

Dietary Management of Eosinophilic Esophagitis

Bethany Doerfler, MS, RD,¹ Angela Y. Lam, MD,² and Nirmala Gonsalves, MD¹

¹Division of Gastroenterology and Hepatology, Northwestern University Feinberg School of Medicine, Chicago, Illinois

²Department of Gastroenterology, Kaiser Permanente San Francisco, San Francisco, California

Corresponding author:

Dr Nirmala Gonsalves

Division of Gastroenterology and Hepatology

Northwestern University Feinberg School of Medicine

676 North St Clair Street, Suite 1400 Chicago, IL 60611

Tel: (312) 695-4013

Fax: (312) 695-3999

E-mail: n-gonsalves@northwestern.edu

Abstract: Eosinophilic esophagitis (EoE) is a chronic immune-mediated food antigen–driven disease characterized by tissue eosinophilia and clinical symptoms of esophageal dysfunction. Medical and dietary therapies can be offered as treatment options in both pediatric and adult populations. Advances in nutritional research in EoE have produced different levels of dietary restriction, ranging from elimination of a single food group to more extensive restriction such as the two-food elimination diet, four-food elimination diet, or six-food elimination diet. Efficacy and outcomes vary for each level of restriction. The option of using dietary therapy allows clinicians to partner with patients in shared decision-making to balance the right level of food antigen restriction for the desired outcome. Key considerations when choosing dietary therapy hinge on patient preference and resources, food-related quality of life, and the ability to provide nutritional diversity and maintain nutritional parameters. This article highlights these considerations and offers clinical pearls to guide clinicians who wish to incorporate dietary therapy of EoE into their practice.

Eosinophilic esophagitis (EoE) is a chronic immune-mediated food antigen–driven disease characterized by tissue eosinophilia and clinical symptoms of esophageal dysfunction.¹ Common presenting symptoms include dysphagia, food impaction, heartburn and atypical chest pain in adults with reflux symptoms, abdominal discomfort, and feeding difficulty in children. Patients with untreated disease have been shown to be at higher risk of stricture development and fibrosis; therefore, earlier recognition and treatment of disease is advocated.² The pathophysiology is thought to be multifactorial, involving genetic predisposition, food allergen exposure, and exposure to T helper 2 (TH2) immune-mediated tissue inflammatory mediators. Important endpoints of treatment include symptomatic relief with improvement in dysphagia, resolution of histopathologic inflammation with fewer than 15 eosinophils per high-power field (eos/hpf) on biopsies, and improvement in endoscopic changes with an esophageal diameter over 15 mm. This article focuses on dietary therapy in EoE and provides strategies to

Keywords

Eosinophilic esophagitis, dietary therapy, six-food elimination diet, dysphagia, food allergy

address education, nutritional wellness, and food preferences while providing clinicians with practical tips for implementation of dietary therapy in clinical practice.

Background

The role of dietary therapy for EoE first emerged from pediatric studies in the late 1990s. In an initial case series of 10 children who had esophageal eosinophilia, failure to respond to acid suppression therapy led to speculation that the underlying pathophysiology was not persistent gastroesophageal reflux. The authors hypothesized that the patients may have had hypersensitivity to dietary proteins, and after treatment with elemental formula, all 10 patients had either improvement or resolution of symptoms as well as decreased intraepithelial eosinophil counts.³ This case series was followed by larger retrospective pediatric studies of the elemental diet in the early 2000s, which produced similar results; pediatric and adolescent patients with EoE reliably had improvement of symptoms and esophageal eosinophilia after treatment with an elemental diet.⁴⁻⁶ One of these studies also supported efficacy of an empiric six-food elimination diet (SFED) in addition to the elemental diet.⁶ These pioneering studies in the pediatric population supported the concept that EoE is an antigen-mediated inflammatory disorder triggered by food antigens and, thus, is manageable by food elimination diets.

Different Approaches of Dietary Therapy

Building upon the evidence for dietary elimination in the pediatric EoE population, the first prospective study of an elemental diet in adult patients with EoE found that 72% responded histologically, although symptoms and strictures did not reliably improve.⁷ Overall, the data in support of utilizing an elemental diet for EoE have been limited to observational studies primarily in pediatrics. A technical review summarizing these data showed that the histologic response rate to an elemental diet was 93.6% compared with 13.3% in a placebo historical comparison group taken from swallowed topical corticosteroid data.⁸ However, there are several important therapeutic limitations to consider. The poor palatability of formula affects dietary adherence, and the extremely restrictive nature of the diet has implications for quality of life and ultimately feasibility. In an adult observational study, for instance, over one-third (38%) of patients failed to adhere to the diet.⁷ There is additional concern for potential nutritional deficiencies, as some adult patients who adhered to an elemental diet proceeded to have significant weight loss (hypothesized by the authors to be related to inadequate consumption of the formula). Therefore, the use of

elemental formula necessitates oversight by a registered dietitian monitoring for these side effects. Finally, treatment with elemental formula is costly for patients, accounting for the cost of the formula as well as the need for multiple repeated endoscopies in a lengthy reintroduction process to identify food triggers. Although the American Gastroenterological Association (AGA) and the Joint Task Force (JTF) of Allergy-Immunology Practice Parameters recommend an elemental diet over no treatment for EoE,⁹ the elemental diet is ultimately complicated by these limitations, which negatively impact feasibility.

