

## Eosinophilic Esophagitis



Benjamin L. Wright, MD<sup>a,b</sup>, and Jonathan M. Spergel, MD, PhD<sup>c,d</sup>

### INSTRUCTIONS

MOC as well as CME credit can now be obtained, free for a limited time, by reviewing this Difficult Cases presentation. Please note the following instructions.

1. Review the target audience, learning objectives, and author disclosures.
2. Follow the online instructions to review the full online version of the presentation.
3. Complete the post-test. At this time, you will have earned 1.00 AMA PRA Category 1 CME Credit™.
4. Approximately 4 weeks later you will receive an online assessment regarding your application of this article to your practice. Once you have completed this assessment, you will be eligible to receive 2 MOC Part II Self-Assessment credits from the American Board of Allergy and Immunology.

**Method of Physician Participation in Learning Process:** The core material for these activities can be found online at the *JACI: In Practice* Web site: [www.jaci-inpractice.org/](http://www.jaci-inpractice.org/). The accompanying tests may only be submitted online at [www.jaci-inpractice.org/](http://www.jaci-inpractice.org/). Fax or other copies will not be accepted.

**Date of Original Release:** September 1, 2018. Credit may be obtained for these courses until August 31, 2018.

**Copyright Statement:** Copyright © 2018-2020. All rights reserved.

**Overall Purpose/Goal:** To provide excellent case-based reviews on key aspects of allergic disease to those who research, treat, or manage allergic disease.

**Target Audience:** Physicians and researchers within the field of allergic disease.

**Accreditation/Provider Statements and Credit Designation:** The American Academy of Allergy, Asthma & Immunology (AAAAI) is

accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. The AAAAI designates this journal-based CME activity for 1.00 AMA PRA Category 1 Credit™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

**List of Design Committee Members:** Benjamin L. Wright, MD, and Jonathan M. Spergel, MD, PhD (authors); Michael Schatz, MD, MS (editor)

### Learning objectives:

1. To distinguish eosinophilic esophagitis (EoE) from other causes of esophageal eosinophilia.
2. To develop an approach for food trigger identification and monitoring response to therapy.
3. To list risks and benefits of swallowed corticosteroid therapy in EoE.
4. To identify emerging therapies that may be effective for EoE in the future.

**Recognition of Commercial Support:** This CME has not received external commercial support.

**Disclosure of Relevant Financial Relationships with Commercial Interests:** B.L.W. receives funding through the Mayo Clinic Foundation, Phoenix Children's Hospital, and the Don and Kathy Levin Family Foundation. J.M.S. receives funding from the Consortium for Gastrointestinal Eosinophilic Researchers (CEGIR). CEGIR (grant no. U54 AI117804) is part of the Rare Diseases Clinical Research Network, an initiative of the Office of Rare Diseases Research, NCATS, and is funded through collaboration between NIAID, NIDDK, and NCATS. J.M.S. also receives funds from DBV Technologies, and Stuart Starr Chair of Pediatrics, The Children's Hospital of Philadelphia Eosinophilic Esophagitis Fund. M. Schatz declares no relevant conflicts of interest.

The Difficult Cases Feature is based on the *Difficult Cases* Course presented at the AAAAI Annual Meeting and coordinated by the AAAAI New Allergist-Immunologist Assembly (NAIA). View the entire presentation and obtain CME or MOC credit by visiting the *JACI: In Practice* homepage [www.jaci-inpractice.org](http://www.jaci-inpractice.org).

<sup>a</sup>Division of Allergy, Asthma and Clinical Immunology, Department of Medicine, Mayo Clinic Arizona, Scottsdale, Ariz

<sup>b</sup>Division of Pulmonology, Phoenix Children's Hospital, Phoenix, Ariz

<sup>c</sup>Department of Pediatrics, Division of Allergy and Immunology, The Children's Hospital of Philadelphia, Philadelphia, Pa

<sup>d</sup>Institute for Immunology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pa

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

B.L.W. receives funding through the Mayo Clinic Foundation, Phoenix Children's Hospital, and the Don and Kathy Levin Family Foundation. J.M.S. receives funding from the Consortium for Gastrointestinal Eosinophilic Researchers (CEGIR). CEGIR (grant no. U54 AI117804) is part of the Rare Diseases Clinical Research Network, an initiative of the Office of Rare Diseases Research, National

Center for Advancing Translational Sciences (NCATS), and is funded through collaboration between National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), and NCATS. J.M.S. also receives funds from DBV Technologies, and Stuart Starr Chair of Pediatrics, The Children's Hospital of Philadelphia Eosinophilic Esophagitis Fund.

Received for publication May 17, 2018; revised June 19, 2018; accepted for publication June 20, 2018.

