Dietary Management of Eosinophilic Esophagitis: When, which approach and why?

Presenters: Amir F. Kagawalla, MD
Sally Schwartz, RD, CSP, LDN

Financial Disclosures

FINANCIAL INTERESTS
I have disclosed below information about all organizations and commercial interests, other than my employer, from which I or a member of my immediate family or household receive remuneration in any amount (including consulting fees, grants, honoraria, investments, etc.) or invest money which may create or be perceived as a conflict of interest.

<table>
<thead>
<tr>
<th>Name of Organization</th>
<th>Nature of Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutricia</td>
<td>Speaker</td>
</tr>
</tbody>
</table>

It is my obligation to disclose to you (the audience) that I am on the Speakers Bureau for Nutricia. However, I acknowledge that today’s activity is certified for CEU credit for Registered Dietitians and thus cannot be promotional. I will give a balanced presentation using the best available evidence to support my conclusions and recommendations.

RESEARCH INTERESTS
I have disclosed below information about all organizations which support research projects for which I or a member of my immediate family or household serve as an investigator.

Objectives

At the conclusion of the webinar presentation, participants should be able to:

• Define and describe the prevalence and clinical spectrum of eosinophilic esophagitis

• Describe the different dietary approaches to managing eosinophilic esophagitis

• Understand the principles underlying elimination diets and the importance of avoiding cross-contamination
Overview

- Review EoE
- Therapy Options
- Nutrition Therapy

Review of EoE

Definition from 2011 consensus guidelines:

- Eosinophilic Esophagitis (EoE) is a chronic, immune/antigen-mediated esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically with presence of dense isolated esophageal eosinophilia.

- EoE has become the most common eosinophilic disease of the gastrointestinal tract

EoE - Definition

- Clinicopathologic diagnosis
  - Presence of clinical symptoms related to esophageal dysfunction
    - Dysphagia, vomiting, abdominal pain, heartburn, feeding difficulty, etc.
  - Isolated esophageal eosinophilia
    - 15 or more eosinophils per hpf
    - Histology of remainder of GI tract normal
  - Exclusion of other GI disorders
    - Absence of pathologic GERD
      - Lack of response to PPI therapy or normal pH probe
    - Infection, Crohn’s disease, hypereosinophilic syndrome

Review of EoE

EoE – An Emerging Epidemic?

1975-1994: Sporadic case reports of patients with EoE
1995: EoE first identified by Kelly et al, showing relationship between EoE and food antigens following Neocate One+ trial
2004: Incidence – children 1:10,000
2007: Actual prevalence in US pediatric population unknown but rising rapidly with 1-4 occurrence in every 10,000 children
   • Higher in US than Europe, Incidence in Africa not known
2010: Just under 600 published articles relating to EoE, around 80% published in the last 5 years!
   • Increasing reports of disease in adult population (1: 2,500)
   • May be combination of increased incidence and recognition
2014: Over a 1,200 publications on eosinophilic esophagitis listed on Pubmed.com

Review of EoE

Pathophysiology

• Strong association between EoE and other allergic diseases
• The majority of patients with EoE have sensitization to food allergens, aeroallergens, or both
• EoE patients have significant over expression of gene eotaxin-3, a chemokine responsible for attracting eosinophils to the esophagus
• Initially EoE considered to be a mixed condition with features of both IgE and cell-mediated food hypersensitivity disorder but newer data supports it as a predominantly a cell-mediated disorder (mostly non-IgE)

Future research directed toward genetic analysis

Gastrointestinal Food Hypersensitivity

IgE mediated

• Oral allergy syndrome
• Gastrointestinal anaphylaxis

Mixed

• Eosinophilic esophagitis
• Eosinophilic gastroenteropathy

Cell mediated

• Food protein induced:
  • enterocolitis
  • proctocolitis
  • enteropathy
• Celiac disease
Eosinophilic Esophagitis: Primary presenting complaint by age

Age (Years)

Percentage of Pop.