Elimination diets directed by allergy testing have been a theoretically appealing alternative, considering the pathophysiology of EoE as a chronic TH2-associated inflammatory disorder mediated by food antigens. However, observational studies of allergy testing-based diets have had limited success. Although dairy and wheat have emerged as the 2 most common foods implicated in EoE, skin prick testing was less than 30% sensitive for both in an early pediatric study.¹⁰ In an adult case series of 15 patients with EoE undergoing elimination diets directed by multimodal allergy testing, 67% failed to achieve either clinical or histologic remission.¹¹ A larger prospective study of 50 adults undergoing an empiric SFED for EoE found that skin prick testing predicted only 13% of identified food triggers.¹² Similar results were demonstrated in a separate study of 67 adults undergoing SFED in which allergy testing showed no concordance with identified offending food antigens.¹³ Finally, a technical review of 12 single-arm observational studies reported a histologic response rate of 50.8%.⁸ Although the AGA-JTF guidelines recommend all dietary therapies over no treatment for EoE,⁹ the sensitivity of traditional allergy testing for food triggers has been suboptimal. On a molecular pathophysiologic level, this may be because EoE is not an immunoglobulin E (IgE)-driven disease. Supporting this, a randomized trial of the anti-IgE antibody omalizumab (Xolair, Genentech) found that the drug did not change symptoms nor histology in treated patients.¹⁴ Interestingly, however, the same study found that esophageal tissue in patients with EoE had a 45-fold increase in immunoglobulin G4 (IgG4) compared with controls. Patients with EoE were also found to have increased serum IgG4 levels reactive to milk, wheat, egg, and nuts. These results generated the hypothesis that EoE may be an IgG4-associated, rather than IgE-induced, allergic disorder. A recent randomized trial between milk elimination and SFED found that milk-specific IgG4 was associated with response to milk elimination, supporting this theory.¹⁵ Recently presented data from a prospective trial evaluating the efficacy of food-specific IgG4-directed elimination diet reported histologic remission in 50% of patients.¹⁶ Although the role of IgG4 testing in dietary

Table 1. Considerations for the Clinical Assessment of Patients With EoE Receiving Dietary Therapy

Clinical assessment	Clinical pearls
Nutritional status	<ul style="list-style-type: none"> Patients should be screened for restrictive eating. Patients with >5% unintentional weight loss in <3 months and patients who have symptoms with high nutritional impact such as dysphagia, pain, or loose stools are considered to be at increased nutritional risk for malnutrition. Dietitian assessment with addition of oral enteral supplements and nutritional monitoring minimize risk.
Timeline and endoscopy scheduling	<ul style="list-style-type: none"> The level of food antigen removal (eliminating 6 foods vs 4 foods vs 2 foods vs 1 food), along with endoscopy schedules, can determine intervention length. Patients should be prepared that dietary therapy can take >6 months. Timing the start date to avoid difficult times (eg, travel, holidays, life events) should be part of the shared decision-making process.
Co-occurring food allergies and intolerances	<ul style="list-style-type: none"> Patients with EoE are highly atopic. Dietary intake may be severely restricted at baseline. Nutritional assessment identifies whether patients can maintain healthy dietary patterns while opting for dietary therapy. Nutritional care plans should consider religious, cultural, and personal values associated with food.
Culinary interest and food environment	<ul style="list-style-type: none"> Limiting dining out can reduce cross-contamination. Access to cooking equipment and ability to purchase and store groceries are important when considering the level of dietary restriction. Nutritional care plans should include optimizing nutritional intake, mapping out meal preparation and snack ideas, and providing resources for patients and families.

EoE, eosinophilic esophagitis.

therapy for EoE is yet to be fully elucidated, these results suggest that more research is needed to understand whether it may be superior to standard allergy testing. Therefore at this time, empiric elimination diets are favored over allergy testing-directed diets.

Of the empiric dietary therapies available for EoE, the empiric SFED has been the best-studied approach to date. In the SFED, the common allergens of milk, wheat, soy, egg, nuts/peanuts, and fish/shellfish are empirically removed from the patient's diet. A technical review of 10 single-arm observational studies demonstrated a 67.9% histologic remission rate.⁸ Initially studied in a pediatric patient population, the SFED provided clinical and histologic improvement in EoE with more favorable acceptance, cost, and adherence compared with an elemental diet.⁶ The SFED was subsequently shown to be effective in adults; a prospective study of 50 patients with EoE demonstrated that 70% achieved histologic remission (≤ 10 eos/hpf) and 94% had reduced symptom scores.¹² Wheat and milk were the most implicated food antigens (60% and 50% of cases, respectively). These results were replicated in a separate European study of 67 patients with EoE in which 73.1% achieved histologic remission (< 15 eos/hpf).¹³ A single offending food antigen was identified in 35.7% of patients, 2 triggers in 30.9%, and 3 or more triggers in 33.3%, with milk being the most common

trigger (in 61.9%), followed by wheat (in 28.6%), egg (in 26.2%), and legumes (in 23.8%). Despite the efficacy of SFED, significant challenges remain, including the need for multiple endoscopies to identify food triggers with this approach owing to poor correlation between symptoms and histologic activity.¹⁷⁻¹⁹ Recent research has shown that use of SFED in clinical practice can lead to 54% to 58% complete histologic remission, and completing food reintroduction has identified only 1 food trigger in 69% of patients.²⁰

These limitations of the empiric SFED have led to more recent research into an alternative, step-up elimination diet approach. In an initial prospective, multicenter Spanish study, a step-up approach starting with dairy and wheat elimination (ie, a two-food elimination diet) reduced endoscopic procedures and diagnostic process time by 20% compared with empiric SFED.²¹ This initial elimination diet achieved remission in 43% of children and adults in the study. Patients who did not respond to this two-food elimination diet moved on to a four-food elimination diet (avoidance of wheat, dairy, egg, and soy), and patients who did not respond to that diet moved on to a SFED. In computer-based simulation model analyses, a step-up dietary elimination approach maximized efficiency in identifying food triggers while balancing the number of endoscopies required.²² Additional data

Table 2. Suggested Substitutes for Key Nutrients Eliminated in Six-Food Elimination Diet

