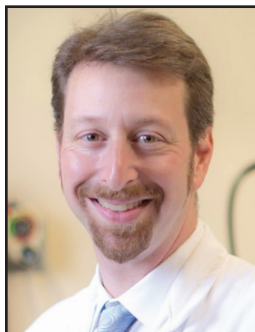


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Nutritional Care of the Patient with Eosinophilic Esophagitis



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Eosinophilic Esophagitis (EoE) is a chronic allergic disease that is characterized by esophageal inflammation and dysfunction. The symptoms vary by age and represent a spectrum from growth failure, vomiting, abdominal pain, and heartburn in children, to dysphagia and food impaction in adolescents and adults. EoE can be treated with dietary elimination, swallowed topical corticosteroids, and, in cases where there are esophageal strictures, dilation. Dietary elimination is the strategic removal of food antigens felt to trigger disease activity. With the elimination of food groups, concerns arise for nutritional risk. Education should be provided to teach techniques on food antigen avoidance as well as strategies to implement a diet that is nutritionally dense, diverse enough to maintain adherence and ensures adequate growth and nutrition status.

INTRODUCTION AND EOSINOPHILIC ESOPHAGITIS OVERVIEW

Eosinophilic Esophagitis (EoE) is a chronic allergic disease that is characterized histologically by eosinophil-predominate esophageal inflammation and clinically by symptoms of esophageal dysfunction that vary by age.¹ The most recent prevalence data demonstrates 56.7/100,000 persons with EoE in the United States, affecting all ages;² both incidence and prevalence of EoE are rapidly increasing.³

In infants and toddlers, symptoms may

include growth failure and feeding difficulties. In elementary school-aged children, symptoms are typically abdominal pain, vomiting, heartburn or regurgitation. In adolescents and adults, dysphagia and food impaction predominate.⁴ (Table 1).

Consensus recommendations provide guidelines on diagnosis and treatment of EoE.⁵⁻⁶ Diagnosis is based on symptoms of esophageal dysfunction, esophageal biopsy with eosinophil predominate inflammation of ≥ 15 eosinophils per high power field (eos/hpf), and persistence of eosinophils isolated to the esophagus after a trial of proton pump inhibitors (PPI) in the absence of secondary causes of eosinophilia.¹ However, these diagnostic criteria have been under debate recently,

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and European guidelines from 2017 have suggested that failure of response to a PPI be eliminated as a diagnostic criterion.⁷ This suggestion is largely based on observations that patients with EoE who do and do not respond to PPI treatment share many similar clinical, endoscopic, histologic, immunologic, and molecular characteristics.⁸⁻⁹

There are three general treatment approaches for EoE: dietary elimination, pharmacotherapy, or, in cases of esophageal strictures, dilation.¹ When considering the optimal treatment method, an individualized plan of care should consider medical, nutritional, and practical barriers to adherence, and a shared decision-making framework should be used to select a therapy.¹⁰ There are currently no FDA-approved medications to treat EoE. However, it has been demonstrated that off label use of topical corticosteroids, when swallowed, effectively treat EoE.^{11,12} Specifically, asthma steroid preparations can be swallowed rather than inhaled to coat the esophagus and provide an anti-inflammatory effect. This approach is effective in many patients,¹³ and formulations of topical steroids are under commercial development.^{14,15} However, a downside of these medications is that when they are stopped, symptoms quickly recur, and long-term maintenance therapy is required.¹⁶ Non-pharmacologic therapies might therefore be desirable.

Dietary Treatment of EoE and Nutritional Implications

Dietary management strategies have been discussed extensively by Groetch et al. in the 2017 Dietary Therapy and Nutrition Management of Eosinophilic Esophagitis: A Work Group Report from the American Academy of Allergy, Asthma and Immunology (AAAAI).¹⁷ The overall concept

Quick Reference to Acronyms Throughout Manuscript
AAF: amino acid based formula
SPT: skin prick testing
APT: atopy patch testing
INDANA: International Network for Diet and Nutrition in Allergy
AAAAI: American Academy of Allergy, Asthma & Immunology
PAL: precautionary allergen labels
FALCPA: Food Allergen Labeling and Consumer Protection Act
CEGiRs: Consortium of Eosinophilic Gastrointestinal Disease Researchers
GF: Gluten Free

is to identify and remove food allergy triggers of EoE from the diet. To do this, dietary elimination is managed with one of three options: elemental formula, empiric dietary elimination, and test-directed dietary modification.

