

Eosinophilic Esophagitis (EoE) Management Guidelines Summary

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What is EoE?

EoE is:

- an allergic GI disorder characterized by abnormally high levels of eosinophils in the esophagus (>15 eos/hpf), leading to esophageal inflammation and narrowing
- concomitant with other allergic disorders, like IgE mediated food allergy, asthma, and atopic dermatitis
- likely to cause symptoms which are not always isolated to the esophagus and vary by age. Infants and toddlers present with feeding refusal and disordered feeding behaviors, young children with vomiting and abdominal pain, and adolescents and adults with dysphagia and, at times, food impaction
- most often triggered by milk, and closely followed by wheat
- often managed by diet and may require the use of AAF as sole source or supplemental nutrition - eHF's are not recommended for EoE

Here we summarize guidelines for the management of EoE. This summary can help keep practitioners abreast of the latest principles to maximize management effectiveness and minimize the discrepancy in care which was highlighted in the Chang et al. survey.¹

Chang et al.'s 2019 survey of US gastroenterologists who manage patients with EoE revealed:

- a wide variation in management plans
- that almost half (47%) spend less than 10 minutes discussing management options with patients on their first visit
- physicians attributed variations to confusion around evolution of guidelines, particularly the use of PPIs for diagnosis or therapy and repeat endoscopy.¹

Dietary Therapy and Nutrition Management of EoE - AAAAI Work Group Report

Groetch, et al. *Allergy Clin Immunol Pract.* 2017;5:312-24.e29.²

These guidelines were developed by the AAAAI work group, specific to dietary management of EoE. Notably, the authors were primarily dietitians from the US but also included allergists and a pediatric gastroenterologist. They highlight that, unlike dilation and topical corticosteroid treatment, dietary management offers long-term clinical and histologic remission without potential drug-related side effects.



Summary of the following dietary management approaches:

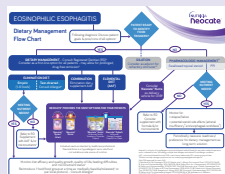
- **Empiric Elimination Diet**, which removes common food allergens without allergy testing. The 6-FED results in a 70-74% histologic remission rate for adults and children. The 4-FED and 2-FED are also common variations of the empiric elimination diet.
- **Elemental Diet**, comprises AAF, free from intact proteins or peptides. The most effective dietary management choice for EoE with a 90.8% histologic remission rate and the same efficacy seen with topical steroids for symptom resolution.
- **Test-directed Elimination Diet**, wherein foods are eliminated from the diet based on allergy testing. Histologic remission is highly variable among studies. Adults have a lower response rate to test-directed elimination diets than children.

Challenges of implementing dietary approaches are manageable.

- Individuals on elimination diets are at risk for nutritional gaps that can delay development and stunt growth.
- Clinicians should monitor nutritional adequacy, anthropometric measures, and quality of life.
- Supplementation with AAF is recommended as a “nutritional safety net” for individuals on elimination diets with nutritional deficiencies and/or poor growth.

Summary of Key Steps to Successfully Implement Elimination Diets

- 1 RD Referral** - Consider referral to RD for any elimination diet for EoE
- 2 Nutrition Assessment** - Assess nutritional status, screen for barriers to diet management
- 3 Eliminate antigens** - Requires adequate training and education to minimize incidental exposure
- 4 Nutritional Adequacy** - Ensure individual nutritional needs are met
- 5 Supplementation as needed** - Substitute eliminated foods with alternative foods and/or supplements, e.g. AAF
- 6 Monitoring** - Monitor to ensure effective elimination and adequate nutrition
- 7 Endoscopy** - Confirm remission following intervention
- 8 Reintroduction** - When successful, work with multidisciplinary team to add eliminated foods back to diet one at a time to identify EoE triggers



EoE Dietary Management Flow Chart which considers these guidelines is available on Nutricia Learning Center



Updated International Consensus Diagnostic Criteria for EoE

AGREE 

Dellon, et al. *Gastroenterology*. 2018;155:1022-33.e10.³

The members of the AGREE conference reviewed the collective evidence for PPI use in EoE in adults and children and made the following recommendations:



- PPIs should be classified as a treatment for EoE rather than as a diagnostic criterion.
- Don't rule out EoE diagnosis in patients with an initial endoscopy while on PPI who demonstrate no abnormalities.
- PPI, swallowed steroids, and dietary elimination should all be considered options for early or initial management of EoE. These options can be used individually or in combination based on patient response.
- Patients with EoE on PPI therapy: regularly assess symptoms, endoscopy, and histology to ensure continued response to PPI.

Evolving Perspective on PPI Use And Years When Major EoE Guidelines Were Published

2007

EoE defined as an immune- or antigen-related condition with symptoms of esophageal dysfunction and histology demonstrating ≥ 15 eos/hpf. GERD and EoE thought to be mutually exclusive. Recommended ruling out GERD-associated inflammation with PPI trial.

