EoE: The Allergy Professional's Role

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Disclosers

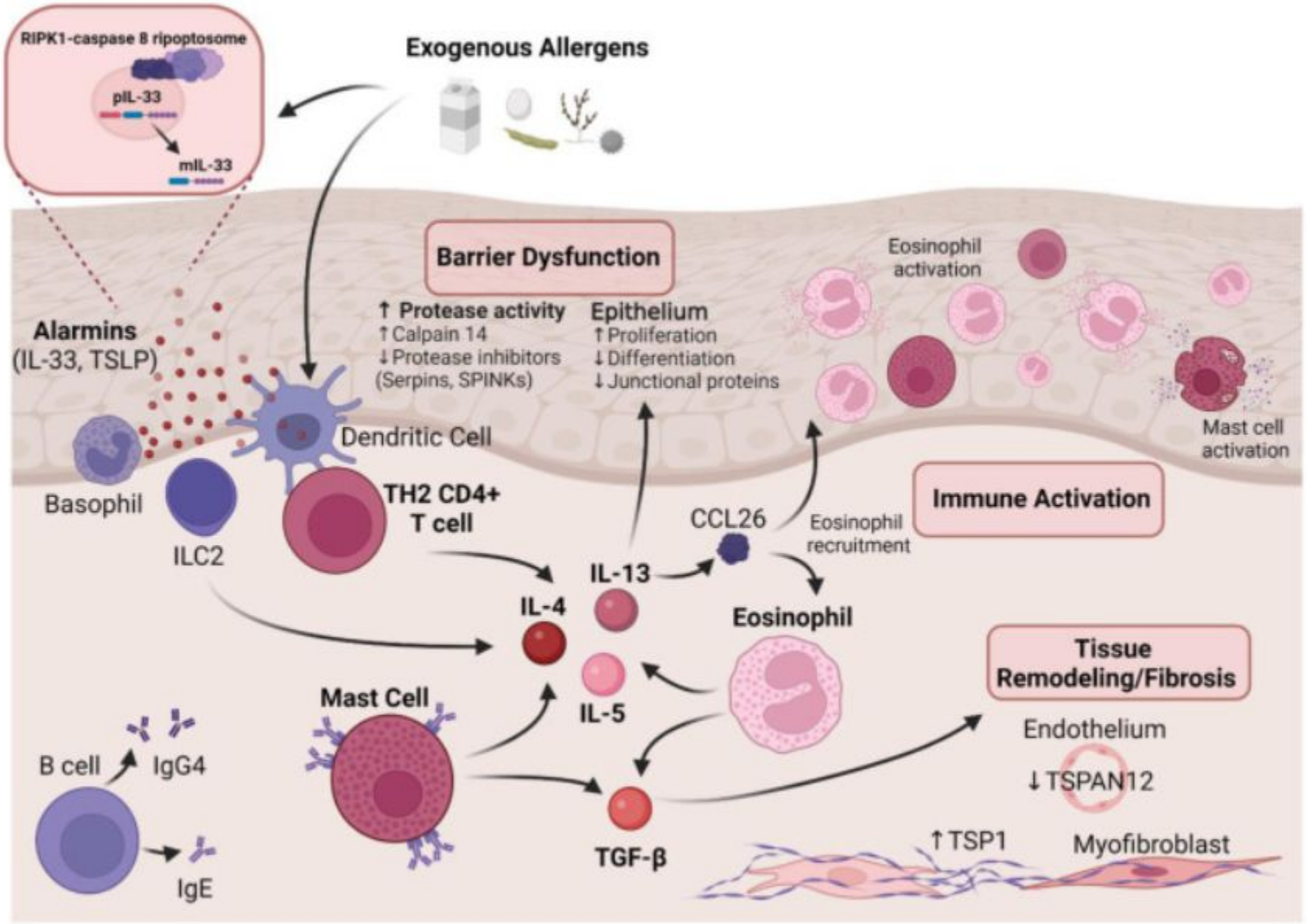
None

Eosinophilic Esophagitis

- **History and Epidemiology**
- **Pathophysiology**
- **Presentation and Diagnosis**
- **Current and Future Treatment Options**
- **Considerations for the Allergy Professional**

