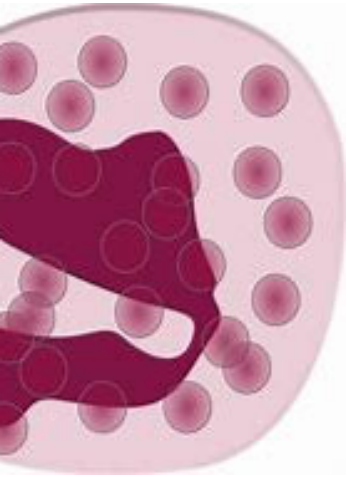

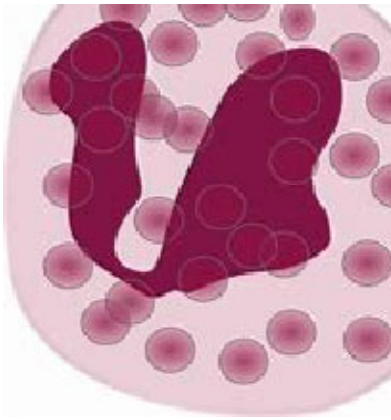

GI & Allergy Perspectives in Eosinophilic Esophagitis

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&

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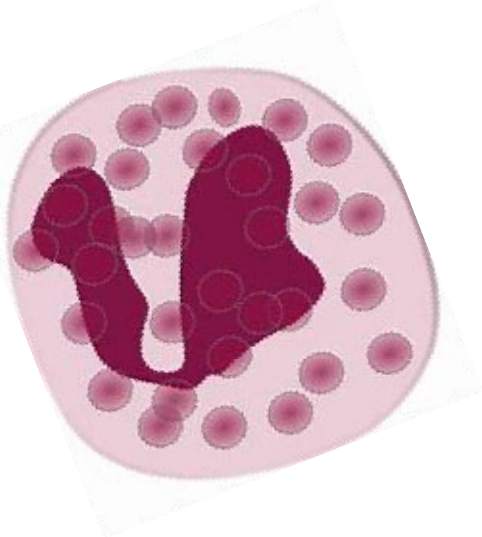
Division of Allergy & Immunology
National Jewish Health



Objectives

- Review the presenting symptoms of EoE
- Review epidemiology of EoE and association with atopic disease
- Discuss the evaluation, treatment and complications of EoE
- Discuss the new treatments and methods for disease monitoring

Eosinophilic Esophagitis:
2007- First consensus recommendations

AGA INSTITUTE

Eosinophilic Esophagitis in Children and Adults: A Systematic Review and Consensus Recommendations for Diagnosis and Treatment

Sponsored by the American Gastroenterological Association (AGA) Institute and North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition

GLENN T. FURUTA,[*] CHRIS A. LIACOURAS,[‡] MARGARET H. COLLINS,[§] SANDEEP K. GUPTA,[‖] CHRIS JUSTINICH,[¶] PHIL E. PUTNAM,[#] PETER BONIS,[**] ERIC HASSALL,[‡‡] ALEX STRAUMANN,[§§] MARC E. ROTHENBERG,[‖‖] and Members of the First International Gastrointestinal Eosinophil Research Symposium (FIGERS) Subcommittees[##]

- Eosinophilic Esophagitis (EoE) is a clinico-pathologic disease
- Clinically characterized by esophageal dysfunction
- Pathologically 1 or more biopsies show eosinophil predominant inflammation (>15 eos/high power field)

Furuta et al. Gastroenterology 2007.

Epidemiology of Eosinophilic Esophagitis (EoE)

- Prevalence is 1-4 in 10,000
- 75% of patients are male
- 75% of patients have associated atopic diseases
- Most common cause for food impaction
- Seen in 12-23% of patients undergoing endoscopy for difficulty swallowing

Waasdorp-Hurtado et al. JPGN 2011.
Dellon et al. Gastroenterology Clinics of North America 2014.
Furuta et al. Gastroenterology 2007.

Symptoms of EoE can vary by age

Young children

- Feeding difficulties
- Gagging
- Vomiting
- Refusal of food
- Regurgitation/ Reflux
- Food or foreign body impaction
- Dysphagia
- Abdominal pain
- Coughing with eating

Teenagers & Adults

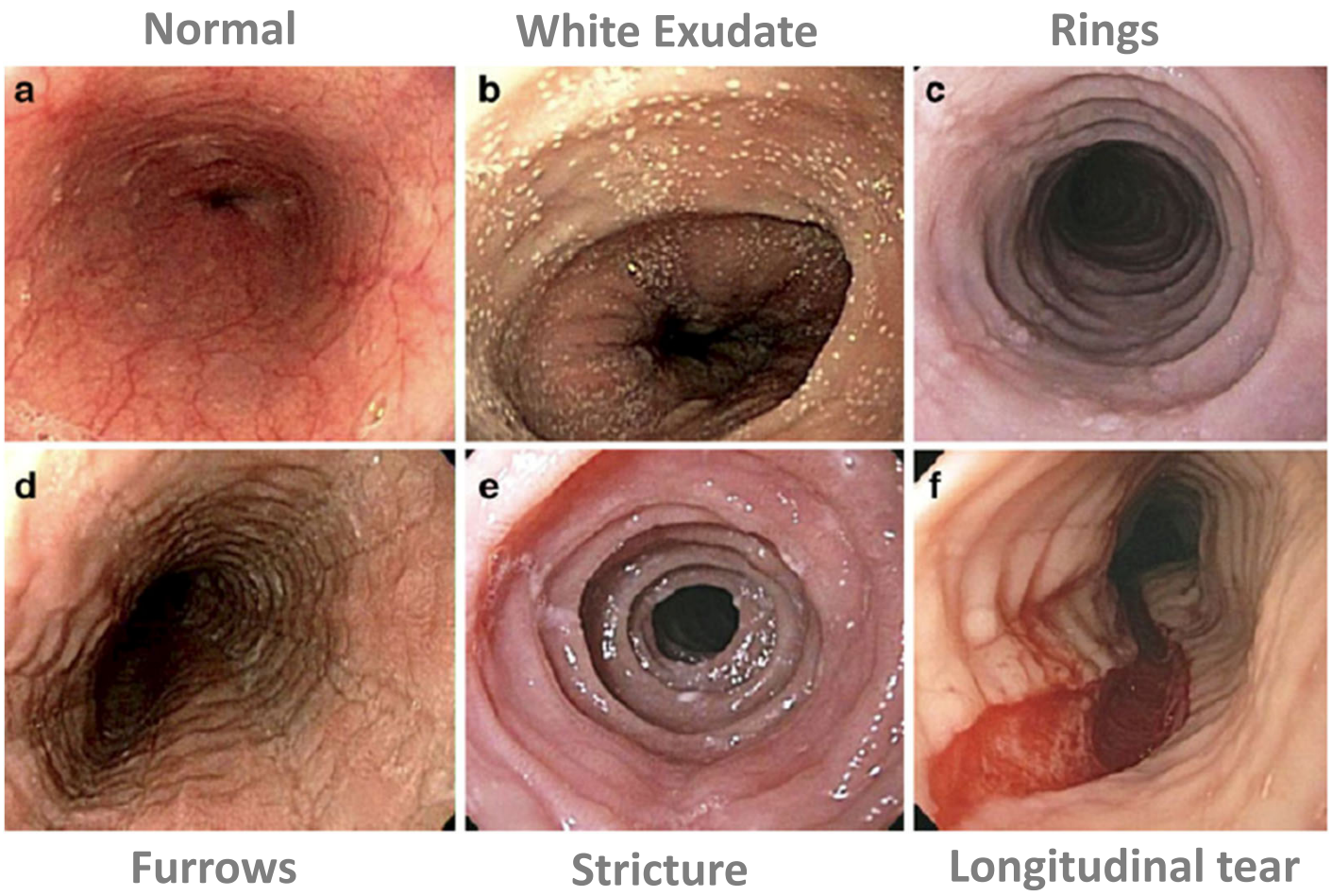
- Dysphagia
- Food impaction
- Chest pain
- Regurgitation/ Reflux

