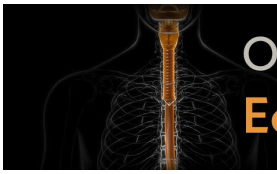


Optimizing Treatment in the Underdiagnosed Eosinophilic Esophagitis: An Interactive Guide

Overview

Eosinophilic esophagitis (EoE) is a chronic, allergic, and inflammatory esophageal disease. It is an allergen-driven T-helper (Th) type-2 cell response that triggers infiltration of eosinophils leading to esophageal dysfunction. It is common for patients diagnosed with EoE to have at least 1 comorbid type-2 inflammatory disease. The etiology of EoE is multifactorial, involving an interplay between host factors, genetics, environment, and immunity. Environmental factors can include airborne substances, such as pollen, and food antigens, including milk, wheat, soy, eggs, peanuts and tree nuts, fish and shellfish, as well as genetic and chemically modified food.[1,2] The pathophysiology of EoE is commonly based on food allergy triggers that result in epithelial dysfunction. Penetration of the epithelial barrier by antigens triggers an inflammatory response that can lead to chronic inflammation, with eventual fibrosis and narrowing of the esophagus. There is a rising global incidence and prevalence, with a higher prevalence in Western, industrialized countries. EoE affects males 3 to 4 times more than females, and Caucasians are afflicted more than other races. EoE can present in all age groups, but is more common in patients younger than 50 years of age.

Clinical Presentation

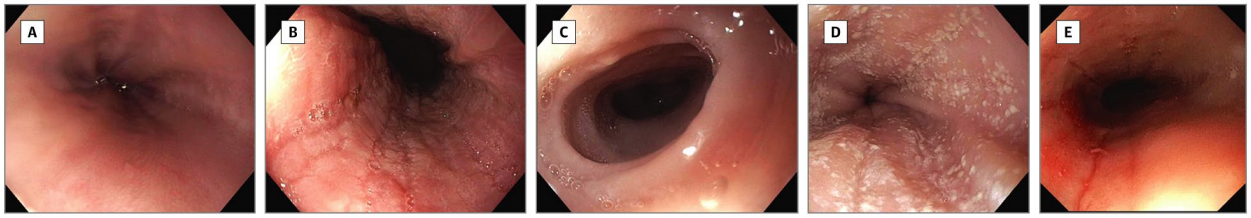
Eosinophilic esophagitis presents differently at different ages.

Toddlers and Young Children	Children	Adolescents and Adults
Feeding difficulties Vomiting and regurgitation Failure to thrive Cough after eating Abdominal pain	Abdominal/epigastric pain GERD-like symptoms Vomiting Dysphagia Food impaction	Dysphagia Food impaction

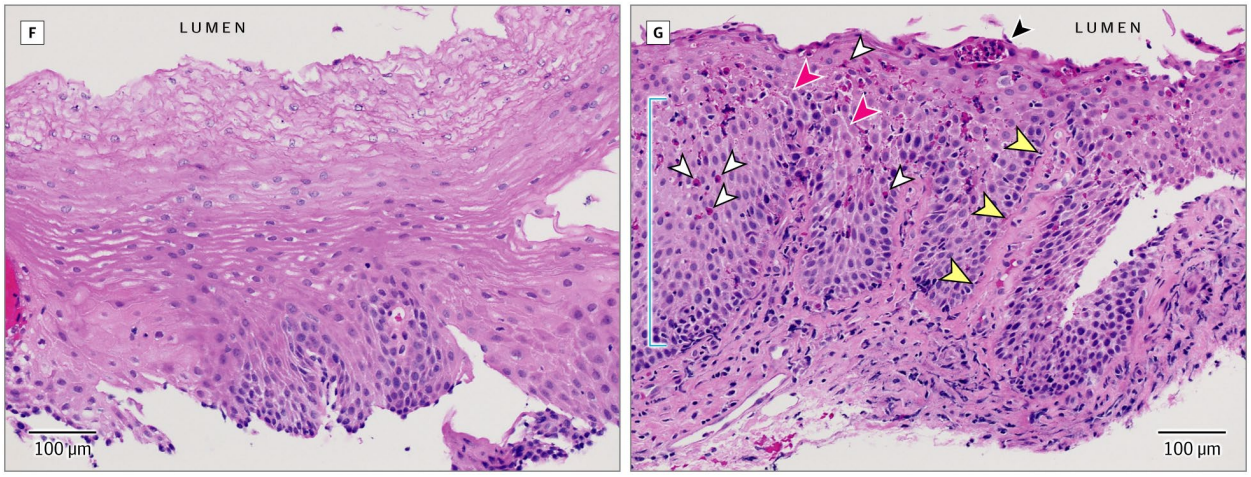
Testing Strategies for an Earlier Diagnosis