Foods	Nutrients	Substitutes
Cow and mammalian milk, cheese (including goat), butter, yogurt	Protein, calories, calcium, vitamin D, vitamin A, vitamin B12, phosphorus	Fortified vegan milk, meats, legumes, whole grains, fortified juices
Wheat/gluten ^a	Folate, B complex, fiber, iron, calories	Fortified grains, dark green leafy vegetables, root vegetables, legumes, whole wheat-free grains such as millet, oats, quinoa, buckwheat
Egg	Protein, vitamin A, riboflavin, pantothenic acid, biotin, selenium	Meats, legumes, whole grains (wheat-free), orange/yellow root vegetables
Soy	Protein, vitamin B6, folate, calcium, phosphorus, magnesium, iron, zinc	Meats, legumes, seeds, dark green leafy vegetables, gluten-free whole grains, fortified beverages
Peanuts and tree nuts	Protein, selenium, manganese, magnesium, niacin, phosphorus, vitamin E, vitamin B6, essential fatty acids	Meats, seeds, plant-based oils and butter substitutes, legumes and lentils, dark green leafy vegetables
Fish and shellfish	Protein, omega-3 fatty acids, vitamin A, vitamin D, phosphorus, selenium, zinc	Meats, seeds, plant-based oils, seed butter, fortified plant-based milk alternatives

^aWheat is most often excluded, but some centers may recommend gluten-free grains owing to cross-contamination of wheat with other grains such as oats.

in support of a less-restrictive diet elimination approach come from recent randomized trials. In one trial comparing milk elimination and SFED in adult patients with EoE, efficacy was surprisingly similar (histologic response rates of 34% compared with 40%, respectively; $P=.58$).¹⁵ However, more patients randomized to SFED achieved complete remission (0-1 eos/hpf) compared with dairy elimination (19% compared with 6%, respectively; $P=.03$). In nonresponders to dairy elimination, 43% ultimately responded to salvage therapy with SFED. Early data from a pediatric trial of dairy elimination compared with a four-food elimination diet also found similar response rates between the 2 diets, although the latter was superior in reducing symptoms.²³ The optimal choice for dietary therapy in clinical practice is ultimately the one that patients and families can successfully adhere to and have the resources to complete, and should be chosen after careful consideration of patient preferences in partnered decision-making (as discussed in a later section).

Discussing Dietary Therapy With Patients

The goal of dietary therapy is to identify causative triggers and ultimately restore the most nutritionally balanced and least-restrictive eating pattern that meets overall health recommendations. Dietary therapy should be viewed as a 3-phased approach offering an elimination phase lasting 6 weeks, a reintroduction phase to identify the food

triggers, and then a maintenance phase.²⁴ Even if patients choose medical therapy over food antigen avoidance after dietary therapy is completed, there is value in identifying causative agents. In a survey of patients who had completed SFED, 57% remained on the diet for long-term maintenance.²⁵

When considering candidates for EoE dietary therapy, several factors, including baseline nutritional status, religious and cultural food patterns, lifestyle, and the ability to purchase and cook alternative foods, are important considerations. Table 1 offers nutritional considerations for clinicians. In pediatric populations, a registered dietitian also considers growth, development, and screening for feeding dysfunction. Interestingly, in a survey of patients who completed dietary therapy with SFED, the majority of patients would advise dietary elimination to other patients irrespective of whether they were still maintaining dietary therapy.²⁵ This supports the concept that knowing one's food trigger(s) can provide some meaningful benefit in a patient's ability to control their disease.^{20,25}

Nutritional Considerations/Assessment for Implementing Dietary Therapy

An initial nutritional assessment by a registered dietitian integrates nutritional status, anthropometry, diet history, and relevant cultural and values-based considerations

to diet. For adult patients, recording height and weight to calculate body mass index is an important first step in nutritional assessment. Unintentional weight loss of more than 5% in less than 3 months is a good screening benchmark to assess nutritional risk level. Symptoms such as dysphagia and texture aversion can affect patients' nutrition. Avoidance of food antigens can inadvertently result in decreased calorie and protein intake if patients are not monitored closely. Some adults, however, have a specific goal of weight reduction and seek dietary therapy in EoE as a mechanism to improve eating patterns and nutritional intake. When appropriate, intentional weight loss in adults does not increase nutritional risk.²⁶

In addition to weight patterns, nutritional assessment should include relevant laboratory values in conjunction with dietary patterns, which can result in micronutrient and macronutrient deficiencies if not monitored. For example, a gluten-free diet can place several nutrients at risk, including folic acid, vitamin B6, thiamin, riboflavin, niacin, iron, and dietary fiber. These nutrients may need to be assessed quarterly and supplemented as appropriate if the patient is on the diet long term.²⁶ Cow milk protein is a major source of calcium and vitamin D in American diets. Careful use of fortified foods and oral supplementation of missing nutrients is warranted.²⁷ Commonly avoided foods such as egg, nuts, fish, and soy provide protein, B vitamins, selenium, and essential fatty acids, so nutritional care plans should integrate appropriate and nutrient-dense food substitutes. Table 2 highlights common nutrients at risk and acceptable substitutes.²⁸

Screening for eating behavior patterns such as avoidant/restrictive food intake disorder (ARFID) by registered dietitians is important. ARFID occurs when a feeding disturbance leads to the inability to meet appropriate nutritional and/or energy needs, evidenced by significant weight loss or nutritional deficiency, or dependence on enteral feeding or oral nutritional supplements. Food avoidance or restriction in ARFID is not motivated by fear of weight gain or body image disturbance, but is driven by lack of appetite, aversion to the sensory characteristics of food (pickiness), and/or concern about symptoms arising from eating (fear of symptoms). More sensitive measurement tools are needed to accurately identify patients with ARFID and other maladaptive eating behaviors,²⁹ and research capturing the prevalence of ARFID among adult patients with EoE is lacking. Among pediatric patients, elimination diets need to be carefully managed, as there are additional concerns for both growth and proper oral motor development. Clinical patterns such as intentional weight loss or diminished diet variety and quality are red flags that warrant assessment by a registered dietitian and perhaps a feeding therapist.²⁶ In addition, owing to the social restrictions that dietary elimination may place on

an individual, these situations need to be discussed prior to initiating dietary therapy and should be carefully monitored. If the restrictions of dietary therapy have too great of an impact on a patient's quality of life, transitioning to medical therapy should be considered.

