In this regard, a number of studies are now seeking to provide characterization of symptoms, quality of life and endoscopic appearances of patients with EoE with the hopes of developing Patient Reported Outcomes and other metrics that can be used in prospective therapeutic trials^{130–135}

Developing new therapeutic approaches

EoE treatments, that include topical steroids and diet exclusion of antigens, induce remission in 50–75% of patients, representing excellent therapeutic responses. But topical steroids can

be difficult to administer and carry potential side effects. Diet treatment can be complicated by identifying the specific allergen and maintaining adherence. To date, no cure has been identified for EoE thus emphasizing the urgent need for future studies dedicated to developing Food and Drug Agency approved treatments^{136, 137}.

Summary

Initial case series describing children and adults with symptoms related to esophageal dysfunction and dense esophageal eosinophilia lead to recognition of a “new” disease, EoE. Clinical experiences and a growing body of research have rapidly lead to diagnostic criteria, therapeutic interventions and identification of complications. Future works will delineate more refined approaches to diagnosis, new therapeutic targets and the natural history of this enigmatic disease^{136, 137}.

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References

1. Biller JA, Winter HS, Grand RJ, et al. Are endoscopic changes predictive of histologic esophagitis in children? *J Pediatr*. 1983; 103:215–218. [PubMed: 6875711]
2. Brown LF, Goldman H, Antonioli DA. Intraepithelial eosinophils in endoscopic biopsies of adults with reflux esophagitis. *Am J Surg Pathol*. 1984; 8:899–905. [PubMed: 6517181]
3. Lee RG. Marked eosinophilia in esophageal mucosal biopsies. *Am J Surg Pathol*. 1985; 9:475–9. [PubMed: 4091182]
4. Landres RT, Kuster GG, Strum WB. Eosinophilic esophagitis in a patient with vigorous achalasia. *Gastroenterology*. 1978; 74:1298–1301. [PubMed: 648822]
5. Picus D, Frank PH. Eosinophilic esophagitis. *AJR Am J Roentgenol*. 1981; 136:1001–3. [PubMed: 6784497]
6. Feczko P, Halpert R, Zonca M. Radiographic abnormalities in eosinophilic esophagitis. *Gastrointest Radiol*. 1985; 10:321–324. [PubMed: 4054495]
7. Matzinger MA, Daneman A. Esophageal involvement in eosinophilic gastroenteritis. *Pediatr Radiol*. 1983; 13:35–8. [PubMed: 6844053]
8. Munch R, Kuhlmann U, Makek M, et al. Eosinophilic esophagitis, a rare manifestation of eosinophilic gastroenteritis. *Schweiz Med Wochenschr*. 1982; 112:731–4. [PubMed: 7100870]
9. Attwood SEA, Smyrk TC, Demeester TR. Eosinophilic asthma-episodic dysphagia with eosinophilic infiltrates. *Gut*. 1989; 30:A1493.
10. Attwood SEA, Smyrk TC, Demeester TC, Jones JB. Esophageal eosinophilia with dysphagia. A distinct clinicopathologic syndrome. *Dig Dis Sci*. 1993; 38:109–116. [PubMed: 8420741]
11. Straumann A, Spichtin HP, Bernoulli R, et al. Idiopathic eosinophilic esophagitis: a frequently overlooked disease with typical clinical aspects and discrete endoscopic findings. *Schweiz Med Wochenschr*. 1994; 124:1419–29. [PubMed: 7939509]
12. Schmidt-Sommerfeld E, Kirschner BS, Stephens JK. Endoscopic and histologic findings in the upper gastrointestinal tract of children with Crohn's disease. *J Pediatr Gastroenterol Nutr*. 1990; 11:448–54. [PubMed: 2262833]
13. Kelly KJ, Lazenby AJ, Rowe PC, et al. Eosinophilic esophagitis attributed to gastroesophageal reflux: improvement with an amino acid-based formula. *Gastroenterology*. 1995; 109:1503–12. [PubMed: 7557132]
14. Mahajan L, Wyllie R, Petras R, et al. Idiopathic eosinophilic esophagitis with stricture formation in a patient with long-standing eosinophilic gastroenteritis. *Gastrointest Endosc*. 1997; 46:557–60. [PubMed: 9434228]