Corresponding author: Benjamin L. Wright, MD, Mayo Clinic Arizona, 13400 E Shea Blvd, Scottsdale, AZ 85259. E-mail: [wright.benjamin@mayo.edu](mailto:wright.benjamin@mayo.edu). 2213-2198

© 2018 American Academy of Allergy, Asthma & Immunology  
<https://doi.org/10.1016/j.jaip.2018.06.019>

## CASE REPORT

A 24-year-old man with a history of asthma and allergic rhinitis presents with a food impaction after eating steak. He has a history of food sticking in his throat, uses condiments to lubricate his foods, and drinks large quantities of water with meals. An upper endoscopy is notable for a food bolus, exudates, linear furrowing with rings, and narrowing of the esophagus. Esophageal dilation is performed after removal of the piece of steak. Esophageal biopsy reveals greater than 100 eosinophils per hpf in all segments of the esophagus.

The patient is started on a high-dose proton pump inhibitor (PPI), but his esophageal eosinophilia persists. Treatment options including swallowed topical budesonide and dietary elimination are reviewed with the patient. The PPI is discontinued, and he begins an empiric 2-food elimination diet, avoiding all dairy and wheat products. A repeat upper endoscopy is performed 2 months later that reveals resolution of esophageal eosinophilia. Wheat is reintroduced into the patient's diet, and a third esophageal biopsy demonstrates continued disease remission.

## DISCUSSION

Eosinophilic esophagitis (EoE) is a clinicopathologic diagnosis characterized by symptoms of esophageal dysfunction and esophageal eosinophilia ( $\geq 15$  eos/hpf).<sup>1</sup> It is the leading cause of food impaction in the United States,<sup>2</sup> and, if left untreated, can result in fibrosis and narrowing of the esophagus, requiring mechanical dilation.<sup>3</sup> Diagnosis requires exclusion of other primary causes of esophageal eosinophilia including celiac disease, connective tissue disorders, inflammatory bowel disease, parasitic infection, gastroesophageal reflux disease, and so forth. Previous diagnostic guidelines required a 6- to 8-week PPI trial to exclude PPI-responsive esophageal eosinophilia (PPI-REE).<sup>1</sup> Strong evidence suggests that EoE and PPI-REE are most likely spectrum of the same disease<sup>4,5</sup>; as a result, new criteria have removed a PPI trial from the diagnostic algorithm.<sup>6</sup> Notwithstanding, PPIs are still an important therapeutic tool because up to 50% of patients with EoE improve with PPI therapy.<sup>7</sup>

After PPIs, treatment options include swallowed corticosteroids, elimination diets, and esophageal dilation. Currently, patients swallow corticosteroids from inhalers or viscous formulations of liquid corticosteroids intended for nebulization. Several new viscous corticosteroid suspensions are currently under investigation.<sup>8</sup> Corticosteroids induce histologic remission in 50% to 90% of patients; however, in almost all patients they must be continued indefinitely to maintain disease remission.<sup>9</sup> The most common side effect is esophageal candidiasis, which is often asymptomatic.<sup>10</sup> Other potential adverse effects include adrenal suppression,<sup>8</sup> growth deceleration,<sup>8</sup> and bone loss.<sup>11</sup>

Approaches to diet elimination may be allergy test-directed, empiric, or completely exclude dietary proteins (ie, elemental formula). Recent studies suggest that skin and atopy patch testing do not confer advantages over empiric elimination approaches.<sup>12</sup> Most patients with EoE have only 1 to 2 food triggers; therefore, a "step-up" approach in which common foods are progressively eliminated until histologic remission is achieved reduces the number of required endoscopies.<sup>13</sup> This is in contrast to "step-down" strategies in which 6-food (dairy, wheat, egg, soy, peanut/tree nuts, fish/shellfish) or 8-food (dairy, wheat, egg, soy,

peanut/tree nuts, fish/shellfish, corn, meats) elimination diets are used and foods are gradually reintroduced.

Trials of biologic therapies targeting IgE<sup>14,15</sup> and eosinophils (ie, anti-IL-5,<sup>16,17</sup> IL-13 agents<sup>18</sup>) have been largely disappointing. Early results of phase II trials of dupilumab (anti-IL-4/IL-13 agent) show promise with improvement in both symptoms and histologic end points.<sup>19</sup>