Approach to Treatment in Patients Who Fail Dietary Therapy Initially

When patients have partial or poor response to dietary therapy, it is important to consider other factors impacting responsiveness such as antigen contamination or failure to remove causative agents. It may be helpful to have a dietitian scan food records and talk with patients about possible areas of contamination, increased dining out, and accidental consumption of ingredients that should be avoided. If patients began with eliminating 1 or 2 foods, then a step-up approach should be offered. An alternative consideration is the increase of allergy-free foods available to patients since the inception of SFED that may introduce naive food proteins. Lucendo and colleagues reported that 23.8% and 19% of a cohort of 42 patients with EoE reacted to all legumes and other wheat-free grains such as rice and corn, respectively.¹³ Conversely in the United States, early dietary intervention trials did not integrate legume-based milk options or protein powders that are now widely available with the growing business interest in meeting food product substitutions associated with allergy-reduced foods.^{12,30}

If patients truly fail dietary therapy, an important consideration is whether there may be untreated acid reflux contributing to persistent esophageal eosinophilia. When proton pump inhibitor (PPI) use is reported in clinical studies, many patients remained on PPI therapy throughout the dietary elimination process. For example, 84% of patients continued twice-daily PPI therapy while undergoing SFED in one prospective study in adults,¹² and 61% to 69% of patients in a recent randomized trial of milk elimination vs SFED were on concomitant PPI therapy.¹⁵ Most observational studies of elimination diets were conducted prior to the 2018 AGREE consensus, which eliminated the need for a PPI trial for the diagnosis of EoE³¹; thus, study inclusion criteria prior to the consensus often required failure to respond to PPI therapy, and many patients remained on concomitant PPI therapy during elimination diets. Since the consensus, patients and providers may reasonably elect to select dietary elimination as their initial therapy without a preceding PPI trial.⁹ However, uncontrolled reflux can lead to impaired epithelial barrier function and integrity of the esophageal mucosa, which may facilitate transepithelial food allergen exposure.^{32,33} Furthermore, reflux alone may independently contribute to esophageal eosinophilia.³⁴

Table 3. Tips From the Authors for the Implementation of Dietary Therapy in Adults With Eosinophilic Esophagitis

Timing of diet initiation is important for success. We often avoid starting dietary therapy before the winter holidays or if patients are about to go on extensive travel or are leaving for college. In these scenarios, we advise patients to hold off on dietary therapy until their schedules are more predictable and diet contamination can be minimized.
During dietary therapy, we advise patients to reach out to us if contamination or adherence issues are encountered. If so, we push back endoscopy an additional 2–4 weeks depending on the degree of contamination.
During the strict elimination phase, we counsel patients to try to avoid eating out at restaurants if possible to decrease the chance of cross-contamination.
In patients who started initially on PPI therapy and did not respond completely, we do not stop the PPI therapy during diet elimination but rather continue it throughout the entire process to minimize additional confounders that can contribute to esophageal eosinophilia.
If patients started initially on dietary therapy upfront without PPI therapy and do not respond, we sometimes add a PPI at that time to control any silent reflux that could be contributing, instead of changing to only PPI therapy.
We typically advise a step-down approach to dietary therapy with either the six-food elimination diet or four-food elimination diet, as it tends to be easier for patients to add foods back to their diets after response rather than sequentially take foods away with the step-up approach. However, if patients want a less-restrictive diet or want to use step-up therapy, we proceed in that manner, as the ultimate decision is based on shared decision-making with patients after extensive discussion about the efficacy of different diets.
During food reintroduction, we add the least likely culprits back first in a sequential manner and leave the most likely triggers to the end to help minimize risk of exposure to trigger foods early in the reintroduction process. Our typical reintroduction path is seafood → nuts → soy → egg → milk or wheat (and then vice versa).
An endoscopy is performed after the food elimination and food reintroduction phases to document histologic response and recurrence given the poor correlation with symptoms and histology.
Once food triggers are identified, we counsel patients on ways to help maintain their diet for long-term success. If they are traveling for holidays, have times at work when it is difficult to be adherent to dietary therapy, or have special occasions when they would like to eat without restriction, we suggest the use of topical corticosteroids to allow for some liberalization of dietary therapy.
We provide detailed nutritional education materials focusing on foods that patients can eat as well as tips for eating outside of the home. Supplemental materials are provided reflecting sample meal ideas, snack options, and success for dining out.

PPI, proton pump inhibitor.

The interaction between EoE and reflux can be complex, and clinicians should screen for overlapping diagnoses. In cases where dietary therapy has failed and a PPI trial has not yet been conducted, clinicians should consider stopping the diet and proceeding with a PPI trial alone to see whether this would resolve inflammation. If there has been partial improvement with dietary therapy and a course of PPI treatment has not been attempted, another option is to add a PPI and continue dietary therapy to assess response. In cases where a PPI trial has already demonstrated a lack of (or incomplete) response yet there remains suspicion for possible untreated reflux, clinicians should consider continuing the PPI concurrently with dietary elimination.