History and Epidemiology

- Recognized as a distinct clinical entity in the early 1990's
- Initial guidelines for diagnosis and management in 2007
- Most recent update to guidelines in 2017
- Prevalence 55/100,000 in 2006
- Healthcare cost; $500-$947 million/year
- Incidence increasing
  - Partially due to recognition bias
  - Does not account for degree of increase
- More common in males vs females in both adult and pediatric populations (3:1)
- Biphasic age of presentation
  - Children; 6-10 years of age
  - Adults; 30-40 years of age


RIPK1-caspase 8 ripoptosome
pIL-33
mIL-33
Exogenous Allergens
Barrier Dysfunction
↑ Protease activity
↑ Calpain 14
↓ Protease inhibitors
(Serpins, SPINKs)
Epithelium
↑ Proliferation
↓ Differentiation
↓ Junctional proteins
Eosinophil activation
Mast cell activation
Alarmins
(IL-33, TSLP)
Dendritic Cell
Basophil
ILC2
TH2 CD4+
T cell
CCL26
Eosinophil recruitment
Immune Activation
IL-13
IL-4
IL-5
Eosinophil
Mast Cell
Tissue
Remodeling/Fibrosis
Endothelium
↓ TSPAN12
B cell
IgG4
IgE
TGF-β
↑ TSP1
Myofibroblast

Presentation

Adults (Older than 12 y/o)

- Dysphagia
- Food impaction
- Heartburn
- Chest pain

Children:

- Vomiting
- Heartburn
- Regurgitation
- Abdominal pain
- Poor weight gain/Feeding refusal

Diagnosis

Increased intraepithelial esophageal eosinophil count

- Greater than 15 eosinophils/HPF (6 biopsies)
- Clinical symptoms of esophageal dysfunction
- Exclusion of other causes of esophageal eosinophilia

Other histologic findings common with EoE

- Superficial layering of eosinophils
- Eosinophilic microabscesses
- Epithelial hyperplasia
- Intercellular edema/spongiosis
- Eosinophil degranulation

Diagnosis

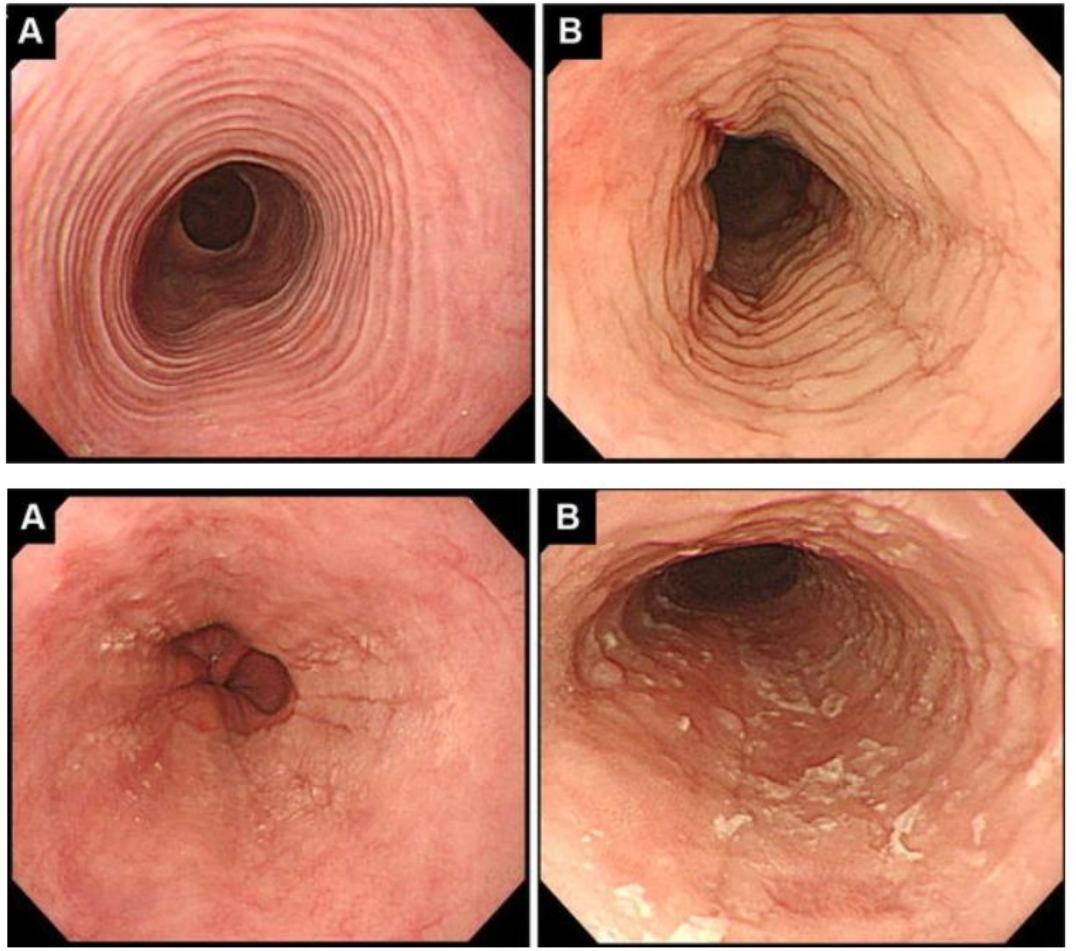
Differential Diagnosis must be ruled out