0 %

4 %

8 %

12 %

16 %

20 %

26 %

26 %

27 %

7 %

Feeding Disorder
Vomiting
Abdominal Pain
Dysphagia
Food Impaction

N = 103


**Review of EoE**

**Endoscopic findings**

Normal

Rings

**Endoscopic and histologic findings...**

Normal

Furrows

40-50 eos/hpf

White exudates

Trachealization
Review of EoE

EoE – Histology

Normal

EoE – Histology

Esophageal eosinophilia

Abscess

Therapy Options

EoE diagnosis made
Educate family on options

Nutrition Therapy

Elimination diet

Combination Elimination diet with Elemental diet to supplement

Elemental diet

Pharmacologic Therapy

Steroids
Topical or Systemic
Kelly (n=10)
• 10/10 Clinically Improved
• 41 → 0.5 p=0.005

Liacouras (n=164)
• 160/164 Clinically resolved
• 38.7 → 1.1 p<0.001

Kagalwalla (n=25)
• 25/25 Clinically Improved
• 58.8 → 3.7 p<0.001

Peterson (n=18)
• No clinical improvement
• 54 → 10 p=0.0006


Foods tested for
Meats: Chicken, turkey, beef & pork
Vegetables: Peas, string beans, squash, carrots, potatoes & sweet potatoes
Fruits: Apples, pears & peaches
Grains: Wheat, rice, rye, oats, barley & corn
Other foods: Milk, soy, eggs & peanuts

N = 146


Clinical improvement: 89% (131/146)
Histologic improvement: 72% (105/146)
Specific foods identified in 39 pts.
Average # food allergens identified = 4.7/patient
Most common foods: milk, egg, soy, meats, grains.

Children (N = 35)
- 97% Clinically improved
- 80.2 ± 9.4 p<0.0001
- 74.66% ≤ 10 eos/hpf
- Most common foods: milk (80%), soy, wheat, egg

Adults (N = 50)
- 94% Clinically Improved
- 44 ± 13 p<0.0001
- 72% ≤ 10 eos/hpf
- Most common foods: wheat (60%), milk (50%), soy, nuts & egg
Six Food Elimination Diet (SFED)
1. Milk
2. Wheat
3. Egg
4. Soy
5. Peanut/Tree nuts
6. Seafood

**Results with SFED in Children & Adults in USA and Europe are Consistent and Reproducible**


**Different Stages of Elimination Diet**

1. **Remission stage:** Food antigen exclusion

2. **Reintroduction stage:** Sequentially reintroducing the excluded foods back in the diet one food at a time followed by EGD every 6-8 weeks

3. **Maintenance stage:** Excluding only trigger food(s) that resulted in recurrence of inflammation during the food reintroduction phase

**Therapy Options**

- **EdE diagnosis made**
  - Educate family on options

- **Elimination diet**
  - Nutrition Therapy
  - Combination Elimination diet with Elemental diet to supplement

- **Elemental diet**
  - Pharmacologic Therapy
  - Steroids: Topical or Systemic
Nutrition Therapy

Elimination Diets

- **6 Food Elimination (unguided/empiric)** – Remove based on history of the most likely foods
  - 80% of food allergies to children: milk, soy, egg, wheat, peanut/tree nut, fish/shellfish

- **Tailored Elimination (guided/directed)** – Remove specific allergic food based on allergy testing/symptoms
  - skin prick or atopy patch testing, blood
  - clinical history


Empiric Elimination Diets

SFED: Elimination of most common food allergens: milk, soy, egg, wheat, peanut/tree nut, fish/shellfish
  - Lurie experience: 74% patients had histological improvement

4-FED: Elimination of milk, soy, wheat & egg
  - Lurie experience/ongoing multicenter study: 73% patients had histological improvement

Single food elimination: milk
  - Lurie experience: 65% histological improvement


Nutritional Therapy

- **Common deficiencies found in children on elimination diets**

<table>
<thead>
<tr>
<th>Nutrient Deficiencies</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca, Fe, Vit D, Vit E, Zn</td>
<td>Salman et al. 2002</td>
</tr>
<tr>
<td>Ca, Vit D, Vit E</td>
<td>Christie et al. 2002</td>
</tr>
<tr>
<td>Kcal, Protein, Fat, Ca, B6, B12</td>
<td>Henniksen et al. 2000</td>
</tr>
</tbody>
</table>