Often, patients are concerned about the safety of PPI therapy and whether it increases the risk of other chronic health issues. A recent randomized, placebo-controlled trial assessed the risk of the incident adverse events of respiratory illness, enteric infections, bone fractures, kidney disease, dementia, and cardiovascular disease in more than 17,000 adult patients taking PPI therapy vs placebo. There was no higher risk other than enteric infections among PPI users. Patients should be counseled on the risks and safety of PPI therapy compared with other medical and dietary treatment options.³⁵

Initial options for salvage therapy in disease unresponsive to dietary elimination include PPIs and/or swallowed topical corticosteroids. In cases where a PPI trial has not yet been completed, this may reasonably be considered first, given its favorable safety and accessibility profile. If patients have been adherent to dietary therapy and contamination is not suspected, options include further diet elimination with additional foods, including corn, beef, and legumes, or transitioning to another available medical therapy.²⁰ The desire to proceed with either direction is largely driven by the patient's goal of therapy being the identification of their food triggers.

Helping Patients Individualize Dietary Therapy

Patients often ask which dietary therapy they should try first. Providers should counsel them on the available data and the effectiveness of different dietary therapies: elemental diet (94%), SFED (70%), four-food elimination diet (50%), two-food elimination diet (44%), and one-food elimination diet (35%).^{8,24} Reviewing the histologic efficacy of these varied approaches helps patients decide which path they wish to pursue. When deciding between step-up vs step-down approaches, it is important to review exactly what is added and taken away at each step. For instance, if milk and wheat elimination fails in a step-up diet, then 2 more foods are removed. As a result,

the patient moves on to eliminating milk, wheat, soy, and egg, not simply switching to eliminating just soy and egg. In some cases, it can be more discouraging for patients to eliminate more items as the diet progresses vs using a top-down approach. At each stage, clinical monitoring should assess nutritional intake and quality of life during treatment to determine whether modifications to the treatment plan are needed. Ultimately, the decision on which direction to pursue is based on a shared decision-making process with the patient. Table 3 highlights some clinical management pearls that the authors have used to help patients with EoE achieve success with dietary therapy.

Assessing Response to Treatment During Dietary Therapy

Guidelines from the AGA, American College of Gastroenterology, and American Society for Gastrointestinal Endoscopy advocate for repeated endoscopic assessment after treatment intervention with either dietary or medical therapy, as symptoms alone are not a reliable indicator of disease activity.^{1,9,36} This can pose a challenge for patients undergoing dietary therapy and food reintroduction, which can result in as many as 6 additional endoscopies.²⁰ However, minimally invasive tools to assess esophageal inflammation have recently been developed and may be considered for use in patients undergoing food reintroduction. One such tool is the Esophageal String Test (Enterotrack), which has shown high sensitivity and specificity in identifying esophageal inflammation in a 1-hour test in adults³⁷ that can identify inactive and active EoE.³⁸ This test consists of a string housed in a capsule that patients swallow in an outpatient office-based setting without sedation. The string is taped to the patient's cheek and left in the esophagus for a minimum of an hour and then withdrawn and sent to the laboratory for evaluation of eosinophil byproducts absorbed on the string. A report is then generated from the laboratory that gives a score with the likelihood of esophageal inflammation present. Another test evaluated in EoE is Cytosponge (Medtronic), which has been used clinically for the assessment of Barrett esophagus.³⁹ This test has been studied in patients with EoE and has shown good correlation with esophageal biopsies; it also has been studied in patients undergoing food reintroduction in a recent study.^{40,41} In addition, studies in children have shown that the use of transnasal endoscopy has been an effective way to monitor disease inflammation in patients undergoing food reintroduction.^{42,43} All of these tests are promising and will hopefully improve patient care by minimizing the need for patients to undergo endoscopy with sedation after reintroducing each food. However, these tests are not all available for standard-of-care use at this time.

Conclusion

Dietary therapy is an effective treatment approach to help control histologic, symptomatic, and endoscopic abnormalities in children and adults with EoE. Empiric elimination diets are favored over elemental and allergy testing-directed diets. There are many available options for empiric elimination diets, and discussion with patients about the pros and cons of each diet in a shared decision-making approach is critical for successful implementation. Consultation with a registered dietitian or utilization of nutritional resources when dietitian services are not available can be helpful for patients and clinicians. (See eFigures at www.gastroenterologyandhepatology.net for supplemental patient resources, including nutrient-dense SFED-friendly meal ideas, a dining-out checklist for patients, and produce and protein snack ideas.) Once dietary therapy is started, it is important to complete food reintroduction to identify food triggers and liberalize diet for long-term management. Areas of active research include long-term outcomes of dietary therapy and the development of testing to predict food triggers, which are critical for personalizing this approach for patients.

Disclosures

Ms Doerfler has done consulting for Nutricia and has been on the speakers bureau for Nutricia. Dr Lam has no relevant conflicts of interest to disclose. Dr Gonsalves has done consulting for AstraZeneca, AbbVie, BMS, Sanofi-Regeneron, and Knopp, and she has been on the speakers bureau for Sanofi-Regeneron.

References

1. Dellow ES, Gonsalves N, Hirano I, Furuta GT, Liacouras CA, Katzka DA; American College of Gastroenterology. ACG clinical guideline: evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis (EoE). *Am J Gastroenterol.* 2013;108(5):679-692.
2. Schoepfer AM, Safroneva E, Bussmann C, et al. Delay in diagnosis of eosinophilic esophagitis increases risk for stricture formation in a time-dependent manner. *Gastroenterology.* 2013;145(6):1230-1236.e1-e2.
3. Kelly KJ, Lazenby AJ, Rowe PC, Yardley JH, Perman JA, Sampson HA. Eosinophilic esophagitis attributed to gastroesophageal reflux: improvement with an amino acid-based formula. *Gastroenterology.* 1995;109(5):1503-1512.
4. Markowitz JE, Spergel JM, Ruchelli E, Liacouras CA. Elemental diet is an effective treatment for eosinophilic esophagitis in children and adolescents. *Am J Gastroenterol.* 2003;98(4):777-782.
5. Liacouras CA, Spergel JM, Ruchelli E, et al. Eosinophilic esophagitis: a 10-year experience in 381 children. *Clin Gastroenterol Hepatol.* 2005;3(12):1198-1206.
6. Kagalwalla AF, Sentongo TA, Ritz S, et al. Effect of six-food elimination diet on clinical and histologic outcomes in eosinophilic esophagitis. *Clin Gastroenterol Hepatol.* 2006;4(9):1097-1102.
7. Peterson KA, Byrne KR, Vinson LA, et al. Elemental diet induces histologic response in adult eosinophilic esophagitis. *Am J Gastroenterol.* 2013;108(5):759-766.
8. Rank MA, Sharaf RN, Furuta GT, et al; AGA Institute; Joint Task Force on Allergy-Immunology Practice Parameters collaborators. Technical review on the management of eosinophilic esophagitis: a report from the AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters. *Gastroenterology.*

