Clinical manifestations and diagnosis of eosinophilic esophagitis (EoE)

AUTHORS: Peter A L Bonis, MD, Sandeep K Gupta, MD
SECTION EDITOR: Nicholas J Talley, MD, PhD
DEPUTY EDITOR: Kristen M Robson, MD, MBA, FACG

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Sep 2023.**
This topic last updated: **Sep 15, 2023.**

INTRODUCTION

Esophageal eosinophils were once considered to be a hallmark of gastroesophageal reflux disease. However, it has become apparent that the esophagus, which is normally devoid of eosinophils, is an immunologically active organ that is capable of recruiting eosinophils in response to a variety of stimuli.

When the gastrointestinal eosinophilia is limited to the esophagus, is accompanied by characteristic symptoms, and other causes of esophageal eosinophilia have been ruled out, it is termed eosinophilic esophagitis. A panel of experts defined eosinophilic esophagitis as "a chronic, immune/antigen-mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation" [1]. In the past, eosinophilic esophagitis was abbreviated as "EE," but because of confusion with erosive esophagitis, many prefer the abbreviation "EoE."

This topic will review the clinical manifestations and diagnosis of EoE in adults and children. The genetics, immunopathogenesis, and management of EoE; eosinophilic gastroenteritis; and other diseases with eosinophilic involvement of specific organs are discussed separately. (See "Eosinophilic esophagitis (EoE): Genetics and immunopathogenesis" and "Treatment of eosinophilic esophagitis (EoE)" and "Eosinophilic gastrointestinal diseases" and "Eosinophil biology and causes of eosinophilia", section on 'Disorders with eosinophilic involvement of specific organs'.)

EPIDEMIOLOGY

EoE has been reported in several countries in North and South America, Europe, Asia, and Australia. A study of a pathology database from the United States found that the disease has been detected in most states that reported data [2]. The results of one survey suggested there may be regional variation, with a higher prevalence in northeastern states and lower prevalence in western states [3]. The diagnosis also appeared to be more common in urban as opposed to rural settings. In contrast, another study that evaluated a national pathology database, revealed the opposite patterns with an increased odds of EoE in the west and in rural settings [4]. Prevalence within the United States may also differ between climate zones with a higher prevalence in cold and arid zones as compared with the tropical zones [5]. Seasonal exacerbations of symptoms that have been described suggested a possible role of aeroallergens [6-8].

Early reports of EoE described patients with multiple esophageal rings, which were attributed to gastroesophageal reflux disease or a congenital origin [9-12]. The assumed association with gastroesophageal reflux disease (GERD) was based upon the observation that biopsies from patients with a ringed esophagus had basal zone hyperplasia, papillary lengthening, and intraepithelial eosinophils, findings that are seen in patients with documented reflux disease. However, careful review of these reports has raised questions about the association with GERD, since many of the patients did not respond to antisecretory therapy or have objective evidence of reflux on a 24-hour pH study [13,14]. In addition, esophageal dilation in some of these patients was associated with deep mucosal tears and esophageal perforation, complications also seen in patients with EoE who undergo dilation [12,15-18].

The incidence of EoE appears to be increasing [19-23]. Some of the increase may be due to increased recognition of the disorder, but increased recognition is unlikely to fully account for the rising incidence. One reason that increased recognition is unlikely to be the sole explanation is that gastrointestinal barium radiography has been practiced for many decades and it is likely that the characteristic ringed pattern in the esophagus would have been described earlier. While some studies evaluating the prevalence of EoE in biopsy samples from patients undergoing endoscopy have not detected an increase [24,25], population-based studies have supported an increasing incidence:

- A population-based study evaluated the incidence of EoE in Olmsted County Minnesota over 30 years [26]. The incidence increased significantly during the last three of the five-year intervals examined (from 0.35 per 100,000 population between 1991 and 1995 to 9.45

per 100,000 between 2001 and 2005). The prevalence was estimated to be 55 per 100,000 in 2006.

- Two population-based studies from Switzerland concluded that the incidence of EoE was increasing, and in one study, the incidence was approaching that of inflammatory bowel disease [20,27].

- A population-based study in children focused on 103 patients who had been identified from a single institution's pathology database in Hamilton County, Ohio [19]. The overall incidence per 10,000 population was estimated to be 1.28 in 2003, an increase from 0.91 in 2000. The authors noted that the most recent incidence rates exceed those of inflammatory bowel disease in children.

Most adults have been males in their 20s or 30s, although later presentations have been described [15,28-30]. In a series of 31 adults (24 males and 7 females), the mean age at diagnosis was 34 years (range 14 to 77 years) [28]. Symptoms (predominantly dysphagia) had been present for an average of 4.5 years prior to diagnosis. The male predominance may be related to variations in a gene located on the X-chromosome that have been associated with EoE. (See "Eosinophilic esophagitis (EoE): Genetics and immunopathogenesis", section on 'Overview of pathogenesis'.)

Among children, the disease is also more common in males (71 percent in the series described above) [19]. In another pediatric population-based study, significantly more of those with EoE were White children (84 percent compared with 73 percent of the surrounding community as a whole) [31]. Pediatric patients with EoE were also more likely to be male compared with the general population (76 versus 48 percent).

There are limited data on risk factors for EoE [32,33]. In a case-control study that included 115 patients with EoE and 225 controls, patients with EoE were significantly less likely to have ever smoked cigarettes or actively use NSAIDs (odds ratio [OR] 0.36 and 0.47, respectively) [33]. However, there was no significant difference in rates of smoking or NSAID exposure between cases with or without fibrostenosing disease or among patients with a post-treatment histologic response. Other potential risk factors include antibiotic exposure, acid suppressive medication use, and admission to neonatal intensive care unit during childhood, whereas exposure to breastmilk may be protective [34,35]. Exposure to *Helicobacter pylori* may also be associated with a reduced risk of EoE [36]. It is unclear if this apparent protective effect is due to *H. pylori*-induced immunomodulation [37].

Subtypes — Three pathogenically distinct subtypes of EoE have been described. In a cross-sectional study in which an EoE diagnostic panel of 96 molecular targets, in tandem with

endoscopic and histological assessment, were used to evaluate adult and pediatric patients with active EoE, three distinct endotypes with unique features were identified [38]:

- **EoEe1** – A mild subtype with normal-appearing esophagus, and mild histological, endoscopic, and molecular changes.
- **EoEe2** – An inflammatory endotype with highest expression of inflammatory cytokines and steroid-responding genes and a steroid refractory phenotype.
- **EoEe3** – A fibrostenotic endotype associated with a narrow-caliber esophagus, and characterized by the highest degree of endoscopic and histological severity and the lowest expression of epithelial differentiation genes.

Additional studies are needed to determine if endophenotyping patients with EoE can effectively guide management and improve patient outcomes. (See 'Laboratory tests' below.)

CLINICAL MANIFESTATIONS

The clinical manifestations of EoE vary with age [39]. Adults and teenagers frequently present with dysphagia and food impactions, whereas in younger children, symptoms often include feeding difficulties, gastroesophageal reflux symptoms, and abdominal pain.

Clinical manifestations in adults — Common clinical manifestations seen in adults include [2,15,18,26,40-66]:

- Dysphagia
- Food impaction
- Chest pain that is often centrally located and may not respond to antacids
- Gastroesophageal reflux disease-like symptoms/refractory heartburn
- Upper abdominal pain

Dysphagia to solid foods is the most common symptom [2,40-44]. Up to 15 percent of patients being evaluated for dysphagia with endoscopy are found to have EoE [42,44,67]. A history of food impaction is present in up to 54 percent of patients [18,45,46] and esophageal strictures have been noted in up to 31 percent of patients [26,47-52]. In one community-based series, 17 of 31 patients presenting with food impaction over a three-year period were diagnosed with EoE [45]. Psychosocial factors such as anxiety and hypervigilance may contribute to symptom reporting, particularly after food impaction [66].

Esophageal dysmotility may also be observed, suggesting possible eosinophil involvement of the muscular layers of the esophagus [53,54,68-70]. High-resolution endoscopic ultrasonography in affected children and adults has shown expansion of the esophageal wall and all individual tissue layers [55-57]. In a study including 109 patients (mean age 37 years) with a recent diagnosis of EoE who underwent high-resolution esophageal manometry, 17 patients (15 percent) had an obstructive motor disorder (eg, achalasia, esophagogastric junction outlet obstruction [EGJOO]) [70].

EoE has been noted in 1 to 4 percent of patients with refractory reflux in prospective studies [43,71]. However, cost-effectiveness models suggest that evaluating for EoE in patients with refractory reflux is only cost-effective when the prevalence of EoE is greater than 8 percent [72].

Finally, spontaneous esophageal perforation (Boerhaave syndrome), esophageal perforation following endoscopy, and mucosal tears associated with endoscopy have been reported [15,17,18,58-60]. (See "Boerhaave syndrome: Effort rupture of the esophagus" and "Complications of endoscopic esophageal stricture dilation", section on 'Risk factors'.)

Clinical manifestations in children — Symptoms in children vary depending in part upon their age [19,73-78]. In one series, the most common presenting symptoms included [19]:

- Feeding dysfunction (median age 2.0 years)
- Vomiting (median age 8.1 years)
- Abdominal pain (median age 12.0 years)
- Dysphagia (median age 13.4 years)
- Food impaction (median age 16.8 years)

The possibility of disease progression was supported in a case-control study that suggested an increased rate of dysphagia (49 versus 6 percent) and food impaction (40 versus 3 percent) in children with esophageal eosinophilia who had been followed for an average of 15 years [79].

Feeding dysfunction continues to be defined but is an increasingly recognized presentation of EoE [80]. It includes failure to develop normal eating patterns (eg, not advancing past liquids or soft foods) and adopting coping strategies (eg, refusing to eat solids after previously eating them, eating slowly, chewing excessively, drinking excessive liquids with meals). In addition, studies suggested that failure to thrive is more common in Black pediatric patients with EoE [81].

Similar findings were described in a single center report involving a total of 381 children. The mean age was nine years and 66 percent were male. Patients most commonly presented with symptoms suggestive of gastroesophageal reflux (85 percent) or dysphagia (18 percent) [74].

The esophageal mucosa was abnormal by endoscopy in 68 percent, whereas in 32 percent it appeared normal despite severe histologic eosinophilia.

ASSOCIATIONS WITH OTHER DISORDERS

There is a strong association of EoE with allergic conditions such as food allergies, environmental allergies, asthma, and atopic dermatitis. It has been estimated that 28 to 86 percent of adults and 42 to 93 percent of children with EoE have another allergic disease [19,26,82-88]:

- In one series, 10 of 13 patients (77 percent) had a history of an allergic disorder defined as asthma, allergic rhinitis, urticaria, hay fever, atopic dermatitis, food allergy, or medicine allergy, and/or positive radioallergosorbent test (RAST) or positive allergic skin tests [89]. Twelve of 13 patients (92 percent) had an absolute peripheral eosinophilia, and 9 of 12 patients (75 percent) had concurrent eosinophilic gastroenteritis.
- In another report, 13 of 19 children (68 percent) had positive skin or RAST testing to a median of seven foods [82].
- In a third series, 18 of 23 adults (78 percent) had an atopic diathesis (most commonly allergic rhinitis) [83]. Most patients were sensitized to several environmental allergens.