2011

2013

2014

Some patients with EoE but with no symptoms of GERD respond clinically and histologically to high-dose PPI therapy – defined as a new condition called PPI-REE.

2017

In May of 2017, a group of pediatric and adult clinicians and researchers in gastroenterology, allergy and pathology from 14 countries convened to address the issue of PPI use in EoE. This meeting was dubbed the AGREE Conference.

See 'Further Reading' for details

Clinical Guidelines for the Management of EoE



Hirano, et al. *Gastroenterology*. 2020;158:1776-86.⁴

These guidelines were created by the AGA and the JTF with approval from the AAAAI and the ACAAI. The purpose was to establish consensus guidelines built on the totality of evidence for the various EoE management approaches. The authors included allergists and adult gastroenterologists, with no dietitians.



Each management option's efficacy in achieving histologic remission of <15 eos/hpf was considered as the primary outcome. Outcomes such as symptom resolution and endoscopic features were not assessed. Based on the existing literature, Hirano et al. outline the following:

Summary of Findings and Recommendations						
	ED	6-FED	Test-directed Elimination Diet	Topical Corticosteroids	PPIs	Dilation
Effectiveness	~94%	~68%	~51%	~66%	~42%	No effect on histology
Recommendation based on panel opinion	Conditional	Conditional	Conditional	Strong	Conditional	Conditional (Adults)
Confidence in evidence quality	Moderate	Low	Very low	Moderate	Very low	Very low

In summary:

- Diet, topical corticosteroids, and PPIs are all viable EoE management option. Decision aids may help evaluate “Conditional” options against patient values and preferences. Dilation can be considered in adults with dysphagia from EoE strictures but does not address esophageal inflammation.
- **Diet options** have high efficacy rates: the panel felt a majority of patients would want diet options. Cited challenges for ED were adherence and a prolonged process of dietary reintroduction. Empiric elimination diets reduce the burden of repeated endoscopies and can improve lifestyle and adherence vs ED.
- **Topical corticosteroids** require continued use: the panel indicated most patients would want this option and this approach requires less clinician time to help make a decision compared to “Conditional” options. Longer-term studies assessing safety are ongoing.
- **PPIs** are considered an effective option for certain patients: comparison of efficacy with other options is limited in existing literature.
- **Other drugs** such as Montelukast, cromolyn sodium, and immunomodulators are not recommended. Newer biologic agents such as anti IL-5 and IL-13 are currently limited to clinical trials.

Guidelines on EoE

GRADE AGREE 



Lucendo, et al. *United European Gastroenterol J.* 2017;5:335-58.⁵

These European guidelines for EoE management were written by an interdisciplinary panel of 21 gastroenterologists, allergist, and researchers, with no dietitians. These guidelines were developed on behalf of the UEG, ESPGHAN, EAACI, and EUREOS. Their recommendations for management of EoE are as follows:

Elemental Diet	Empiric Elimination Diet	Test-directed Elimination Diet
Should be considered after other treatments and the elimination diet have failed. 90% of adults and children see remission on the ED.	The 6-FED induces remission in ¾ of adults and children. 4-FED and 2-FED may also be effective. Can lead to drug-free sustained remission.	Induces remission in less than 1/3 of adults. Remission may be higher in children. Not recommended.
Topical (Swallowed) Corticosteroids	PPIs	Dilation
Induce remission in adults and children. Long-term therapy maintains remission in a proportion of patients.	Induce remission in a proportion of adults and children. Long-term therapy may be effective in maintaining remission.	Is safe and improves dysphagia in ¾ of adult patients. Helps manage symptoms but does not replace therapy for underlying inflammation.

In summary, “PPIs, diet, or topical steroids might be offered as first line anti-inflammatory therapy. The choice of therapy should be individually discussed with the patient and might be potentially interchangeable over time. The efficacy of any therapy should be checked by a follow-up endoscopy after a 6- to 12-week initial course.”

Other EGIDs can be successfully managed with ED using AAF

There is evidence that an elemental diet with AAFs is effective in the management of other EGIDs.

- In 2005, a study by Chehade et al. at the Mount Sinai School of Medicine examined the response to therapy and the long-term outcomes in patients with allergic EG with concurrent protein-losing enteropathy.
 - Conclusion: individuals whose management plan was composed exclusively of an AAF demonstrated “rapid resolution of clinical symptoms, hypoalbuminemia, and anemia in less than 4 weeks” on this diet.
 - In comparison, alternative therapies including empiric elimination, systemic steroids, montelukast, and oral cromolyn sodium produced partial, temporary, or no clinical response.⁶
- First shared in May 2020, the ELEMENT pilot study by Gonsalves et al. found that an elemental diet can effectively improve histologic, molecular, endoscopic, and symptomatic disease activity in adults with EG/EGE.⁷