- 2020;158(6):1789-1810.e15.
9. Hirano I, Chan ES, Rank MA, et al; AGA Institute Clinical Guidelines Committee; Joint Task Force on Allergy-Immunology Practice Parameters. AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters clinical guidelines for the management of eosinophilic esophagitis. *Gastroenterology*. 2020;158(6):1776-1786.
 10. Spergel JM, Brown-Whitehorn TF, Cianferoni A, et al. Identification of causative foods in children with eosinophilic esophagitis treated with an elimination diet. *J Allergy Clin Immunol*. 2012;130(2):461-467.e5.
 11. Molina-Infante J, Martin-Noguerol E, Alvarado-Arenas M, Porcel-Carreño SL, Jimenez-Timon S, Hernandez-Arbeiza FJ. Selective elimination diet based on skin testing has suboptimal efficacy for adult eosinophilic esophagitis. *J Allergy Clin Immunol*. 2012;130(5):1200-1202.
 12. Gonsalves N, Yang G-Y, Doerfler B, Ritz S, Ditto AM, Hirano I. Elimination diet effectively treats eosinophilic esophagitis in adults; food reintroduction identifies causative factors. *Gastroenterology*. 2012;142(7):1451-1459.e1.
 13. Lucendo AJ, Arias Á, González-Cervera J, et al. Empiric 6-food elimination diet induced and maintained prolonged remission in patients with adult eosinophilic esophagitis: a prospective study on the food cause of the disease. *J Allergy Clin Immunol*. 2013;131(3):797-804.
 14. Clayton F, Fang JC, Gleich GJ, et al. Eosinophilic esophagitis in adults is associated with IgG4 and not mediated by IgE. *Gastroenterology*. 2014;147(3):602-609.
 15. Kliewer KL, Gonsalves N, Dellow ES, et al. One-food versus six-food elimination diet therapy for the treatment of eosinophilic oesophagitis: a multicentre, randomised, open-label trial. *Lancet Gastroenterol Hepatol*. 2023;8(5):408-421.
 16. Lim A, Ngoi B, Hissaria P, et al. Serum food-specific IgG4-led targeted elimination diet in patients with eosinophilic esophagitis [abstract 466]. Presented at Digestive Disease Week; Chicago, IL; May 7, 2023.
 17. Safroneeva E, Pan Z, King E, et al; Consortium of Eosinophilic Gastrointestinal Disease Researchers. Long-lasting dissociation of esophageal eosinophilia and symptoms after dilation in adults with eosinophilic esophagitis. *Clin Gastroenterol Hepatol*. 2022;20(4):766-775.e4.
 18. Chang JW, Yeow RY, Waljee AK, Rubenstein JH. Systematic review and meta-regressions: management of eosinophilic esophagitis requires histologic assessment. *Dis Esophagus*. 2018;31(8):31.
 19. Hirano I, Furuta GT. Approaches and challenges to management of pediatric and adult patients with eosinophilic esophagitis. *Gastroenterology*. 2020;158(4):840-851.
 20. Zalewski A, Doerfler B, Krause A, Hirano I, Gonsalves N. Long-term outcomes of the six-food elimination diet and food reintroduction in a large cohort of adults with eosinophilic esophagitis. *Am J Gastroenterol*. 2022;117(12):1963-1970.
 21. Molina-Infante J, Arias Á, Alcedo J, et al. Step-up empiric elimination diet for pediatric and adult eosinophilic esophagitis: the 2-4-6 study. *J Allergy Clin Immunol*. 2018;141(4):1365-1372.
 22. Zhan T, Ali A, Choi JG, et al. Model to determine the optimal dietary elimination strategy for treatment of eosinophilic esophagitis. *Clin Gastroenterol Hepatol*. 2018;16(11):1730-1737.e2.
 23. Kliewer K, Aceves SS, Atkins D, et al. Efficacy of 1-food and 4-food elimination diets for pediatric eosinophilic esophagitis in a randomized multi-site study. *Gastroenterology*. 2019;156(6):S-172-S-173.
 24. Chang JW, Kliewer K, Haller E, et al; Consortium of Eosinophilic Gastrointestinal Disease Researchers. Development of a practical guide to implement and monitor diet therapy for eosinophilic esophagitis. *Clin Gastroenterol Hepatol*. 2023;21(7):1690-1698.
 25. Wang R, Hirano I, Doerfler B, Zalewski A, Gonsalves N, Taft T. Assessing adherence and barriers to long-term elimination diet therapy in adults with eosinophilic esophagitis. *Dig Dis Sci*. 2018;63(7):1756-1762.
 26. Groetch M, Venter C, Skypala I, et al; Eosinophilic Gastrointestinal Disorders Committee of the American Academy of Allergy, Asthma and Immunology. Dietary therapy and nutrition management of eosinophilic esophagitis: a work group report of the American Academy of Allergy, Asthma, and Immunology. *J Allergy Clin Immunol Pract*. 2017;5(2):312-324.e29.
 27. Jamieson JA, Neufeld A. Food sources of energy and nutrients among Canadian adults following a gluten-free diet. *PeerJ*. 2020;8:e9590.
 28. Doerfler B, Bryce P, Hirano I, Gonsalves N. Practical approach to implementing dietary therapy in adults with eosinophilic esophagitis: the Chicago experience. *Dis Esophagus*. 2015;28(1):42-58.
 29. Fink M, Simons M, Tomasino K, Pandit A, Taft T. When is patient behavior indicative of avoidant restrictive food intake disorder (ARFID) vs reasonable response to digestive disease? *Clin Gastroenterol Hepatol*. 2022;20(6):1241-1250.
 30. Gupta RS, Warren CM, Smith BM, et al. Prevalence and severity of food allergies among US adults. *JAMA Netw Open*. 2019;2(1):e185630.
 31. Dellow ES, Liacouras CA, Molina-Infante J, et al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. *Gastroenterology*. 2018;155(4):1022-1033.e10.
 32. Calabrese C, Bortolotti M, Fabbri A, et al. Reversibility of GERD ultrastructural alterations and relief of symptoms after omeprazole treatment. *Am J Gastroenterol*. 2005;100(3):537-542.
 33. van Rhijn BD, Weijenborg PW, Verheij J, et al. Proton pump inhibitors partially restore mucosal integrity in patients with proton pump inhibitor-responsive esophageal eosinophilia but not eosinophilic esophagitis. *Clin Gastroenterol Hepatol*. 2014;12(11):1815-1823.e2.
 34. Winter HS, Madara JL, Stafford RJ, Grand RJ, Quinlan JE, Goldman H. Intraepithelial eosinophils: a new diagnostic criterion for reflux esophagitis. *Gastroenterology*. 1982;83(4):818-823.
 35. Moayyedi P, Eikelboom JW, Bosch J, et al; COMPASS Investigators. Safety of proton pump inhibitors based on a large, multi-year, randomized trial of patients receiving rivaroxaban or aspirin. *Gastroenterology*. 2019;157(3):682-691.e2.
 36. Aceves SS, Alexander JA, Baron TH, et al. Endoscopic approach to eosinophilic esophagitis: American Society for Gastrointestinal Endoscopy Consensus Conference. *Gastrointest Endosc*. 2022;96(4):576-592.e1.
 37. 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(10):1395-1405.
 38. 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(10):1614-1625.
 39. Pilonis ND, Killcoyne S, Tan WK, et al. Use of a Cytospunge biomarker panel to prioritise endoscopic Barrett's oesophagus surveillance: a cross-sectional study followed by a real-world prospective pilot. *Lancet Oncol*. 2022;23(2):270-278.
 40. Alexander JA, Katzka DA, Ravi K, et al. 310 - Efficacy of Cytospunge directed food elimination diet in eosinophilic esophagitis. A pilot trial. *Gastroenterology*. 2018;154(6):S-76.
 41. Katzka DA, Smyrk TC, Alexander JA, et al. Accuracy and safety of the Cytospunge for assessing histologic activity in eosinophilic esophagitis: a two-center study. *Am J Gastroenterol*. 2017;112(10):1538-1544.
 42. Friedlander JA, DeBoer EM, Soden JS, et al. Unsedated transnasal esophagoscopy for monitoring therapy in pediatric eosinophilic esophagitis. *Gastrointest Endosc*. 2016;83(2):299-306.e1.
 43. Friedlander JA, Fleischer DM, Black JO, et al. Unsedated transnasal esophagoscopy with virtual reality distraction enables earlier monitoring of dietary therapy in eosinophilic esophagitis. *J Allergy Clin Immunol Pract*. 2021;9(9):3494-3496.

