



The Global Face of Eosinophilic Esophagitis: Advocacy and Research Groups

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Abstract

Although eosinophilic esophagitis (EoE) has been described in the literature for a substantial period, its recognition as a disease entity on the global stage is still relatively new. It has become a major diagnosis of consideration by medical providers when both adult and pediatric patients present with dysphagia, food impaction, and gastroesophageal reflux-like symptoms. In addition to the clinical work of specialists such as allergy-immunologists and gastroenterologists, the evolution of research organizations and advocacy groups focused on EoE have greatly assisted in bringing attention to, and raising awareness about, this disease. As a result of their efforts, diagnosis and treatment guidelines have been developed, and medical providers now have a specific ICD code for EoE. This represents a new model for the interaction of patients and medical provider, where patients not only advocate for their disorder, but also drive physician education and a patient-centered research agenda and its funding. It should be noted, though, that these organizations and advocacy groups are mainly located in North America and Europe, and as a result, EoE has largely been associated with the Caucasian demographic. However, it has been described in Asia, the Middle East, Latin America, and Africa. Physicians from these areas have increased awareness and understanding in the medical and research communities in their countries through case reports and the establishment and analysis of potential patient cohorts. At this time, the prevalence of EoE in these regions is comparably lower, but this may be due to less recognition and understanding of EoE, as well as medical efforts being directed towards more ubiquitous disease processes, such as infectious diseases. With the support and ongoing work of researchers, patients, and their family members, understanding and recognition of EoE as a clinically significant disease entity will continue to grow.

Keywords Eosinophilic esophagitis · Global advocacy · Research groups · Guidelines · ICD

Abbreviations

EoE Eosinophilic esophagitis
GERD Gastroesophageal reflux

Introduction

Eosinophilic esophagitis (EoE), a chronic allergic/immune condition characterized by eosinophilic infiltration of the

esophagus leading to esophageal dysfunction, may be considered a relatively new disease in that a formal name and description of this disease came forth only in the last two decades. The first descriptions of EoE occurred in the late 1970s to early 1980s, during which gastroenterologists reported cases of patients whose complaints of dysphagia or achalasia were found to be in the setting of extensive eosinophils found in the esophagus, an organ typically free of these types of cells [1, 2].

As EoE has emerged as one of the major causes of dysphagia and food impaction in adults, as well as gastroesophageal reflux (GERD)-like symptoms in children, the push for awareness and advocacy has also increased; however, these social aspects of the disease have not expanded as quickly to some parts of the world. This article seeks to review the history of EoE from an advocacy standpoint, both in the clinical and research settings.

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Recognition of Eosinophilic Esophagitis as a Disease

Two investigations by Attwood et al. and Straumann et al. were among the first to attempt to describe eosinophilic esophagitis by both its clinical symptoms and pathology [3, 4], though the latter was the first to coin the term for this disease process. Key clinical findings from the case series noted that patients experienced dysphagia with a notably normal pH and elevated eosinophils in the esophagus. Both also emphasized the importance of performing endoscopy to obtain mucosal biopsies of the esophagus to make the diagnosis, but this procedure was not commonplace at that time, leading to underdiagnosis.

It should be noted that the above series were done in adults, and recognition of EoE in the pediatric community occurred as a result of routine biopsies done during endoscopy. This method of practice became the standard of care due to the fact that pediatric patients could have normal-appearing mucosa on endoscopy, but inflammation would be present by histology [5]. Children complained of similar symptoms as adults with EoE and were also found to have similar pathology with dense eosinophil infiltrates in the esophagus [6, 7].

The Rise in Literature

As the number of patients with findings consistent with EoE began to rise, so too did the number of publications. Prior to 2000, the rate of publication on EoE was about 0–1 per year, whereas in 2013, this rate increased to >200 publications [8]. This change in number could be attributed to a variety of reasons.

Attention had turned to demographic parameters, as the disease was noted to be more common than previously expected—Rothenberg et al. reported an incidence rate of at least 1 in 10,000 Caucasian males [9]. Researchers then began to consider associated risk factors or an underlying mechanism for the development of this health process. It had been noted that both adult and pediatric patients in some of the groups seemed to have atopic disease as well, particularly food allergy, eczema, and asthma. Focus also turned to potential therapeutic options. These included elimination diets of the six most common food allergens, inhaled corticosteroids, immune therapy, and dilatation for fixed narrowing [10–15].