- Inflammatory Bowel Disease (Crohn's Disease)
- Celiac Disease
- GERD
- Extra-esophageal Gastrointestinal Disease

Presentation

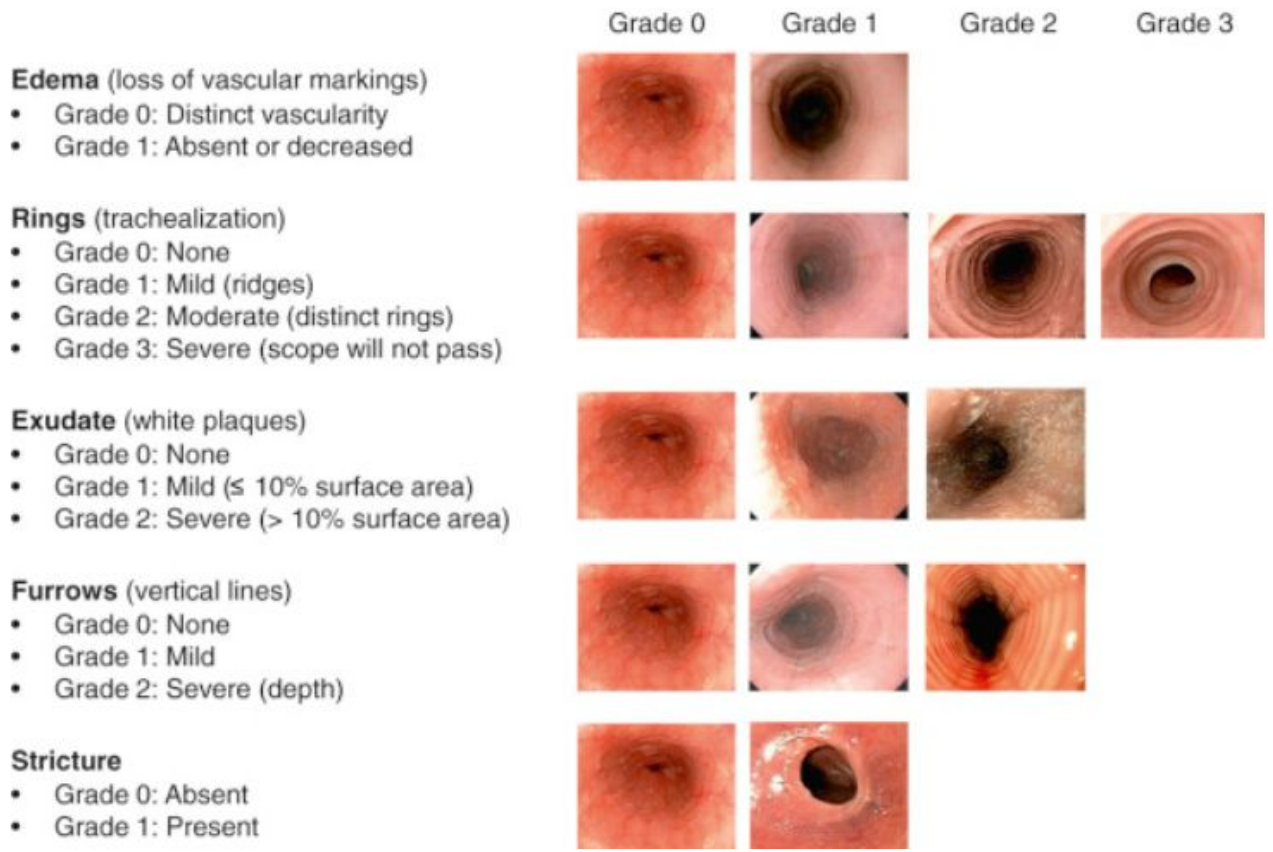
Endoscopic Findings

- **Adults**
  - Linear Furrows (80%)
  - Mucosal Rings (64%)
  - Small Caliber (28%)
  - White Plaques/Exudate (16%)
  - Stricture (12%)
- **Children**
  - Normal Appearance (32%)
  - Linear Furrows (41%)
  - Esophageal Rings (12%)
  - White Plaques (15%)



Treatment

EoE **E**ndoscopic **R**e**F**erence **S**core (EREFS)