15. Faubion WA Jr, Perrault J, Burgart LJ, et al. Treatment of eosinophilic esophagitis with inhaled corticosteroids. *J Pediatr Gastroenterol Nutr.* 1998; 27:90–3. [PubMed: 9669733]
16. 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. [PubMed: 9552132]
17. Orenstein SR, Shalaby TM, Di Lorenzo C, et al. The spectrum of pediatric eosinophilic esophagitis beyond infancy: a clinical series of 30 children. *Am J Gastroenterol.* 2000; 95:1422–30. [PubMed: 10894574]
18. Siafakas CG, Ryan CK, Brown MR, et al. Multiple esophageal rings: an association with eosinophilic esophagitis: case report and review of the literature. *Am J Gastroenterol.* 2000; 95:1572–5. [PubMed: 10894599]
19. Fox VL, Nurko S, Teitelbaum JE, et al. High-resolution EUS in children with eosinophilic “allergic” esophagitis. *Gastrointest Endosc.* 2003; 57:30–6. [PubMed: 12518127]
20. Khan S, Orenstein SR, Di Lorenzo C, et al. Eosinophilic esophagitis: strictures, impactions, dysphagia. *Dig Dis Sci.* 2003; 48:22–9. [PubMed: 12645786]
21. 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; 4:1097–102. [PubMed: 16860614]
22. Spergel JM, Andrews T, Brown-Whitehorn TF, et al. Treatment of eosinophilic esophagitis with specific food elimination diet directed by a combination of skin prick and patch tests. *Ann Allergy Asthma Immunol.* 2005; 95:336–43. [PubMed: 16279563]
23. Teitelbaum J, Fox V, Twarog F, et al. Eosinophilic esophagitis in children: immunopathological analysis and response to fluticasone propionate. *Gastroenterology.* 2002; 122:1216–1225. [PubMed: 11984507]
24. Arora AS, Perrault J, Smyrk TC. Topical corticosteroid treatment of dysphagia due to eosinophilic esophagitis in adults. *Mayo Clin Proc.* 2003; 78:830–5. [PubMed: 12839078]
25. Aceves SS, Dohil R, Newbury RO, et al. Topical viscous budesonide suspension for treatment of eosinophilic esophagitis. *J Allergy Clin Immunol.* 2005; 116:705–6. [PubMed: 16159647]
26. 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. [PubMed: 17101314]
27. Remedios M, Campbell C, Jones DM, et al. Eosinophilic esophagitis in adults: clinical, endoscopic, histologic findings, and response to treatment with fluticasone propionate. *Gastrointest Endosc.* 2006; 63:3–12. [PubMed: 16377308]
28. Aceves SS, Bastian JF, Newbury RO, et al. Oral Viscous Budesonide: A Potential New Therapy for Eosinophilic Esophagitis in Children. *Am J Gastroenterol.* 2007
29. Lucendo AJ, De Rezende L, Comas C, et al. Treatment with topical steroids downregulates IL-5, eotaxin-1/CCL11, and eotaxin-3/CCL26 gene expression in eosinophilic esophagitis. *Am J Gastroenterol.* 2008; 103:2184–93. [PubMed: 18844613]
30. Schaefer ET, Fitzgerald JF, Molleston JP, et al. Comparison of oral prednisone and topical fluticasone in the treatment of eosinophilic esophagitis: a randomized trial in children. *Clin Gastroenterol Hepatol.* 2008; 6:165–73. [PubMed: 18237866]
31. Aceves SS, Newbury RO, Chen D, et al. Resolution of remodeling in eosinophilic esophagitis correlates with epithelial response to topical corticosteroids. *Allergy.* 2010; 65:109–16. [PubMed: 19796194]
32. Caldwell JM, Blanchard C, Collins MH, et al. Glucocorticoid-regulated genes in eosinophilic esophagitis: a role for FKBP51. *J Allergy Clin Immunol.* 2010; 125:879–888 e8. [PubMed: 20371398]
33. 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. [PubMed: 20457157]
34. Peterson KA, Thomas KL, Hilden K, et al. Comparison of esomeprazole to aerosolized, swallowed fluticasone for eosinophilic esophagitis. *Dig Dis Sci.* 2010; 55:1313–9. [PubMed: 19533356]