Development of Formal Guidelines Around the World

Part of the gap in such a difference in publication rate could be attributed to a lack of formal criteria to make a definitive diagnosis of eosinophilic esophagitis. There had been ongoing debate regarding which clinical characteristics and pathology requirements should be used in order to define EoE, and one systematic review demonstrated a significant amount of variability in diagnostic criteria [16]; however, in 2006, the North

American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) held the First International Gastrointestinal Eosinophil Research Symposium (FIGERS). This multidisciplinary task force consisted of 31 physicians who developed diagnostic recommendations and treatment options, and in the year after the meeting, published the First Consensus Recommendations [17]. These recommendations were taken from a systematic review of the literature, in addition to the expert opinion of the symposium's participants. The International Gastrointestinal Research Symposium (TIGERS) presented another consensus report in 2011 after a survey from the American Academic of Allergy, Asthma, and Immunology (AAAAI) and NASPGHAN revealed that only one third of physicians were following the 2007 guidelines [18, 19].

Following these consensus reports, other international groups developed their own guidelines as well. In 2016, members from the United European Gastroenterology (UEG), the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), the European Academy of Allergy and Clinical Immunology (EAACI), and the European Society of Eosinophilic Oesophagitis (EUREOS) formed a Working Committee to publish a European set of guidelines [20]. The updated Food Allergy Practice Parameters from the AAAAI in 2014 also included summary statements regarding evaluation of EoE [21], particularly in regard to diagnosis. Interestingly, these directives from US-based and European-based groups seemed to be used as standards across the world, as other regions did not seem to develop specific guidelines of their own.

Development of ICD Codes

Although eosinophilic esophagitis had been recognized as a distinct disease in 1995, official coding from the International Classification of Diseases was not approved until 2008 [22]. Until that point, coding had largely relied on symptoms associated with the disease or disease processes with similar clinical presentations. However, with the advent of guidelines from TIGERS and the strong advocacy efforts of the American Partnership for Eosinophilic Disorders (APFED), eosinophilic esophagitis was designated with the ICD-9 classification 530.13 [23]. This code was updated in 2015 to K20.0 in alignment with ICD-10 classification.

Advocacy and Research Groups for EoE

Much of the recognition that EoE received as a unique disease could be credited to a number of advocacy organizations. Some of these groups grew out of necessity for parents whose children were struck with symptoms that had not been seen before in the medical community, and the rarity of the clinical presentation at the time resulting

in a dearth of dedicated research, particularly in relation to treatment. Others were started by clinician and research experts from multiple fields who came together to provide a forum for both eosinophilic awareness and ongoing research (Table 1).

American Partnership for Eosinophilic Disorders (APFED)

APFED was the most important advocacy organization to be created for patients with eosinophilic disorders, and it was the first one to be accepted as an expansion of the AAAAI lay organizations committee [24]. The group was formed in 2001 by three parents and was able to achieve nonprofit status within the same year. Their initial efforts focused on bringing parents of children with eosinophilia together in an annual conference and writing a newsletter solely dedicated to raise awareness and increase education about eosinophilic disease.

However, members of the organization felt that their advocacy goals should go further in differentiating the types of eosinophilic diseases and ensuring their recognition in the larger medical community. This conviction led to the development of specific ICD codes for EoE and sponsorship of TIGERS. In addition, APFED encouraged research on this health problem by creating grants through the Hope on the Horizon Research Program [25]. The HOPE grants are unique to APFED, but the organization also collaborates with a number of organizations to provide funding. Its connection with the AAAAI gives awards to early career investigators who are interested in EoE research, and the Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR) receives supplemental funding from APFED. Through its collaboration with NASPGHAN and the American Gastroenterology Association (AGA), APFED provides smaller monetary awards for outstanding research abstracts at national conferences.

Campaign Urging Research for Eosinophilic Disease (CURED)

Like APFED, the Campaign Urging Research for Eosinophilic Disease (CURED) grew out of a necessity from families caring for members with eosinophilic disease [26]. The main focus of the organization is to raise money towards eosinophilic disease research, especially in regard to finding a cure. Their website features the stories of multiple children living with eosinophilic diseases such as EoE, and it highlights multiple ongoing clinical trials that patients may be eligible to join. The organization has also organized multiple patient education conferences, which help families to understand both the medical and social aspects of the disease. CURED has raised 4 million dollars, to date, towards eosinophilic research funding through local and national fundraisers.

Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR)

The Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR) is part of the Rare Disease Clinical Research Network (RDCRN), which is a National Institutes of Health (NIH)-funded group [27]. It is a multidisciplinary team that relies on expertise from pediatric and adult gastroenterologists, allergists, immunologists, and pathologists, and it seeks to improve patient care in eosinophilic gastrointestinal disorders through research, clinical expertise, and education. The disorders that CEGIR is focused on include eosinophilic esophagitis, eosinophilic gastritis (EG), and eosinophilic colitis (EC).

CEGIR has four primary cores: Clinical Research Projects 1 and 2, a Pilot/Demonstration Clinical Research Program, and the Training (Career Development) Program. Clinical Research Project 1 is called the OMEGA Trial (Outcome Measures for Eosinophilic Gastrointestinal Diseases Across

Table 1 Advocacy and research organizations for eosinophilic esophagitis

Patient advocacy groups	Both started by pediatric patients' parents.
APFED	Primarily involved in ICD coding, development of guidelines for eosinophilic disease, education/awareness, research funding
CURED	Focused primarily on awareness through fundraising for research efforts.
Research organizations	
CEGIR	All three professional organizations are comprised of physicians and researchers across fields dedicated to research in eosinophilic disease. Contributions include: -Diagnosis and management guidelines for eosinophilic disease -Development of research studies -Increasing awareness of eosinophilic disease in the medical community and among the public -Training and grant funding for new investigators
EUREOS	
IES	

Ages). It is a multicenter, longitudinal study of children and adults with EoE, EG, and EC, and it seeks to correlate clinical outcome measures with mucosal eosinophil counts and to correlate the molecular profile of these diseases with clinical outcomes measures and mucosal eosinophilia. Clinical Research Project 2 is called the SOFEED Trial (Six Versus One Food Eosinophilic Esophagitis Diet). It is a multicenter study that aims to compare the efficacy of a one-food elimination diet versus six-food elimination diets, to see if patients remain responsive to swallowed glucocorticoids if they fail either elimination diets, and to develop a personalized treatment approach based on biomarker analysis.

The Pilot/Demonstration Clinical Research Program supports two Pilot/Demonstration Clinical Research Projects each year that are focused on investigating EoE, EG, and EC. The project funding lasts for 2 years and encourages collaboration among CEGIR members and members outside of CEGIR. The Training (Career Development) Program is dedicated to training new investigators in clinical and translational research in eosinophilic gastrointestinal disease.

European Society of Eosinophilic Oesophagitis (EUREOS)

The European Society of Eosinophilic Oesophagitis (EUREOS) is a nonprofit organization comprised of eosinophilic esophagitis professionals in medicine and research [28]. Members hail from 11 countries: Belgium, Finland, France, Germany, Italy, Netherlands, Portugal, Spain, Sweden, Switzerland, and the UK, and their professions include adult and pediatric gastroenterology, allergy, immunology, and pathology. The goal of this international organization is to coordinate education and research specific to eosinophilic esophagitis. Its website also serves as a portal to connect patients in the region to EoE centers for evaluation and treatment.

Most recently, the group released its first consensus document that determined a new definition for proton pump inhibitor-responsive esophageal eosinophilia (PPI-REE) [29]. Prior to this, there had been questions regarding the location of PPI-REE on the spectrum of disease between EoE and GERD; however, the EUREOS task force report provided new recommendations. In addition, its members have published multiple research articles on EoE, which are summarized on the organization's website. These articles assist in providing the public more information about the evolving knowledge on EoE and future directions of research.

International Eosinophil Society (IES)

The International Eosinophil Society (IES) is an organization solely focused on research surrounding eosinophilic disease that was started in 1999 [30]. For a time, the organization struggled to find its footing in terms of

establishing itself as a needed entity, as the significance of eosinophils was questioned in the scientific community; however, with continued perseverance by its members, the group now has an official constitution and interactive membership. The society also hosts a biennial symposium featuring the most up-to-date research on eosinophils from around the world.

How Global Is Eosinophilic Esophagitis?