EoE is underdiagnosed and often misdiagnosed because symptoms are nonspecific and oftentimes present alongside extraesophageal manifestations. Also, patients often develop adaptive behaviors that obscure symptoms.[4] Signs and symptoms include dysphagia, feeding difficulties, symptoms mimicking gastroesophageal reflux, abdominal pain, vomiting, and failure to thrive.[3] Food impaction or other esophageal foreign body should prompt further evaluation such as mucosal biopsy. To confirm the diagnosis, an upper endoscopy with a biopsy is required showing >15 eosinophils per high power field, mucosal edema, basal cell hyperplasia, vascular papillae elongation, eosinophil microabscesses, and lamina propria fibrosis. Other features can include esophageal rings, linear or longitudinal furrows, white plaques, and pale and/or congested fragile mucosa with loss of vascularity.

Endoscopic appearance of normal esophagus tissue and eosinophilic esophagitis

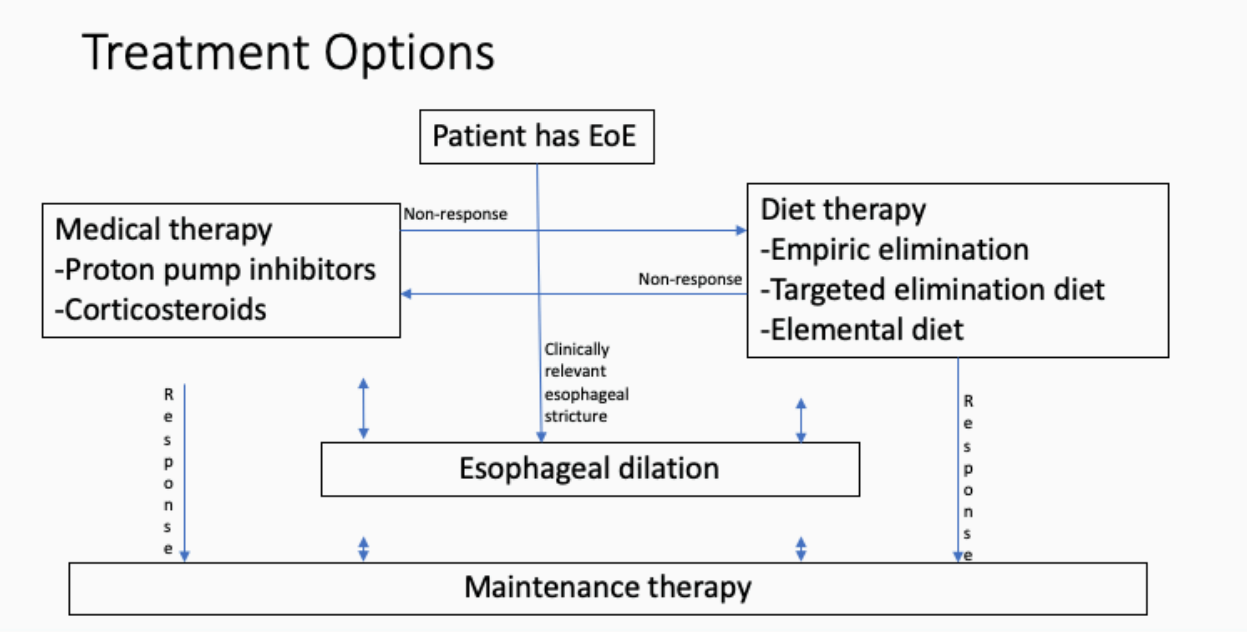


Histologic appearance of normal esophagus tissue and eosinophilic esophagitis



Endoscopy of EoE: normal esophagus (A); linear furrows (B); mucosal pallor representing edema, decreased vascular pattern, and concentric rings or trachealization (C); small white plaques (D); and esophageal narrowing and rent due to endoscope passage (E). Histology (hematoxylin and eosin) of EoE: F, Normal esophageal squamous epithelium with inconspicuous basal layer, luminal squamous differentiation, and absence of inflammation. G, EoE mucosa demonstrating elongated papilla (yellow arrowheads), basal cell hyperplasia (blue line), infiltrating eosinophils (white arrowheads), eosinophil microabscess (black arrowhead), and epithelial spongiosis (pink arrowheads). Images courtesy of Benjamin Wilkins, MD, PhD, Children's Hospital of Philadelphia.[5]