An association with celiac disease has been reported in multiple studies, and in one series a response to a gluten-free diet was also noted [90,91]. In addition, an association with inflammatory bowel disease, chronic rhinosinusitis, connective tissue disorders, caustic injury, antibiotic exposure in infancy, herpes simplex virus esophagitis, and a Schatzki ring have also been described, although the strength of the associations is unclear [92-99].

DIAGNOSIS

Clinical suspicion and evaluation — The diagnosis of EoE is based upon symptoms, endoscopic appearance, and histological findings. EoE should be suspected in patients with chronic symptoms of esophageal dysfunction (eg, dysphagia, food impaction, food refusal, abdominal pain, heartburn, regurgitation, chest pain, odynophagia). A history of atopic comorbidities (eg, asthma, atopic dermatitis, allergic rhinitis, or immediate food-type allergies) and a family history of EoE or dysphagia should raise the index of suspicion. A history of esophageal perforation or severe pain after dilation of a stricture should also raise suspicion of this disorder.

The diagnosis is established by upper endoscopy with esophageal biopsies and an evaluation to exclude other disorders that can cause esophageal eosinophilia (table 1). Radiographic and laboratory findings may support the diagnosis and help establish baseline esophageal luminal integrity but are not required to establish the diagnosis. (See 'Differential diagnosis' below.)

Since the symptoms of EoE are not specific, the diagnosis may be missed. In one retrospective study that included 200 patients with symptomatic EoE, the median delay in diagnosis was six years (interquartile range 2 to 12 years) [100]. Increasing duration of delay in the diagnosis was associated with an increase in the prevalence of fibrotic features of EoE on biopsy and esophageal strictures.

Diagnostic criteria — The diagnosis of EoE requires all of the following [101]:

- Symptoms related to esophageal dysfunction.
- Eosinophil-predominant inflammation on esophageal biopsy, characteristically consisting of a peak value of ≥15 eosinophils per high power field (HPF) (or 60 eosinophils per mm^2).
- Exclusion of other causes that may be responsible for or contributing to symptoms and esophageal eosinophilia (table 2).

Diagnostic criteria for EoE have evolved since EoE was first conceptually defined. In contrast to prior guidelines, persistence of mucosal eosinophilia in the esophagus after two months of treatment with a high-dose proton pump inhibitor (PPI) (eg, twice daily) is no longer a diagnostic criterion for EoE [101,102]. The rationale for exclusion of a PPI trial is that patients with clinical and histologic features compatible with EoE but who respond histologically to a PPI, (PPI-responsive esophageal eosinophilia [PPI-REE]), do not appear to be distinct from those with EoE [102-111]. Furthermore, patients with an initial response to PPIs may subsequently develop recurrent symptoms and eosinophilia consistent with EoE [112]. It is also recognized that GERD and EoE frequently co-exist and PPIs can improve esophageal eosinophilia by mechanisms independent of their effect on gastric acid secretion [113]. PPI-responsive esophageal eosinophilia is therefore considered a subset of EoE rather than a distinct disease [101,114].

The requirement of more than 15 eosinophils per HPF as a cutoff has not been extensively validated. One study supporting this cutoff confirmed endoscopic healing and symptomatic improvement when eosinophil counts decreased below this threshold [115]. Ongoing studies are helping to further clarify whether different cutoffs may be better at discriminating those with EoE versus other disorders. It is possible, for example, that patients with persistent esophageal eosinophilia after treatment with a PPI but who do not reach the 15 eosinophils per HPF threshold may still respond to treatment for EoE.

Endoscopy — A variety of morphologic features in the esophagus have been described in patients with EoE and a classification and grading scheme for these findings has been proposed [28,116-121]. A scoring system that relies on the assessment of Exudate, Rings, Edema, Furrows and Strictures has been developed and validated in children and adults and may be useful in clinical trials [121-124]. However, the assessment of endoscopic severity varies between endoscopists [125]. In addition, the endoscopic appearance alone has limited utility in the diagnosis of EoE. A meta-analysis that compared 4678 patients with EoE and 2742 controls estimated the frequency of the following endoscopic features [126]:

- Stacked circular rings ("feline" esophagus) (picture 1): 44 percent
- Strictures (particularly proximal strictures) (image 1): 21 percent
- Attenuation of the subepithelial vascular pattern: 41 percent
- Linear furrows (picture 2): 48 percent
- Whitish specks (representing eosinophil microabscesses) (picture 1): 27 percent
- Small caliber esophagus: 9 percent

Individual endoscopic features suggestive of EoE had low sensitivity ranging from 15 to 48 percent but high specificity ranging from 90 to 95 percent. Positive and negative predictive values ranged from 51 to 73 percent and 74 to 83 percent, respectively. Given the low sensitivity of endoscopic findings for EoE and variable positive predictive value, histology remains important in making a diagnosis of EoE, regardless of the endoscopic appearance. (See 'Histology' below.)

Complications associated with endoscopy in patients with EoE (even in the absence of esophageal dilation) include esophageal perforation and mucosal tears [17,58-60].

Histology — Esophageal biopsies from patients with EoE show an increased number of eosinophils. The vast majority of patients have at least 15 eosinophils per high power field (peak value) in at least one biopsy specimen [101]. Esophageal eosinophilia in the absence of clinical features is not sufficient to make a diagnosis of EoE.

During endoscopy, biopsies should be obtained from the distal esophagus as well as either the mid or proximal esophagus [127]. The sensitivity of biopsies for diagnosing EoE depends upon the number of biopsies obtained:

- In a report of 66 adults, the sensitivity was 100 percent after obtaining five biopsies compared with 55 percent with one biopsy [47].
- A second study found that the sensitivity for two, three, and six biopsies was 84, 97, and 100 percent, respectively [128].

- A third series evaluated biopsies obtained from the mid and distal esophagus in 102 consecutive patients with EoE [129]. The probability of one, four, five, and six biopsy fragments containing >15 eosinophils per high power field was 0.63, 0.98, 0.99, and >0.99, respectively.

We suggest that two to four biopsies be obtained from the distal esophagus, as well as another two to four from the mid or proximal esophagus.

Biopsy specimens should be fixed in formalin or paraformaldehyde rather than Bouin's fixative since formalin is more effective at preserving the integrity of eosinophils. Immunohistochemical studies have demonstrated that the number of eosinophils and amount of degranulation are underestimated by standard (hematoxylin and eosin) staining, although the clinical relevance for making a diagnosis is unclear [130].

As noted above, a threshold of 15 eosinophils per high power field is generally required for the diagnosis (picture 3) [131]. Approaches to improved diagnostic accuracy (and response to treatment) continue to be evaluated. One approach involves a scoring system (the EoE Histology Scoring system [EoEHSS]) that evaluates certain histologic features such basal zone hyperplasia [132]. The EoEHSS can discriminate between treated and untreated patients and provides a comprehensive assessment of esophageal mucosa.

Other histologic findings suggestive of EoE include [103,131,133-140]:

- Eosinophil microabscesses
- Superficial layering of eosinophils
- Sheets of eosinophils
- Extracellular eosinophil granules
- Subepithelial and lamina propria fibrosis and inflammation
- Basal cell hyperplasia
- Papillary lengthening
- Increased numbers of mast cells, B cells, and IgE-bearing cells

The association between histologic findings and symptoms is incompletely understood. Some studies suggest that histologic findings correlate with symptom severity [2,104,141,142], but discordant data have also been published [42,49,73,143]. One of the most detailed studies found that symptoms were only modestly predictive of histologic or endoscopic findings [144].

Biopsies of the gastric antrum and duodenum should also be obtained in patients with symptoms suggestive of eosinophilic gastroenteritis (eg, abdominal pain, nausea, vomiting, diarrhea, weight loss, ascites), visible mucosal abnormalities, or when there is a high index of

suspicion [101]. Establishing the diagnosis of eosinophilic gastroenteritis rather than/in addition to EoE is important since it will influence treatment [102]. More controversial is the presence of incidental gastric eosinophils in patients without compatible symptoms. At least one report found that such patients had a similar clinical presentation and response to treatment as patients with EoE who did not have gastric eosinophilia [145]. There are renewed interests in gastrointestinal eosinophilia including nomenclature [146]. (See "Eosinophilic gastrointestinal diseases".)

Radiology — Barium studies are not sensitive for diagnosing EoE, but can help characterize anatomic abnormalities and provide information on the length and diameter of strictures [147,148]. Findings described in patients with EoE undergoing barium studies include strictures and a ringed esophagus (picture 4) [120]. In addition, other causes for symptoms can be ruled out (eg, malrotation as a cause for vomiting). In addition, barium studies can help to assess luminal narrowing that is not evident at endoscopy [149,150]. They can be especially helpful in children or when combined with the use of a barium-coated pill [150].

Laboratory tests — Approximately 50 to 60 percent of patients with EoE will have elevated serum IgE levels (>114,000 units/L) [83,87]. Peripheral eosinophilia is seen in 40 to 50 percent of patients but is generally mild [48,75,151,152]. In some reports, the peripheral blood eosinophil level decreased with topical glucocorticoid therapy [153].

Genetic and molecular markers of disease activity continue to be studied [154]. A 96-gene EoE diagnostic panel, for example, has been developed based upon analysis of esophageal biopsies [155]. This diagnostic panel, which appears to be able to differentiate EoE from control individuals, including those with GERD, may also be able to differentiate patients with active and inactive disease and identify glucocorticoid exposure. Genetic testing for the EoE molecular transcriptome is commercially available but its role in clinical management is still evolving [38]. (See 'Subtypes' above.) Measurement of eosinophil progenitor cells correlate with histopathology and thus may provide a method of monitoring disease activity [156].

Evaluation for allergies — Because of the strong association of EoE with allergies, we suggest that patients with EoE undergo evaluation by an allergist. Children are often treated with dietary therapy, and uncontrolled data suggest that the information gained from allergy testing may help guide therapy. In addition, dietary therapy is sometimes used in the treatment of adults who are willing to make dietary modifications. Allergy testing may also help with the management of concomitant atopic disease, which is common in patients with EoE. (See "Treatment of eosinophilic esophagitis (EoE)", section on 'Dietary therapy' and "Overview of skin testing for IgE-mediated allergic disease" and "Diagnostic evaluation of IgE-mediated food allergy".)

