



# Multidisciplinary Approach to Eosinophilic Esophagitis (EoE) Management in Children and Adults

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May 20, 2020

## Disclosures



- Disclosures:
  - Honorarium provided by Nutricia

*The opinions reflected in this presentation are those of the speaker and independent of Nutricia North America*

## Polling Question



What is your profession?

- A. Registered Dietitian
- B. Registered Nurse
- C. MD, PA, NP
- D. Other



## An Illustrative Case



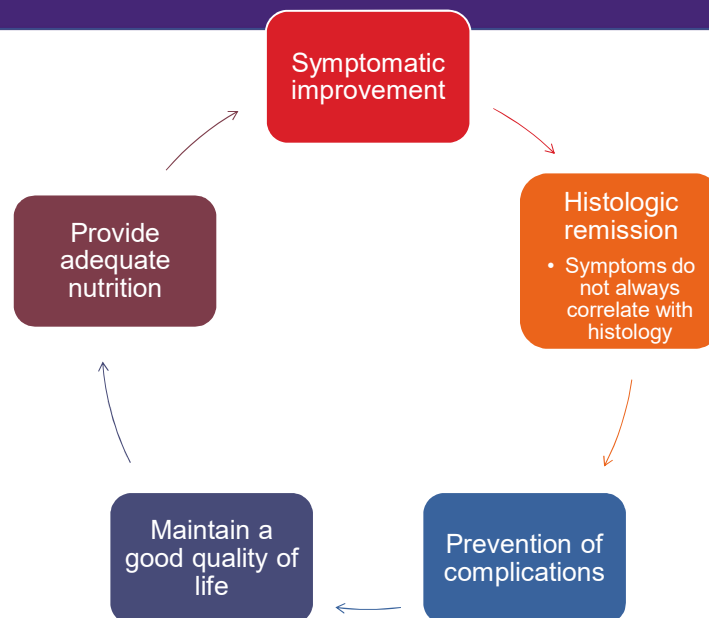
- A 12 yo boy presented to my office, referred from their pediatrician, with a chief complaint of dysphagia
  - ▣ Long-standing history of reflux, dating to infancy
  - ▣ 1 year of episodic dysphagia
    - Episodes becoming more frequent and more severe
  - ▣ Also complains of reflux symptoms
    - Regurgitation and heartburn
    - Abdominal pain
  - ▣ Had been on ranitidine until recent FDA recall
    - Minimal improvement in reflux symptoms
- Mother has been diagnosed with EoE and asthma

## Learning Objectives



- Learning objectives relating to this case:
  - ▣ Understand the symptoms of EoE and how these may change with age
  - ▣ Review the management options for EoE
  - ▣ Discuss an approach to dietary management for EoE
  - ▣ Introduce a multidisciplinary approach to EoE management to optimize care