eFigure 1: Nutrient-Dense Six-Food Elimination Diet–Friendly Meal Ideas**BREAKFAST OPTIONS****Option 1**

$\frac{1}{2}$ cup cooked gluten free oats: topped with 1 tbsp ground flax seeds, $\frac{1}{2}$ cup berries, 1 cup fortified flax milk, coffee or tea

Option 2

Breakfast wrap: Fill 2 corn or brown rice tortilla with: $\frac{1}{2}$ cup cooked leftover potatoes, turkey breakfast sausage, $\frac{1}{2}$ sliced avocado. Add cilantro & salsa if desired. 1 cup fresh melon, coffee or tea

Option 3

Plant based smoothie: Blend: 1 cup hemp milk or flax milk with protein (6 gm protein) + 1 cup frozen fruit of choice (bananas, sliced peaches, berries) + 2 tbsp sunflower seed butter or pumpkin butter + $\frac{1}{2}$ cup ice.

Optional mix ins: 1 handful baby spinach, $\frac{1}{2}$ cup canned pumpkin, 2 pitted dates, dash cinnamon or vanilla extract, cold brew coffee, vegan protein powder

LUNCH & DINNER OPTIONS**Option 1: Make Your Own Burrito Bowl**

Base: 2 cups mixed greens, 1 cup cooked brown rice or quinoa. Top with: canned & rinsed black beans, cooked ground beef or turkey (optional to add spices: cumin, chili powder, smoked paprika and garlic), diced cherry tomatoes, cooked corn, salsa and guacamole

Round out meal with fruit (clementines, fresh melon or grapes) and cup of fortified nondairy milk or nondairy yogurt with allowed ingredients

Option 2: Chicken Vegetable Soup (great for batch cooking)

In large stock pot or crock pot: Add 8 cups gluten free chicken or vegetable broth, 1 pound boneless skinless chicken breasts, 1 cup each diced: carrots, celery, onions, parsnips. Simmer for 3+ hours. Shred chicken with 2 forks and add back to broth and vegetable mixture. Cook either rice or gluten free orzo separately to add if desired.

