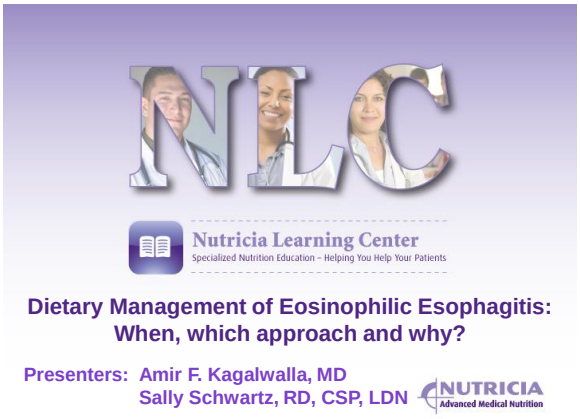


Financial Disclosures

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.

Name of Organization	Nature of Relationship
Nutricia	Speaker

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

Liacouras, et al. *J Allergy Clin Immunol*. 2011
Spergel et al. *J Pediatr Gastroenterol Nutr.* 2009

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

Furuta, et al; *Gastroenterology* 2007; 133:1342.

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

Liacouras, et al. *J Allergy Clin Immunol*. 2011
Furuta, et al. *Gastroenterology*. 2007

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)

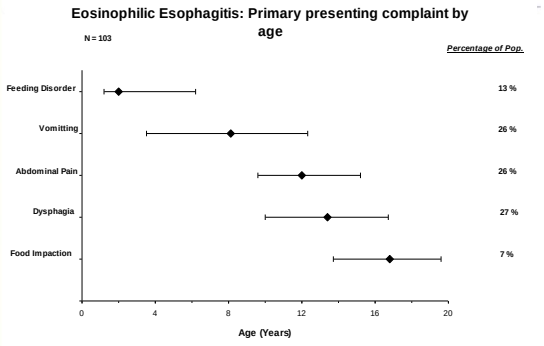
Future research directed toward genetic analysis

Liacouras, et al. *J Allergy Clin Immunol*. 2011
Furuta, et al. *Gastroenterology*. 2007

Gastrointestinal Food Hypersensitivity

IgE mediated	Mixed	Cell mediated
▪ Oral allergy syndrome	▪ Eosinophilic esophagitis	▪ Food protein induced: ▪ enterocolitis ▪ proctocolitis ▪ enteropathy
▪ Gastrointestinal anaphylaxis	▪ Eosinophilic gastroenteropathy	▪ Celiac disease

EoE Presentation by Age



Noel, et al. *N Eng J Med.* 2004;351:940.

Review of EoE

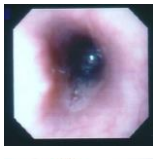
Endoscopic findings

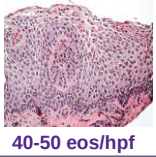
Normal

Rings

Endoscopic and histologic findings…

Normal

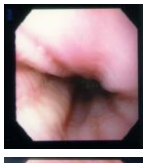




40-50 eos/hpf

Furrows . . . . . .