35. 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. [PubMed: 20682320]
36. Abu-Sultaneh SM, Durst P, Maynard V, et al. Fluticasone and food allergen elimination reverse sub-epithelial fibrosis in children with eosinophilic esophagitis. *Dig Dis Sci*. 2011; 56:97–102. [PubMed: 20458625]
37. 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
38. Alexander JA, Jung KW, Arora AS, et al. Swallowed fluticasone improves histologic but not symptomatic response of adults with eosinophilic esophagitis. *Clin Gastroenterol Hepatol*. 2012; 10:742–749 e1. [PubMed: 22475741]
39. Dellon ES, Sheikh A, Speck O, et al. Viscous topical is more effective than nebulized steroid therapy for patients with eosinophilic esophagitis. *Gastroenterology*. 2012; 143:321–4 e1. [PubMed: 22561055]
40. Schroeder S, Fleischer DM, Masterson JC, et al. Successful treatment of eosinophilic esophagitis with ciclesonide. *J Allergy Clin Immunol*. 2012; 129:1419–21. [PubMed: 22480537]
41. Attwood SE, Lewis CJ, Bronder CS, et al. Eosinophilic oesophagitis: a novel treatment using Montelukast. *Gut*. 2003; 52:181–5. [PubMed: 12524397]
42. Garrett JK, Jameson SC, Thomson B, et al. Anti-interleukin-5 (mepolizumab) therapy for hypereosinophilic syndromes. *J Allergy Clin Immunol*. 2004; 113:115–9. [PubMed: 14699394]
43. Assa'ad AH, Gupta SK, Collins MH, et al. An antibody against IL-5 reduces numbers of esophageal intraepithelial eosinophils in children with eosinophilic esophagitis. *Gastroenterology*. 2011; 141:1593–604. [PubMed: 21835135]
44. 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. [PubMed: 22206777]
45. Otani IM, Anilkumar AA, Newbury RO, et al. Anti-IL-5 therapy reduces mast cell and IL-9 cell numbers in pediatric patients with eosinophilic esophagitis. *J Allergy Clin Immunol*. 2013; 131:1576–82. [PubMed: 23623266]
46. Straumann A, Hoesli S, Bussmann C, et al. Anti-eosinophil activity and clinical efficacy of the CRTH2 antagonist OC000459 in eosinophilic esophagitis. *Allergy*. 2013; 68:375–85. [PubMed: 23379537]
47. Lucendo AJ, De Rezende L. Endoscopic dilation in eosinophilic esophagitis: a treatment strategy associated with a high risk of perforation. *Endoscopy*. 2007; 39:376. author reply 377. [PubMed: 17427083]
48. Jacobs JW Jr, Spechler SJ. A systematic review of the risk of perforation during esophageal dilation for patients with eosinophilic esophagitis. *Dig Dis Sci*. 2010; 55:1512–5. [PubMed: 20238250]
49. Riley SA, Attwood SE. Guidelines on the use of oesophageal dilatation in clinical practice. *Gut*. 2004; 53 (Suppl 1):i1–6. [PubMed: 14724139]
50. 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. [PubMed: 19935783]
51. Noel RJ, Putnam PE, Rothenberg ME. Eosinophilic esophagitis. *N Engl J Med*. 2004; 351:940–1. [PubMed: 15329438]
52. Croese J, Fairley SK, Masson JW, et al. Clinical and endoscopic features of eosinophilic esophagitis in adults. *Gastrointest Endosc*. 2003; 58:516–22. [PubMed: 14520283]
53. Liacouras CA. Eosinophilic esophagitis in children and adults. *J Pediatr Gastroenterol Nutr*. 2003; 37 (Suppl 1):S23–8. [PubMed: 14685074]
54. 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. [PubMed: 14724818]
55. Lucendo AJ, Carrion G, Navarro M, et al. Eosinophilic esophagitis in adults: an emerging disease. *Dig Dis Sci*. 2004; 49:1884–8. [PubMed: 15628721]