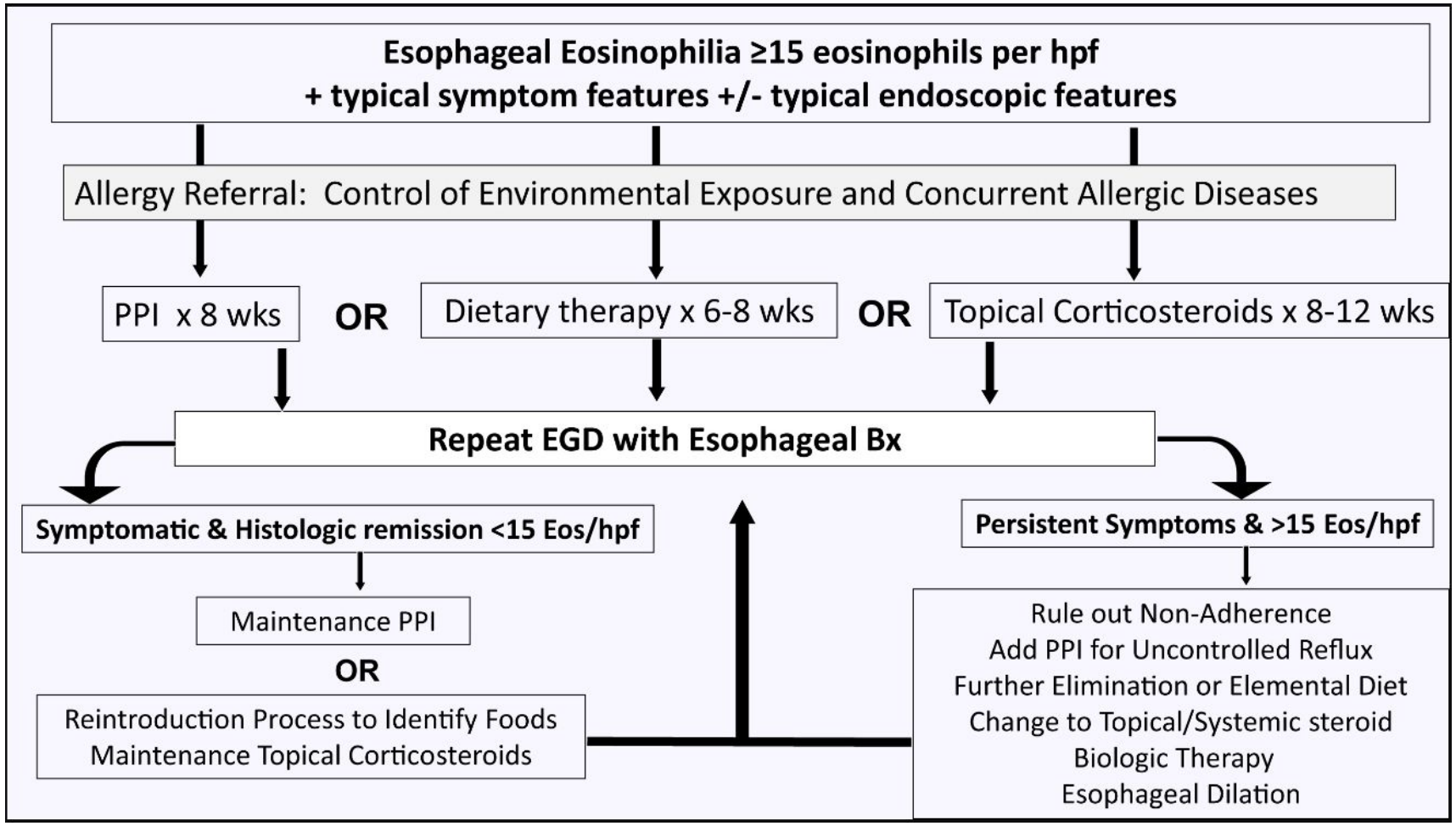


Treatment

- High Dose PPI
- Swallowed/Topical Corticosteroids
- Elimination Diets
- Esophageal Dilatation
- Biologics

- Emerging Therapies

Treatment


Esophageal Eosinophilia ≥15 eosinophils per hpf
+ typical symptom features +/- typical endoscopic features
Allergy Referral: Control of Environmental Exposure and Concurrent Allergic Diseases
PPI x 8 wks
OR
Dietary therapy x 6-8 wks
OR
Topical Corticosteroids x 8-12 wks
Repeat EGD with Esophageal Bx
Symptomatic & Histologic remission <15 Eos/hpf
Maintenance PPI
OR
Reintroduction Process to Identify Foods
Maintenance Topical Corticosteroids
Persistent Symptoms & >15 Eos/hpf
Rule out Non-Adherence
Add PPI for Uncontrolled Reflux
Further Elimination or Elemental Diet
Change to Topical/Systemic steroid
Biologic Therapy
Esophageal Dilation

Treatment

High Dose Proton Pump Inhibitors

- 30-50% of EOE patients respond (41.7% PPI vs 13.3% placebo)
- Pediatric dosing 2mg/kg/day divided BID
- Adult dosing:
  - Lansoprazole- 30mg BID
  - Omeprazole 20-40 mg divided BID
  - Pantoprazole 20-40 mg BID
  - Esomeprazole 20-40 mg daily
  - Rabeprazole 20 mg BID
  - Dexlansoprazole 60 mg daily