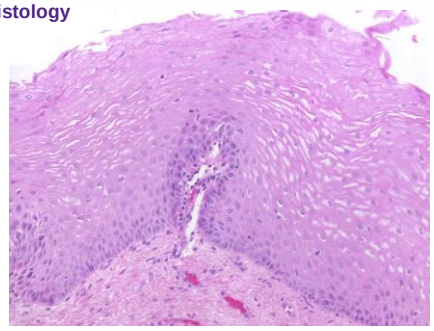
White exudates



Trachealization

Review of EoE

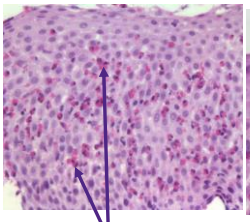
EoE – Histology

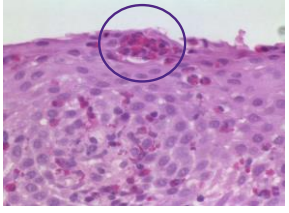


Normal

Review of EoE

EoE – Histology

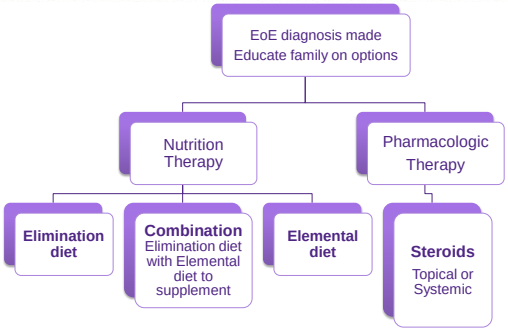




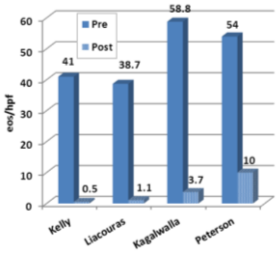
Esophageal eosinophilia

Abscess

Therapy Options



Elemental Diet



- 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

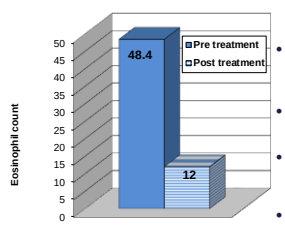
Kelly K, et al. *Gastroenterology*. 1995;109:1503-12.
Liacouras C, et al. *Clin Gastroenterology Hepat*. 2005;3:1198.
Kagalwalla A, et al. *Clin Gastroenterology Hepat*. 2006;4:1097.
Peterson K, et al. *Am J of Gastroenterol*. 2013;Online.

Diet based on combination of skin prick & atopy patch tests in children

N = 146	
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

Spergel J, et al. *Ann Allergy Asthma Immunol*. 2005;95:336-43.

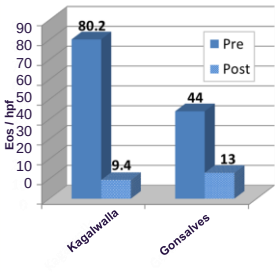
Response to Elimination Diet based on SPT & APT Tests in children



- 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.

Spergel J, et al. *Ann Allergy Asthma Immunol*. 2005;95:336-43.

Non-directed or empiric elimination diet: SFED

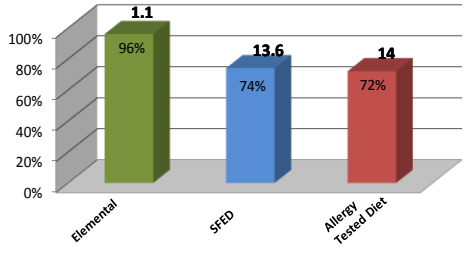


Children (N = 35)
- 97% Clinically improved
- 80.2 → 9.4 p<0.0001
- 74.06% ≤ 10 eos/hpf
- Most common foods: milk (80%), soy, wheat, egg

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

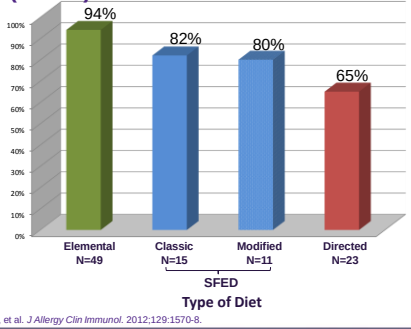
Kagalwalla A. *Clin Gastroenterol Hepat.* 2006;4:1097.
Gonsalves N. *Gastroentrology.* 2012;142(7):1451-9.

Comparison of Different Dietary Treatments in Children



Liacouras C, et al. *Clin Gastroenterol Hepatol.* 2005;3:1198–206.
Kagalwalla A, et al. *Clin Gastroenterol Hepatol.* 2006;4: 1097-102.
Spergel J, et al. *Ann Allergy Asthma Immunol.* 2005;95:336–43.

Single Center Experience Responses to the three different diets (N = 98)

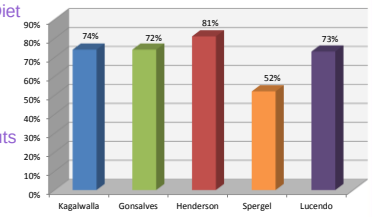


Henderson C, et al. *J Allergy Clin Immunol.* 2012;129:1570-8.

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

Six Food Elimination Diet (SFED)

1. Milk
2. Wheat
3. Egg
4. Soy
5. Peanut/Tree nuts
6. Seafood

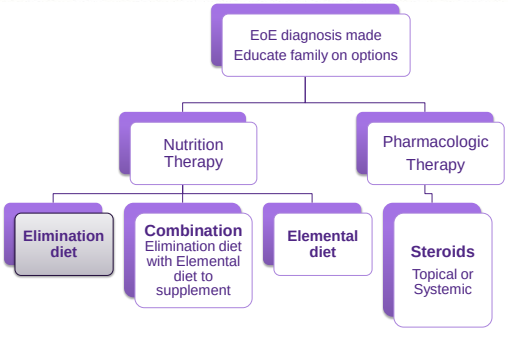


Kagalwalla A, et al. *Clin Gastroenterol Hepatol*. 2006;4:1097-102.
Gonsalves N, et al. *Gastroenterology*. 2012;142:1451-9.
Henderson C, et al. *J Allergy Clin Immunol*. 2012;129:1570-8.
Spergel J, et al. *J Allergy Clin Immunol*. 2012;130:461-7.
Lucendo et al. *J Allergy Clin Immunol*. 2013;E-pub ahead of print.