Elimination diet

- Significant challenges to families and patients
- Milk and wheat proteins are the most difficult to omit and have greatest nutritional impact
- Inadequate nutrition may have long lasting implications i.e. poor growth, delayed development, and failure to thrive.
### Example of diet: 13 yr boy

<table>
<thead>
<tr>
<th>Diet pre-elimination</th>
<th>Pre-elimination diet following SFED</th>
<th>SFED with appropriate substitutes</th>
<th>SFED + elemental formulas to supplement</th>
</tr>
</thead>
<tbody>
<tr>
<td>cheerios 1 cup</td>
<td>cheerios 1 cup</td>
<td>corn flakes 1 cup</td>
<td>corn flakes 1 cup</td>
</tr>
<tr>
<td>2% milk 1/2 cup</td>
<td>orange juice 1 cup</td>
<td>orange juice 1 cup (pH 4.5)</td>
<td>orange juice 1 cup</td>
</tr>
<tr>
<td>banana 1 cup</td>
<td>peanut butter jelly sandwich</td>
<td>peanut butter jelly sandwich</td>
<td>peanut butter jelly sandwich</td>
</tr>
<tr>
<td>orange juice 1 cup</td>
<td>granola bar 1</td>
<td>granola bar 1</td>
<td>granola bar 1</td>
</tr>
<tr>
<td>water</td>
<td>pretzels 1 oz</td>
<td>pretzels 1 oz</td>
<td>pretzels 1 oz</td>
</tr>
<tr>
<td>baked chicken 3/4 w/rice (1/2c)</td>
<td>green beans 1/2c</td>
<td>baked chicken 3/4 w/rice</td>
<td>baked chicken 3/4 w/rice</td>
</tr>
<tr>
<td>dinner roll 2% milk 1 cup</td>
<td>strawberry 1/2c</td>
<td>strawberry 1/2c</td>
<td>strawberry 1/2c</td>
</tr>
<tr>
<td>chocolate chip cookies 2-3</td>
<td>chocolate chip cookies 2-3</td>
<td>chocolate chip cookies 2-3</td>
<td>chocolate chip cookies 2-3</td>
</tr>
<tr>
<td>25 milk 1 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calories: 2,326</td>
<td>Calories: 1,980</td>
<td>Calories: 2,284</td>
<td></td>
</tr>
<tr>
<td>Protein: 88gm</td>
<td>Protein: 65gm</td>
<td>Protein: 76gm</td>
<td></td>
</tr>
<tr>
<td>Calcium: 1,200mg</td>
<td>Calcium: 60mg</td>
<td>Calcium: 594.872mg</td>
<td></td>
</tr>
</tbody>
</table>

### Therapy Options

- **EoE diagnosis made
  - Educate family on options

  **Nutrition Therapy**
  - **Elimination diet**
  - **Combination Elimination diet with Elemental diet to supplement**
  - **Elemental diet**
  - **Pharmacologic Therapy**
  - **Stereoids**
    - Topical or Systemic

### Nutrition Therapy

**Elemental Diet**

- Amino acid-based (AAB) diet using 100% non-allergenic free amino acids as protein source.
- 95%-98% pts respond to elemental diet showing both clinical improvement and complete histologic resolution
- Extremely effective nutritional treatment for EoE
- After resolution of disease, foods may be reintroduced
  - Few foods at a time followed by periodic endoscopy
  - Minimum of 9 months – 1 year as elemental diet being main source of nutrition

An elemental diet is superior at inducing histologic remission compared with other nutrition therapy options for EoE.