A majority of EoE cases seem to be located in the USA, Western Europe, and Australia, and this coincides with the most commonly described demographic of the EoE patient: Caucasian male. This data is likely skewed by the fact that these regions have developed large cohorts from which to study the disease, and the advocacy organizations that have been started to bring recognition to this disease process are largely from these areas of the world. Also, despite guidelines to guide the diagnosis, these recommendations were not present until 2007, and even then, multiple physicians were not necessarily following these guidelines. EoE has also evolved such that there seems to be a growing spectrum rather than only one type of the disease. However, the concern for EoE among patients is evident in other regions, including countries in Latin America, East and Southeast Asia, the Middle East, and Africa (Fig. 1).

Among the Hispanic population, it has been observed that the overall prevalence seems to be lower when compared to studies done in Caucasian populations. A study done by Yu et al. evaluated complaints of dysphagia and/or food impaction among Hispanic and Caucasian patients through esophagogastroduodenoscopy (EGD) and esophageal biopsies. Caucasian patients had at least a three- to sevenfold increase in EoE diagnosis when compared to Hispanic patients [31]. Of note, the aforementioned study was done in two medical centers within the USA with high proportions of Hispanic patients. However, studies completed in medical centers in Mexico also confirmed the idea that EoE is a less prevalent diagnosis. In Northeastern Mexico, EoE was the cause of refractory gastroesophageal reflux disease (GERD) symptoms in 4% of the patients examined [32], while patients from medical facilities in Southeastern Mexico only had a 1.7% prevalence of EoE [33]. Reasons for these differences have been hypothesized, including environmental, cultural, or racial factors, but still need to be extensively studied.

In East and Southeast Asia, EoE is garnering more interest among the medical community. The first case was reported in 2007 in a Japanese patient [34], and since that time, EoE has been recognized as a disease entity in South Korea [35], Thailand [36], India [37], and China [38]. In the latter two countries, studies had been conducted to hypothesize about disease prevalence. Baruah et al. evaluated EoE in patients

Fig. 1 Map of global distribution of EoE reports



from a hospital in northern India who had symptoms suggestive of GERD and found the prevalence in their group to be 3.2% [39]. A retrospective analysis of 3490 patients within a Chinese hospital system who underwent EGD and subsequent esophageal biopsies found that the esophageal biopsies of 12 patients met the criteria for EoE diagnosis (0.34%) [40]. The clinical characteristics that warranted these interventions included dysphagia, GERD-like symptoms, abdominal pain, chest pain, and chronic cough.

EoE has also become a pediatric concern in countries in the Middle East. Two retrospective chart analyses conducted by hospitals in Saudi Arabia identified at least 3/351 patients and 15/229 patients with EoE by histology and clinical context. [40, 41] These studies attempted to find specific clinical characteristics within their populations, with Hasosah et al. noting that failure to thrive and abdominal pain in school-aged, atopic males seemed to be the most common features [40]. However, in the second study, dysphagia followed by vomiting and epigastric pain was the most dominant characteristic [41]. Another Saudi Arabian study noted the importance of esophageal trachealization as a potential feature of EoE [42]. In Turkey, at least four case reports have been published with five patients who presented with dysphagia and were then diagnosed with EoE [43–46]. One study in Israel looked at pediatric and adult gastroenterologist management of EoE, suggesting that the disease has gained enough of a foothold in the medical community there to look at and address variations in practice [47].

At this time, there is very little information regarding the prevalence of EoE within Africa. One cohort has been described out of Cape Town, South Africa, in which eight patients were diagnosed with EoE and were placed on treatment with subsequent improvement [48]. It is not clear whether this is due to differences in presentation that have not yet been noted or differences in physician practice in regard to gastrointestinal diseases. Countries in this region may also be focusing their research efforts on other disease processes that are more prevalent in their societies, such as infectious diseases.

Conclusion

Despite its relatively new presence on the scene, EoE has become a significant health concern, particularly in the gastroenterology and allergy/immunology community. The amount of research has nearly doubled annually within the last 10 years, and this is due in large part to the advocacy efforts of both patients and researchers. It should be noted, though, that these organizations are largely in North America and Europe. Although EoE is not as prevalent in other regions of the world, this may be due in part to a lack of knowledge about EoE on the part of physicians and researchers in these regions, or focus being given to other more prevalent disease entities. However, this may change over time, as further advocacy and research opportunities get underway in the future.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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References