## Management Goals in EoE

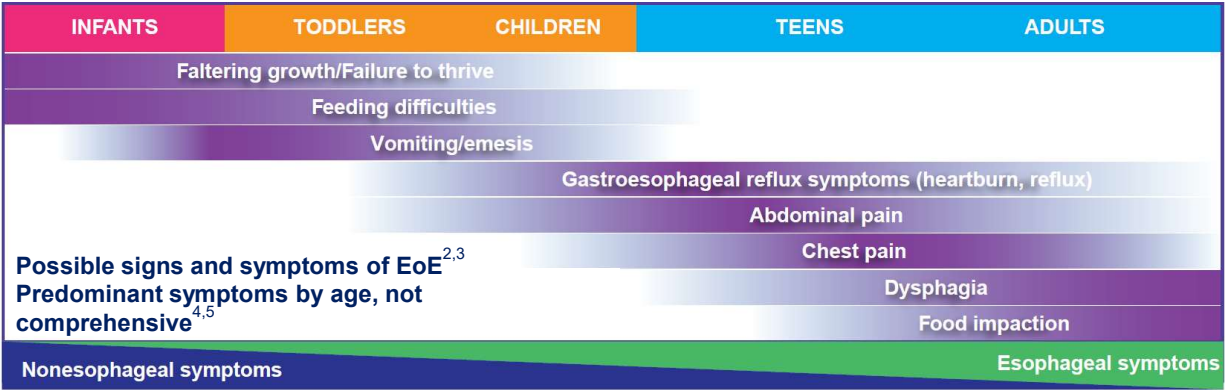


# Presenting Symptoms Vary By Age



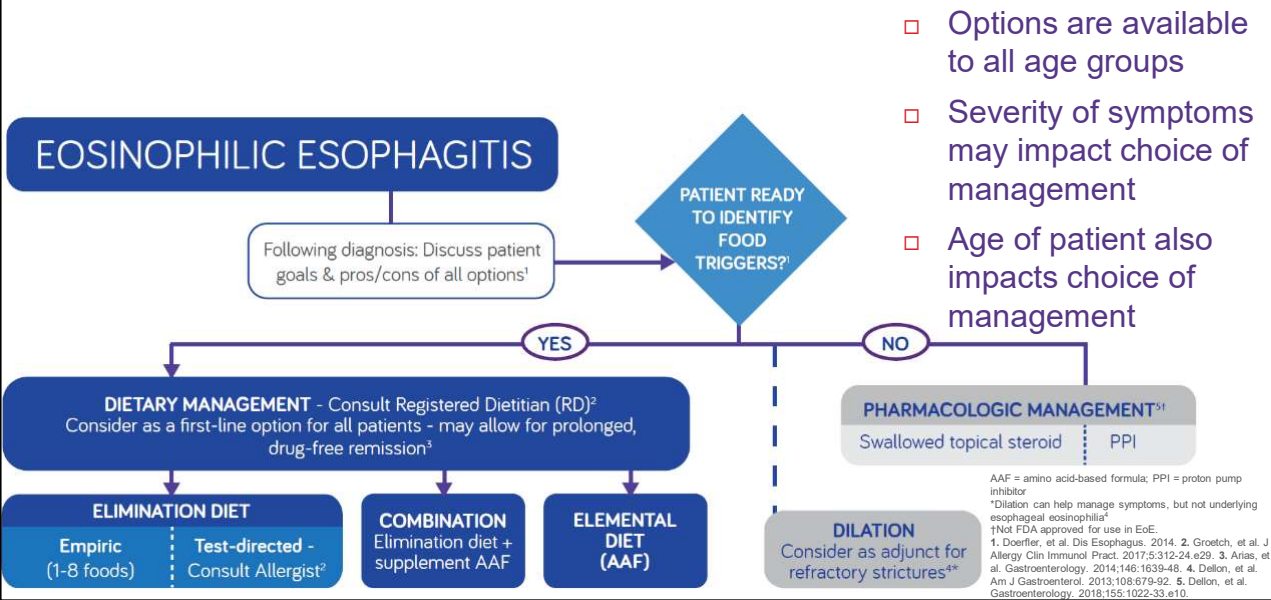
Most prominent symptoms	Feeding disorder	Vomiting	Abdominal pain	Dysphagia	Food impaction
Median age at presentation	2.0 years	8.1 years	12.0 years	13.4 years	16.8 years
Prevalence	13.6%	26.2%	26.2%	27.2%	6.8%

Based on Noel et al, 2004<sup>1</sup>



1. Noel RJ, et al. NEJM 351:9, 2004. 2. Spergel, et al. Allergy. 2020. 3. Furuta, et al. Gastroenterology. 2007;133:1342-63. 4. Dellon, et al. Am J Gastroenterol. 2013;108:679-92. 5. Durban, et al. Pract Gastroenterol. 2018;42:40-51. Illustration courtesy of Nutricia Medical and Scientific Affairs, North America.