Other diagnostic tests — Other diagnostic tests that have been evaluated but that are not routinely used include functional lumen imaging probe [157], endoscopic ultrasound [158,159], impedance planimetry to measure esophageal pressures and distensibility [160-162], mucosal impedance contour analysis that evaluates esophageal mucosal integrity [163], esophageal manometry [54,164,165], and endoscopic confocal laser microscopy [166,167]. In addition, an esophageal string test has been developed as a tool to measure esophageal inflammation in patients with esophagitis. In one study that included 41 children, measurement of eosinophil-derived protein biomarkers distinguished between children with active EoE, treated EoE in remission, GERD, and those with a normal esophagus [168,169].

The Cytosponge has been developed for use in diagnosis and monitoring of EoE. This test captures esophageal cells that can then be assessed for levels of eosinophil derived neurotoxin (EDN). In several studies of adult patients, the levels of EDN was highly correlated with mucosal eosinophilia [170-172].

Findings on standard esophageal manometry in most patients with EoE are nonspecific [54,164,165].

DEFINING DISEASE SEVERITY

Several instruments have been developed for assessment of disease severity that consider the range of findings associated with the disease. Some are used mainly for clinical trials while others were developed with an intention they be used for routine care, although adoption is mixed [173,174]. As an example, one instrument for patients with an established diagnosis of EoE is based on a scoring system developed by a panel of experts in gastroenterology and allergy immunology [175]. The following clinical features are assigned a point value ranging from 1 to 15 (see 'Diagnosis' above):

- Symptoms and associated complications – Symptom frequency, food impaction, hospitalization
- Endoscopic features – Edema, furrows, exudates, rings, strictures
- Histology – Eosinophil burden per high power field

The sum of the values determines the Index of Severity for Eosinophilic Esophagitis (I-SEE; mild [1 to 6 points], moderate [7 to 14 points] or severe [15 points or higher]). The severity index can be assessed at initial diagnosis and then at subsequent visits. Further studies that validate and refine the I-SEE are awaited before using it routinely in clinical practice. One study retrospectively examined I-SEE in data from prior randomized clinical trials [176].

DIFFERENTIAL DIAGNOSIS

The differential diagnosis includes a variety of conditions that can cause morphologic or histologic findings that resemble EoE.

Other causes of esophageal eosinophilia — Esophageal eosinophilia is the finding of eosinophils in the squamous epithelium of the esophagus [102]. Esophageal eosinophilia can be seen in association with multiple conditions. These include gastroesophageal reflux disease (GERD), recurrent vomiting due to other causes, parasitic and fungal infections, congenital rings, Crohn disease, periarteritis, allergic vasculitis, drug injury, connective tissue diseases, bullous pemphigoid, pemphigoid vegetans, graft-versus-host disease, achalasia, drug hypersensitivity, celiac disease, vasculitis, carcinoma, and a number of causes of peripheral eosinophilia in which the esophagus (along with other organ systems) may become involved (table 2). (See "Eosinophil biology and causes of eosinophilia", section on 'Disorders with eosinophilic involvement of specific organs'.)

There are occasional patients who have characteristic findings of esophageal rings but do not have esophageal eosinophilia. In addition to considering the diagnoses above, it is important to ensure that adequate biopsies were obtained. In our clinical experience, some of these patients have responded to dietary elimination therapy used to treat EoE. Whether such patients have eosinophilia in deeper layers of the esophagus not sampled by standard biopsies is unknown.

Distinction from GERD — The most common consideration in the differential diagnosis of EoE is GERD. Case reports have described children with a dense eosinophilic infiltrate that resolved after treatment with a proton pump inhibitor (PPI) alone [177], suggesting that the histologic findings may have been due to GERD:

- In a series of 36 children with ≥15 eosinophils/HPF, 14 (39 percent) responded histologically to high-dose PPIs alone [103].
- In a study of 712 patients with upper gastrointestinal symptoms undergoing endoscopy, 35 (5 percent) had ≥15 eosinophils/HPF on biopsies obtained from the upper-middle esophagus [178]. Twenty-six patients (75 percent) had a clinicopathologic remission on treatment with a PPI, including half of the patients with a typical EoE phenotype. Based upon these findings, the authors concluded that using histologic criteria alone to diagnose EoE may lead to an overestimation of the prevalence of the disorder.

Histologic features suggestive of EoE rather than GERD include:

- Large numbers of intraepithelial eosinophils on histologic examination [136,179-181]. In two reports, the presence of more than 20 eosinophils/HPF was typically associated with non-acid-related causes of esophagitis [181] and patients with EoE had significantly more eosinophils than patients who responded to therapy for GERD (28 to 31 versus 5 per HPF overall, and 19 to 32 versus 1 per HPF with biopsies from the proximal esophagus) [179]. Patients with EoE are also more likely to have ≥15 eosinophils/HPF in three or more biopsies taken at different levels [103].

- Other histologic findings favoring EoE include proximal esophageal involvement, subepithelial and lamina propria fibrosis [135], eosinophilic abscesses [75,180], more severe basal cell hyperplasia [182], activated mucosal mast cells/increased epithelial tryptase density [137,140,183,184], and degranulating eosinophils [48].

- Assessment of eotaxin-3 and major basic protein levels in esophageal biopsy specimens (by immunohistochemistry or real-time polymerase chain reaction [PCR]) has been suggested to help differentiate GERD from EoE, but further studies are needed [136,185,186]. (See "Eosinophilic esophagitis (EoE): Genetics and immunopathogenesis", section on 'Role of the immune system and environmental factors'.)

Prediction models have also been developed to identify patients with EoE and distinguish them from patients with GERD [48,180]. One such model that incorporated eight clinical and endoscopic features (younger age; male sex; presence of dysphagia and food allergies; presence of esophageal rings, furrows, and plaques; and lack of a hiatal hernia) predicted EoE with an accuracy, sensitivity, and specificity of 84, 97, and 92 percent, respectively [187].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Eosinophilic esophagitis".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more

sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

In addition, manufacturers of elemental formulas have template letters for medical necessity of amino acid diets available on their websites.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Upper endoscopy (The Basics)" and "Patient education: Eosinophilic esophagitis (The Basics)")
- Beyond the Basics topic (see "Patient education: Upper endoscopy (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Clinical presentation –** Eosinophilic esophagitis (EoE) should be considered in adults with a history of food impaction, with persistent dysphagia, or with gastroesophageal reflux disease that fails to respond to medical therapy. In children, symptoms that may be associated with EoE vary by age and include feeding disorders, vomiting, abdominal pain, dysphagia, and food impaction.

  In particular, the diagnosis should be considered in young males or boys, and in those with a history of food or environmental allergies, asthma, or atopy. A history of esophageal perforation or severe pain after dilation of a stricture should also raise suspicion of this disorder. (See 'Clinical manifestations' above and 'Clinical suspicion and evaluation' above.)

- **Diagnosis –** Making a diagnosis of EoE requires the presence of both symptoms and histologic findings. In addition, other disorders that can cause esophageal eosinophilia, should be ruled out. (See 'Diagnostic criteria' above and 'Differential diagnosis' above.)

  The diagnosis of EoE no longer requires a trial of proton pump inhibitor treatment.

  In patients suspected of having EoE, the first diagnostic test is typically an upper endoscopy with esophageal biopsies. We suggest that, at a minimum, two to four biopsies be obtained from the distal esophagus, as well as another two to four from the mid or proximal esophagus. (See 'Diagnosis' above.)

- **Endoscopic features –** A variety of morphologic features in the esophagus have been described in patients with EoE. Endoscopic findings include (see 'Endoscopy' above):
  - Stacked circular rings ("feline" esophagus) (picture 1)
  - Strictures (particularly proximal strictures) (image 1)
  - Attenuation of the subepithelial vascular pattern
  - Linear furrowing that may extend the entire length of the esophagus (picture 2)
  - Whitish papules (representing eosinophil microabscesses) (picture 1)
  - Small caliber esophagus
- **Histologic features –** Histologic findings suggestive of EoE include (see 'Histology' above):
  - Peak eosinophil count of ≥15 eosinophils per high power field (picture 3)
  - Eosinophil microabscesses
  - Superficial layering of eosinophils
  - Sheets of eosinophils
  - Extracellular eosinophil granules
  - Subepithelial and lamina propria fibrosis and inflammation
  - Basal cell hyperplasia
  - Papillary lengthening
- **Evaluation for allergies –** Because of the strong association of EoE with allergies, we suggest that patients with EoE undergo evaluation by an allergist. The results of the evaluation may have treatment implications (eg, elimination diets). (See "Allergy testing in eosinophilic esophagitis" and "Dietary management of eosinophilic esophagitis".)

ACKNOWLEDGMENT

The UpToDate editorial staff thank Dr. Glenn Furuta, MD, for his contributions as author to prior versions of this topic review.

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.

2. Kapel RC, Miller JK, Torres C, et al. Eosinophilic esophagitis: a prevalent disease in the United States that affects all age groups. Gastroenterology 2008; 134:1316.
3. Spergel JM, Book WM, Mays E, et al. Variation in prevalence, diagnostic criteria, and initial management options for eosinophilic gastrointestinal diseases in the United States. J Pediatr Gastroenterol Nutr 2011; 52:300.
4. Jensen ET, Hoffman K, Shaheen NJ, et al. Esophageal eosinophilia is increased in rural areas with low population density: results from a national pathology database. Am J Gastroenterol 2014; 109:668.
5. Hurrell JM, Genta RM, Dellon ES. Prevalence of esophageal eosinophilia varies by climate zone in the United States. Am J Gastroenterol 2012; 107:698.
6. Ram G, Lee J, Ott M, et al. Seasonal exacerbation of esophageal eosinophilia in children with eosinophilic esophagitis and allergic rhinitis. Ann Allergy Asthma Immunol 2015; 115:224.
7. Reed CC, Iglesia EGA, Commins SP, Dellon ES. Seasonal exacerbation of eosinophilic esophagitis histologic activity in adults and children implicates role of aeroallergens. Ann Allergy Asthma Immunol 2019; 122:296.
8. Wang FY, Gupta SK, Fitzgerald JF. Is there a seasonal variation in the incidence or intensity of allergic eosinophilic esophagitis in newly diagnosed children? J Clin Gastroenterol 2007; 41:451.
9. McKinley MJ, Eisner TD, Fisher ML, et al. Multiple rings of the esophagus associated with gastroesophageal reflux [case report]. Am J Gastroenterol 1996; 91:574.
10. Langdon DE. Corrugated ringed and too small esophagi. Am J Gastroenterol 1999; 94:542.
11. Katzka DA, Levine MS, Ginsberg GG, et al. Congenital esophageal stenosis in adults. Am J Gastroenterol 2000; 95:32.
12. Morrow JB, Vargo JJ, Goldblum JR, Richter JE. The ringed esophagus: histological features of GERD. Am J Gastroenterol 2001; 96:984.
13. Bousvaros A, Antonioli DA, Winter HS. Ringed esophagus: an association with esophagitis. Am J Gastroenterol 1992; 87:1187.
14. Gluck M, Schembre D, Jiranek G. Multiple esophageal rings: Histology, EUS, and manometric findings (abstract). Am J Gastroenterol 2001; 96:S14.
15. 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.