- Landres RT, Kuster GG, Strum WB (1978) Eosinophilic esophagitis in a patient with vigorous achalasia. *Gastroenterology* 74:1298–1301
- Picus D, Frank PH (1981) Eosinophilic esophagitis. *AJR Am J Roentgenol* 136:1001–1003
- Attwood SEA, Smyrk TC, Demeester TC, Jones JB (1993) Esophageal eosinophilia with dysphagia. A distinct clinicopathologic syndrome. *Dig Dis Sci* 38:109–116
- Straumann A, Spichtin HP, Bernoulli R, Loosli J, Vögtlin J (1994) Idiopathic eosinophilic esophagitis: a frequently overlooked disease with typical clinical aspects and discrete endoscopic findings. *Schweiz Med Wochenschr* 124:1419–1429
- Schmidt-Sommerfeld E, Kirschner BS, Stephens JK (1990) Endoscopic and histologic findings in the upper gastrointestinal tract of children with Crohn's disease. *J Pediatr Gastroenterol Nutr* 11:448–454
- Liacouras CA, Wenner WJ, Brown K, Ruchelli E (1998) Primary eosinophilic esophagitis in children: successful treatment with oral corticosteroids. *J Pediatr Gastroenterol Nutr* 26:380–385
- Orenstein SR, Shalaby TM, Di Lorenzo C et al (2000) The spectrum of pediatric eosinophilic esophagitis beyond infancy: a clinical series of 30 children. *Am J Gastroenterol* 95:1422–1430
- Dellon E (2014) Epidemiology of eosinophilic esophagitis. *Gastroenterol Clin N Am* 43(2):201–218
- Noel RJ, Putnam PE, Rothenberg ME (2004) Eosinophilic esophagitis. *N Engl J Med* 351:940–941
- Kagalwalla AF, Sentongo TA, Ritz S, Hess T, Nelson SP, Emerick KM, Melin-Aldana H, Li BUK (2006) Effect of six-food elimination diet on clinical and histologic outcomes in eosinophilic esophagitis. *Clin Gastroenterol Hepatol* 4:1097–1102
- Spergel JM, Andrews T, Brown-Whitehorn TF et al (2005) Treatment of eosinophilic esophagitis with specific food elimination diet directed by a combination of skin prick and patch tests. *Ann Allergy Asthma Immunol* 95:336–343
- Aceves SS, Dohil R, Newbury RO, Bastian JF (2005) Topical viscous budesonide suspension for treatment of eosinophilic esophagitis. *J Allergy Clin Immunol* 116:705–706
- Aceves SS, Bastian JF, Newbury RO, Dohil R (2007) Oral viscous budesonide: a potential new therapy for eosinophilic esophagitis in children. *Am J Gastroenterol* 102:2271–2279
- Otani IM, Anilkumar AA, Newbury RO, Bhagat M, Beppu LY, Dohil R, Broide DH, Aceves SS (2013) Anti-IL-5 therapy reduces mast cell and IL-9 cell numbers in pediatric patients with eosinophilic esophagitis. *J Allergy Clin Immunol* 131:1576–1582
- Schoepfer AM, Gonsalves N, Bussmann C, Conus S, Simon HU, Straumann A, Hirano I (2010) Esophageal dilation in eosinophilic esophagitis: effectiveness, safety, and impact on the underlying inflammation. *Am J Gastroenterol* 105:1062–1070
- Dellon ES, Aderoju A, Woosley JT, Sandler RS, Shaheen NJ (2007) Variability in diagnostic criteria for eosinophilic esophagitis: a systematic review. *Am J Gastroenterol* 102(10):2300–2313
- Furuta GT, Liacouras CA, Collins MH, Gupta SK, Justinich C, Putnam PE, Bonis P, Hassall E, Straumann A, Rothenberg ME, First International Gastrointestinal Eosinophil Research Symposium (FIGERS) Subcommittees (2007) Eosinophilic esophagitis in children and adults: a systematic review and consensus recommendations for diagnosis and treatment. *Gastroenterology* 133(4):1342–1363