Furuta et al. Gastroenterology 2007.

Evaluation

- May present initially to primary care, GI, allergy, ENT or other subspecialties

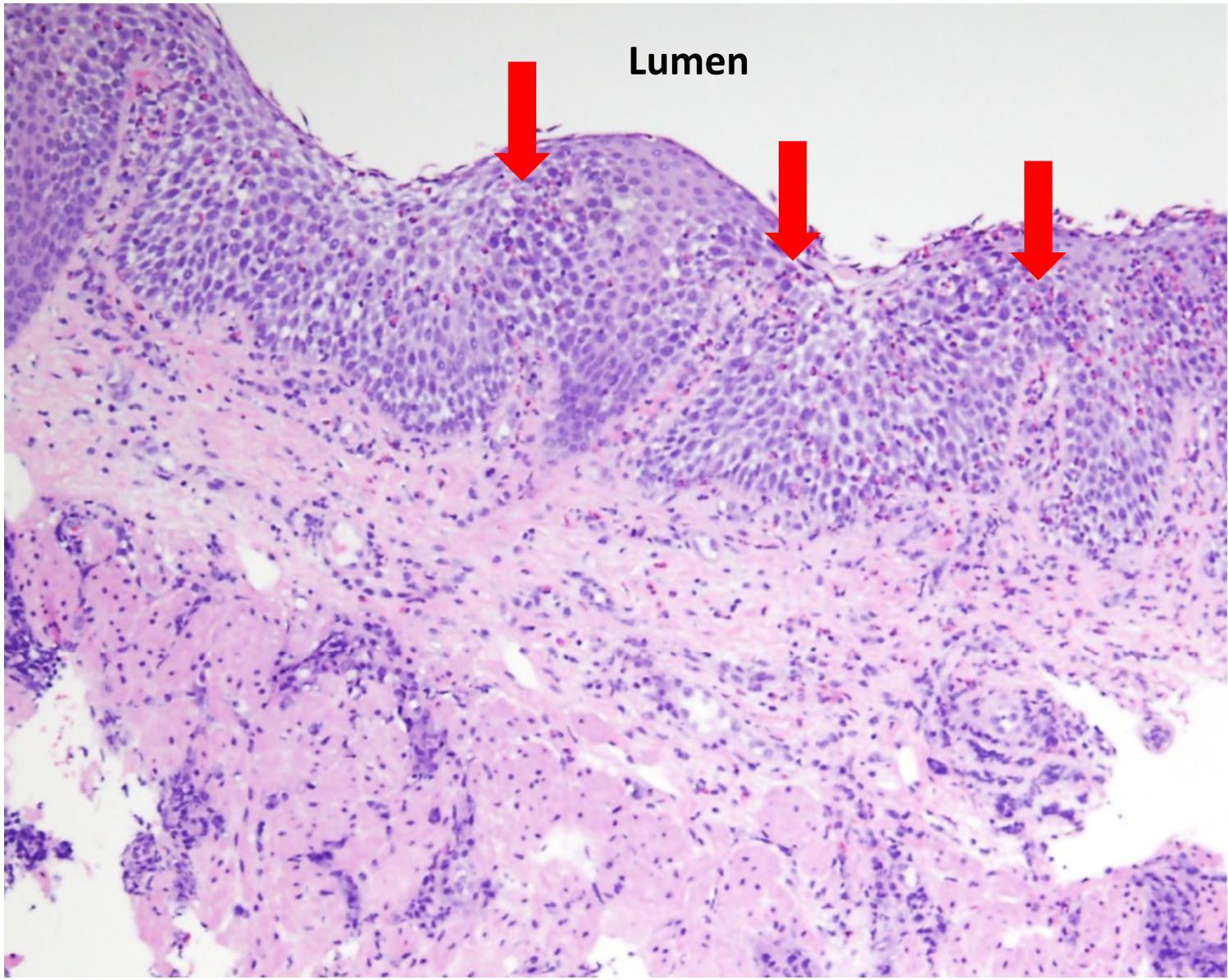
- Diagnosis requires endoscopy with biopsy