- Ideally dosed 30 min before meals

Treatment

High Dose Proton Pump Inhibitors

- Work beyond just acid suppression
- Immunosuppression is occurring
  - Inhibits eotaxin-3
- Frequently a first line treatment.
- Initial EGD should be done before starting PPI

Treatment

Topical Corticosteroids

- 65% histologic response (overall better than PPI) vs 13% in placebo
  - 52% for FDA-approved budesonide oral suspension vs 1% placebo over 12 weeks.
- No eating, drinking or brushing teeth for 30 min after dosing
- Side effects: oral/esophageal candidiasis, adrenal insufficiency
- Recurrence when TCS removed

Treatment

Topical Corticosteroids

- “Puff and Swallow” fluticasone propionate 220mcg inhaler
  - Pediatric dose: 4-8 actuations/day initially, 2-4 actuations maintenance
  - Adult dose: 8 actuations/day initially, 4-8 actuations maintenance
- Budesonide Slurry 0.5mg/2cc respule in thickening agent
  - Pediatric dose: 1mg/d initially, 0.5 mg/d maintenance
  - Adult dose: 2mg/d initially, 1mg/d maintenance
- FDA-approved budesonide oral suspension (Eohilia)
  - 11yo and older
  - Viscous budesonide, 2mg/ml
  - Dosed twice a day for 12 weeks