While an elemental diet is the most effective of the dietary elimination options in inducing remission with response rates above 90%, it is also the most restrictive of the diets.⁸⁻²¹ Patients following an elemental diet are only allowed to consume amino acid based formula (AAF) (Table 2), and a few non-nutritious treats (Table 3). There are several available choices of AAF, each with unique macronutrient and micronutrient

Table 1. Eosinophilic Esophagitis Symptoms by Age

Age Group	Symptoms
Child	Growth failure, feeding refusal, emesis, regurgitation/reflux
Adolescent	Emesis, regurgitation/reflux, stomach pain, chest pain, difficulty swallowing, prolonged chewing, food impaction
Adult	Regurgitation/reflux, stomach pain, chest pain, difficulty swallowing, prolonged chewing, food impaction

Table 2. Amino Acid Based Formulas and Cost

Manufacturer	Website	Product	Cost (\$) per 500mL of Formula
Abbott	elecare.com	Elecare Infant	8.17
		Elecare Junior	12.67
Mead Johnson	enfamil.com	PurAmino Infant	7.14
		PurAmino Toddler	10.13
Nestle	nestlenutritionstore.com	Alfamino Infant	8.13
		Alfamino Jr	12.62
Nutricia	neocate.com	Neocate Infant	6.64
		Neocate Syneo Infant	7.64
		Neocate Junior	11.12
		Neocate Junior with Prebiotics	11.12
		Neocate Splash	11.29

Table 3. Ingredients/Candies Allowed While on Strict Elemental Diet (Oral or Enteral)

Acceptable Ingredients	Acceptable Candies
Sugar/dextrose/sucrose	Pixie Sticks
Corn syrup/high fructose corn syrup/corn syrup solids	Smarties brand candy canes and candies
Maltodextrin	Rock Candy
Artificial flavors/sugars/colors	Dum Dum lollipops (artificial flavors only)
Citric and malic acid	Charms Cotton Candy
Soy oil/lecithin	Fun Dip
Refined oils	Nesquik strawberry syrup
Salt/sodium nitrate	Kool-Aid powdered drink mixes

Table 4. Empiric Elimination Diet Options

Empiric Elimination diet options	Foods removed*
Six Food elimination diet (SFED)	Milk, egg, wheat, soy, peanut/tree nuts, fish/shellfish
Four Food elimination diet (FFED)	Milk, egg, wheat, soy
Two food elimination diet	Milk, wheat
One food elimination diet	Milk

*Food groups based on Consortium of Eosinophilic Gastrointestinal Diseases Researchers

content, so it is crucial that attention be given to specific formula selection. Use of an elemental diet in young children may impede development of feeding skills.²² Due to the volume required to meet nutritional requirements, some patients may require a feeding tube for formula administration. Patients on an elemental diet also have prolonged food reintroduction periods to reach a stable diet and may experience social isolation.¹⁷ Finally, expense can be prohibitive, as only a minority of states offer insurance coverage for AAFs, so patients must work with their physicians to explore coverage options.

Because of the restrictive nature of elemental diets, empiric elimination diets were developed as these were easier to adhere to, but still achieved good efficacy, typically in the 60-70% range. The initial empiric elimination diet, which is still the standard, was the so-called six-food elimination diet (SFED), where the “top six” allergens were

eliminated (dairy, wheat, egg, soy, nuts, and seafood). SFED has been shown to be effective in adults²³ and children²⁴ Nevertheless, this diet is still quite restrictive, so newer iterations have tested empiric elimination of one food (dairy),²⁵ four foods (dairy, wheat, egg, soy),^{26,27} or most recently a “step-up” approach where two foods (dairy and wheat) are eliminated initially, followed by four and then six food groups, depending on patient response.²⁸ Studies demonstrate histological and symptom improvement; however, they lack consistency in their specific food group eliminations and efficacy rates in adults and pediatrics. The Consortium for Eosinophilic Gastrointestinal Researchers, an NIH-funded multicenter research network, includes the food groups outlined in Table 4 when conducting empiric diet elimination efficacy studies.

Allergy test-directed diets eliminate foods based on the interpretation of skin prick testing (SPT) and/or atopy patch testing (APT), but these

Table 5. Sample Food Label Information

Section of Label	What to Expect on Label
Ingredient List	Enriched wheat flour, sugar, dark chocolate chunk (chocolate liquor, sugar, dextrose, cocoa butter, cream, soy lecithin, natural flavor), cocoa powder, egg, butter, salt, sodium bicarbonate, baking powder, soybean oil
FALCPA allergen statement	Wheat, soy, milk
PAL statement	Manufactured in a facility that also processes peanuts and tree nuts.