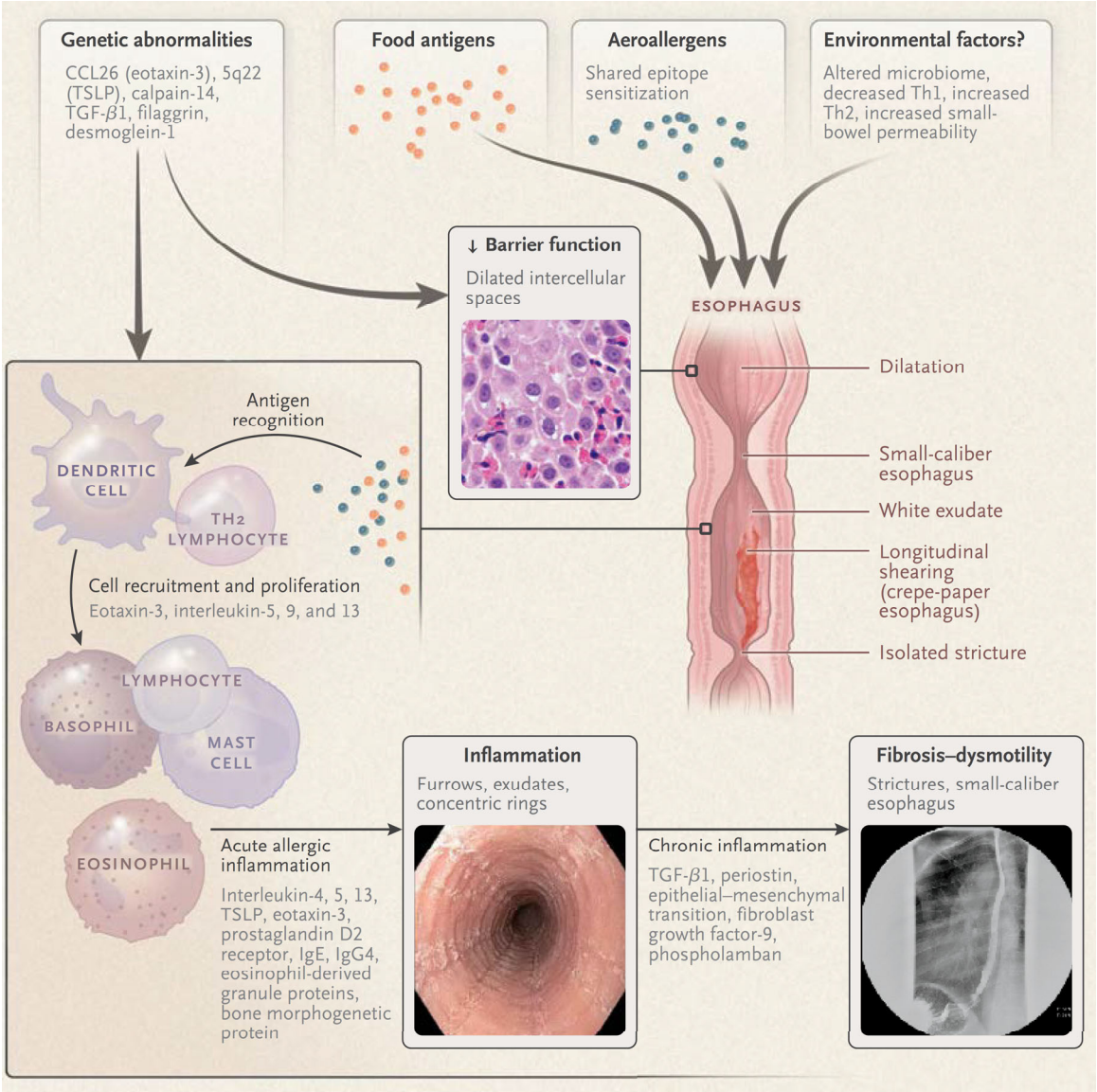


Aceves et al. Sem Immunopath 2012.

Esophageal Epithelium

Lamina Propria





Furuta et al. NEJM 2015.

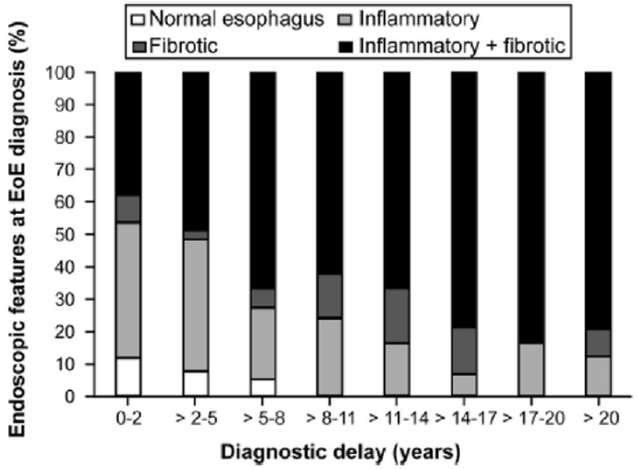
Goals of Treatment of EoE

- Improve symptoms
- Prevent complications
- Balance risks and benefits of treatment with Quality of Life

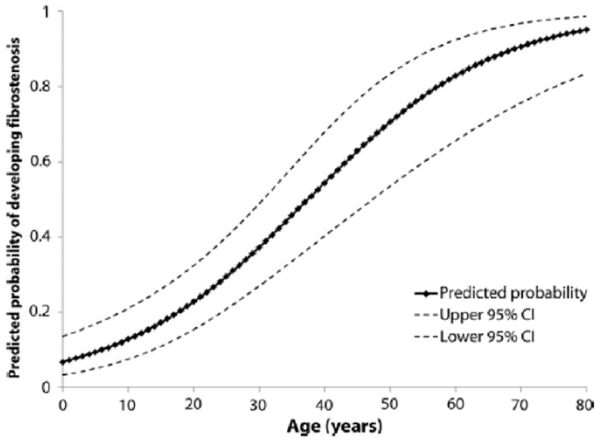
Furuta et al. Gastroenterology 2007.

EoE Natural History

Diagnostic delay and fibrostenosis – consistent results in 4 studies



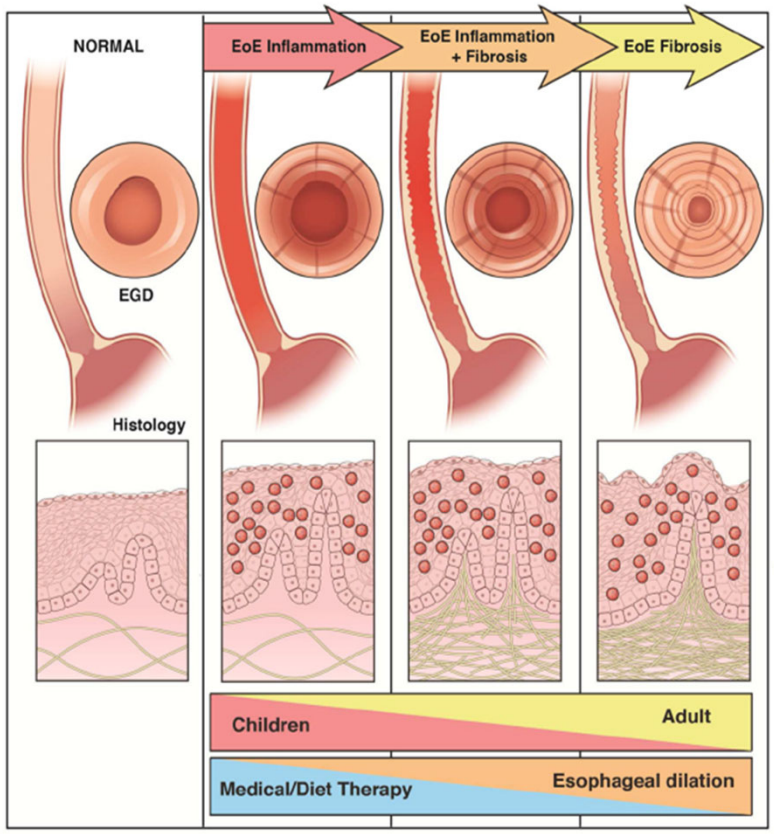
Prevalence of fibrotic features increased **from 47%** (diagnostic delay-2 years) **to 88%** (diagnostic delay, >20 years)