56. Potter JW, Saeian K, Staff D, et al. Eosinophilic esophagitis in adults: an emerging problem with unique esophageal features. *Gastrointest Endosc.* 2004; 59:355–61. [PubMed: 14997131]
57. Sant'Anna AM, Rolland S, Fournet JC, et al. Eosinophilic Esophagitis in Children: Symptoms, Histology and pH Probe Results. *J Pediatr Gastroenterol Nutr.* 2004; 39:373–377. [PubMed: 15448427]
58. Desai TK, Stecevic V, Chang CH, et al. Association of eosinophilic inflammation with esophageal food impaction in adults. *Gastrointest Endosc.* 2005; 61:795–801. [PubMed: 15933677]
59. Liacouras CA, Spergel JM, Ruchelli E, et al. Eosinophilic esophagitis: a 10-year experience in 381 children. *Clin Gastroenterol Hepatol.* 2005; 3:1198–206. [PubMed: 16361045]
60. Cherian S, Smith NM, Forbes DA. Rapidly increasing prevalence of eosinophilic oesophagitis in Western Australia. *Arch Dis Child.* 2006; 91:1000–4. [PubMed: 16877474]
61. Gonsalves N, Policarpio-Nicolas M, Zhang Q, et al. Histopathologic variability and endoscopic correlates in adults with eosinophilic esophagitis. *Gastrointest Endosc.* 2006; 64:313–9. [PubMed: 16923475]
62. Parfitt JR, Gregor JC, Suskin NG, et al. Eosinophilic esophagitis in adults: distinguishing features from gastroesophageal reflux disease: a study of 41 patients. *Mod Pathol.* 2006; 19:90–6. [PubMed: 16258505]
63. Aceves SS, Newbury RO, Dohil R, et al. Distinguishing eosinophilic esophagitis in pediatric patients: clinical, endoscopic, and histologic features of an emerging disorder. *J Clin Gastroenterol.* 2007; 41:252–6. [PubMed: 17426462]
64. Chehade M, Sampson HA, Morotti RA, et al. Esophageal subepithelial fibrosis in children with eosinophilic esophagitis. *J Pediatr Gastroenterol Nutr.* 2007; 45:319–28. [PubMed: 17873744]
65. Cohen MS, Kaufman A, Dimarino AJ Jr, et al. Eosinophilic Esophagitis Presenting as Spontaneous Esophageal Rupture (Boerhaave's Syndrome). *Clin Gastroenterol Hepatol.* 2007; 5:A24. [PubMed: 16863702]
66. Kerlin P, Jones D, Remedios M, et al. Prevalence of eosinophilic esophagitis in adults with food bolus obstruction of the esophagus. *J Clin Gastroenterol.* 2007; 41:356–61. [PubMed: 17413601]
67. Pasha SF, DiBaise JK, Kim HJ, et al. Patient characteristics, clinical, endoscopic, and histologic findings in adult eosinophilic esophagitis: a case series and systematic review of the medical literature. *Dis Esophagus.* 2007; 20:311–9. [PubMed: 17617880]
68. Prasad GA, Talley NJ, Romero Y, et al. Prevalence and Predictive Factors of Eosinophilic Esophagitis in Patients Presenting With Dysphagia: A Prospective Study. *Am J Gastroenterol.* 2007
69. Sundaram S, Sunku B, Nelson SP, et al. Adherent white plaques: an endoscopic finding in eosinophilic esophagitis. *J Pediatr Gastroenterol Nutr.* 2004; 38:208–12. [PubMed: 14734886]
70. Kaplan M, Mutlu EA, Jakate S, et al. Endoscopy in eosinophilic esophagitis: "feline" esophagus and perforation risk. *Clin Gastroenterol Hepatol.* 2003; 1:433–7. [PubMed: 15017642]
71. Straumann A, Rossi L, Simon HU, et al. Fragility of the esophageal mucosa: a pathognomonic endoscopic sign of primary eosinophilic esophagitis? *Gastrointest Endosc.* 2003; 57:407–12. [PubMed: 12612531]
72. Nurko S, Teitelbaum JE, Husain K, et al. Association of Schatzki ring with eosinophilic esophagitis in children. *J Pediatr Gastroenterol Nutr.* 2004; 38:436–41. [PubMed: 15085025]
73. Straumann A, Spichtin HP, Bucher KA, et al. Eosinophilic esophagitis: red on microscopy, white on endoscopy. *Digestion.* 2004; 70:109–16. [PubMed: 15383737]
74. Prasad GA, Arora AS. Spontaneous perforation in the ringed esophagus. *Dis Esophagus.* 2005; 18:406–9. [PubMed: 16336613]
75. Mecklenburg I, Weber C, Folwaczny C. Spontaneous recovery of dysphagia by rupture of an esophageal diverticulum in eosinophilic esophagitis. *Dig Dis Sci.* 2006; 51:1241–2. [PubMed: 16944019]
76. Zuber-Jerger I, Ratiu N, Kullman F. Long-lasting effect of endoscopic dilatation of an esophageal stenosis due to eosinophilic esophagitis. *J Gastrointest Liver Dis.* 2006; 15:167–70. [PubMed: 16802012]