Other add in options: drained and rinsed white beans, baby spinach, canned black beans and frozen corn
Round out soup meal with: side salad topped with oil & vinegar and fruit or nondairy yogurt topped with fruit and pumpkin seeds

Option 3: Grilled Chicken & Vegetables

Make marinade: $\frac{1}{2}$ cup apple cider vinegar, $\frac{1}{2}$ cup olive oil or vegetable oil, 1 smashed garlic clove, salt & pepper to taste

Use with chicken breasts or thighs and vegetables such as: bell peppers, zucchini, asparagus, yellow squash

Round out meal by: serving with roasted potatoes or quinoa or tortilla. Use leftover grilled veggies and chicken on salad greens for meal next day

Finish meal with fruit and fortified nondairy beverage

Option 4: Pulled Pork or Chicken and Roasted Sweet Potatoes

Pulled chicken or pork: In Dutch oven or crock pot: add 2-3# boneless skinless chicken thighs or 2-3# of lean pork roast plus 1 cup gluten free broth. Simmer on low-medium heat for 4 hours until meat is falling apart. Shred in juices.

Sweet potatoes: Cut 2 large sweet potatoes into wedges- brush with vegetable or olive oil, salt & pepper and baked at 375 degrees F until fork tender

Serve: Serve shredded meat with allergy free BBQ, Allergy free Brown Rice Bun and sweet potatoes on the side

Round out meal with additional vegetable such as side salad, cooked green beans or broccoli, coleslaw made with vinegar & oil

Tip: use leftover meat for tacos or salads or bowls

eFigure 2

DINING OUT CHECKLIST

Scan Menu Ahead of Visit

CALL AT NON-PEAK TIMES TO SPEAK WITH RESTAURANT STAFF



- Inquire about ingredients in food
- Special attention to marinades & sauces
- Ask Staff to verify ingredients if they aren't sure

Preparation Matters

INQUIRE ABOUT COOKING METHODS



- Avoid Fried food unless dedicated fryer
- Ask if your food can be made in clean pan using clean utensils
- Request fresh gloves when preparing your food
- Choose simply prepared foods: lean meats, vegetables and potatoes or rice cooked in oil
- Request vegetable oils over butter and avoid fried foods

Prepare Plan B



- Eat a light snack before dining to prevent excess hunger
- Bring safe snack or protein shake just in case the restaurant makes a mistake
- Be aware of what beverages you can enjoy at meal

Drinking Safely



- Enjoy alcoholic beverages moderately if at all: 1 drink for women and 1-2 for men
- Clear, distilled spirits are best
- Wine can be enjoyed but aim for vegan wines fined without animal proteins
- Juices, soda, sports drinks, sparkling water and iced teas and coffees can be enjoyed on diet

Dine In



- Eating at home is safest
- Weekend batch cooking allows for quick meal assembly
- Verbalize diet needs to friends and family
- Bring allergy free dish to share for group dinners
- Allergy free diners get to make a plate first to avoid cross contamination from others

eFigure 3: Produce & Protein Snacks

Be Ready with Allergy Friendly Snacks

Sweet Snacks

- Nonfat, Oatmilk yogurt + frozen berries
- 1 cup mango
- 1 tbsp. sunflower seed butter + 1 small apple + 1 tsp. flax seeds
- Popcorn + 1 tsp. honey & 1 tsp EVOO + dash cinnamon
- 6"rice tortilla + 1 tbsp pumpkin seed butter + raspberries
- 2 tbsp coconut milk whip + berries
- 2 rice cakes + 1 tbsp. almond butter + 1 tbsp. craisins
- 1 Bunch grapes + 1 oz dairy free chocolate y
- 1/4 cup seeds + 1 tbsp. shredded coconut + 1 tbsp. raisins
- 1, 6-inch tortilla + 1 tbsp. seed butter + 1/2 banana
- Brown rice English muffin + SF jam
- Bars: The GFB®, 88 Acres®, Blake's Seed®, Enjoy Life®
- Made Good® Bar + 1 handful pumpkin seeds
- Pear + 1 oz. non dairy cheese + 1 tbsp. sugar free jam
- OWYN protein shake + 1 cup melon
- 1 cup diced Melon
- 2 clementines + 1/4 cup seeds
- Smoothie: handful spinach + 1 cup fruit + vegan protein powder
- Gluten free oatmeal + blueberries + 1 tbsp ground flax
- 1 oz. Biona® sea salt chickpeas + fruit
- Fruit dip: Pumpkin seed butter + drizzle honey + apple

Savory Snacks

- 2 mini cucumbers + 1 Tbsp Humuse
- 1 corn tortilla + 2 oz. vegetarian refried beans + tomatoes
- Boursin® dairy free cheese spread+ 1 cup cucumbers
- 3 cups popcorn + 1 tsp. EVOO + 2 tbsp. pumpkin seeds
- 6-8 Gluten Free crackers + 1/4-1/2 avocado
- lettuce wraps: 2 oz chicken breast + salsa
- 4 mini peppers + 2-3 tbsp hummus
- 1/2 cup grits + 1 cup baby spinach + 1/4 vegan margarine
- 1/4 cup sunflower seeds + 1 cup raw veggies
- 2 Brown rice cakes topped with 1 tbsp hummus & tomatoes
- 4 celery sticks + 1 tbsp. seed butter
- 1 cup veggie soup®, Amy's Organic®, Pacific®, Imagine® 8 fl. oz low sodium vegetable juice + 3 cup popcorn
- Brown Rice tortilla + 2 oz turkey+ greens & EVOO
- 1 cup crudité + 2 tbsp.Boursin dairy free cheese spread®
- 1/4 quinoa + 1/4 cup black beans + fresh pico de gallo
- 2 veggie dolmas + 2 tbsp. hummus
- 1/4 cup chickpeas + cucumbers + tomatoes + 2 tsp. EVOO
- 1 serving Harvest Snaps Crisps + handful seeds
- grape tomatoes + basil + olive oil & vinegar
- black bean hummus + peppers
- 1 turkey jerky + 1 cup baby carrots