Every ten year increase in age, odds of fibrostenotic phenotype **more than doubled**

Schoepfer AM, et al. *Gastroenterology.* 2013
Dellon ES, et al. *Gastrointest Endosc*. 2014

EoE as a Continuum From Inflammation to Fibrosis



Inflammation leads to fibrosis over time

- Explains different symptoms in children vs adults

Diagnostic delay leads to greater rates of stricture

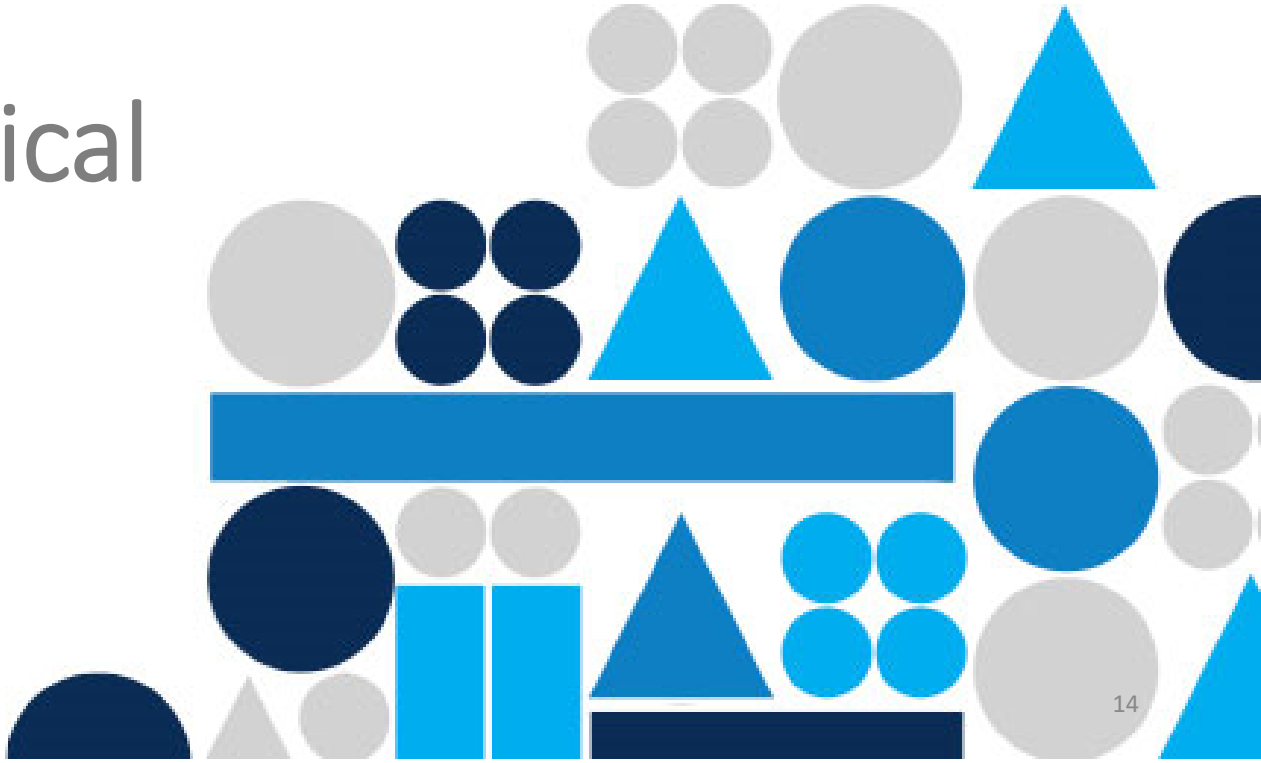
- Necessitates both anti-inflammatory and dilation treatments in some patients

Eosinophilic Esophagitis Guideline Education Program
Dellon ES, Hirano I. *Gastroenterology*. 2018.

Treatment: the 3 D's

- Drugs
  - Swallowed Topical Corticosteroids
  - PPI- Proton Pump Inhibitors
  - Biologics
- Dietary therapy
  - Elimination Diets
  - Allergy Directed Diets
  - Elemental diets
- Dilation

Treatment: Topical Corticosteroids



Swallowed Topical Corticosteroids

- Efficacy of topical corticosteroids ranges from 60-87%
- Typically taken twice daily
- Most commonly used:
  - Flovent or Alvesco: 2 puffs swallowed without a spacer
  - Oral Viscous Budesonide: 1-2 respules mixed for thick slurry
    - Splenda or Neocate Nutra

Konikoff et al. Gastroenterology 2006.
Aceves et al. Am J Gastroenterol 2007.
Dohil et al. Gastroenterology 2010.
Straumann et al. Gastroenterology 2010.
Alexander et al. Clin Gastroenterol Hepatol 2012.
Butz Gastroenterology 2014.