# EoE Initial Management



## PPI as Treatment for EoE



- PPI trial should be considered in patients diagnosed with EoE
  - **Option A:**
    - Treat symptoms with PPI before EGD
      - If symptoms resolve, continue to treat based on symptoms
      - May miss a PPI-responsive EoE case
    - Perform EGD if symptoms do not resolve
      - If findings are consistent with EoE, diagnosis is confirmed
      - Can assume EoE is not PPI responsive in that patient
  - **Option B:**
    - Perform EGD before any treatment
    - If findings suggest EoE, treat with PPI
      - High dose, 8 weeks
    - Repeat EGD at end of treatment
      - If still looks like EoE, non PPI responsive EoE
      - If findings resolve, PPI responsive EoE
- If PPI responsive EoE is diagnosed, ongoing treatment with PPI is needed
  - Patients with PPI responsive EoE do not need other treatments

## Topical Steroids for EoE



- As opposed to PPI, topical steroids should be reserved for confirmed diagnosis of EoE
  - From MDI (fluticasone, mometasone, ciclesonide)
  - Budesonide in slurry form (Splenda<sup>1</sup>, Nutra<sup>2</sup>, honey)

**Advantages**

- Relatively easy to administer
- Minimal systemic absorption

**Disadvantages**

- Cost
- Disease relapses when discontinued
- Potential side effects:
  - Esophageal candidiasis (not necessarily candidal esophagitis) in up to 20%
  - Growth

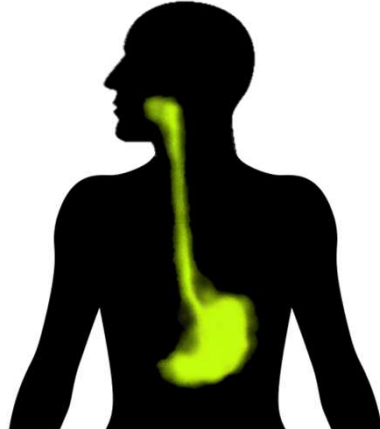
Splenda® is a registered trademark of McNeil Nutritionals, LLC.

1. Gupta SK, et al. Clin Gastroenterol Hepatol 2014. 2. Rubinstein, et al. J Pediatr Gastroenterol Nutr. 2014;59:317-20.

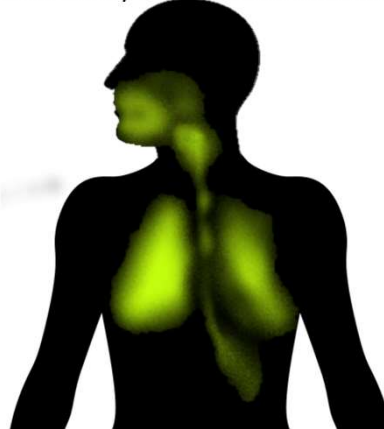
# Viscous vs. Aerosolized Budesonide



**Example oral viscous budesonide distribution**



**Example nebulized (inhaled-aerosolized) budesonide distribution**



Artist illustrations of medication distribution and tissue deposition. Illustrations courtesy of Nutricia Medical and Scientific Affairs, North America, based on nuclear scintigraphy esophageal emptying scans using a nuclear-labeled tracer<sup>1</sup>.

1. Dellon et al. Gastroenterology, 2012.

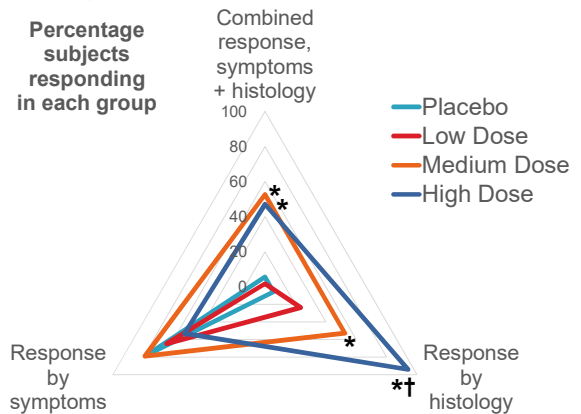
# Effectiveness of Topical Steroids



## Efficacy and Safety of Oral Budesonide Suspension in Pediatric Patients With Eosinophilic Esophagitis

Sandeep K. Gupta, Joanne M. Vitanza, Margaret H. Collins

- N = 71 (18, 17, 19, 17 in the placebo, low, mid, and high dose groups)
- Age-based dosing:
  - low: 0.35 – 0.5 mg/d
  - mid: 1.4 – 2 mg/d
  - high: 2.8 – 4 mg/d
- Unvalidated composite symptom score used (heartburn, abd pain, nocturnal awakening, nausea, regurg, vomiting, anorexia, dysphagia)
- Histologic response: ≤ 6 eos/hpf
- Sx response: ≥ 50% decr in sx score



Gupta SK, et al. Clin Gastroenterol Hepatol 2015.