16. Vasilopoulos S, Murphy P, Auerbach A, et al. The small-caliber esophagus: an unappreciated cause of dysphagia for solids in patients with eosinophilic esophagitis. Gastrointest Endosc 2002; 55:99.
17. Cohen MS, Kaufman AB, Palazzo JP, et al. An audit of endoscopic complications in adult eosinophilic esophagitis. Clin Gastroenterol Hepatol 2007; 5:1149.
18. 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.
19. Noel RJ, Putnam PE, Rothenberg ME. Eosinophilic esophagitis. N Engl J Med 2004; 351:940.
20. Straumann A, Simon HU. Eosinophilic esophagitis: escalating epidemiology? J Allergy Clin Immunol 2005; 115:418.
21. Erwin EA, Asti L, Hemming T, Kelleher KJ. A decade of hospital discharges related to eosinophilic esophagitis. J Pediatr Gastroenterol Nutr 2012; 54:427.
22. Soon IS, Butzner JD, Kaplan GG, deBruyn JC. Incidence and prevalence of eosinophilic esophagitis in children. J Pediatr Gastroenterol Nutr 2013; 57:72.
23. Navarro P, Arias Á, Arias-González L, et al. Systematic review with meta-analysis: the growing incidence and prevalence of eosinophilic oesophagitis in children and adults in population-based studies. Aliment Pharmacol Ther 2019; 49:1116.
24. Lee JJ, Baker RD, Khan AR, Baker SS. Childhood esophagitis: then and now. J Pediatr Gastroenterol Nutr 2009; 48:37.
25. Vanderheyden AD, Petras RE, DeYoung BR, Mitros FA. Emerging eosinophilic (allergic) esophagitis: increased incidence or increased recognition? Arch Pathol Lab Med 2007; 131:777.
26. Prasad GA, Alexander JA, Schleck CD, et al. Epidemiology of eosinophilic esophagitis over three decades in Olmsted County, Minnesota. Clin Gastroenterol Hepatol 2009; 7:1055.
27. Hruz P, Straumann A, Bussmann C, et al. Escalating incidence of eosinophilic esophagitis: a 20-year prospective, population-based study in Olten County, Switzerland. J Allergy Clin Immunol 2011; 128:1349.
28. Croese J, Fairley SK, Masson JW, et al. Clinical and endoscopic features of eosinophilic esophagitis in adults. Gastrointest Endosc 2003; 58:516.
29. Dellon ES, Jensen ET, Martin CF, et al. Prevalence of eosinophilic esophagitis in the United States. Clin Gastroenterol Hepatol 2014; 12:589.
30. Trifan A, Stoica O, Chihaia CA, et al. Eosinophilic esophagitis in an octogenarian: A case report and review of the literature. Medicine (Baltimore) 2016; 95:e5169.

31. Franciosi JP, Tam V, Liacouras CA, Spergel JM. A case-control study of sociodemographic and geographic characteristics of 335 children with eosinophilic esophagitis. Clin Gastroenterol Hepatol 2009; 7:415.
32. Lipka S, Kumar A, Richter JE. Impact of Diagnostic Delay and Other Risk Factors on Eosinophilic Esophagitis Phenotype and Esophageal Diameter. J Clin Gastroenterol 2016; 50:134.
33. Koutlas NT, Eluri S, Rusin S, et al. Impact of smoking, alcohol consumption, and NSAID use on risk for and phenotypes of eosinophilic esophagitis. Dis Esophagus 2018; 31:1.
34. Witmer CP, Susi A, Min SB, Nylund CM. Early Infant Risk Factors for Pediatric Eosinophilic Esophagitis. J Pediatr Gastroenterol Nutr 2018; 67:610.
35. Jensen ET, Kuhl JT, Martin LJ, et al. Early-life environmental exposures interact with genetic susceptibility variants in pediatric patients with eosinophilic esophagitis. J Allergy Clin Immunol 2018; 141:632.
36. Shah SC, Tepler A, Peek RM Jr, et al. Association Between Helicobacter pylori Exposure and Decreased Odds of Eosinophilic Esophagitis-A Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol 2019; 17:2185.
37. Molina-Infante J, Gutierrez-Junquera C, Savarino E, et al. Helicobacter pylori infection does not protect against eosinophilic esophagitis: results from a large multicenter case-control study. Am J Gastroenterol 2018; 113:972.
38. Shoda T, Wen T, Aceves SS, et al. Eosinophilic oesophagitis endotype classification by molecular, clinical, and histopathological analyses: a cross-sectional study. Lancet Gastroenterol Hepatol 2018; 3:477.
39. Furuta GT, Katzka DA. Eosinophilic Esophagitis. N Engl J Med 2015; 373:1640.
40. Sgouros SN, Bergele C, Mantides A. Eosinophilic esophagitis in adults: a systematic review. Eur J Gastroenterol Hepatol 2006; 18:211.
41. 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.
42. 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; 102:2627.
43. García-Compeán D, González González JA, Marrufo García CA, et al. Prevalence of eosinophilic esophagitis in patients with refractory gastroesophageal reflux disease symptoms: A prospective study. Dig Liver Dis 2011; 43:204.

44. Mackenzie SH, Go M, Chadwick B, et al. Eosinophilic oesophagitis in patients presenting with dysphagia--a prospective analysis. Aliment Pharmacol Ther 2008; 28:1140.

45. Desai TK, Stecevic V, Chang CH, et al. Association of eosinophilic inflammation with esophageal food impaction in adults. Gastrointest Endosc 2005; 61:795.

46. Remedios M, Campbell C, Jones DM, Kerlin P. Eosinophilic esophagitis in adults: clinical, endoscopic, histologic findings, and response to treatment with fluticasone propionate. Gastrointest Endosc 2006; 63:3.

47. Gonsalves N, Policarpio-Nicolas M, Zhang Q, et al. Histopathologic variability and endoscopic correlates in adults with eosinophilic esophagitis. Gastrointest Endosc 2006; 64:313.

48. 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.

49. 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.

50. Bohm M, Richter JE, Kelsen S, Thomas R. Esophageal dilation: simple and effective treatment for adults with eosinophilic esophagitis and esophageal rings and narrowing. Dis Esophagus 2010; 23:377.

51. Kanakala V, Lamb CA, Haigh C, et al. The diagnosis of primary eosinophilic oesophagitis in adults: missed or misinterpreted? Eur J Gastroenterol Hepatol 2010; 22:848.

52. 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.

53. Lucendo AJ, Castillo P, Martín-Chávarri S, et al. Manometric findings in adult eosinophilic oesophagitis: a study of 12 cases. Eur J Gastroenterol Hepatol 2007; 19:417.

54. 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.

55. Fox VL, Nurko S, Teitelbaum JE, et al. High-resolution EUS in children with eosinophilic "allergic" esophagitis. Gastrointest Endosc 2003; 57:30.

56. Bhutani MS, Moparty B, Chaya CT, et al. Endoscopic ultrasound-guided fine-needle aspiration of enlarged mediastinal lymph nodes in eosinophilic esophagitis. Endoscopy 2007; 39 Suppl 1:E82.

57. Furuta K, Adachi K, Kowari K, et al. A Japanese case of eosinophilic esophagitis. J Gastroenterol 2006; 41:706.
58. Kaplan M, Mutlu EA, Jakate S, et al. Endoscopy in eosinophilic esophagitis: "feline" esophagus and perforation risk. Clin Gastroenterol Hepatol 2003; 1:433.
59. Shim LS, Grehan M. Education and Imaging. Gastrointestinal: oesophageal perforation during endoscopy for food impaction in eosinophilic oesophagitis. J Gastroenterol Hepatol 2010; 25:428.
60. Nantes O, Jiménez FJ, Zozaya JM, Vila JJ. Increased risk of esophageal perforation in eosinophilic esophagitis. Endoscopy 2009; 41 Suppl 2:E177.
61. Achem SR, Almansa C, Krishna M, et al. Oesophageal eosinophilic infiltration in patients with noncardiac chest pain. Aliment Pharmacol Ther 2011; 33:1194.
62. 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 Endosc 2011; 74:985.
63. Menard-Katcher P, Marks KL, Liacouras CA, et al. The natural history of eosinophilic oesophagitis in the transition from childhood to adulthood. Aliment Pharmacol Ther 2013; 37:114.
64. Mahesh VN, Holloway RH, Nguyen NQ. Changing epidemiology of food bolus impaction: is eosinophilic esophagitis to blame? J Gastroenterol Hepatol 2013; 28:963.
65. Okimoto K, Arai M, Ishigami H, et al. A Prospective Study of Eosinophilic Esophagitis and the Expression of Tight Junction Proteins in Patients with Gastroesophageal Reflux Disease Symptoms. Gut Liver 2018; 12:30.
66. Taft TH, Carlson DA, Simons M, et al. Esophageal Hypervigilance and Symptom-Specific Anxiety in Patients with Eosinophilic Esophagitis. Gastroenterology 2021; 161:1133.
67. Kidambi T, Toto E, Ho N, et al. Temporal trends in the relative prevalence of dysphagia etiologies from 1999-2009. World J Gastroenterol 2012; 18:4335.
68. Melchior C, Chiavelli H, Leroi AM, et al. Recovery of a "Jackhammer esophagus" after the treatment of an eosinophilic esophagitis. Am J Gastroenterol 2012; 107:952.
69. Spechler SJ, Konda V, Souza R. Can Eosinophilic Esophagitis Cause Achalasia and Other Esophageal Motility Disorders? Am J Gastroenterol 2018; 113:1594.
70. Ghisa M, Laserra G, Marabotto E, et al. Achalasia and Obstructive Motor Disorders Are Not Uncommon in Patients With Eosinophilic Esophagitis. Clin Gastroenterol Hepatol 2021; 19:1554.