Potential side effects of Topical steroids

Candida infection

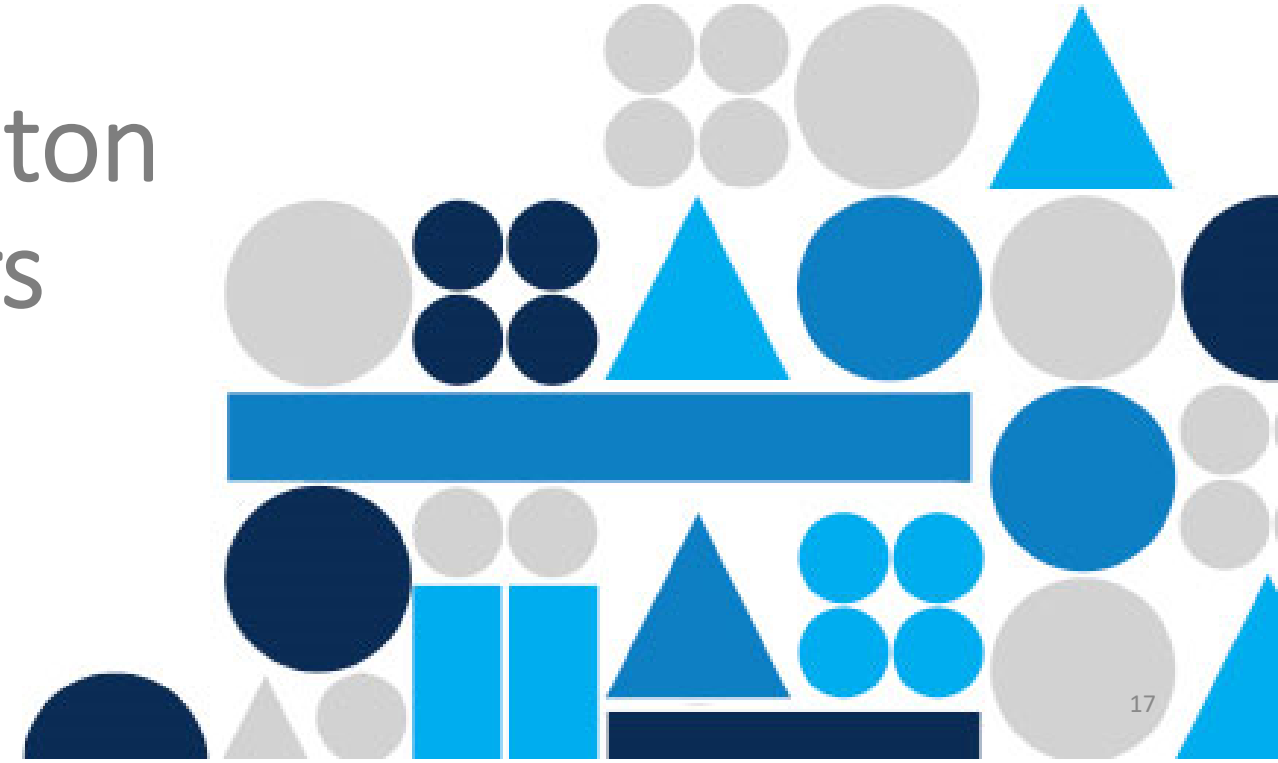
- Typically asymptomatic
- Oral (2-3%) esophageal (4-16%) in clinical trials
- Can treat with topical antifungals and try to reduce steroid dose

Adrenal insufficiency is uncommon, asymptomatic and can be difficult to assess.

- Systematic review 1950-2017, 17 studies*
- 6/119 (5%) of those that excluded concomitant use of other steroids
- Prospective assessment of 106 children, TCS for >4 months**
- 3 had abnormal ACTH stimulation test *(3%)-all on other steroids*

Eosinophilic Esophagitis Guideline Education Program
*Philpott H, et al. *Aliment Pharmacol Ther*. 2018
**Hsu S, et al. *Pediatr Allergy Immunol Pulmonol*. 2017
Ahmet A, et al. *Allergy Asthma Clin Immunol*. 2016
Golekoh MC, et al. *J Pediatr*. 2016
Bose P, et al. J Pediatr Gastroenterol Nutr. 2020
Hirano I, et al. *Aliment Pharmacol Ther*. 2020

Treatment: Proton Pump Inhibitors



Proton Pump Inhibitors

- Previous guidelines recommend PPI trial or normal pH impedance probe to “rule out” GERD as a cause of esophageal eosinophilia

- Evidence now suggests that PPIs are better classified as treatment for EoE rather than as diagnostic criteria

- Data on PPI effectiveness varies, 40-60% response

Molina-Infante et al. Gut 2016.
Lucendo et al. Clinical Gastroenterology and Hepatology 2016.

Side Effects of Long Term PPI Use:

Side Effect	Strength of Association
Bone fractures	Weak
GI infections	**Moderate**
Pneumonia	Weak
Kidney events	Weak
Dementia	Weak
Hypomagnesemia	Weak
Rebound acid hypersecretion	**Moderate**
Iron & B12 absorption	Weak
Liver Disease	Weak

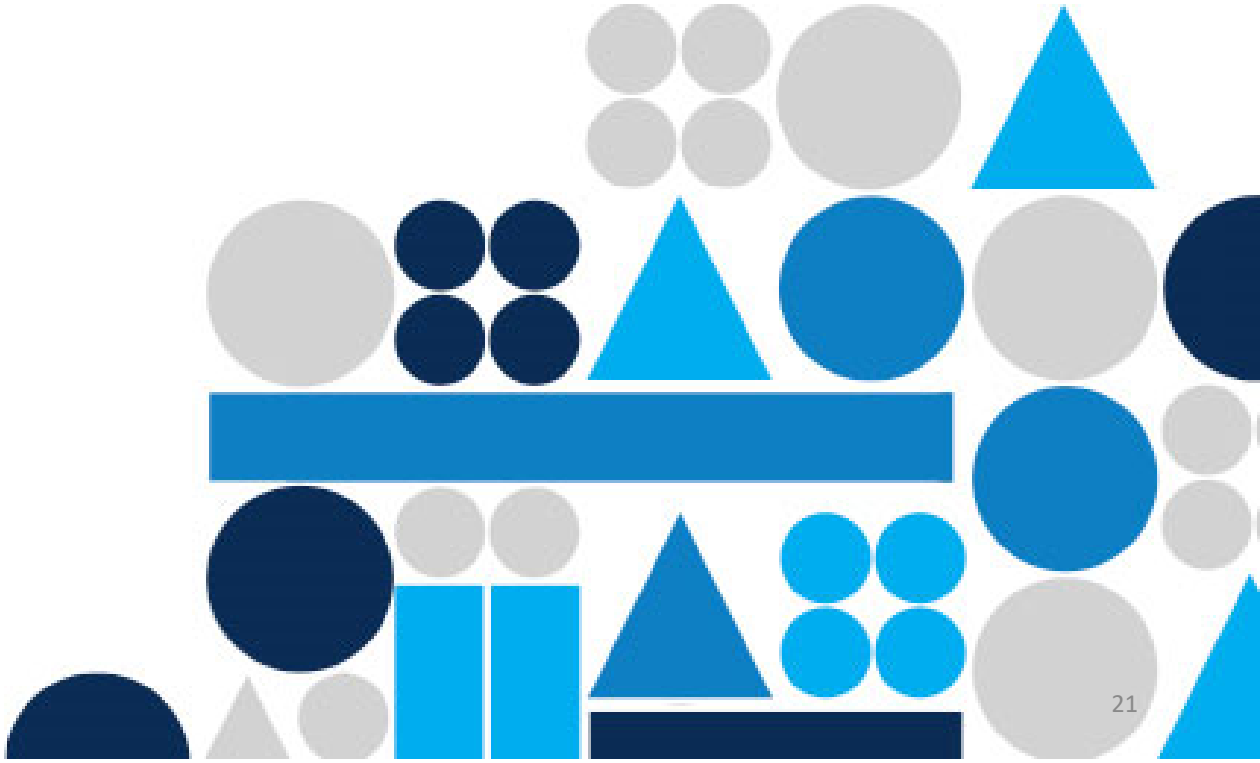
Hastrup et al. Basic & Clinical Pharmacology & Toxicology 2018.