\* = significant response vs placebo  
 † = significant response vs. OBS medium-dose

## Dietary Elimination



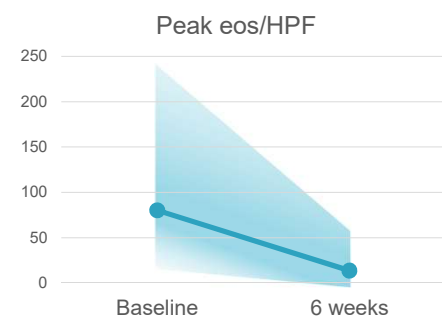
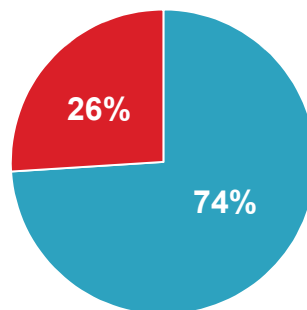
- **Empiric:** selecting the most likely antigenic triggers
  - **6FED-** eliminates the top allergens in U.S. - milk, soy, egg, wheat, peanut/tree nut, fish/shellfish
  - **4FED-** eliminates milk, soy, egg, wheat
  - **2FED-** eliminates milk, wheat
- **Allergy test-directed:** based on results of allergy testing
  - Requires specialized testing to increase accuracy
- **Elemental:** remove all foods and use just an amino acid-based formula
  - Most effective, most life-altering

## Empiric Food Elimination is Effective in Children



### Effect of six-food elimination diet on clinical and histologic outcomes in eosinophilic esophagitis

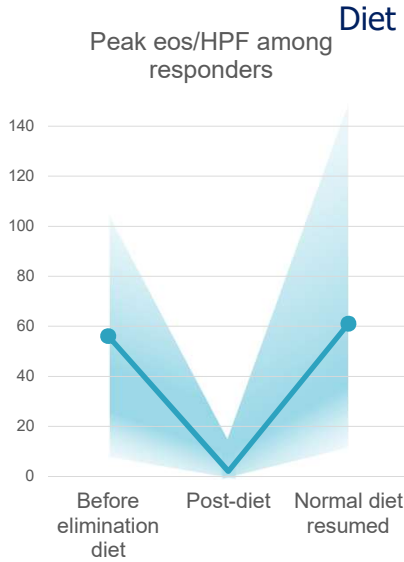
- 35 children on 6 weeks of SFED:
  - **74%** histologic response (<10 eos/hpf)
  - Peak eosinophils dropped from 80.2 to 13.6 eos/hpf



- **Histologic response**
- **Non-response**

Kagalwalla, et al. Clin Gastroenterol Hepatol, 2006.

# Empiric Food Elimination is Effective in Adults



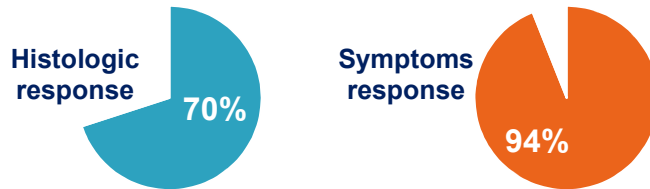
Diet effectively manages eosinophilic esophagitis in adults; Food reintroduction identifies causative factors

⑩ 50 adults with EoE managed with SFED

- 70% histologic response (<10 eos/hpf)
- 94% symptom response
- Recurrence of symptoms with food reintroduction (n=20 patients)

⑩ Most common foods: milk and wheat

⑩ Skin prick testing not predictive



Gonsalves N et al. Gastroenterol, 2012.