71. Sá CC, Kishi HS, Silva-Werneck AL, et al. Eosinophilic esophagitis in patients with typical gastroesophageal reflux disease symptoms refractory to proton pump inhibitor. Clinics (Sao Paulo) 2011; 66:557.
72. Miller SM, Goldstein JL, Gerson LB. Cost-effectiveness model of endoscopic biopsy for eosinophilic esophagitis in patients with refractory GERD. Am J Gastroenterol 2011; 106:1439.
73. Baxi S, Gupta SK, Swigonski N, Fitzgerald JF. Clinical presentation of patients with eosinophilic inflammation of the esophagus. Gastrointest Endosc 2006; 64:473.
74. Liacouras CA, Spergel JM, Ruchelli E, et al. Eosinophilic esophagitis: a 10-year experience in 381 children. Clin Gastroenterol Hepatol 2005; 3:1198.
75. 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.
76. Gill R, Durst P, Rewalt M, Elitsur Y. Eosinophilic esophagitis disease in children from West Virginia: a review of the last decade (1995-2004). Am J Gastroenterol 2007; 102:2281.
77. Rodrigues M, D'Amico MF, Patiño FR, et al. Clinical manifestations, treatment, and outcomes of children and adolescents with eosinophilic esophagitis. J Pediatr (Rio J) 2013; 89:197.
78. Ettyreddy AR, Sink JR, Georg MW, et al. Association between Eosinophilic Esophagitis and Esophageal Food Impaction in the Pediatric Population. Otolaryngol Head Neck Surg 2018; 159:750.
79. DeBrosse CW, Franciosi JP, King EC, et al. Long-term outcomes in pediatric-onset esophageal eosinophilia. J Allergy Clin Immunol 2011; 128:132.
80. Mukkada VA, Haas A, Maune NC, et al. Feeding dysfunction in children with eosinophilic gastrointestinal diseases. Pediatrics 2010; 126:e672.
81. Edwards-Salmon S, Moraczewski J, Offerle T, et al. Comparing Eosinophilic Esophagitis in a Black and Non-Black Pediatric Cohort. J Pediatr Gastroenterol Nutr 2022; 75:485.
82. 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.
83. Roy-Ghanta S, Larosa DF, Katzka DA. Atopic characteristics of adult patients with eosinophilic esophagitis. Clin Gastroenterol Hepatol 2008; 6:531.
84. Almansa C, Krishna M, Buchner AM, et al. Seasonal distribution in newly diagnosed cases of eosinophilic esophagitis in adults. Am J Gastroenterol 2009; 104:828.

85. Moawad FJ, Veerappan GR, Lake JM, et al. Correlation between eosinophilic oesophagitis and aeroallergens. Aliment Pharmacol Ther 2010; 31:509.

86. 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.

87. Erwin EA, James HR, Gutekunst HM, et al. Serum IgE measurement and detection of food allergy in pediatric patients with eosinophilic esophagitis. Ann Allergy Asthma Immunol 2010; 104:496.

88. 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.

89. Vitellas KM, Bennett WF, Bova JG, et al. Idiopathic eosinophilic esophagitis. Radiology 1993; 186:789.

90. Quaglietta L, Coccorullo P, Miele E, et al. Eosinophilic oesophagitis and coeliac disease: is there an association? Aliment Pharmacol Ther 2007; 26:487.

91. Stewart MJ, Shaffer E, Urbanski SJ, et al. The association between celiac disease and eosinophilic esophagitis in children and adults. BMC Gastroenterol 2013; 13:96.

92. Limketkai BN, Shah SC, Hirano I, et al. Epidemiology and implications of concurrent diagnosis of eosinophilic oesophagitis and IBD based on a prospective population-based analysis. Gut 2019; 68:2152.

93. Padia R, Curtin K, Peterson K, et al. Eosinophilic esophagitis strongly linked to chronic rhinosinusitis. Laryngoscope 2016; 126:1279.

94. Abonia JP, Wen T, Stucke EM, et al. High prevalence of eosinophilic esophagitis in patients with inherited connective tissue disorders. J Allergy Clin Immunol 2013; 132:378.

95. Homan M, Orel R, Liacouras C. Caustic ingestion: a possible cause of eosinophilic esophagitis? Pediatrics 2013; 131:e1284.

96. Jensen ET, Kappelman MD, Kim HP, et al. Early life exposures as risk factors for pediatric eosinophilic esophagitis. J Pediatr Gastroenterol Nutr 2013; 57:67.

97. Zimmermann D, Criblez DH, Dellon ES, et al. Acute Herpes Simplex Viral Esophagitis Occurring in 5 Immunocompetent Individuals With Eosinophilic Esophagitis. ACG Case Rep J 2016; 3:165.

98. Sgouros SN, Bergele C, Mantides A. Schatzki's rings are not associated with eosinophilic esophagitis. Gastrointest Endosc 2006; 63:535.

99. Nurko S, Teitelbaum JE, Husain K, et al. Association of Schatzki ring with eosinophilic esophagitis in children. J Pediatr Gastroenterol Nutr 2004; 38:436.

100. 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; 145:1230.

101. Dellon ES, Liacouras CA, Molina-Infante J, et al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. Gastroenterology 2018; 155:1022.

102. 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). Am J Gastroenterol 2013; 108:679.

103. 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.

104. Peterson KA, Thomas KL, Hilden K, et al. Comparison of esomeprazole to aerosolized, swallowed fluticasone for eosinophilic esophagitis. Dig Dis Sci 2010; 55:1313.

105. Dranove JE, Horn DS, Davis MA, et al. Predictors of response to proton pump inhibitor therapy among children with significant esophageal eosinophilia. J Pediatr 2009; 154:96.

106. Molina-Infante J, Ferrando-Lamana L, Mateos-Rodríguez JM, et al. Overlap of reflux and eosinophilic esophagitis in two patients requiring different therapies: a review of the literature. World J Gastroenterol 2008; 14:1463.

107. Poh CH, Gasiorowska A, Navarro-Rodriguez T, et al. Upper GI tract findings in patients with heartburn in whom proton pump inhibitor treatment failed versus those not receiving antireflux treatment. Gastrointest Endosc 2010; 71:28.

108. Krarup AL, Villadsen GE, Mejlgaard E, et al. Acid hypersensitivity in patients with eosinophilic oesophagitis. Scand J Gastroenterol 2010; 45:273.

109. Schroeder S, Capocelli KE, Masterson JC, et al. Effect of proton pump inhibitor on esophageal eosinophilia. J Pediatr Gastroenterol Nutr 2013; 56:166.

110. Dellon ES, Speck O, Woodward K, et al. Clinical and endoscopic characteristics do not reliably differentiate PPI-responsive esophageal eosinophilia and eosinophilic esophagitis in patients undergoing upper endoscopy: a prospective cohort study. Am J Gastroenterol 2013; 108:1854.

111. Dellon ES, Speck O, Woodward K, et al. Markers of eosinophilic inflammation for diagnosis of eosinophilic esophagitis and proton pump inhibitor-responsive esophageal eosinophilia: a prospective study. Clin Gastroenterol Hepatol 2014; 12:2015.

112. 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.

113. 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.

114. Katzka DA. Eosinophilic esophagitis and proton pump-responsive esophageal eosinophilia: what is in a name? Clin Gastroenterol Hepatol 2014; 12:2023.

115. Reed CC, Wolf WA, Cotton CC, et al. Optimal Histologic Cutpoints for Treatment Response in Patients With Eosinophilic Esophagitis: Analysis of Data From a Prospective Cohort Study. Clin Gastroenterol Hepatol 2018; 16:226.

116. Siafakas CG, Ryan CK, Brown MR, Miller TL. Multiple esophageal rings: an association with eosinophilic esophagitis: case report and review of the literature. Am J Gastroenterol 2000; 95:1572.

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

118. Noel RJ, Putnam PE, Collins MH, et al. Clinical and immunopathologic effects of swallowed fluticasone for eosinophilic esophagitis. Clin Gastroenterol Hepatol 2004; 2:568.

119. Lim JR, Gupta SK, Croffie JM, et al. White specks in the esophageal mucosa: An endoscopic manifestation of non-reflux eosinophilic esophagitis in children. Gastrointest Endosc 2004; 59:835.

120. Zimmerman SL, Levine MS, Rubesin SE, et al. Idiopathic eosinophilic esophagitis in adults: the ringed esophagus. Radiology 2005; 236:159.

121. 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.

122. Wechsler JB, Bolton SM, Amsden K, et al. Eosinophilic Esophagitis Reference Score Accurately Identifies Disease Activity and Treatment Effects in Children. Clin Gastroenterol Hepatol 2018; 16:1056.

123. van Rhijn BD, Warners MJ, Curvers WL, et al. Evaluating the endoscopic reference score for eosinophilic esophagitis: moderate to substantial intra- and interobserver reliability. Endoscopy 2014; 46:1049.

124. Rodríguez-Sánchez J, Barrio-Andrés J, Nantes Castillejo O, et al. The Endoscopic Reference Score shows modest accuracy to predict either clinical or histological activity in adult patients with eosinophilic oesophagitis. Aliment Pharmacol Ther 2017; 45:300.

125. Schoepfer AM, Hirano I, Coslovsky M, et al. Variation in Endoscopic Activity Assessment and Endoscopy Score Validation in Adults With Eosinophilic Esophagitis. Clin Gastroenterol Hepatol 2019; 17:1477.

126. Kim HP, Vance RB, Shaheen NJ, Dellon ES. The prevalence and diagnostic utility of endoscopic features of eosinophilic esophagitis: a meta-analysis. Clin Gastroenterol Hepatol 2012; 10:988.

127. Collins MH. Histopathologic features of eosinophilic esophagitis. Gastrointest Endosc Clin N Am 2008; 18:59.

128. Shah A, Kagalwalla AF, Gonsalves N, et al. Histopathologic variability in children with eosinophilic esophagitis. Am J Gastroenterol 2009; 104:716.

129. Nielsen JA, Lager DJ, Lewin M, et al. The optimal number of biopsy fragments to establish a morphologic diagnosis of eosinophilic esophagitis. Am J Gastroenterol 2014; 109:515.

130. Mueller S, Aigner T, Neureiter D, Stolte M. Eosinophil infiltration and degranulation in oesophageal mucosa from adult patients with eosinophilic oesophagitis: a retrospective and comparative study on pathological biopsy. J Clin Pathol 2006; 59:1175.

131. 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.

132. Collins MH, Martin LJ, Alexander ES, et al. Newly developed and validated eosinophilic esophagitis histology scoring system and evidence that it outperforms peak eosinophil count for disease diagnosis and monitoring. Dis Esophagus 2017; 30:1.

133. Genta RM, Spechler SJ, Souza RF. The Twentieth Eosinophil. Adv Anat Pathol 2007; 14:340.

134. Chehade M, Sampson HA, Morotti RA, Magid MS. Esophageal subepithelial fibrosis in children with eosinophilic esophagitis. J Pediatr Gastroenterol Nutr 2007; 45:319.

135. Lee S, de Boer WB, Naran A, et al. More than just counting eosinophils: proximal oesophageal involvement and subepithelial sclerosis are major diagnostic criteria for eosinophilic oesophagitis. J Clin Pathol 2010; 63:644.

136. Protheroe C, Woodruff SA, de Petris G, et al. A novel histologic scoring system to evaluate mucosal biopsies from patients with eosinophilic esophagitis. Clin Gastroenterol Hepatol 2009; 7:749.