Practical Considerations for PPI Therapy in EoE

- PPIs are no longer required for the diagnosis of EoE
- Histologic benefits of PPIs in children and adults with variable effect size (approximately 30-50%)
- Mechanism of therapeutic benefit maybe related to improvement in epithelial barrier function and an acid-independent anti-inflammatory effect
- Effectiveness, widespread availability, ease of administration and safety position PPIs as a popular first line treatment option
- **Loss of therapeutic benefit with prolonged use reported but uncommon**

Eosinophilic Esophagitis Guideline Education Program
Hirano I, Furuta G. *Gastroenterology.* 2020

Treatment: Biologics



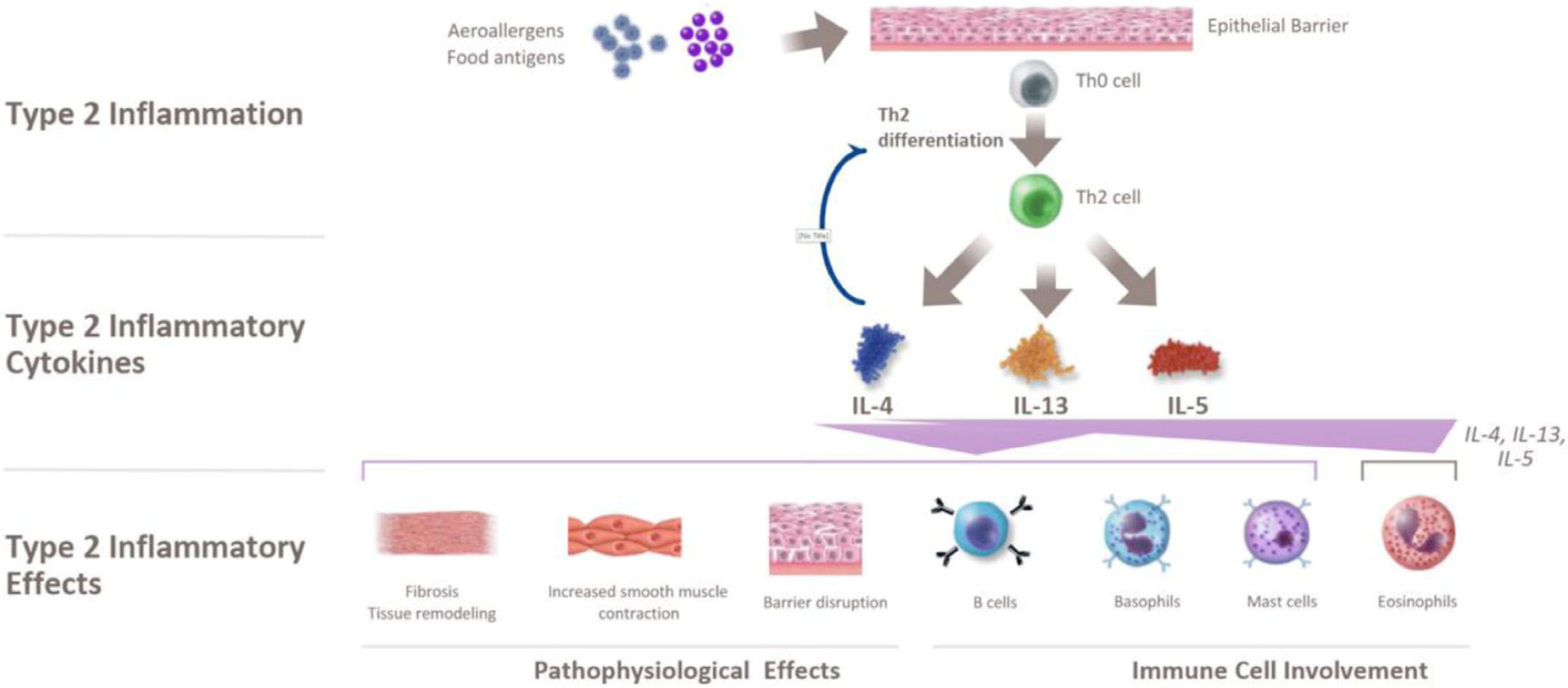
FDA NEWS RELEASE

FDA Approves First Treatment for Eosinophilic Esophagitis, a Chronic Immune Disorder

For Immediate Release: May 20, 2022

Today, the U.S. Food and Drug Administration approved Dupixent (dupilumab) to treat eosinophilic esophagitis (EoE) in adults and pediatric patients 12 years and older weighing at least 40 kilograms (which is about 88 pounds). Today's action marks the first FDA approval of a treatment for EoE.

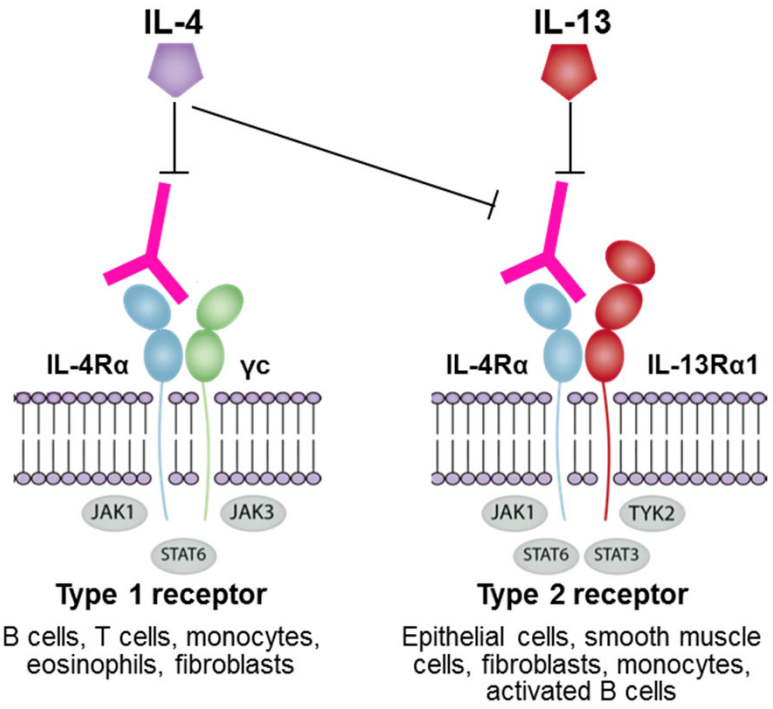
Q.M. Nhu and S.S. Aceves / Ann Allergy Asthma Immunol 00 (2022) 1–5



Nhu et al. Ann Allergy Asthma Immunol 2022.