77. Lee GS, Craig PI, Freiman JS, et al. Intermittent Dysphagia for solids associated with a multiringed esophagus: clinical features and response to dilatation. *Dysphagia*. 2007; 22:55–62. [PubMed: 17216404]
78. Lucendo AJ, Pascual-Turrión JM, Navarro M, et al. Endoscopic, bioptic, and manometric findings in eosinophilic esophagitis before and after steroid therapy: a case series. *Endoscopy*. 2007; 39:765–71. [PubMed: 17703383]
79. Muller S, Puhl S, Vieth M, et al. Analysis of symptoms and endoscopic findings in 117 patients with histological diagnoses of eosinophilic esophagitis. *Endoscopy*. 2007; 39:339–44. [PubMed: 17427070]
80. Zeiter DK, Hyams JS. Gastroesophageal reflux: pathogenesis, diagnosis, and treatment. *Allergy Asthma Proc*. 1999; 20:45–9. [PubMed: 10076709]
81. 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. [PubMed: 12738455]
82. Noel RJ, Putnam PE, Collins MH, et al. Clinical and immunopathologic effects of swallowed fluticasone for eosinophilic esophagitis. *Clin Gastroenterol Hepatol*. 2004; 2:568–75. [PubMed: 15224281]
83. Stein ML, Collins MH, Villanueva JM, et al. Anti-IL-5 (mepolizumab) therapy for eosinophilic esophagitis. *J Allergy Clin Immunol*. 2006; 118:1312–9. [PubMed: 17157662]
84. Shah A, Hirano I. Treatment of eosinophilic esophagitis: drugs, diet, or dilation? *Curr Gastroenterol Rep*. 2007; 9:181–8. [PubMed: 17511914]
85. Dellon ES, Aderoju A, Woosley JT, et al. Variability in Diagnostic Criteria for Eosinophilic Esophagitis: A Systematic Review. *Am J Gastroenterol*. 2007
86. 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. [PubMed: 17919504]
87. 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. quiz 21–2. [PubMed: 21477849]
88. Dellon ES, Gonsalves N, Hirano I, et al. ACG clinical guideline: Evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis (EoE). *Amer J Gastroenterol*. 2013; 108:679–92. quiz 693. [PubMed: 23567357]
89. Papadopoulou A, Koletzko S, Heuschkel R, et al. Management guidelines of eosinophilic esophagitis in childhood. *J Pediatr Gastroenterol Nutr*. 2014; 58:107–18. [PubMed: 24378521]
90. Focht DR, Kaul A. Food impaction and eosinophilic esophagitis. *J Pediatr*. 2005; 147:540. [PubMed: 16227043]
91. Lucendo Villarin AJ, Carrion Alonso G, Navarro Sanchez M, et al. Eosinophilic esophagitis in adults, an emerging cause of dysphagia. Description of 9 cases. *Rev Esp Enferm Dig*. 2005; 97:229–39. [PubMed: 15982178]
92. Luis AL, Rinon C, Encinas JL, et al. Non stenotic food impaction due to eosinophilic esophagitis: a potential surgical emergency. *Eur J Pediatr Surg*. 2006; 16:399–402. [PubMed: 17211786]
93. Smith CR, Miranda A, Rudolph CD, et al. Removal of impacted food in children with eosinophilic esophagitis using Saeed banding device. *J Pediatr Gastroenterol Nutr*. 2007; 44:521–3. [PubMed: 17414157]
94. Nonevski IT, Downs-Kelly E, Falk GW. Eosinophilic esophagitis: an increasingly recognized cause of dysphagia, food impaction, and refractory heartburn. *Cleve Clin J Med*. 2008; 75:623–6. 629–33. [PubMed: 18788223]
95. Hurtado CW, Furuta GT, Kramer RE. Etiology of esophageal food impactions in children. *J Pediatr Gastroenterol Nutr*. 2011; 52:43–6. [PubMed: 20975581]
96. Sperry SL, Crockett SD, Miller CB, et al. Esophageal foreign-body impactions: epidemiology, time trends, and the impact of the increasing prevalence of eosinophilic esophagitis. *Gastrointest Endo*. 2011; 74:985–91.