137. Kirsch R, Bokhary R, Marcon MA, Cutz E. Activated mucosal mast cells differentiate eosinophilic (allergic) esophagitis from gastroesophageal reflux disease. J Pediatr Gastroenterol Nutr 2007; 44:20.

138. Vicario M, Blanchard C, Stringer KF, et al. Local B cells and IgE production in the oesophageal mucosa in eosinophilic oesophagitis. Gut 2010; 59:12.

139. Mueller S, Neureiter D, Aigner T, Stolte M. Comparison of histological parameters for the diagnosis of eosinophilic oesophagitis versus gastro-oesophageal reflux disease on oesophageal biopsy material. Histopathology 2008; 53:676.

140. Dellon ES, Chen X, Miller CR, et al. Tryptase staining of mast cells may differentiate eosinophilic esophagitis from gastroesophageal reflux disease. Am J Gastroenterol 2011; 106:264.

141. Aceves SS, Ackerman SJ. Relationships between eosinophilic inflammation, tissue remodeling, and fibrosis in eosinophilic esophagitis. Immunol Allergy Clin North Am 2009; 29:197.

142. 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.

143. Pentiuk S, Putnam PE, Collins MH, Rothenberg ME. Dissociation between symptoms and histological severity in pediatric eosinophilic esophagitis. J Pediatr Gastroenterol Nutr 2009; 48:152.

144. Safroneeva E, Straumann A, Coslovsky M, et al. Symptoms Have Modest Accuracy in Detecting Endoscopic and Histologic Remission in Adults With Eosinophilic Esophagitis. Gastroenterology 2016; 150:581.

145. Ammoury RF, Rosenman MB, Roettcher D, Gupta SK. Incidental gastric eosinophils in patients with eosinophilic esophagitis: do they matter? J Pediatr Gastroenterol Nutr 2010; 51:723.

146. Dellon ES, Gonsalves N, Abonia JP, et al. International Consensus Recommendations for Eosinophilic Gastrointestinal Disease Nomenclature. Clin Gastroenterol Hepatol 2022; 20:2474.

147. Binkovitz LA, Lorenz EA, Di Lorenzo C, Kahwash S. Pediatric eosinophilic esophagitis: radiologic findings with pathologic correlation. Pediatr Radiol 2010; 40:714.

148. Nelson MJ, Miller FH, Moy N, et al. Comparison of endoscopy and radiographic imaging for detection of esophageal inflammation and remodeling in adults with eosinophilic esophagitis. Gastrointest Endosc 2018; 87:962.

149. Gentile N, Katzka D, Ravi K, et al. Oesophageal narrowing is common and frequently under-appreciated at endoscopy in patients with oesophageal eosinophilia. Aliment Pharmacol Ther 2014; 40:1333.

150. Menard-Katcher C, Swerdlow MP, Mehta P, et al. Contribution of Esophagram to the Evaluation of Complicated Pediatric Eosinophilic Esophagitis. J Pediatr Gastroenterol Nutr 2015; 61:541.

151. Dellon ES, Aderoju A, Woosley JT, et al. Variability in diagnostic criteria for eosinophilic esophagitis: a systematic review. Am J Gastroenterol 2007; 102:2300.

152. Chehade M, Sampson HA. Epidemiology and etiology of eosinophilic esophagitis. Gastrointest Endosc Clin N Am 2008; 18:33.

153. Straumann A, Conus S, Degen L, et al. Budesonide is effective in adolescent and adult patients with active eosinophilic esophagitis. Gastroenterology 2010; 139:1526.

154. Hines BT, Rank MA, Wright BL, et al. Minimally invasive biomarker studies in eosinophilic esophagitis: A systematic review. Ann Allergy Asthma Immunol 2018; 121:218.

155. Wen T, Stucke EM, Grotjan TM, et al. Molecular diagnosis of eosinophilic esophagitis by gene expression profiling. Gastroenterology 2013; 145:1289.

156. Schwartz JT, Morris DW, Collins MH, et al. Eosinophil progenitor levels correlate with tissue pathology in pediatric eosinophilic esophagitis. J Allergy Clin Immunol 2019; 143:1221.

157. Carlson DA. Editorial: Widening the Use of the Functional Lumen Imaging Probe to Kids With Eosinophilic Esophagitis: Esophageal Narrowing is not Just an Adult Problem. Am J Gastroenterol 2017; 112:1474.

158. Dalby K, Nielsen RG, Kruse-Andersen S, et al. Gastroesophageal reflux disease and eosinophilic esophagitis in infants and children. A study of esophageal pH, multiple intraluminal impedance and endoscopic ultrasound. Scand J Gastroenterol 2010; 45:1029.

159. Korsapati H, Babaei A, Bhargava V, et al. Dysfunction of the longitudinal muscles of the oesophagus in eosinophilic oesophagitis. Gut 2009; 58:1056.

160. Kwiatek MA, Hirano I, Kahrilas PJ, et al. Mechanical properties of the esophagus in eosinophilic esophagitis. Gastroenterology 2011; 140:82.

161. Roman S, Hirano I, Kwiatek MA, et al. Manometric features of eosinophilic esophagitis in esophageal pressure topography. Neurogastroenterol Motil 2011; 23:208.

162. Nicodème F, Hirano I, Chen J, et al. Esophageal distensibility as a measure of disease severity in patients with eosinophilic esophagitis. Clin Gastroenterol Hepatol 2013; 11:1101.

163. Patel DA, Higginbotham T, Slaughter JC, et al. Development and Validation of a Mucosal Impedance Contour Analysis System to Distinguish Esophageal Disorders. Gastroenterology 2019; 156:1617.

164. Martín Martín L, Santander C, Lopez Martín MC, et al. Esophageal motor abnormalities in eosinophilic esophagitis identified by high-resolution manometry. J Gastroenterol Hepatol

2011; 26:1447.

165. Moawad FJ, Maydonovitch CL, Veerappan GR, et al. Esophageal motor disorders in adults with eosinophilic esophagitis. Dig Dis Sci 2011; 56:1427.
166. Rogart JN, Nagata J, Loeser CS, et al. Multiphoton imaging can be used for microscopic examination of intact human gastrointestinal mucosa ex vivo. Clin Gastroenterol Hepatol 2008; 6:95.
167. Hiremath G, Gupta SK. Promising Modalities to Identify and Monitor Eosinophilic Esophagitis. Clin Gastroenterol Hepatol 2017; 15:1655.
168. 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.
169. Ackerman SJ, Kagalwalla AF, Hirano I, et al. One-Hour Esophageal String Test: A Nonendoscopic Minimally Invasive Test That Accurately Detects Disease Activity in Eosinophilic Esophagitis. Am J Gastroenterol 2019; 114:1614.
170. Katzka DA, Geno DM, Ravi A, et al. Accuracy, safety, and tolerability of tissue collection by Cytosponge vs endoscopy for evaluation of eosinophilic esophagitis. Clin Gastroenterol Hepatol 2015; 13:77.
171. Januszewicz W, Tan WK, Lehovsky K, et al. Safety and Acceptability of Esophageal Cytosponge Cell Collection Device in a Pooled Analysis of Data From Individual Patients. Clin Gastroenterol Hepatol 2019; 17:647.
172. Iqbal U, Siddique O, Ovalle A, et al. Safety and efficacy of a minimally invasive cell sampling device ('Cytosponge') in the diagnosis of esophageal pathology: a systematic review. Eur J Gastroenterol Hepatol 2018; 30:1261.
173. Schoepfer AM, Schürmann C, Trelle S, et al. Systematic Review of Outcome Measures Used in Observational Studies of Adults with Eosinophilic Esophagitis. Int Arch Allergy Immunol 2021; 182:1169.
174. Schoepfer AM, Straumann A, Panczak R, et al. Development and validation of a symptom-based activity index for adults with eosinophilic esophagitis. Gastroenterology 2014; 147:1255.
175. Dellon ES, Khoury P, Muir AB, et al. A Clinical Severity Index for Eosinophilic Esophagitis: Development, Consensus, and Future Directions. Gastroenterology 2022; 163:59.
176. Cotton CC, Moist SE, McGee SJ, et al. A Newly Proposed Severity Index for Eosinophilic Esophagitis is Associated With Baseline Clinical Features and Successful Treatment Response. Clin Gastroenterol Hepatol 2023; 21:2534.

177. Ngo P, Furuta GT, Antonioli DA, Fox VL. Eosinophils in the esophagus--peptic or allergic eosinophilic esophagitis? Case series of three patients with esophageal eosinophilia. Am J Gastroenterol 2006; 101:1666.

178. 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.

179. Walsh SV, Antonioli DA, Goldman H, et al. Allergic esophagitis in children: a clinicopathological entity. Am J Surg Pathol 1999; 23:390.

180. 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.

181. Steiner SJ, Gupta SK, Croffie JM, Fitzgerald JF. Correlation between number of eosinophils and reflux index on same day esophageal biopsy and 24 hour esophageal pH monitoring. Am J Gastroenterol 2004; 99:801.

182. Steiner SJ, Kernek KM, Fitzgerald JF. Severity of basal cell hyperplasia differs in reflux versus eosinophilic esophagitis. J Pediatr Gastroenterol Nutr 2006; 42:506.

183. Abonia JP, Blanchard C, Butz BB, et al. Involvement of mast cells in eosinophilic esophagitis. J Allergy Clin Immunol 2010; 126:140.

184. Sridhara S, Ravi K, Smyrk TC, et al. Increased numbers of eosinophils, rather than only etiology, predict histologic changes in patients with esophageal eosinophilia. Clin Gastroenterol Hepatol 2012; 10:735.

185. Bhattacharya B, Carlsten J, Sabo E, et al. Increased expression of eotaxin-3 distinguishes between eosinophilic esophagitis and gastroesophageal reflux disease. Hum Pathol 2007; 38:1744.

186. Dellon ES, Chen X, Miller CR, et al. Diagnostic utility of major basic protein, eotaxin-3, and leukotriene enzyme staining in eosinophilic esophagitis. Am J Gastroenterol 2012; 107:1503.

187. Dellon ES, Rusin S, Gebhart JH, et al. A Clinical Prediction Tool Identifies Cases of Eosinophilic Esophagitis Without Endoscopic Biopsy: A Prospective Study. Am J Gastroenterol 2015; 110:1347.

Topic 2243 Version 63.0

GRAPHICS

The International Gastrointestinal Eosinophil Researchers (TIGERS) Summary of 2011 eosinophilic esophagitis updated consensus recommendations

Below is a summary version of the 2011 consensus recommendations for eosinophilic esophagitis (EoE) diagnosis and treatment.[1] Since 2007, the number of EoE publications doubled, providing new disease insight. A panel of 33 physicians with expertise in pediatric and adult allergy/immunology, gastroenterology and pathology conducted a systematic review of the EoE literature (since September 2006) using electronic databases. Based on the literature review and expertise of the panel, a summary of the recommendations is provided here.