Treatment

Elemental Diet

- Amino acid based elemental diet
- 80-90% histologic response
- Poor palatability, high cost, poor insurance reimbursement

Diagnosis

Directed Elimination Diet

- Used previously to direct elimination diet based on percutaneous testing and/or patch testing
- Non-IgE mediated mechanism
- Prick skin test positive predictive value 44%
- Not predictive for elimination, but may be helpful prior to reintroduction
- Atopy patch testing technically challenging and unreliable
- Overall limited predictive value of food allergy testing

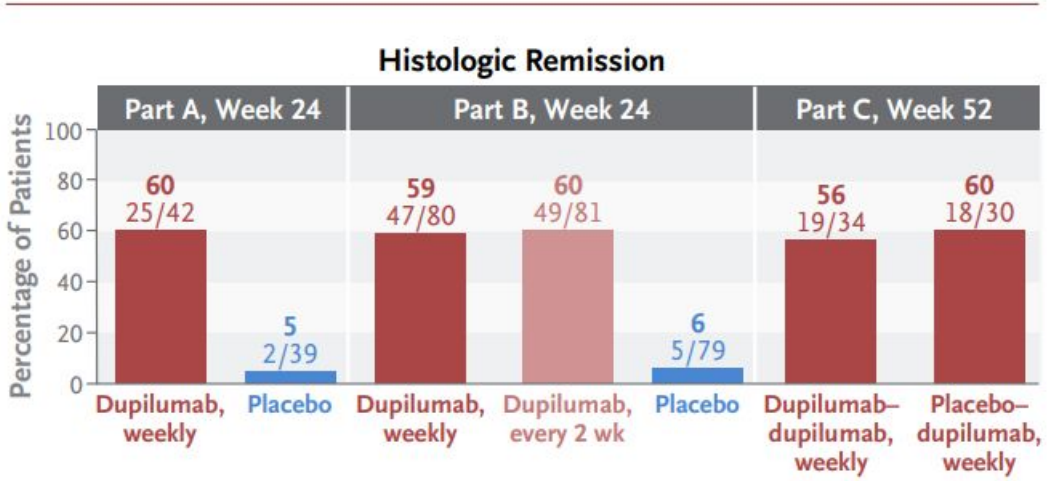
Treatment

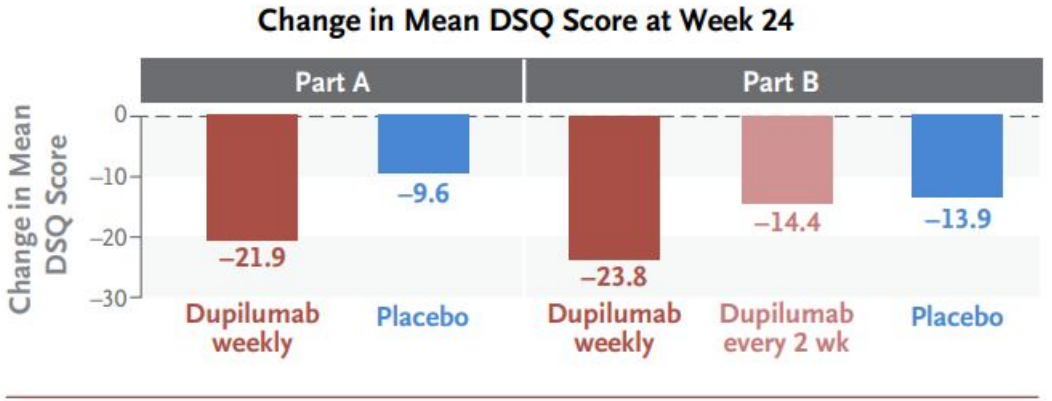
Empiric Elimination Diets

- Milk most common in pediatric patients (50-70%)
- Wheat most common in adults (40-50%)
- Empiric elimination diets
  - Six Food: milk, egg, wheat, soy, peanut/tree nut, fish/shellfish (65-75%)
  - Four Food: milk, egg, wheat, soy (50-65%)
  - Two Food: Milk and Wheat (40-50%)
  - One Food: Milk (particularly in pediatrics, 35%)
- Lancet study, 2023; No difference in clinical or histologic remission between 1 and 6 food elimination diet
- 8-12 week trial and repeat endoscopy
- Reintroduction of foods if response
- 2-4-6 food approach: 43% response after 2 foods, 20% less endoscopies