Anti-IL-4Rα (Dupilumab)

- IL-4 receptor α monoclonal antibody
- Inhibits signaling of IL-4 and IL-13
- Approved for multiple atopic conditions



Eosinophilic Esophagitis Guideline Education Program

Gandhi N, et al. *Expert Rev Clin Immunol*. 2017
Simpson E, et al. *N Engl J Med*. 2016
Wenzel S, et al. *Lancet*. 2016
Bachert C, et al. *JAMA*. 2016

Table 2
Current Approved Use for Dupilumab

- Atopic dermatitis: Adult and pediatric patients age 6 months and older with moderate-to-severe atopic dermatitis whose diseases are not adequately controlled with topical prescription therapies or when those therapies are not advisable.
- Asthma: Add-on maintenance treatment of adult and pediatric patients age 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid-dependent asthma.
- Chronic rhinosinusitis with nasal polyposis: Add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis.
- EoE: for the treatment of adult and pediatric patients 12 years and older, weighing at least 40 kg, with EoE
- Prurigo nodularis: For the treatment of adult patients with prurigo nodularis.

Aceves et al. Ann Allergy Asthma Immunol 2022.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

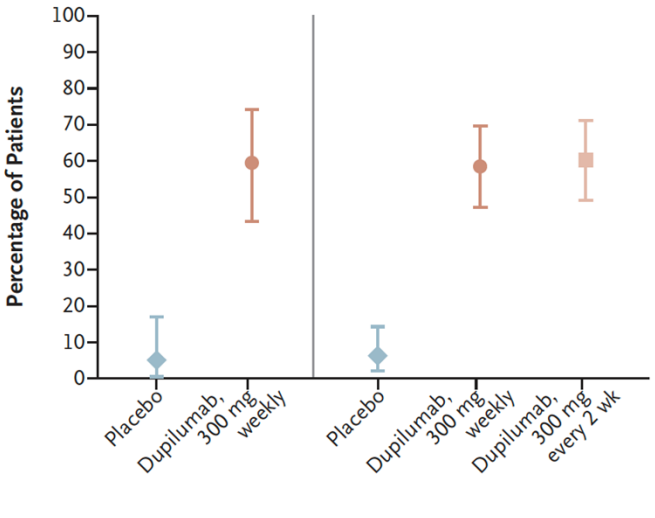
Dupilumab in Adults and Adolescents with Eosinophilic Esophagitis

E.S. Dellon, M.E. Rothenberg, M.H. Collins, I. Hirano, M. Chehade, A.J. Bredenoord, A.J. Lucendo, J.M. Spergel, S. Aceves, X. Sun, M.P. Kosloski, M.A. Kamal, J.D. Hamilton, B. Beazley, E. McCann, K. Patel, L.P. Mannent, E. Laws, B. Akinlade, N. Amin, W.K. Lim, M.F. Wipperman, M. Ruddy, N. Patel, D.R. Weinreich, G.D. Yancopoulos, B. Shumel, J. Maloney, A. Giannelou, and A. Shabbir

Dellon ES, Rothenberg ME et al. NEJM. 2022

Histologic Improvement
Dupilumab vs Placebo

A Histologic Remission at Wk 24 in Parts A and B

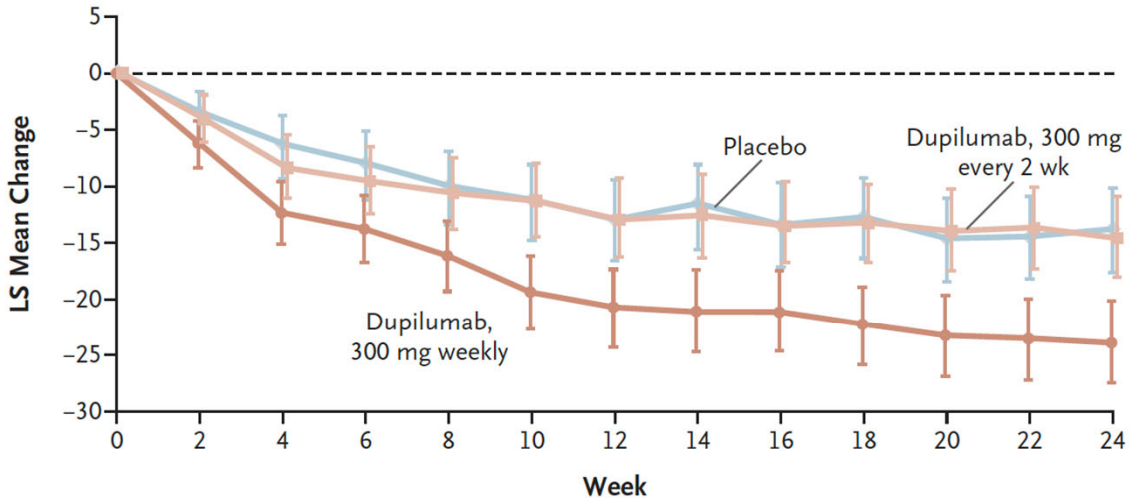


	Part A, Wk 24		Part B, Wk 24		
No. of Patients	39	42	79	80	81
No. of Patients with Response (%)	2 (5)	25 (60)	5 (6)	47 (59)	49 (60)

Dellon ES, Rothenberg ME et al. NEJM. 2022

Change in Dysphagia Symptom Score (DSQ)

B **Change from Baseline in DSQ Score in Part B**



No. of Patients/No. with Imputed Values													
Placebo	78/0	75/3	73/5	66/12	68/10	69/9	65/13	62/16	64/14	62/16	62/16	62/16	59/19
Dupilumab, 300 mg weekly	80/0	80/0	76/4	78/2	75/5	72/8	71/9	69/11	68/12	65/15	60/20	64/16	63/17
Dupilumab, 300 mg every 2 wk	81/0	77/4	78/3	76/5	68/13	70/11	66/15	65/16	69/12	65/16	61/20	63/18	62/19