*Note that soy lecithin and soybean oil are allowable ingredients

Table 6. Milk and Milk Alternative Nutritional Comparison Based on 8 Ounces

Milk	Kcal	Fat (g)	Pro (g)	Carbohydrate (g)
Cow's milk	150	8	8	12
Hemp	80	8	2	1
Rice/Quinoa	60	2.5	<1	9
Flax	25	2.5	0	1
Coconut	60	5	0	1
Rice	70	2.5	0	11
Pea	70	8	4.5	0
Almond	60	2.5	1	8
Cashew	60	2.5	<1	9

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are the least effective option, with response rates in the 40% range.²⁰ Because of this, the updated Food Allergy Practice Parameters²⁹ report that IgE blood testing, and SPT and APT alone are not sufficient to diagnose food triggers of EoE. In addition to being the least effective treatment modality, testing for directed diets can be cumbersome,³⁰ as APT requires small metal disks to be affixed to the patient’s skin for 48 hours and a return visit for result interpretation at 72 hours. As well, SPT may cause localized discomfort. Test direct elimination diets may result in the removal of foods not recognized by the allergen labeling laws, thus increasing the risk for accidental allergen exposure due to difficulty in identifying the allergen within ingredient list.

With any elimination diet, dietary education is necessary to ensure adequate nutrition and reduce the risk of accidental allergen ingestion while maintaining quality of life (QoL). Dietary elimination education must consider a patient’s

current nutritional status and ensure effective development of individualized strategies to aid in diet prescription adherence. Note that after a patient achieves remission of EoE based on histological reevaluation using dietary elimination, education is also important for food reintroduction. Enlisting consultation with a registered dietitian should also be considered for patients experiencing treatment failure due to poor adherence, unintentional weight changes, unbalanced diet or factors related to QoL.¹⁷ INDANA, the International Network for Diet and Nutrition in Allergy, <http://www.indana-allergynetwork.org/>, can aid in locating a registered dietitian savvy in dietary elimination related to food allergy or EoE. There are also many available tools and further guidance in the AAAAI Workgroup Report on Dietary Therapy and Nutrition Management of Eosinophilic Esophagitis.¹⁷

Education provided will guide the patient to shop and purchase allergen free and nutritionally appropriate foods independent of the health care

Table 7. Alternatives for Allergen in Food Preparation

Ingredient/Allergen	Substitution
Milk	Equivalent amount of water, juice or milk alternative (see Table 5)
Butter (1 stick)	Equivalent amount avocado or safe margarine 2 Tbsp vegetable oil mixed with 6 Tbsp applesauce 1/3 cup pumpkin puree or refined vegetable oil
Egg (1 large egg)	1/4 cup applesauce or pureed avocado or pumpkin puree 1 Tbsp Vinegar mixed with 1 Tbsp water and 1 tsp baking powder 1/4 cup of warm water to dissolve 1 tsp yeast 1 ripened banana Commercially available egg replacer, dry 3 Tbsp chickpea or white bean juice
Wheat Flour (1 cup)	1 cup commercially available gluten free flour 1 1/3 cup oats* 1 cup tapioca flour 3/4 cup potato starch
Nuts	Toasted coconut Seeds (sunflower, pumpkin) Crushed plain chips (potato or corn) Crushed plain cereal (corn, rice)

*If prescribed a gluten free diet, barley and rye should be avoided in addition to wheat. Oats should be labeled as gluten free to avoid those with possible cross contact with wheat.

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provider. This is particularly important, as prior research has shown that the cost of elimination diets and specialty foods is not negligible.³¹ Label reading education is also crucial, and has two key components, the ingredient panel and the precautionary allergen labels (PAL). The ingredient panel is regulated by the United States Food Allergen Labeling and Consumer Protection Act (FALCPA) and requires that the top 8 most common food allergens in the United States (cow’s milk, wheat, egg, soy, peanut, tree nut, shellfish and fish) be labeled by its common name in a clear and distinct fashion. Soy and peanut oil (highly refined oils), as well as soy lecithin³² are allowable ingredients. While FALCPA is beneficial for patients following an empiric elimination diet, which encompasses only these foods, test directed

diets may eliminate foods outside of the scope of FALCPA and may increase potential for accidental allergen exposure. Other ingredients may have unknown origins such as “natural flavorings” or “modified food starch” and it may be helpful to contact the manufacturer for ingredient source details.