Treatment

- Anti IL4 receptor α subunit (anti IL4 and anti IL13)
  - Dupilumab
  - 12 week study showed significant decrease in symptoms, and decreased endoscopic and histologic findings
  - Now approved down to 1 year of age/33lbs
  - 60% histologic remission





Body Weight	Recommended Dosage in Adult and Pediatric Patients 1 Year and Older, Weighing At Least 15 kg
15 to less than 30 kg	200 mg every other week (Q2W)
30 to less than 40 kg	300 mg every other week (Q2W)
40 kg or more	300 mg every week (QW)

Treatment

Esophageal Dilatation

- Food Impaction and stricture common presentation in adults
- Treats structural changes and can relieve some symptoms
- Will not alter inflammatory aspect of disease
- May need to be repeated if only treatment

Treatment

Investigatory Treatments

- Anti-Thymic stromal lymphoproteins (TSLP)
  - TSLP functions as a TH2 switch promoting inflammatory response
  - Anti TSLP (tezepelumab) promising in murine models
- Anti-IL5
  - mepolizumab, reslizumab
  - 54% reduction in esophageal eosinophilia, but only minor decrease in symptoms
- Anti-IL13
  - 2 mAbs developed with mixed results

So Why Allergy Professionals?

Most of what I have presented can be performed by gastroenterology

- Diagnosis
  - EGD
- Management
  - PPI
  - Swallowed Steroids
  - Food elimination (allergy testing isn't particularly helpful)
  - Dupilumab
- Follow up
  - Repeat EGD

So Why Allergists?

Patients are highly atopic

- EoE may be an additional part of the allergic march
  - Allergic Rhinitis – 30-90%
  - Asthma – 25-50%
  - Atopic Dermatitis – 10-25%
  - IgE-mediated food allergy – 10-25%

Aeroallergen Sensitization and EoE

Data is inconsistent

- 2015 case series
  - 1,180 patients with EoE
  - 14% with history suggesting seasonality of symptoms
  - 3% had biopsy proven seasonal variation
- Multiple other studies have suggested an association between EoE and seasonal pollen counts.

99. Wang FY, Gupta SK, Fitzgerald JF. Is there a seasonal variation in the incidence or intensity of allergic eosinophilic esophagitis in newly diagnosed children? *J Clin Gastroenterol*. 2007;41(5):451–3. [PubMed] [Google Scholar]

100. Moawad FJ, Veerappan GR, Lake JM, Maydonovitch CL, Haymore BR, Kosisky SE, et al. Correlation between eosinophilic oesophagitis and aeroallergens. *Aliment Pharmacol Ther*. 2010;31(4):509–15. [PubMed] [Google Scholar]

101. Prasad GA, Alexander JA, Schleck CD, Zinsmeister AR, Smyrk TC, Elias RM, et al. Epidemiology of Eosinophilic Esophagitis Over Three Decades in Olmsted County, Minnesota. *Clin Gastroenterol Hepatol*. 2009;7(10): 1055–61. [PMC free article] [PubMed] [Google Scholar]

102. Almansa C, Krishna M, Buchner AM, Ghabril MS, Talley N, DeVault KR, et al. Seasonal distribution in newly diagnosed cases of eosinophilic esophagitis in adults. *Am J Gastroenterol*. 2009;104(4):828–33. [PubMed] [Google Scholar]

103. Iwanczak B, Janczyk W, Ryzko J, Banaszkiewicz A, Radzikowski A, Jarocka-Cyrta E, et al. Eosinophilic esophagitis in children: Frequency, clinical manifestations, endoscopic findings, and seasonal distribution. *Adv Med Sci*. 2011;56(2):151–7. [PubMed] [Google Scholar]

104. Fahey L, Robinson G, Weinberger K, Giambrone AE, Solomon AB. Correlation between aeroallergen levels and new diagnosis of eosinophilic esophagitis in New York City. *J Pediatr Gastroenterol Nutr*. 2017;64(l):22–5. [PMC free article] [PubMed] [Google Scholar]