# Less Restrictive Diets May Be Effective



**Four-food group elimination diet for adult eosinophilic esophagitis: A prospective multicenter study**

Javier Molina-Infante, Angel Arias, Jesus Barrio, Joaquín Rodríguez-Sánchez, Marta Sanchez-Cazalilla, and Alfredo J. Lucendo

- n=52 adults eliminated dairy, wheat, eggs, legumes
- 54% response rate (< 15 eos/hpf)

**Cow's Milk Elimination: A Novel Dietary Approach to Treat Eosinophilic Esophagitis**

Amir F. Kagalwalla, Katie Amsden, Ameesh Shah, Sally Ritz, Maria Manuel-Rubio, Katherine Dunne, Suzanne P. Nelson, Barry K. Wershil, and Hector Melin-Aldana

- n=17 children eliminated cow's milk only
- 65% response rate (≤ 15 eos/hpf) 41% "complete remission" (0-1 eos/hpf)

Molina-Infante et al. JACI, 2014.

Kagalwalla et al. JPGN, 2012.



## Allergy Test-Directed Dietary Elimination

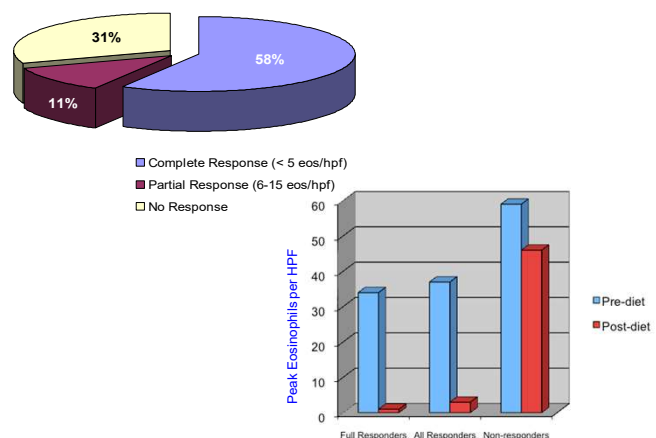


- An alternative approach to empiric elimination and elemental diets
- Based on identification of specific food antigens responsible for EoE
  - ▣ Involves both **IgE-** and **non-IgE-mediated** allergies
  - ▣ Utilizing multiple types of allergy testing that may offer improved results
    - Combination of **skin prick testing (SPT)** and **atopy patch testing (APT)** necessary to get reasonable remission rates

## Using Allergy Testing to Guide Dietary Elimination



- 64 pediatric patients with EoE underwent SPT and APT testing
  - ▣ Repeat EGD 6 weeks after starting restrictions
- **58%** complete remission (<5 eos/hpf)
- **11%** response without remission (5-15 eos/hpf)
- Results comparable to empiric elimination diets



Markowitz JE. J Pediatr Gastroenterol Nutr. 53(S1) 2011.

## Limitations to Elimination Diets



Photo by [Joe Caione](#) on [Unsplash](#)

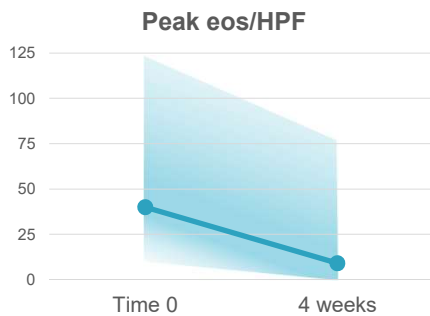
- Difficult to implement
  - Patients need instruction on reading labels, avoiding inadvertent exposure & creating nutritionally adequate diet with allowable foods
- Difficult to maintain long-term
  - Process of identifying food antigens can be long
  - Restrictive diets may be tedious
- May be overly restrictive or not restrictive enough
- May place at risk of nutritional deficiencies
  - Should monitor nutritional status
  - Co-manage with dietitian
  - May need supplemental amino acid-based formula to fill nutritional gaps

## Elemental Diet: Amino Acid-Based Formula

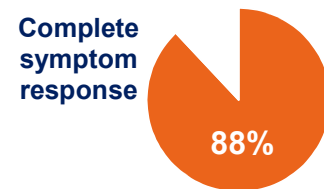
- Exclusive feeding of amino acid-based formula (AAF)
- Up to 97% response rate
- Advantages:
  - Most effective of any published option
- Disadvantages:
  - Most life-altering
  - May require NG or gastrostomy feeds
  - Cost (if paid out of pocket)
    - Increasing state legislative mandates for AAF coverage

Markowitz J et al. Am J Gastroenterol, 2003. Liacouras C et al. Clin Gastroenterol Hepatol, 2005.