Further Reading

Reference	Description	Key Authors	Origin
Madison JM, Bhardwaj V, Braskett M. Strategy for food reintroduction following empiric elimination and elemental dietary therapy in the treatment of eosinophilic gastrointestinal disorders. <i>Curr Gastroenterol Rep.</i> 2020;22:25.	Authors detail the existing data on the efficacy of various dietary therapies for EoE. They offer a strategy for food reintroduction following an elimination or elemental diet, from lowest to highest risk of six food groups, with 6-12 weeks between “new” foods or groups.	Dietitian and physicians	
Atwal K, Hubbard GP, Venter C, et al. The use of amino acid-based nutritional feeds is effective in the dietary management of pediatric eosinophilic oesophagitis. <i>Immun Inflamm Dis.</i> 2019;7:292-303.	Authors reviewed 10 eligible studies measuring the effectiveness of the dietary therapy in the management of pediatric EoE. Remission was demonstrated in 75-100% of children on an elemental diet, with positive growth outcomes where documented.	Dietitians Supported by Nutricia UK	 
Papadopoulou A, Koletzko S, Heuschkel R, et al. Management guidelines of eosinophilic esophagitis in childhood. <i>J Pediatr Gastroenterol Nutr.</i> 2014;58:107-18.	These European guidelines were authored by the ESPGHAN Eosinophilic Esophagitis Working Group and the Gastroenterology Committee.	A panel of 16 primarily EU-based gastroenterologists and pediatricians	
Henry M. Nutrition guidelines for treatment of Children with eosinophilic esophagitis. <i>Pract Gastroenterol.</i> 2014;38:21-30.	These guidelines highlight the nutritional implications of EoE and the benefits and challenges of the common dietary management approaches.	Registered Dietitian	
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). <i>Am J Gastroenterol.</i> 2013;108:679-92.	These guidelines were published by the American College of Gastroenterology.	US-based Gastroenterologists	
Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. <i>Allergy Clin Immunol.</i> 2011;128:320.e6.	This is an update to the 2007 guidelines, published by AAAAI.	Interdisciplinary panel of 33 primarily US-based physicians	
Furuta GT, Liacouras CA, Collins MH, et al. Eosinophilic esophagitis in children and adults: a systematic review and consensus recommendations for diagnosis and treatment. <i>Gastroenterology.</i> 2007;133:1342-63.	These guidelines were sponsored by the AGA Institute and NASPGHAN.	Interdisciplinary panel of 31 primarily US-based physicians	

KEY

- 2-FED – Two Food Elimination Diet (removal of milk and wheat (and in some cases gluten))
- 4-FED – Four Food Elimination Diet (removal of milk, wheat (and in some cases gluten), egg and soy)
- 6-FED – Six Food Elimination Diet (removal of milk, wheat (and in some cases gluten), egg, soy, peanut/tree nut and fish/shellfish)
- AAAAI – American Academy of Allergy, Asthma, and Immunology
- AAF – Amino acid-based formula
- ACAAI – American College of Allergy, Asthma, and Immunology
- AGA – American Gastroenterological Association
- AGREE – A Working Group on PPI-REE
- EAACI – The European Academy of Allergy and Clinical Immunology
- ED – Elemental Diet
- EG – Eosinophilic gastritis
- EGE – Eosinophilic gastroenteritis
- EGIDs – Eosinophilic gastrointestinal disorders
- ELEMENT trial – Prospective study of elemental diet in EGE nutrition trial
- EoE – Eosinophilic esophagitis
- Eos/hpf – eosinophils/high powered field
- ESPGHAN – The European Society of Pediatric Gastroenterology, Hepatology and Nutrition
- EUREOS – The European Society of Eosinophilic Oesophagitis
- GERD – Gastroesophageal reflux disease
- GI – Gastrointestinal
- GRADE – Grading of Recommendations, Assessment, Development, and Evaluation
- IgE – Immunoglobulin E
- IL – Interleukin
- JTF – Joint Task Force on Allergy-Immunology Practice Parameters
- NASPGHAN – North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition
- PPIs – Proton-pump inhibitors
- PPI-REE – PPI-responsive esophageal eosinophilia
- UEG – United European Gastroenterology

References

1. Chang, et al. *Dis Esophagus*. 2019;32.
2. Groetch, et al. *J Allergy Clin Immunol Pract*. 2017;5:312-24.e29.
3. Dellon, et al. *Gastroenterology*. 2018;155:1022-33.e10.
4. Hirano, et al. *Gastroenterology*. 2020;158:1776-86.
5. Lucendo, et al. *United European Gastroenterol J*. 2017;5:335-58.
6. Chehade, et al. *J Pediatr Gastroenterol Nutr*. 2006;42:516-21.
7. Gonsalves, et al. *Gastro*. 2020;158:S-43.

GRADE Developed using the GRADE methodology: Grading of Recommendations Assessment, Development, and Evaluation

AGREE Developed using the AGREE II instrument: Appraisal of Guidelines for Research and Evaluation instrument



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