97. El-Matary W, El-Hakim H, Popel J. Eosinophilic esophagitis in children needing emergency endoscopy for foreign body and food bolus impaction. *Pediatr Emerg Care*. 2012; 28:611–3. [PubMed: 22743755]
98. Akyuz U, Akyuz F, Ozdil K, et al. Food impaction in older age: Think about an eosinophilic esophagitis. *World journal of gastrointestinal endoscopy*. 2013; 5:79–80. [PubMed: 23422854]
99. Hudson S, Sampson C, Muntz HR, et al. Foreign Body Impaction as Presentation of Eosinophilic Esophagitis. *Otolaryngology*. 2013
100. Straumann A, Bussmann C, Zuber M, et al. Eosinophilic esophagitis: analysis of food impaction and perforation in 251 adolescent and adult patients. *Clin Gastroenterol Hepatol*. 2008; 6:598–600. [PubMed: 18407800]
101. Lucendo AJ, Friginal-Ruiz AB, Rodriguez B. Boerhaave's syndrome as the primary manifestation of adult eosinophilic esophagitis. Two case reports and a review of the literature. *Dis Esophag*. 2011; 24:E11–5.
102. Fontillon M, Lucendo AJ. Transmural eosinophilic infiltration and fibrosis in a patient with non-traumatic Boerhaave's syndrome due to eosinophilic esophagitis. *Amer J Gastroenterol*. 2012; 107:1762. [PubMed: 23160304]
103. Hirano I. Editorial: Should patients with suspected eosinophilic esophagitis undergo a therapeutic trial of proton pump inhibition? *Amer J Gastroenterol*. 2013; 108:373–5. [PubMed: 23459046]
104. Molina-Infante J, Ferrando-Lamana L, Ripoll C, et al. Esophageal eosinophilic infiltration responds to proton pump inhibition in most adults. *Clin Gastroenterol Hepatol*. 2010
105. Molina-Infante J, Zamorano J. Distinguishing eosinophilic esophagitis from gastroesophageal reflux disease upon PPI refractoriness: what about PPI-responsive esophageal eosinophilia? *Digestion*. 2012; 85:210. [PubMed: 22354119]
106. Zhang X, Cheng E, Huo X, et al. Omeprazole blocks STAT6 binding to the eotaxin-3 promoter in eosinophilic esophagitis cells. *PloS one*. 2012; 7:e50037. [PubMed: 23185525]
107. 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*. 2013; 62:824–32. [PubMed: 22580413]
108. Straumann A. The natural history and complications of eosinophilic esophagitis. *Thor Surg Clin*. 2011; 21:575–87.
109. Schoepfer AM, Safroneeva E, Bussmann C, et al. Delay in Diagnosis of Eosinophilic Esophagitis Increases Risk for Stricture Formation, in a Time-Dependent Manner. *Gastroenterology*. 2013
110. Blanchard C, Wang N, Stringer KF, et al. Eotaxin-3 and a uniquely conserved gene-expression profile in eosinophilic esophagitis. *J Clin Invest*. 2006; 116:536–547. [PubMed: 16453027]
111. Rothenberg ME, Mishra A, Collins MH, et al. Pathogenesis and clinical features of eosinophilic esophagitis. *J Allergy Clin Immunol*. 2001; 108:891–4. [PubMed: 11742263]
112. Mishra A, Hogan SP, Brandt EB, et al. IL-5 promotes eosinophil trafficking to the esophagus. *J Immunol*. 2002; 168:2464–9. [PubMed: 11859139]
113. Mishra A, Hogan SP, Brandt EB, et al. Enterocyte expression of the eotaxin and interleukin-5 transgenes induces compartmentalized dysregulation of eosinophil trafficking. *J Biol Chem*. 2002; 277:4406–12. [PubMed: 11733500]
114. Mishra A, Rothenberg ME. Intratracheal IL-13 induces eosinophilic esophagitis by an IL-5, eotaxin-1, and STAT6-dependent mechanism. *Gastroenterology*. 2003; 125:1419–27. [PubMed: 14598258]
115. Rothenberg ME, Spergel JM, Sherrill JD, et al. Common variants at 5q22 associate with pediatric eosinophilic esophagitis. *Nat Genet*. 2010; 42:289–91. [PubMed: 20208534]
116. Sherrill JD, Gao PS, Stucke EM, et al. Variants of thymic stromal lymphopoietin and its receptor associate with eosinophilic esophagitis. *J Allergy Clin Immunol*. 2010; 126:160–5 e3. [PubMed: 20620568]
117. Masterson JC, McNamee EN, Hosford L, et al. Local hypersensitivity reaction in transgenic mice with squamous epithelial IL-5 overexpression provides a novel model of eosinophilic oesophagitis. *Gut*. 2012