## AAF Diet is Effective in Adult EoE



- **94%** (16 of 17) showed response to diet
  - **71%** (12 of 17) adult patients had complete remission
- **88%** (15 of 17) had complete symptom response
  - Symptoms improved in **all** patients



Warners, MJ et al., Alimen Pharmacol Therapeutics, 2017.

## Limitations of Elemental Diet



- Most life altering
- No other foods for duration of the trial—usually 4 to 6 weeks
  - Sometimes allow non-antigenic foods (simple sugars, artificial flavors)
- While palatability of AAFs has improved significantly, must take significant volume to maintain adequate caloric intake
- While AAFs are nutritionally complete, micronutrient deficiencies should be considered
  - Monitor height, weight, lab work
- It can take many months or longer before enough food trials to significantly reduce AAF volume

## Steroids vs. Dietary Management



### Steroids

- Relatively easy
- Relatively few side effects
- No allergy testing needed
- Incomplete remission
- Requires long-term medication
- “Band-aid” approach



### Diet

- Can be difficult
- No “side effects”
- May require allergy testing
- Complete remission
- No need for medications
- Addresses the underlying “root cause” of disease

## Empiric vs. Directed Dietary Management



### Empiric

- No allergy testing needed
- Multiple options: (6FED, 4FED, 1FED)
  - The more restrictive, the better the likelihood of response
- Each option restricts dietary “staples”
  - Still lots of kid-friendly foods (meats, fruits, vegetables) are allowable



### Directed

- Relies on allergy testing
  - Highly dependent on allergist
- May bypass elimination of some dietary “staples”
  - Although almost always includes milk restriction

## Polling Question



Which option is most often used as an initial management approach in your center?

- A. Pharmacological (Steroids, PPIs)
- B. Elimination diet (Empiric, test-directed)
- C. Elemental diet (Amino acid-based formula)
- D. Combination of elimination and elemental diet
- E. Varies significantly between patients

## EoE Management Choices Vary By Center

- Comparison of initial management choices in pediatric patients across academic and community allergy and gastroenterology practices in the Carolinas
  - Steroids as initial management choice varied from **1% to 86%**
  - Diet as initial management choice varied from **2% to 81%**
  - Elemental diet as initial management choice varied from **0% to 6%**

Huang et al. Gastroenterol. 150(4):S1:S669.

## Management Choices May Be Driven By Resources



- Vital clinical providers for dietary management
  - ▣ Gastroenterologist
  - ▣ Allergist
  - ▣ Dietitian
- Vital clinical providers for medical management
  - ▣ Gastroenterologist and/or allergist

## Return to the Case: 12 yo with Suspected EoE



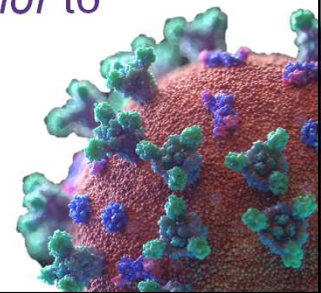
- Trial of PPI initiated
- Awaiting results
  - ▣ If symptoms not improving within first 4 weeks:
    - EGD to be scheduled
    - Allow 6-8 weeks from start of treatment
  - ▣ If symptoms improving:
    - Continued treatment for 3 to 6 months
    - Schedule EGD if lack of complete resolution or symptoms worsen

## Altered Approach in Era of COVID-19?



- ❑ Elective procedures may be postponed indefinitely
  - ❑ Consider empiric topical steroids as first line therapy in newly diagnosed patients
  - ❑ Consider whether an empiric approach *prior* to diagnosis is indicated for highly symptomatic patients
  - ❑ Hold off on any management changes or food trials

Photo by [Fusion Medical Animation](#) on [Unsplash](#)



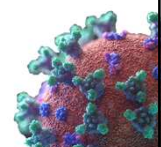
## Polling Question



How have your management practices changed given the current pandemic? Select all that apply.