## REFERENCES

1. Liacouras CA, Furuta GT, Hirano I, Atkins D, Attwood SE, Bonis PA, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. *J Allergy Clin Immunol* 2011;128:3-20.e6.
2. Sperry SL, Crockett SD, Miller CB, Shaheen NJ, Dellon ES. Esophageal foreign-body impactions: epidemiology, time trends, and the impact of the increasing prevalence of eosinophilic esophagitis. *Gastrointest Endosc* 2011;74:985-91.
3. Dellon ES, Kim HP, Sperry SL, Rybnicek DA, Woosley JT, Shaheen NJ. A phenotypic analysis shows that eosinophilic esophagitis is a progressive fibrostenotic disease. *Gastrointest Endosc* 2014;79:577-585.e4.
4. Dellon ES, Speck O, Woodward K, Gebhart JH, Madanick RD, Levinson S, 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;108:1854-60.
5. Wen T, Dellon ES, Moawad FJ, Furuta GT, Aceves SS, Rothenberg ME. Transcriptome analysis of proton pump inhibitor-responsive esophageal eosinophilia reveals proton pump inhibitor-reversible allergic inflammation. *J Allergy Clin Immunol* 2015;135:187-97.
6. Dellon ES, Liacouras CA, Molina-Infante J, Furuta GT, Spergel JM, Zevit N, et al. Updated international consensus criteria for eosinophilic esophagitis: Proceedings of the AGREE conference [published online ahead of print July 12, 2018]. *Gastroenterology*. <https://doi.org/10.1053/j.gastro.2018.07.009>.
7. Lucendo AJ, Arias A, Molina-Infante J. Efficacy of proton pump inhibitor drugs for inducing clinical and histologic remission in patients with symptomatic esophageal eosinophilia: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2016;14:13-22.e1.
8. Dellon ES, Katzka DA, Collins MH, Hamdani M, Gupta SK, Hirano I, et al. Budesonide oral suspension improves symptomatic, endoscopic, and histologic parameters compared with placebo in patients with eosinophilic esophagitis. *Gastroenterology* 2017;152:776-786.e5.
9. Greuter T, Bussmann C, Safroneeva E, Schoepfer AM, Biedermann L, Vavricka SR, et al. Long-term treatment of eosinophilic esophagitis with swallowed topical corticosteroids: development and evaluation of a therapeutic concept. *Am J Gastroenterol* 2017;112:1527-35.
10. Noel RJ, Putnam PE, Collins MH, Assa'ad AH, Guajardo JR, Jameson SC, et al. Clinical and immunopathologic effects of swallowed fluticasone for eosinophilic esophagitis. *Clin Gastroenterol Hepatol* 2004;2:568-75.
11. Martin E, Patterson M, Beckwith S, Rettiganti M, Luo C, Chandler PL, et al. Bone mineral density screening in a pediatric population with eosinophilic esophagitis. *J Allergy Clin Immunol* 2018;141:AB136.
12. Spergel JM, Brown-Whitehorn TF, Cianferoni A, Shuker M, Wang ML, Verma R, et al. Identification of causative foods in children with eosinophilic esophagitis treated with an elimination diet. *J Allergy Clin Immunol* 2012;130:461-467.e5.
13. Molina-Infante J, Arias A, Alcedo J, Garcia-Romero R, Casabona-Frances S, Prieto-Garcia A, et al. Step-up empiric elimination diet for pediatric and adult eosinophilic esophagitis: the 2-4-6 study. *J Allergy Clin Immunol* 2018;141:1365-72.
14. Clayton F, Fang JC, Gleich GJ, Lucendo AJ, Olalla JM, Vinson LA, et al. Eosinophilic esophagitis in adults is associated with IgG4 and not mediated by IgE. *Gastroenterology* 2014;147:602-9.
15. Loizou D, Enav B, Komlodi-Pasztor E, Hider P, Kim-Chang J, Noonan L, et al. A pilot study of omalizumab in eosinophilic esophagitis. *PLoS One* 2015;10:e0113483.
16. Assa'ad AH, Gupta SK, Collins MH, Thomson M, Heath AT, Smith DA, et al. An antibody against IL-5 reduces numbers of esophageal intraepithelial eosinophils in children with eosinophilic esophagitis. *Gastroenterology* 2011;141:1593-604.
17. Spergel JM, Rothenberg ME, Collins MH, Furuta GT, Markowitz JE, Fuchs G III, et al. Reslizumab in children and adolescents with eosinophilic esophagitis: results of a double-blind, randomized, placebo-controlled trial. *J Allergy Clin Immunol* 2012;129:456-63. e1-3.

18. Rothenberg ME, Wen T, Greenberg A, Alban O, Enav B, Hirano I, et al. Intravenous anti-IL-13 mAb QAX576 for the treatment of eosinophilic esophagitis. *J Allergy Clin Immunol* 2015;135:500-7.
19. Hirano I, Dellon ES, Hamilton JD, Collins MH, Peterson K, Chehade M, et al. Dupilumab efficacy and safety in adult patients with active eosinophilic

esophagitis: a randomized double-blind placebo-controlled phase 2 trial. Paper presented at: American College of Gastroenterology Annual Scientific Meeting; October 13-18, 2017; Orlando, Fla. Available at: <http://files.shareholder.com/downloads/REGN/6138593856x0x959724/16AF93AE-DAF8-480A-8301-311C91E8FA41/Presentation.pdf>. Accessed May 5, 2018.