118. Niranjani R, Rayapudi M, Mishra A, et al. Pathogenesis of allergen-induced eosinophilic esophagitis is independent of interleukin (IL)-13. *Immunol Cell Biol.* 2013; 91:408–15. [PubMed: 23689305]
119. Noti M, Wojno ED, Kim BS, et al. Thymic stromal lymphopoietin-elicited basophil responses promote eosinophilic esophagitis. *Nat Med.* 2013; 19:1005–13. [PubMed: 23872715]
120. Wen T, Stucke EM, Grotjan TM, et al. Molecular Diagnosis of Eosinophilic Esophagitis by Gene Expression Profiling. *Gastroenterology.* 2013
121. Ngo P, Furuta G, Antonioli D, et al. Eosinophils in the Esophagus - Peptic or Allergic Eosinophilic Esophagitis? Case series of three patients with esophageal eosinophilia. *Am J Gastroenterol.* 2006
122. Dohil R, Newbury RO, Aceves S. Transient PPI responsive esophageal eosinophilia may be a clinical sub-phenotype of pediatric eosinophilic esophagitis. *Dig Dis Sci.* 2012; 57:1413–9. [PubMed: 22134787]
123. Schroeder S, Capocelli KE, Masterson JC, et al. Effect of proton pump inhibitor on esophageal eosinophilia. *J Pediatr Gastroenterol Nutr.* 2013; 56:166–72. [PubMed: 23325438]
124. Pentiu S, Putnam PE, Collins MH, et al. Dissociation between symptoms and histological severity in pediatric eosinophilic esophagitis. *J Pediatr Gastroenterol Nutr.* 2009; 48:152–60. [PubMed: 19179876]
125. Furuta GT, Kagalwalla AF, Lee JJ, et al. The oesophageal string test: a novel, minimally invasive method measures mucosal inflammation in eosinophilic oesophagitis. *Gut.* 2013; 62:1395–405. [PubMed: 22895393]
126. Lao-Sirieix P, Boussioutas A, Kadri SR, et al. Non-endoscopic screening biomarkers for Barrett's oesophagus: from microarray analysis to the clinic. *Gut.* 2009; 58:1451–9. [PubMed: 19651633]
127. Kwiatek MA, Hirano I, Kahrilas PJ, et al. Mechanical properties of the esophagus in eosinophilic esophagitis. *Gastroenterology.* 2011; 140:82–90. [PubMed: 20858491]
128. Lin Z, Kahrilas PJ, Xiao Y, et al. Functional luminal imaging probe topography: an improved method for characterizing esophageal distensibility in eosinophilic esophagitis. *Ther Adv Gastroenterol.* 2013; 6:97–107.