Nutrition Therapy

Elemental Diet - Clinical evidence

• 1995, Johns Hopkins University
  • First study to use amino acid-based or elemental approach.
• 10 children previously diagnosed with GERD (unresponsive to PPI’s)
• Used Neocate (and Neocate One+ for children > 1 yo) for minimum of 6 weeks followed by a reintroduction of foods
• Discovered that the ingestion of food caused EoE
• When receiving an amino acid based formula,
  • 100% of pts had improvement in number of esophageal eosinophils
  • 80% had complete resolution of EoE symptoms.


Nutrition Therapy

Elemental Diet - Clinical evidence

• 2003, Children’s Hospital of Philadelphia
  • 51 children diagnosed with EoE and treated with elemental diet (Neocate One+) for 1 month
  • At least 95% of pts had significant improvements in symptoms in 8.5 days

At least 95% of pts had significant improvements in symptoms in 8.5 days

<table>
<thead>
<tr>
<th></th>
<th>Pre-diet</th>
<th>Post-diet</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eos/HPF</td>
<td>33.7±10.3</td>
<td>1.0±0.6</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>40</td>
<td>2</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Vomiting</td>
<td>36</td>
<td>1</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>7</td>
<td>0</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>


Nutrition Therapy

Elemental vs elimination vs pharmacological therapy

• 2005, Children’s Hospital of Philadelphia
• 10 year, retrospective study
• Total of 381 patients diagnosed with EoE
• Corticosteroids effective; upon withdrawal, EoE recurs
• Removal of food antigens significantly improved symptoms and histology in 98% of pts.
• Esophageal eosinophils significantly lower in patients treated with strict elemental diet than in those treated with elimination diet

Nutrition Therapy

Common Challenge - Diet Adherence

<table>
<thead>
<tr>
<th>Nutrition Therapy</th>
<th>Challenges/Barriers</th>
</tr>
</thead>
</table>
| 6 Food Elimination| • May under/over restrict diet  
                     • Increases risk of nutritional deficiencies  
                     • Unfamiliar foods  
                     • Potential growth problems |
| Tailored Elimination| • Increased risk of nutritional deficiencies  
                          • Potential growth problems  
                          • Lack of reliable allergen tests  
                          • Extensive allergy testing done on pt |
| Elemental         | • Psychosocial – quality of life  
                     • Developmental – lack of oral motor stimulation  
                     • Volume intake / palatability – NG or PEG tubes often needed  
                     • Cost, patients unaware of how to obtain |

Elements to consider with family and multidisciplinary team

Feeding dysfunction

Feeding dysfunction associated with EoE and EGIDs

- Feeding dysfunction often occurs in patients with EoE/EGID (usually pre-treatment)
- EoE increases risk by disrupting the developmental continuum of learned feeding skills
- When important feeding milestones are missed in infancy, it may be difficult for the child to learn appropriate feeding techniques

Sources:
Red Flags/Signs of feeding problems:
- Avoiding solids foods or textured foods
- Reducing volume of foods
- Reducing variety of foods
- Prolonged mealtimes

For children with feeding dysfunction consult feeding team (speech/occupational therapists/psychologist) to help treat at first sign of problems.

Tips to avoid feeding problems:
- Positive reinforcement while eating
- Slowly transition/wean to new formula/food
- Introduce new food 10-15 times (at minimum)
- Decrease patterns of "grazing"
- Have scheduled mealtimes with family
- Sit at dinner table to practice using utensils
- Introduce pureed textured allergen-free foods
- Give options in foods/formulas

Nutrition Therapy

Combination: Elimination diet with Elemental supplementation

Initiate Elimination diet with Elemental product supplementation to help meet nutrient needs

This method can help solve challenges associated with diet therapy!

- Reduces risk of nutritional deficiencies
- Offers more options in diet
- Can enhance QOL with more diet options
- Less volume needed from strict elemental diet
- Psychosocial developmental needs met
- Decreases risk of growth issues
Nutrition Therapy

Combination: Elimination diet with elemental supplementation
- Reduces risk of nutrient deficiencies, growth failures, and feeding aversions linked to restrictive diets.
- Helps patients & families meet nutritional and social needs.
- Choosing the right products for patients are based on the patients age, severity of condition, nutritional status, and lifestyle.