- A. Increased use of steroids as first-line option
- B. Avoidance of changes to management approach
- C. Avoidance of food trials
- D. Discontinuation of elective procedures (e.g. EGD)
- E. Initiation of telehealth
- F. Other

Photo by [Fusion Medical Animation](#) on [Unsplash](#)



## Proposed Approach for Initial Management NLC NUTRICIA LEARNING CENTER

- Confirm diagnosis
  - Try not to perform EGD until adequate trial of PPI (high dose)
  - If has not had adequate PPI trial, start PPI and plan on repeat EGD to confirm eosinophilia persists

## Proposed Approach for Initial Management NLC NUTRICIA LEARNING CENTER

- Once diagnosis is confirmed, start management approach
  - If **severe** symptoms (dysphagia, weight loss, food impactions), consider temporary topical steroid use
    - If **stricture** present, consider prednisone
  - If mild symptoms, refer to allergist for testing to assist in directing elimination diet
    - Consider restriction of milk +/- wheat pending allergy testing



## Proposed Approach for Initial Management NLC NUTRICIA LEARNING CENTER

- Working with allergist, identify foods to target for elimination
  - ▣ Experience of allergist is important
    - False positives and false negatives are common
    - Reading tests, in particular patch tests, can be subjective
  - ▣ Usually eliminate cow milk regardless of results of testing
    - Allergy testing for milk in EoE is notoriously inaccurate
    - Milk is most common food trigger
  - ▣ Arrange for visit with dietitian to review diet and assess nutritional needs in detail
    - If extensive food allergies identified, recommend supplementation with amino acid based-formula to maintain adequate nutritional intake
    - Younger children commonly need supplemental formula

## Proposed Approach for Initial Management NLC NUTRICIA LEARNING CENTER

- If allergy testing is negative, start empiric approach
  - ▣ Usually 4 or 6 food elimination diet
  - ▣ Meet with dietitian; assess AAF need
- Once dietary elimination is started, discontinue use of steroids (if started)
- Schedule repeat EGD approximately 6 weeks after starting dietary approach
  - ▣ If in remission, can attempt food reintroduction
  - ▣ If not in remission, adjust diet further

## Second Phase of Dietary Management



- If unable to achieve remission:
  - ▣ Consider elemental diet
  - ▣ Consider steroids
- Once new approach started, schedule repeat EGD to confirm remission
- Once in remission:
  - ▣ Start food reintroductions
    - EGD to follow

## Who Captains the Ship?



- GI or Allergy?
- Some factors to consider:
  - ▣ Ease of access
  - ▣ Experience and expertise
  - ▣ Location of other resources
    - Dietitian
    - Psychologist
    - Feeding specialists
- A shared approach is optimal
  - ▣ Requires a shared philosophy
  - ▣ Good communication is vital
  - ▣ Must speak the same language



# Gastroenterology and Allergy



## Gastroenterology

- Make definitive diagnosis (EGD)
- Recommend management approach\*
- Monitor symptoms
- Manage complications
  - Dilation, FB removal
- Instruct on food reintroduction
- Re-evaluate for histologic response
- Manage co-existing GI symptoms

## Allergy

- Identify potential patients
- Diagnose food allergies
- Recommend management approach\*
- Retest prior to food reintroduction
- Instruct on food reintroduction
- Manage co-existing atopic/allergic disease

\*If no agreement on recommended approach, response is likely to be sub-optimal

# Additional Issues



- Many co-morbidities common with EoE patients
  - Anxiety, depression, other psychological issues
  - Behavior problems, particularly around feeding
  - Connective tissue disease
  - Mitochondrial disease
  - POTS/dysautonomia



### ATOPIC:

Asthma, allergic rhinitis, IgE-mediated food allergy, and atopic dermatitis are more common in EoE than the general population<sup>1</sup>