Conceptual definition - To refine perceptions and hypotheses for future EoE studies, the following conceptual definition was developed: "Eosinophilic esophagitis represents a chronic, immune/antigen mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation."

Diagnostic guidelines - Taking into account increasing clinical experiences and research, the following guidelines were proposed: "Eosinophilic esophagitis is a clinico-pathological disease. Clinically, EoE is characterized by symptoms related to esophageal dysfunction. Pathologically, one or more biopsies must show eosinophil predominant inflammation.* With few exceptions, 15 eosinophils/hpf (peak value) is considered a minimum threshold for a diagnosis of EoE. The disease is isolated to the esophagus and other causes of esophageal eosinophilia should be excluded, specifically proton pump inhibitor (PPI)-responsive esophageal eosinophilia.¶ (Table A). The disease should remit with treatments of dietary exclusion and/or topical corticosteroids. EoE should be diagnosed by clinicians taking into consideration all clinical and pathologic information; neither of these parameters should be interpreted in isolation.

Summary statements

History and physical - History should focus on difficulties with eating and swallowing (Table B) and a thorough physical examination should focus on growth and nutrition parameters and to assess potential other causes of esophagitis (Table A).

Endoscopy - Endoscopy with esophageal biopsy is considered the only reliable EoE diagnostic. Two to four biopsies each from the proximal and distal esophagus should be obtained. Gastric and duodenal biopsies should be examined to exclude other potential causes of eosinophil associated gastrointestinal disease (Table A). Endoscopic features can suggest but cannot diagnose EoE.

Radiography - An upper gastrointestinal series is useful to characterize anatomic abnormalities that may escape endoscopic detection such as proximal strictures and long segment narrowing.

Histopathology - See Diagnostic guidelines and Table C.

Allergic evaluation - An evaluation by an allergist or immunologist is recommended to document aeroallergen sensitization and seasonal variability as it may pertain to EoE and to control concurrent atopic diseases. Serum IgE and/or skin prick testing for immediate type hypersensitivity reactions to foods are warranted to help identify food allergic disease in patients with EoE.

Medically supervised food reintroduction may be necessary for patients with previous allergic reactions to a food or IgE-mediated sensitivity documented by IgE testing. Skin prick tests, serum IgE tests, and food patch tests may be used to help identify foods that are associated with EoE, but are **not** sufficient to make the diagnosis of food allergy driven EoE. Foods that trigger EoE can only be identified by documenting disease remission and recrudescence after specific food elimination and addition.

Genetics - EoE runs in families and although specific genes that pre-dispose to EoE susceptibility have been identified (thymic stromal lymphopoietin [TSLP], eotaxin-3), they are not yet ready for usage in clinical settings.

Treatments - (Table D).

Dietary therapy - Amino acid based formulas and dietary elimination are effective therapies for children with EoE and their use in adults requires further study. Patient's lifestyle, adherence to therapy and family resources should be considered when instituting these treatments. Consultation with a registered dietitian is strongly encouraged. EoE foods triggers may need to be restricted indefinitely.

Steroids - Topical corticosteroids are effective therapy for EoE in children and adults. Systemic corticosteroids may be used for emergent situations (severe dysphagia, hospitalization, weight loss) but caution is warranted for chronic management of EoE.

Other treatments - Cromolyn sodium, leukotriene receptor antagonists, and immunosuppressives (azathioprine or 6-mercaptopurine) are not recommended treatments for EoE. Biologic agents require further clinical studies and are currently not recommended for routine use.

Dilation - Esophageal dilation can provide relief of dysphagia in selected EoE patients. If high-grade esophageal stenosis is not present, a trial of medical or dietary therapy prior to esophageal dilation is reasonable.

Table A.[1] Conditions associated with esophageal eosinophilia

Gastroesophageal reflux disease (GERD)
Eosinophilic esophagitis (EoE)
Eosinophilic gastrointestinal diseases (EGIDs)
Celiac disease
Crohn's disease
Infection
Hypereosinophilic syndrome (HES)
Achalasia
Drug hypersensitivity
Vasculitis
Pemphigoid vegetans
Connective tissue disease

Graft versus host disease
Table B.[1] Symptoms related to EoE
Dysphagia and feeding dysfunction
Coping mechanisms - Avoiding highly textured foods such as meats and bulky foods such as bagels, cutting food in small pieces, lubricating foods before eating with liquids or butter, extensive chewing of foods, washing food down with liquids, prolongation of mealtimes
Food impaction
Coping mechanisms - Drinking liquid to wash food down, raising hands above head, jumping up and down, waiting for food to dissolve or to pass
Chest pain
Coping mechanisms - Avoiding foods or liquids that exacerbate pain such as highly textured or bulky foods, alcohol or acidic drinks
GERD like symptoms recalcitrant to medical and surgical GERD management
Abdominal pain
Vomiting
Anorexia and early satiety
Table C.[1] Histological characteristics of EoE
Mucosal eosinophilia
Eosinophil microabscesses
Superficial layering of eosinophils
Extracellular eosinophil granules
Surface epithelial desquamation
Basal zone hyperplasia
Rete peg elongation
Dilated intercellular spaces
Subepithelial fibrosis/sclerosis/lamina propria fibrosis
Table D.[1] Recommended initial treatments for EoE
Topical swallowed corticosteroids (initial doses)[2-4]
Fluticasone (spray metered dose inhaler directly in mouth then swallow)
Adults: 440 to 880 mcg twice daily
Children: 88 to 440 mcg twice to four times daily (maximum 1760 mcg per day)
Budesonide (as a compounded viscous suspension$^{\Delta}$)
Children (<10 years): 1 mg daily

Older children and adults: 2 mg daily
Following administration, patients should not rinse the mouth or eat or drink for 30 minutes
Systemic corticosteroids (severe disease)
Prednisone: 1 to 2 mg/kg per day by mouth in one or two divided doses (maximum 60 mg per day), taper after week 4[4]
Education, advocacy, and/or research support resources:
American Academy of Allergy, Asthma, and Immunology: www.aaaai.org
American Partnership for Eosinophilic Disorders: www.apfed.org
Campaign Urging Research for Eosinophilic Disorders: www.curedfoundation.org
Children's Digestive Health and Nutrition Foundation: https://naspghan.org/naspghan-foundation/
Food Allergy & Anaphylaxis Network: www.foodallergy.org
North American Society of Pediatric Gastroenterology and Nutrition: www.naspghan.org
Registry for Eosinophilic Gastrointestinal Disorders: https://www.rarediseasesnetwork.org/cms/cegir
TIGERS is grateful to the American Partnership for Eosinophilic Disorders for providing financial support of this summary document. APFED (www.apfed.org) is a 501(c)3 non-profit dedicated to education, advocacy, support and advancing research to improve the lives of those with eosinophil associated diseases. Content summarized by TIGERS.

EoE: eosinophilic esophagitis.

* For optimal pathological evaluation, multiple biopsies from the proximal and distal esophagus should be obtained and evaluated for a variety of pathological features. Pathologists should report all abnormalities associated with EoE such as the peak eosinophil count (obtained from the area with the highest density of eosinophils), eosinophilic microabscesses, surface layering of eosinophils, extracellular eosinophil granules, basal cell hyperplasia, dilated intercellular spaces, and lamina propria fibrosis. In a few circumstances, patients may have strong clinical evidence for EoE and have less than 15 eosinophils/hpf with other histological features indicative of eosinophilic inflammation.

¶ An emerging body of literature and clinical experience describes a subset of patients whose symptoms and histopathologic findings are responsive to PPI treatment and who may, or may not, have well documented gastroesophageal reflux disease (GERD). Until more is known, these patients should be diagnosed as "PPI-responsive esophageal eosinophilia."

Δ Viscous budesonide can be compounded by mixing two 0.5 mg/2 mL budesonide inhalation (Pulmicort Respule) ampules for nebulization with sucralose (Splenda), ten 1-gram packets per 1 mg of budesonide, creating a volume of approximately 8 mL[3].

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.*
2. *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.*

3. *Dohil R, Newbury R, Fox L, Bastian J, Aceves SS. Oral viscous budesonide is effective in children with eosinophilic esophagitis in a randomized, placebo-controlled trial. Gastroenterology 2010; 139:418.*
4. *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.*

Graphic 58642 Version 7.0

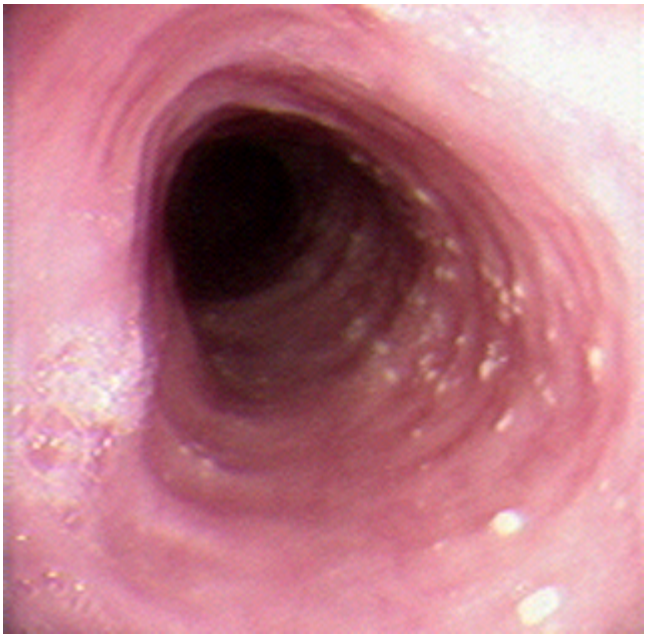
Conditions associated with esophageal eosinophilia

▪ Eosinophilic esophagitis
▪ Eosinophilic gastritis, gastroenteritis, or colitis with esophageal involvement
▪ Gastroesophageal reflux disease
▪ Achalasia and other disorders of esophageal dysmotility
▪ Hypereosinophilic syndrome
▪ Crohn's disease with esophageal involvement
▪ Infections (fungal, viral)
▪ Connective tissue disorders
▪ Hypermobility syndromes
▪ Autoimmune disorders and vasculitides
▪ Dermatologic conditions with esophageal involvement (ie, pemphigus)
▪ Drug hypersensitivity reactions
▪ Pill esophagitis
▪ Graft versus host disease
▪ Mendelian disorders (Marfan syndrome type II, hyper-IgE syndrome, PTEN hamartoma tumor syndrome, Netherton's syndrome, severe atopy metabolic wasting syndrome)

Reproduced from: Dellon ES, Liacouras CA, Molina-Infante, et al. Updated international consensus diagnostic criteria for eosinophilic esophagitis: Proceedings of the AGREE conference. Gastroenterology 2018. Table used with the permission of Elsevier Inc. All rights reserved.