- Dellon ES, Aderoju A, Woosley JT et al (2007) Variability in Diagnostic Criteria for Eosinophilic Esophagitis: A Systematic Review. *Am J Gastroenterol* 102:2300–2313
- Liacouras CA, Furuta GT, Hirano I, Atkins D, Attwood SE, Bonis PA, Burks AW, Chehade M, Collins MH, Dellon ES, Dohil R, Falk GW, Gonsalves N, Gupta SK, Katzka DA, Lucendo AJ, Markowitz JE, Noel RJ, Odze RD, Putnam PE, Richter JE, Romero Y, Ruchelli E, Sampson HA, Schoepfer A, Shaheen NJ, Sicherer SH, Spechler S, Spergel JM, Straumann A, Wershil BK, Rothenberg ME, Aceves SS (2011) Eosinophilic esophagitis: updated consensus recommendations for children and adults. *J Allergy Clin Immunol* 128(1):3–20
- Lucendo AJ, Molina-Infante J, Arias A, von Arnim U, Bredenoord AJ, Bussmann C, Amil Dias J, Bove M, González-Cervera J, Larsson H, Miehke S, Papadopolou A, Rodríguez-Sánchez J, Ravelli A, Ronkainen J, Santander C, Schoepfer AM, Storr MA, Terreehorst I, Straumann A, Attwood SE (2017) Guidelines on eosinophilic esophagitis: evidence-based statements and recommendations for diagnosis and management in children and adults. *United European Gastroenterol J* 5(3):335–358
- Sampson HA, Aceves S, Bock SA, James J, Jones S, Lang D, Nadeau K, Nowak-Wegrzyn A, Oppenheimer J, Perry TT, Randolph C, Sicherer SH, Simon RA, Vickery BP, Wood R, Sampson HA, Randolph C, Bernstein D, Blessing-Moore J, Khan D, Lang D, Nicklas R, Oppenheimer J, Portnoy J, Randolph C, Schuller D, Spector S, Tilles SA, Wallace D, Sampson HA, Aceves S, Bock SA, James J, Jones S, Lang D, Nadeau K, Nowak-Wegrzyn A, Oppenheimer J, Perry TT, Randolph C, Sicherer SH, Simon RA, Vickery BP, Wood R (2014) Food allergy: a practice parameter update—2014. *J Allergy Clin Immunol* 134(5):1016–1025
- Rybnickie DA, Hathorn KE, Pfaff ER (2014) Administrative coding is specific, but not sensitive, for identifying eosinophilic esophagitis. *Dis Esophagus* 27(8):703–708
- Attwood S, Furuta GT (2014) Eosinophilic esophagitis: historical perspective on an evolving disease. *Gastroenterol Clin N Am* 43(2):185–199
- About APFED [Internet] 2001. [Cited 22 June 2017]. Available from: <http://apfed.org/about-apfed>
- APFED'S Hope on the Horizon Research Program [Internet] 2001. [Cited 22 June 2017]. Available from: <http://apfed.org/research/about-the-hope-on-the-horizon-research-fund>
- About CURED [Internet] 2015. [Cited 22 June 2017]. Available from: <https://curedfoundation.org/about-cured>
- About CEGIR [Internet] [Cited 22 June 2017]. Available from: <https://www.rarediseasesnetwork.org/cms/cegir/About-Us/CEGIR>
- European Society of Eosinophilic Oesophagitis (EUREOS) [Internet]. 2015. [Cited 22 June 2017]. Available from: <http://eureos.online>
- Molina-Infante J, Bredenoord AJ, Cheng E et al (2016) Proton pump inhibitor-responsive oesophageal eosinophilia: an entity challenging current diagnostic criteria for eosinophilic oesophagitis. *Gut* 65(3):524–531
- History of IES [Internet]. 2017. [Cited 22 June 2017]. Available from: <http://www.eosinophil-society.org/about-ies/history-of-ies>