### AUTOIMMUNE CONDITIONS:

Celiac disease, inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis and others have been associated with EoE<sup>2</sup>



### MALE:

Two of every three patients diagnosed with EoE are male<sup>3</sup>



### UNUSUAL EATING BEHAVIORS:

Slow eating, lots of fluid with meals,<sup>1</sup> and preference for pureed textures are seen in children<sup>4</sup>

1. Spergel, et al. Allergy. 2020. 2. Dellon, et al. Gastroenterology. 2018;155:1022-33.e10. 3. Dellon, et al. Clin Gastroenterol Hepatol. 2014;12:589-96 e1. 4. Mukkada, et al. Pediatrics. 2010;126:e672-e7.

## Team Approach is Needed for Complicated Patients



- The optimal management team has many members
  - ▣ Gastroenterologist
  - ▣ Allergist
  - ▣ Dietitian
  - ▣ Coordinator
  - ▣ Psychologist
  - ▣ Feeding therapist
  - ▣ Research nurse
  - ▣ Other specialists: Pain, Rheumatology, Cardiology/POTS

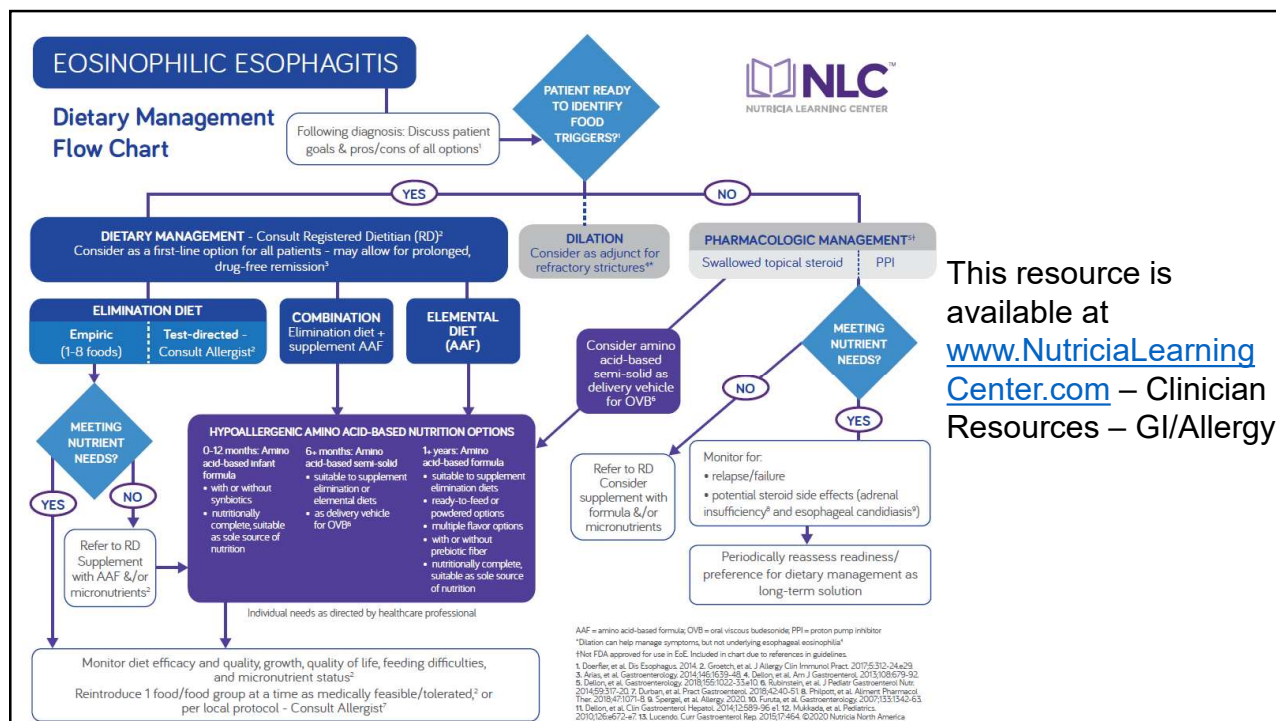


**Questions?**

**Thank you!**

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