- A variety of amino acid-based products are available to boost protein and general nutrient content of restrictive elimination diets.
- Amino Acid-Based (AAB) formula manufacturers have made significant strides to improve flavors, convenience, and variety in textures
  - Semi-solid amino acid-based product
  - AAB formula available with Prebiotic Fiber
  - Variety of flavors for patients to choose from

Tips for Successful Nutritional Therapies
- Involvement of Registered Dietitian (RD) to assess nutritional status, provide education and ongoing support to families
- Education: label reading, appropriate substitutes, cross-contamination, correcting any micronutrient deficiencies, realistic diet plan: focus on balanced nutrition
- Resource identification: FARE, APFED, formula company information for reimbursement help, where/how to purchase
- Planning ahead: for school, snacks, eating out, traveling, celebrations & weeknight meals: Batch cooking, pantry/area of safe foods, research restaurants (call ahead, look up menu online), appropriate substitutes
- Elemental formulas: served chilled in sports/straw bottle, trial safe flavorings

Deciding the best treatment option...
- Consider that EoE is a chronic, lifelong condition and therapy must be individualized
- Multi-disciplinary team should be involved in deciding treatment options
- Physician and family should “discuss” best-fit treatment option
- Patient’s lifestyle, QOL and family resources need to be considered
Case Study: DW

2 year old male presents with poor wt gain, diarrhea and abdominal distension.

Work up:
- Celiac Panel
- Serum IgA
- CBC
- BMP
- Fecal fat
- Folic Acid
- Pre-albumin
- Stool studies
- Vitamin B12
- sweat test

EGD: Duodenum villous atrophy.

- Celiac Panel
- Serum IgA
- CBC
- BMP
- Fecal fat
- Folic Acid
- Pre-albumin
- Stool studies
- Vitamin B12
- sweat test

EGD: Duodenum villous atrophy. Esophagus: 75-90 Eos/HPF

- Plan: Gluten free diet (GFD) and PPI 2x/day for 3 months

Next EGD: Duodenum normal villi. Esophagus: 275-300 Eos/HPF

- Anorexia, aversion to solids.
- Plan: Start SFED in addition to GFD. Provide samples of elemental formulas.

Follow-up visit 1 month later: Poor compliance with SFED and poor caloric intake.
- Plan: G-tube placed and elemental formula only

Case Study: DW

- Elemental formula to provide 100% nutrition needs + apples for oral stimulation
- Repeat EGD: 5 Eos/HPF
- Plan: start food reintroduction with low allergenicity fruits and vegetables, continued elemental diet
- Feeding dysfunction primary problem → Referral to psychologist, feeding team
- Elemental formula providing ~67% calorie needs
- Even though histology improves, symptoms of feeding dysfunction remain.

G-tube placed

Case Study: LM

5 year old female, presents with abdominal pain and vomiting for 6 months. No dysphagia, no food impaction, no difficulty swallowing.

Wt: 19.8kg @ 50-75%ile
Ht: 116.6cm @ 50-75%ile

EGD after PPI 2x/day for 8 weeks

Diagnostic Histology

Diagnostic visual appearance
Case Study: LM

Treatment
- 4FED (milk, wheat, egg, soy, free diet)
- Education by RD
- Sent home w/ elemental formula samples
- Pt taking elemental formula 2x/day.

11 months

2 year follow up:
- Asymptomatic on exclusive milk free diet
- Growth following curve
  - Wt: 50-75%ile
  - Ht: 75-90%ile

Summary: Role of Nutrition in EoE

- Pharmacologic therapy has been shown effective but long term use and possible side effects must be considered
- Elimination diet is effective - keeping in mind nutrient deficiencies may occur
- Elemental diet is the most effective nutrition therapy. Consider family's lifestyle and willingness.

“Dietary therapy should be considered as an effective therapy in all children diagnosed with EoE.”

Combination of elimination diet with elemental supplementation may be the best fit for patients and families dealing with EoE.

Thank you

Thank you for joining us

Please visit NutriciaLearningCenter.com for the recorded version of this webinar as well as other free CEU-eligible recorded webinars.