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



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

Kagalwalla A, et al. *Clin Gastroenterol Hepat.* 2006
Spergel J, et al. *Ann Allergy Asthma Immunol.* 2005
Furuta G, et al. *Gastroenterology.* 2007

Nutritional Therapy

Empiric Elimination Diets

SFED: Elimination of most common food allergens: milk, soy, egg, wheat, peanut/treenut, 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**

Kagalwalla A, et al. *Clin Gastroenterol Hepatol.* 2006;4:1097-102.
Amsden K, Schwartz S, et al. Effect of Four Food Elimination Diet on Clinical and Histologic outcomes in Eosinophilic Esophagitis. Poster session presented at FALK Symposium: Eosinophilic Esophagitis: A Novel Chronic Inflammatory Disease of the GI Tract ;2013 September 6-7; Graz, Austria.
Kagalwalla A, et al. *J Pediatr Gastroenterol Nutr.* 2012;55:711-6.

Nutrition Therapy

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.

Common deficiencies found in children on elimination diets

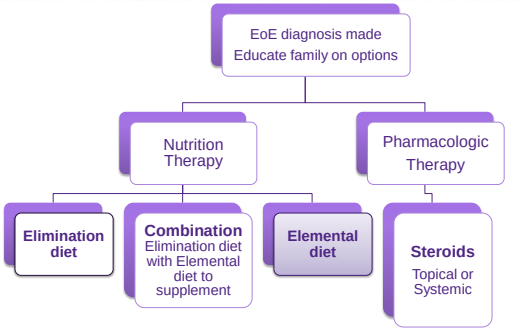
Nutrient Deficiencies	Study
Ca, Fe, Vit D, Vit E, Zn	Salman et al. 2002
Ca, Vit D, Vit E	Christie et al. 2002
Kcal, Protein, Fat, Ca, B_2, B_3	Henriksen et al. 2000

Salman et al. *J Allergy Clin Immunol.* 2002.
Christie L, et al. *J Am Diet Assoc.* 2002.
Hendriksen C, et al. *Acta Paediatr.* 2000.
Spergel J, et al. *Gastrointest Endo Clin N Am.* 2008.

Example of diet: 13 yr boy

Diet pre-elimination	Pre-elimination diet following SFED	SFED with appropriate substitutes	SFED + elemental formulas to supplement
cheerios 1cup 2% milk 1/2 cup banana 1 orange juice 1 cup	~~cheerios 1 cup~~ ~~2% milk 1/2 cup~~ banana 1 orange juice 1 cup	corn chex 1 cup rice milk 4 oz banana 1 orange juice 1 cup (ca/vit D fortified)	corn chex 1 cup rice milk 4 oz banana 1 elemental formula 1 cup 30kcal/oz
peanut butter jelly sandwich (2tbsp pb) granola bar 1 grapes 1 cup lemonade 8floz	~~peanut butter jelly sandwich~~ ~~granola bar (peanut butter)~~ grapes 1 cup lemonade 8floz	ham sandwich (2oz ham) ener-g bread, mustard, lettuce,tomato enjoy life bar 1 grapes 1 cup lemonade 8 floz	ham sandwch (2 oz ham) ener-g bread, mustard, lettuce, tomato enjoy life bar1 grapes 1 cup lemonade 8floz
pretzels 1oz, water	~~pretzels~~, water	potato chips/freeze-dried greenbeans 1oz/ water	potato chips/freeze-dried greenbeans 1oz, water
baked chicken 3oz w/rice (1/2c) green beans (1/2c) dinner roll 1 2% milk 1 cup strawberries 1 cup vanilla ice cream ½ cup	baked chicken w/rice green beans ~~dinner roll~~ ~~2% milk cup~~ strawberries ~~vanilla ice cream~~	baked chicken w/rice green beans slice bread rice milk 1 cup strawberries homemade banana ice cream	baked chicken w/rice green beans slice bread rice milk 1/2 cup strawberries homemade banana ice cream
chocolate chip cookies 2-3 2% milk 1 cup	~~chocolate chip cookies~~ ~~2% milk 1 cup~~	enjoy life foods cookies 2	enjoy life foodscookies 2 elemental formula 8floz
Calories: 2,326 Protein: 88gm Calcium: 1,200mg	Calories: 1,061 Protein: 29gm Calcium: 300mg	Calories: 1,980 Protein: 65gm Calcium: 600mg	Calories: 2,284 Protein: 76gm Calcium: 594-872mg

Therapy Options



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.

Henderson C, et al. *J Allergy Clin Immunology*. 2012.
Liacouras C, et al. *Clin Gastroenterol Hepatol*. 2005.
Markowitz et al. *Am J Gastroenterol*. 2003.
Kelly et al.*Gastroenterology*. 1995.