Design a Treatment Plan



The goal is to improve clinical symptoms and histological findings while reducing long-term complications. Note the 3 Ds: **d**rugs, **d**ietary restriction, and endoscopic **d**ilation. No single agent has been approved by the US Food and Drug Administration to treat EoE. Medication options include proton-pump inhibitors and topical and systemic corticosteroids.[3] Dietary approaches focus on the removal of the offending allergen through an empiric elimination diet, targeted elimination diet, or elemental diet. Patients who are candidates for esophageal dilation include those with esophageal strictures alongside symptoms of dysphagia, those without esophageal strictures alongside symptoms of dysphagia despite histologic remission, and those with esophageal strictures who deny symptoms of dysphagia due to adaptive eating behaviors.[4] Shared decision making is important to individualize therapy, especially when standard of care needs to be modified or combination therapy is warranted.

Emerging Therapies: Efficacy and Safety Data

Numerous treatments are undergoing clinical investigation, including several monoclonal antibodies, as well as new steroid formulations, ie, budesonide orodispersible tablets and fluticasone propionate.[6–8]

Agent	Mechanism	Identifier	Status
Benralizumab	Anti-IL5 receptor alpha	NCT04543409	Recruiting
Cendakimab	Anti-IL13	NCT04753697	Recruiting
Dupilumab	Anti-IL4 receptor alpha	NCT03633617 NCT04394351	Active
Lirentelimab	Siglec-8 inhibitor	NCT04322708	Active
Reslizumab	Anti-IL5 receptor alpha	NCT00538434	Completed

https://clinicaltrials.gov

References

1. Greuter T, Hirano I, Dellon ES. Emerging therapies for eosinophilic esophagitis. *J Allergy Clin Immunol.* 2020;145(1):38-45. doi:10.1016/j.jaci.2019.10.027
2. Fernandez-Becker NQ. Eosinophilic esophagitis: Incidence, diagnosis, management, and future directions. *Gastroenterol Clin North Am.* 2021;50(4):825-841. doi:10.1016/j.gtc.2021.08.001
3. Kumar S, Choi S, Gupta SK. Eosinophilic esophagitis-A primer for otolaryngologists. *JAMA Otolaryngol Head Neck Surg.* 2019;145(4):373-380. doi:10.1001/jamaoto.2018.4177
4. Hirano I, Furuta GT. Approaches and challenges to management of pediatric and adult patients with eosinophilic esophagitis. *Gastroenterology.* 2020;158(4):840-851. doi:10.1053/j.gastro.2019.09.052
5. Muir A, Falk GW. Eosinophilic esophagitis: A review. *JAMA.* 2021;326(13):1310-1318. doi:10.1001/jama.2021.14920
6. Lucendo AJ, Miehlke S, Schlag C, et al; for International EOS-1 Study Group. Efficacy of budesonide orodispersible tablets as induction therapy for eosinophilic esophagitis in a randomized placebo-controlled trial. *Gastroenterology.* 2019;157(1):74-86.e15. doi:10.1053/j.gastro.2019.03.025
7. ClinicalTrials.gov. Efficacy and safety APT-1011 in adult subjects with eosinophilic esophagitis (EoE) (FLUTE-2). Last updated April 14, 2022. Available at https://clinicaltrials.gov/ct2/show/NCT04281108?cond=eosinophilic+esophagitis&phase=2&draw=2&rank=5
8. Dellon ES, Woosley JT, Arrington A, et al. Efficacy of budesonide vs fluticasone for initial treatment of eosinophilic esophagitis in a randomized controlled trial. *Gastroenterology.* 2019;157(1):65-73.e5. doi:10.1053/j.gastro.2019.03.014