129. Nicodeme F, Hirano I, Chen J, et al. Esophageal Distensibility as a Measure of Disease Severity in Patients With Eosinophilic Esophagitis. *Clin Gastroenterol Hepatol.* 2013
130. Dellon ES, Irani AM, Hill MR, et al. Development and field testing of a novel patient-reported outcome measure of dysphagia in patients with eosinophilic esophagitis. *Aliment Pharm Ther.* 2013
131. Franciosi JP, Hommel KA, Bendo CB, et al. PedsQL eosinophilic esophagitis module: feasibility, reliability, and validity. *J Pediatr Gastroenterol Nutr.* 2013; 57:57–66. [PubMed: 23478422]
132. Franciosi JP, Hommel KA, DeBrosse CW, et al. Development of a validated patient-reported symptom metric for pediatric eosinophilic esophagitis: qualitative methods. *BMC Gastroenterology.* 2011; 11:126. [PubMed: 22099448]
133. Franciosi JP, Hommel KA, Greenberg AB, et al. Development of the Pediatric Quality of Life Inventory TM Eosinophilic Esophagitis Module items: qualitative methods. *BMC Gastroenterology.* 2012; 12:135. [PubMed: 23009120]
134. Taft TH, Kern E, Kwiatek MA, et al. The adult eosinophilic oesophagitis quality of life questionnaire: a new measure of health-related quality of life. *Aliment Pharm Ther.* 2011; 34:790–8.
135. Hirano I, Moy N, Heckman MG, et al. Endoscopic assessment of the oesophageal features of eosinophilic oesophagitis: validation of a novel classification and grading system. *Gut.* 2013; 62:489–95. [PubMed: 22619364]
136. Fiorentino R, Liu G, Pariser AR, et al. Cross-sector sponsorship of research in eosinophilic esophagitis: a collaborative model for rational drug development in rare diseases. *J Allergy Clin Immunol.* 2012; 130:613–6. [PubMed: 22857796]
137. Rothenberg ME, Aceves S, Bonis PA, et al. Working with the US Food and Drug Administration: progress and timelines in understanding and treating patients with eosinophilic esophagitis. *J Allergy Clin Immunol.* 2012; 130:617–9. [PubMed: 22935588]

Key Points

- Mild to severe dysphagia and food impaction are the most common symptoms of eosinophilic esophagitis in adults and teenagers
- Vomiting, feeding difficulties and abdominal pain are the most common symptoms of eosinophilic esophagitis in children.
- Eosinophilic esophagitis is diagnosed by clinical features and esophageal biopsy.