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.**

Kelly et al. *Gastroenterology.* 1995.

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

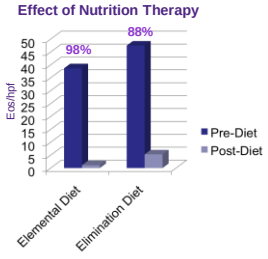
	Pre-diet	Post-diet	p-value
Eos/HPF	**33.7±10.3**	**1.0±0.6**	**< 0.01**
# of pts – Abdominal Pain	**40**	**2**	**< 0.01**
# of pts – Vomiting	**36**	**1**	**< 0.01**
# of pts – Dysphagia	**7**	**0**	**< 0.01**

Markowitz et al. *Am J Gastroenterol.* 2003.

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



Liacouras C, et al. *Clin Gastroenterol Hepatol.* 2005.

Nutrition Therapy

Common Challenge - Diet Adherence

Nutrition Therapy

Nutrition Therapy	Challenges/Barriers
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

Chafen et al. *JAMA*. 2010.

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

Illingworth et al. *J Pediatr.* 1984.
Haas AM, Maune NC. *Immunol Allergy Clin North Am.* 2009.

Nutrition Therapy

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 pt choices in food/formulas

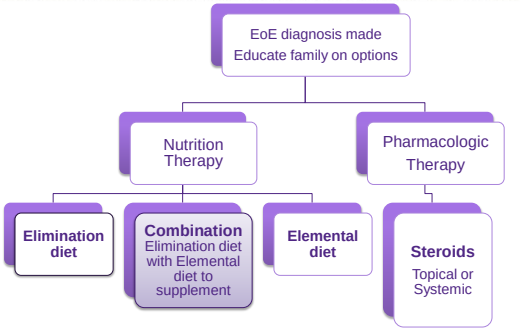
Red Flags/Signs of feeding problems:

- 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.

Illingworth et al. *J Pediatr.* 1984.
Haas AM, Maune NC. *Immunol Allergy Clin North Am.* 2009.

Therapy Options



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

Feuling, Noel. *Nutr Clin Pract.* 2010.
Spergel.,*Gastrotintest Endoscopy Clin N Am.* 2008.

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

Feuling, Noel. *Nutr Clin Pract.* 2010.
Spergel,.*Gastrotintest Endoscopy Clin N Am*. 2008.

Nutrition Therapy

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

http://physicianinfosource.com/

Furuta et al. *Gastroenterology.* 2007.

Case Study: DW

2 year old 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 B_{12}
- 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.

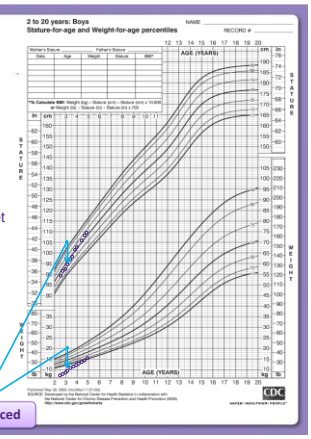
- Plan: Start SFED in additional to GFD. Provide samples of elemental formulas.

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.



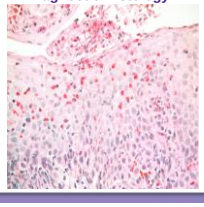
Case Study: LM

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

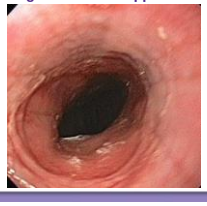
Wt: 19.8kg @ 50-75%ile
Ht: 116.6cm @ 50-75%ile

EGD after PPI 2x/day for 8 weeks

Diagnostic Histology

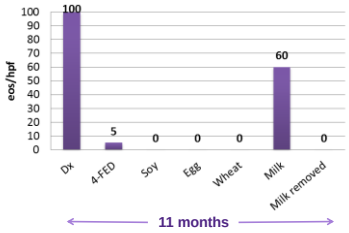


Diagnostic visual appearance



Case Study: LM

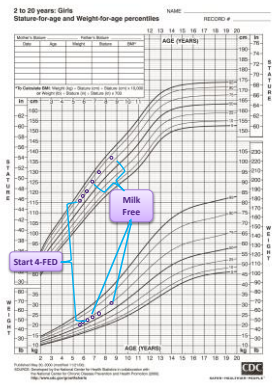
Treatment
- 4FED (milk, wheat, egg, soy, free diet)
- Education by RD
- Sent home w/elemental formula samples
- Pt taking elemental formula 2x/day.



11 months

Case Study: LM

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.

Furuta et al. *Gastroenterology.* 2007.
Feuling, Noel. *Nutr Clin Pract.* 2010.

Thank you

Thank you for joining us

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