Graphic 118557 Version 1.0

Endoscopic image of eosinophilic esophagitis

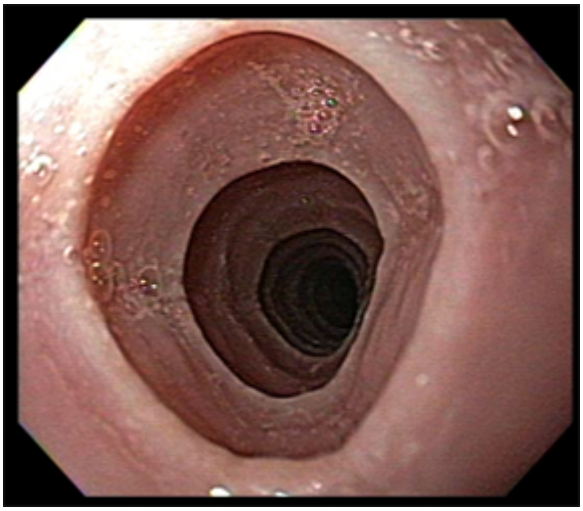


This upper endoscopy in a 36-year-old man with dysphagia showed multiple rings in the proximal to mid esophagus, giving it the appearance of a trachea. Small whitish papules are also visible representing eosinophilic abscesses on histology. The patient's symptoms responded to swallowed (ie, topical) fluticasone.

Courtesy of Eric D Libby, MD.

Graphic 51432 Version 4.0

Endoscopic image of the esophagus showing multiple ring-like strictures in a patient with eosinophilic esophagitis

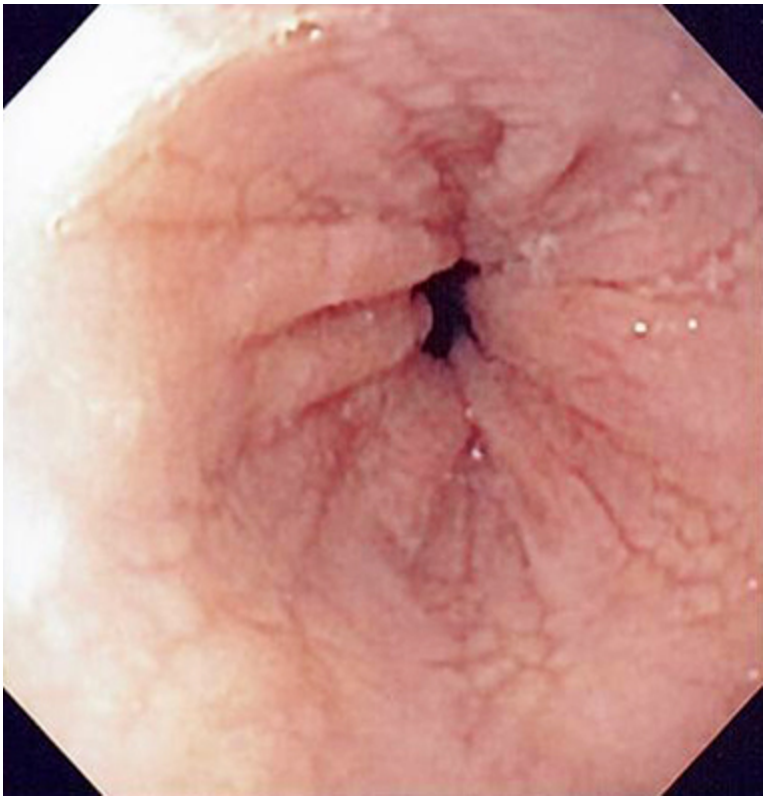


This upper endoscopy in a patient with eosinophilic esophagitis showed multiple ring-like strictures in the proximal and mid-esophagus.

Courtesy of Andres Gelrud, MD and Anthony Lembo, MD.

Graphic 50566 Version 3.0

Eosinophilic esophagitis

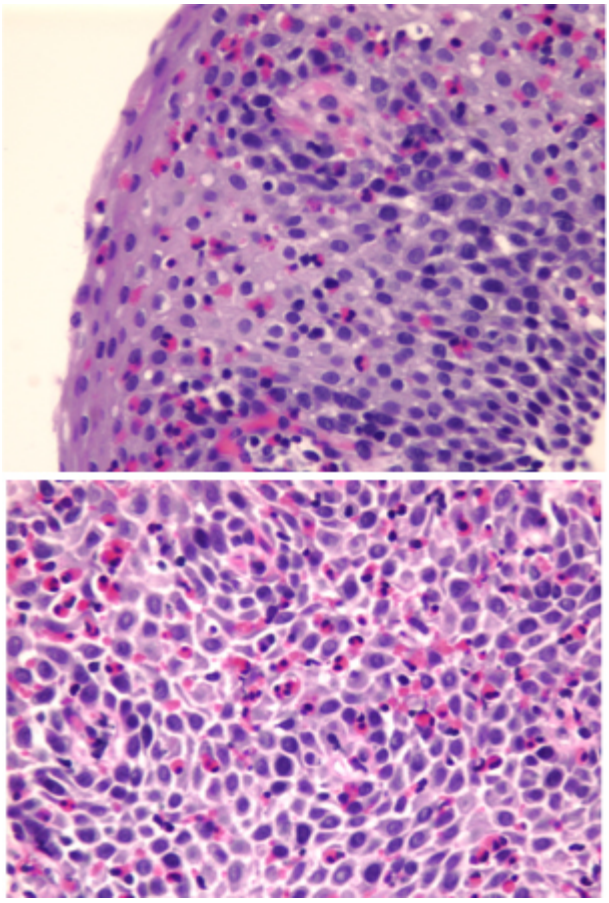


A 14-month-old with failure to thrive and loose stools. Endoscopy demonstrates a thickened furrowed esophagus consistent with eosinophilic esophagitis. These patients commonly have dysphagia with, as well as without, evidence of stricture. Eosinophilic esophagitis is also a common cause of dysphagic in atopic school-aged children. Histology would demonstrate sheets of eosinophils in the lamina propria.

Courtesy of Karen Murray, MD.

Graphic 74737 Version 1.0

Eosinophilic esophagitis

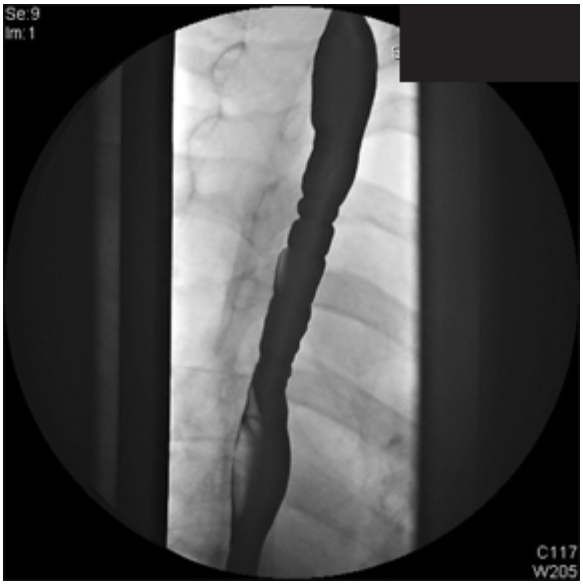


Esophageal biopsies from a patient with eosinophilic esophagitis. There is severe active esophagitis characterized by marked basal zone hyperplasia (top panel) and large numbers of eosinophils (greater than 40 per high power field, bottom panel). Biopsies obtained from the proximal, mid and distal esophagus showed similar findings. The long linear extent of the esophagitis plus the large numbers of eosinophils are characteristic pathologic features of eosinophilic esophagitis.

Courtesy of Maria Botero, MD and Donald Antonioli, MD.

Graphic 70915 Version 2.0

Eosinophilic esophagitis



Barium swallow in a patient with eosinophilic esopahgitis showing mild segmental ring-like areas of narrowing in the proximal and mid esophagus representing "trachealization" of the esophagus.

Courtesy of Norman Joffe, MD.

Graphic 73447 Version 2.0

Contributor Disclosures

Peter A L Bonis, MD No relevant financial relationship(s) with ineligible companies to disclose. **Sandeep K Gupta, MD** Grant/Research/Clinical Trial Support: Allakos [Eosinophil-associated gastrointestinal disorders]; Ellodi [Eosinophilic esophagitis]; Shire [Eosinophilic esophagitis]. Consultant/Advisory Boards: Adare [Eosinophilic esophagitis]; Allakos [Eosinophilic esophagitis/eosinophilic gastrointestinal disease]; Celgene [Eosinophilic esophagitis]; Gossamer [Eosinophilic esophagitis]; QoL [Sucrase deficiency]; Viaskin [Eosinophilic esophagitis]. Speaker's Bureau: Abbott [Eosinophilic esophagitis, GERD]; Medscape [Eosinophilic gastrointestinal diseases]. All of the relevant financial relationships listed have been mitigated. **Nicholas J Talley, MD, PhD** Patent Holder: Australian Provisional Patent [Diagnostic marker for functional gastrointestinal disorders]; Biomarkers of irritable bowel syndrome [Irritable bowel syndrome]; Mayo Clinic [Dysphagia questionnaire]; Mayo Clinic [Bowel Disease questionnaire]; Nepean Dyspepsia Index [Dyspepsia]; Nestec [Irritable bowel syndrome]; Singapore Provisional Patent [BDNF Tissue Repair Pathway]. Grant/Research/Clinical Trial Support: Alimetry [Gastric mapping device research collaboration]; Allakos [Gastric eosinophilic disease]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; Intrinsic Medicine [Bowel syndrome with constipation]; NHMRC Centre for Research Excellence in Digestive Health [NHMRC Investigator grant]. Consultant/Advisory Boards: Adelphi Values [Functional dyspepsia]; Allakos [Gastric eosinophilic disease, AK002]; AstraZeneca [Eosinophilic gastritis, eosinophilic gastroenteritis]; AusEE [Eosinophilic gut diseases]; Bayer [Inflammatory bowel syndrome]; BluMaiden [Microbiome Ad Board]; Comvita Mānuka Honey [Digestive health]; Dr Falk Pharma [Eosinophilia]; GlaxoSmithKline Australia [Educational speaker eosinophilic gut disease]; Glutagen [Celiac disease]; International Foundation for Functional Gastrointestinal Disorders [Advisory board, functional GI disorders]; Intrinsic Medicine [Human milk oligosaccharide]; IsoThrive [Esophageal microbiome]; Planet Innovation [Gas capsule, inflammatory bowel syndrome]; Progenity Inc [Intestinal capsule]; Rose Pharma [IBS]; Viscera Labs [Inflammatory bowel syndrome, diarrhea]. Other Financial Interest: Elsevier textbook royalties [Medical education]. All of the relevant financial relationships listed have been mitigated. **Kristen M Robson, MD, MBA, FACG** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→