PAL statements indicate the possibility of a product containing an allergen due to inadvertent cross contact during the manufacturing process. These statements are not regulated in their verbiage and are voluntary in placement. Table 5 provides an example of the differences in FALCPA and PAL label statements. Threshold levels of exposure to allergens in EoE are currently not known, but accepted management practice suggests avoidance of allergens as well as potential sources of cross contamination.¹⁷ Once

Table 8. A Two-Day Sample Menu for the Six-Food Elimination Diet (SFED)

Meal	Day 1	Day 2
Breakfast	GF Oatmeal (prepared with milk alternative), blueberries, hemp seeds, coffee (w/coconut creamer)	SFED waffle with 100% pure maple syrup, berries Milk alternative
Lunch	Rice with beans, grilled vegetables, GF corn chips, lettuce, salsa, cheese substitute	GF wrap with chicken, SFED mayonnaise, avocado slices Milk alternative
Dinner	GF pasta with vegetables, grilled pork chop Baked apple with cinnamon Milk alternative	Beef tenderloin, rice, SFED butter substitute, steamed broccoli Orange
Snack(s)	Sunflower seed butter with apple	Sliced vegetables with hummus
	Seed mixture with allergen free chocolate chips and dried fruit	Mini rice cakes with sunflower seed butter
	Allergen free pretzels and hummus	Coconut milk ice cream

Table 9. Additional Resources for Patients and Health Care Providers

American Partnership for Eosinophilic Disorders	APFED.org
Campaign Urging Research for Eosinophilic Disease	CUREDfoundation.org
Kids with Food Allergies	kidswithfoodallergies.org
Clinical Trials	clinicaltrials.gov
Consortium of Eosinophilic Gastrointestinal Diseases Researchers (CEGIR)	rarediseasesnetwork.org/cms/cegir

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allergen avoidance techniques have been learned, discussing implementation of the rules into daily practice should be completed. While the ultimate goals are to improve histology and symptoms, as well as to ensure QoL and nutrition, the diet does not have to be implemented immediately or all at once, and patients and families can transition into a diet over a few weeks' time.

During these weeks, patients can build a list of foods and supplies that need to be substituted. For example, milk and milk-based ingredients are a ubiquitous staple of the American diet, and a palatable yet nutritionally appropriate substitution may require trialing a variety of alternative milks (Table 6), cheeses and yogurts. An extensive nutritional comparison of available milk alternatives has recently been published.³³ Each eliminated food group contributes to a balanced diet and care must be taken during replacement selection. Table 7 provides suggestions on allergen replacements to use while cooking. It is important to note that children under the age of two, who are not breastfed and who are required to avoid cow's milk should be prescribed an AAF.³⁴ A two-day sample menu is available in Table 8, and additional materials are available in the AAAAI Work Group Report.¹⁷

After the first phase of an elimination diet has been successfully completed with histological remission, reintroduction of foods may be considered by the care team. The recommendation is to reintroduce only one food or food group back into the diet at a time and wait six weeks¹⁷ before conducting a repeat endoscopy to verify the EoE remains in remission.^{26,27} In patients with known IgE-type immediate allergic reactions to food, it is also important to collaborate with an allergist during the food reintroduction phase to minimize the likelihood of IgE-mediated reactions. There is no set protocol for food reintroduction, though many providers add back the least allergenic food, or the food least likely to trigger EoE, first. Selection of a food to reintroduce should also consider the patient's ability to eat. Children, in particular, may have delays in oral motor development, adaptive behaviors, or require texture modification. Collaboration with a feeding therapist may be beneficial to diet expansion.¹⁷

Throughout dietary elimination phases, the

patient should be monitored to ensure adequate nutrition and/or growth as well as address barriers to adherence. Monitoring methods include tracking anthropometrics and review of patient's dietary recall to identify allergen and nutrition risks while assessing quality of life. If nutritional risks are identified, laboratory tests may be valuable.¹⁷

CONCLUSIONS

Dietary elimination is an effective treatment for initial and long-term management of EoE.^{24,35} However, with the elimination of food groups, concerns arise for nutritional risk and quality of life. Education and resources (Table 9) should be provided to teach food avoidance techniques on the prescribed elimination diet, as well as strategies to implement a diet that is allergen free, nutritionally dense, and diverse enough to maintain adherence, nutrition status and QoL. Successful EoE treatment with dietary modification requires a multidisciplinary approach, with gastroenterologists, allergists and dietitians. ■

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