31. Yu C, Sterling D, Albayati I, Al-Obaidi S, Moraveji S, Bustamante MA et al (2017) The prevalence of biopsy-proven eosinophilic esophagitis in Hispanics undergoing endoscopy is infrequent compared to Caucasians: a cross-sectional study. *Dig Dis Sci* 62(12): 3511–3516. <https://doi.org/10.1007/s10620-017-4791-8>
32. García-Compeán D, González González JA, Marrufo García CA, Flores Gutiérrez JP, Quintana OB, Rodríguez GG et al (2018) Causes of infrequent prevalence of eosinophilic esophagitis in Hispanics may involve social and cultural factors: probable role of digestive microbiota. *Dig Dis Sci* 63(2):534–535. <https://doi.org/10.1007/s10620-017-4902-6>
33. De la Cruz-Patiño E, Ruiz Juárez I, Meixueiro Daza A, Grube Pagola P, Roesch-Dietlen F, Remes-Troche JM (2015) Eosinophilic esophagitis prevalence in an adult population undergoing upper endoscopy in southeastern Mexico. *Dis Esophagus* 28: 524–529. <https://doi.org/10.1111/dote.12238>
34. Furuta K, Adachi K, Kowari K, Mishima Y, Imaoka H, Kadota C, Koshino K, Miyake T, Kadowaki Y, Furuta K, Kazumori H, Sato S, Ishihara S, Amano Y, Honda M, Kinoshita Y (2006) A Japanese case of eosinophilic esophagitis. *J Gastroenterol* 41:706–710. <https://doi.org/10.1007/s00535-006-1827-9>
35. Kim NI, Jo Y, Ahn SB, Son BK, Kim SH, Park YS (2010) A case of eosinophilic esophagitis with food hypersensitivity. *J Neurogastroenterol Motil* 16(3):315–318. <https://doi.org/10.5056/jnm.2010>
36. Aswakul P, Janyangdikul P, Prachayakul V (2016) Thickened esophagus as an unusual manifestation of eosinophilic esophagitis. *Dis Esophagus* 29(6):681–683. <https://doi.org/10.1111/dote.12044>
37. Sandhya P, Danda D, Mathew J, Kurian S, Ramakrishna BS (2012) Eosinophilic esophagitis and pharyngitis presenting as mass lesion in a patient with inactive rheumatoid arthritis. *J Clin Rheumatol* 18: 33–35
38. Shi YN, Sun SJ, Xiong LS, Cao QH, Cui Y, Chen MH (2012) Prevalence, clinical manifestations and endoscopic features of eosinophilic esophagitis: a pathological review in China. *J Dig Dis* 13: 304–309. <https://doi.org/10.1111/j.1751-2980.2012.00593.x>
39. Baruah B, Kumar T, Das P, Thakur B, Sreenivas V, Ahuja V, Gupta SD, Makharia GK (2017) Prevalence of eosinophilic esophagitis in patients with gastroesophageal reflux symptoms: a cross-sectional study from a tertiary care hospital in North India. *Indian J Gastroenterol* 36(5):353–360. <https://doi.org/10.1007/s12664-017-0789-6>
40. Hasosah MY, Sukkar GA, Alsahafi AF, Thabit AO, Fakeeh ME, Al-Zahrani DM, Satti MB (2011) Eosinophilic esophagitis in Saudi children: symptoms, histology and endoscopy results. *Saudi J Gastroenterol* 17(2):119–123. <https://doi.org/10.4103/1319-3767.77242>
41. Assiri AM, Saeed A (2014) Incidence and diagnostic features of eosinophilic esophagitis in a group of children with dysphagia and gastroesophageal reflux disease. *Saudi Med J* 35(3):292–297
42. Al-Hussaini AA, Semaan T, El Hag IA (2009) Esophageal trachealization: a feature of eosinophilic esophagitis. *Saudi J Gastroenterol* 15(3):193–195. <https://doi.org/10.4103/1319-3767.54747>
43. Akyüz U, Akyüz F, Özdil K, Altun H, Ağan AF, Ağan A (2013) Food impaction in older age: think about an eosinophilic esophagitis. *World J Gastrointest Endosc* 5(2):79–80. <https://doi.org/10.4253/wjge.v5.i2.79>
44. Mungan Z, Pinarbaşı B, Kaymakoglu S (2007) Eosinophilic esophagitis: case report. *Turk J Gastroenterol* 18(2):100–102
45. Yilmaz O, Karagol HIE, Topal E et al (2014) Two cases of esophageal eosinophilia: eosinophilic esophagitis or gastro-esophageal reflux disease? *Pediatr Rep* 6(2):5160. <https://doi.org/10.4081/pr.2014.5160>
46. Destek S, Gul VO, Ahioglu S, Tatar Z, Erbil Y (2014) A rare cause of chronic dysphagia: eosinophilic esophagitis. *J Surg Case Rep* 2014(9):rju096. <https://doi.org/10.1093/jscr/rju096>
47. Zifman E, Banai H, Shamir R, Ringel-Kulka T, Zevit N (2018) Practice differences in the diagnosis and management of eosinophilic esophagitis among adult and pediatric gastroenterologists in Israel. *J Pediatr Gastroenterol Nutr*. <https://doi.org/10.1097/MPG.0000000000001909>
48. Levin M, Motala C (2011) Eosinophilic oesophagitis in Cape Town, South Africa. *Clin Transl Allergy* 1(Suppl 1):P26. <https://doi.org/10.1186/2045-7022-1-S1-P26>