105. Larsson H, Bergquist H, Bove M. The incidence of esophageal bolus impaction: Is there a seasonal variation? *Otolaryngol - Head Neck Surg*. 2011; 144(2): 186–90. [PubMed] [Google Scholar]

Aeroallergen Sensitization and EoE

Data is inconsistent

- 2013 study of 700 patients
  - Symptoms did not seem to vary based on seasons
- Meta-analysis of 18 studies
  - No seasonal variation in bolus impaction

Overall, limited data, most data is retrospective

- Difficult to study
  - Repeat EGDs
  - Symptoms may lag onset of allergy season
  - Need prospective data

Aeroallergen Sensitization and EoE

Bottom Line

- **Mixed data on aeroallergens and their impact on EoE**
- **SCIT may improve EoE, but it certainly won't hurt**
- **Don't use SLIT**
    - **Associated worsening of symptoms with ODT formulations**

So Why Allergists?

Esophageal String Test

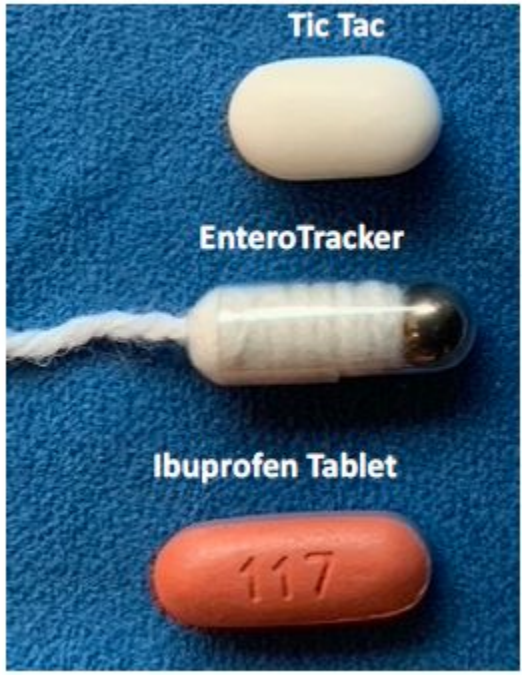
- Now available, Enterotrack
- May decrease the number of EGDs required to manage patients
- Monitors for eosinophil associated proteins in the esophagus and provides a
  - EDGPs eosinophil-derived neurotoxin (EDN)
  - eosinophil peroxidase (EPX)
  - major basic protein 1 (MBP-1)
  - eosinophil cytosolic protein Charcot-Leyden crystal protein/Galectin-10 (CLC/Gal-10)
  - Eot2
  - Eot3

So Why Allergists?

Esophageal String Test

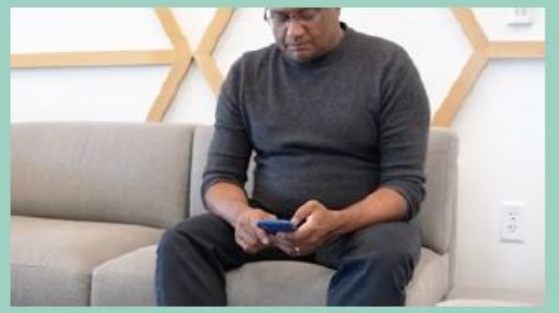
- EoE Score has been shown to correlate with active eosinophilic inflammation of the esophagus.
- Not to be used to diagnose EoE, but could be helpful with stepping up or stepping down therapy.
- Overall, well tolerated.

So Why Allergists?



1 Secure the string to the patient's cheek

2 Mark the string where it lies on the corner of the patient's mouth – this is the 0-cm mark



3 Patient relaxesfor one hour

So Why Allergists?

RETRIEVE

Pull the string back out from the patient's mouth in one smooth motion

PROCESS

pH mark the string to identify the esophageal-gastric transition (or use Cut esophageal section

PREPARE

Transfer the esophageal string segment into the sample buffer vial, mix, and ship to the reference lab

Questions?

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