Dellon ES, Rothenberg ME et al. NEJM. 2022

Biologics Under Investigation

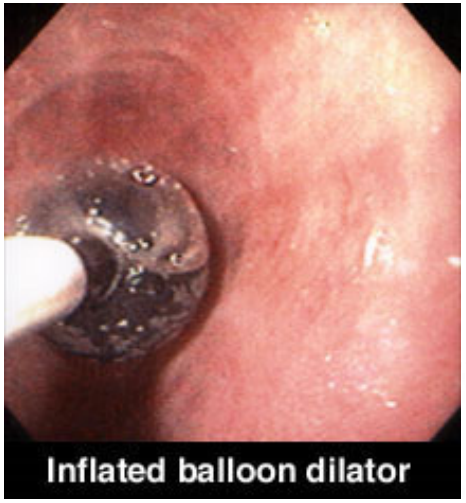
Table 2. Biologics Under Investigation for the Treatment of Patients With Eosinophilic Esophagitis

Medication	Mechanism of Action	FDA-Approved Indications	Eosinophilic Esophagitis Clinical Trial Status
Dupilumab	Monoclonal antibody to IL-4 receptor α subunit	Atopic dermatitis, asthma, rhinosinusitis with nasal polyposis	Phase 3 trials ongoing
Cendakimab	Monoclonal antibody to IL-13 receptor	None	Phase 3 trials ongoing
Lirentelimab	Monoclonal antibody to Siglec-8	None	Phase 2/3 trials ongoing
Benralizumab	Monoclonal antibody to IL-5 receptor	Asthma	Phase 3 trials ongoing
Mepolizumab	Monoclonal antibody to soluble IL-5	Asthma, hypereosinophilic syndrome, chronic rhinosinusitis with nasal polyposis, eosinophilic granulomatosis with polyangiitis	Phase 2 trials ongoing

FDA, US Food and Drug Administration; IL, interleukin; Siglec-8, sialic acid–binding immunoglobulin-like lectin 8.

Syverson et al. Gastroenterol Hepatol 2022.

Treatment: Esophageal Dilation



Practical Approach to Esophageal Dilation

- Stricture Formation (11-31%), Food impaction (30-55%) and Small caliber esophagus (10%) affect dysphagia
- Medical and dietary therapy can help improve stricture caliber but may not resolve it completely
- Dilation is effective therapy but does not affect underlying inflammation – use as adjunctive therapy
- Conservative dilation approach is imperative (start low and go slow) to target endpoint of 16 mm
    - May need multiple dilation sessions
    - Type of dilator should be determined by type of stricture

Eosinophilic Esophagitis Guideline Education Program

Dellon ES, Gonsalves N, Hirano I. *Am J Gastroentero*. 2013
Richter JE. *Am J Gastroenterol.* 2016
Hirano I. *Gastroenterology.* 2018

AGA-JTF Guidelines: Management of Eosinophilic Esophagitis

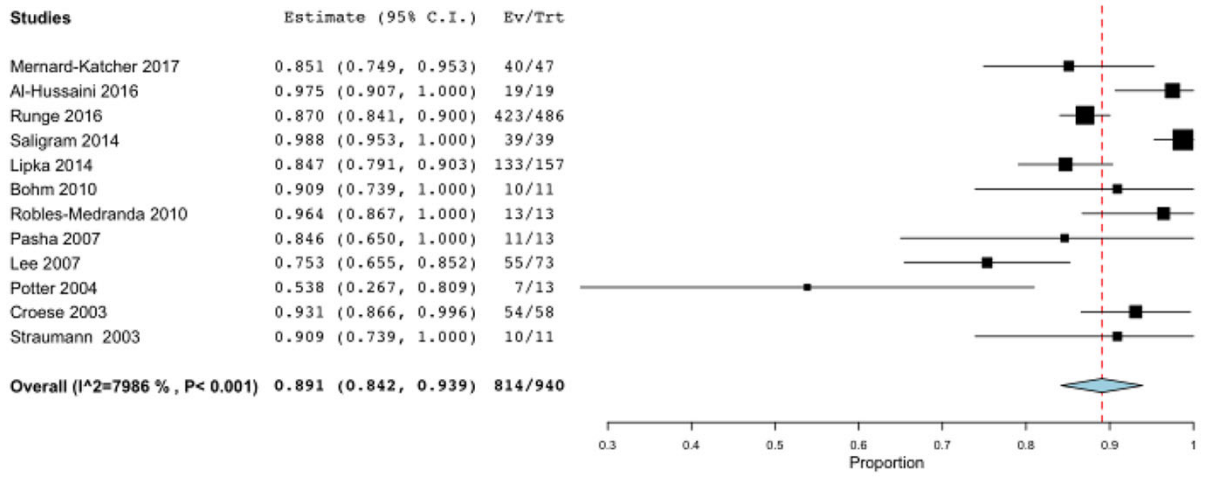
Esophageal Dilation

Recommendation: In adult patients with dysphagia from a stricture associated with eosinophilic esophagitis, the AGA/ JTF suggests endoscopic dilation over no dilation, (Conditional recommendation, very low-quality evidence)

Comment: Esophageal dilation does not address the esophageal inflammation associated with EoE.

87% achieving symptomatic improvement

Forest plot for clinical improvement



Side Effects of Esophageal Dilation

- No mortality associated with dilation
- Pooled Complication Rate
  - Perforation rate was 0.4%
  - Hospitalization 1.2%
  - GI hemorrhage 0.1%
- Chest discomfort or pain reported in prior studies as high as 74%
- Inform patients about side effects/expected symptoms post dilation

Schoepfer AM, et al. *Am J Gastroenterol.* 2010
Dougherty M, et al. *Gastrointest Endosc*, 2017

Treatment: Diet Elimination

Consideration	Dietary intervention		
	Testing-directed elimination	Empiric elimination	Elemental formula
Therapeutic success rate	50 to 70%	50 to 70%	>90%
Number of foods avoided	Typically <6 foods eliminated	Typically 6 foods/food groups eliminated from diet	All food eliminated
Available data	Multiple centers Retrospective Pediatric	Multiple centers Prospective and retrospective Pediatric and adult	Multiple centers Prospective and retrospective Pediatric and adult
Cost	Requires purchase of specific specialty foods	Requires purchase of specific specialty foods	USD ≥$50 per can Not always covered by insurance unless via tube feeding

Elemental Diet

Amino acid based formula

1995 – first paper describing effectiveness of elemental therapy

Systematic review of 6 observational studies

- 431 patients
- 93.6% with histologic remission (< 15 eos/high power field)

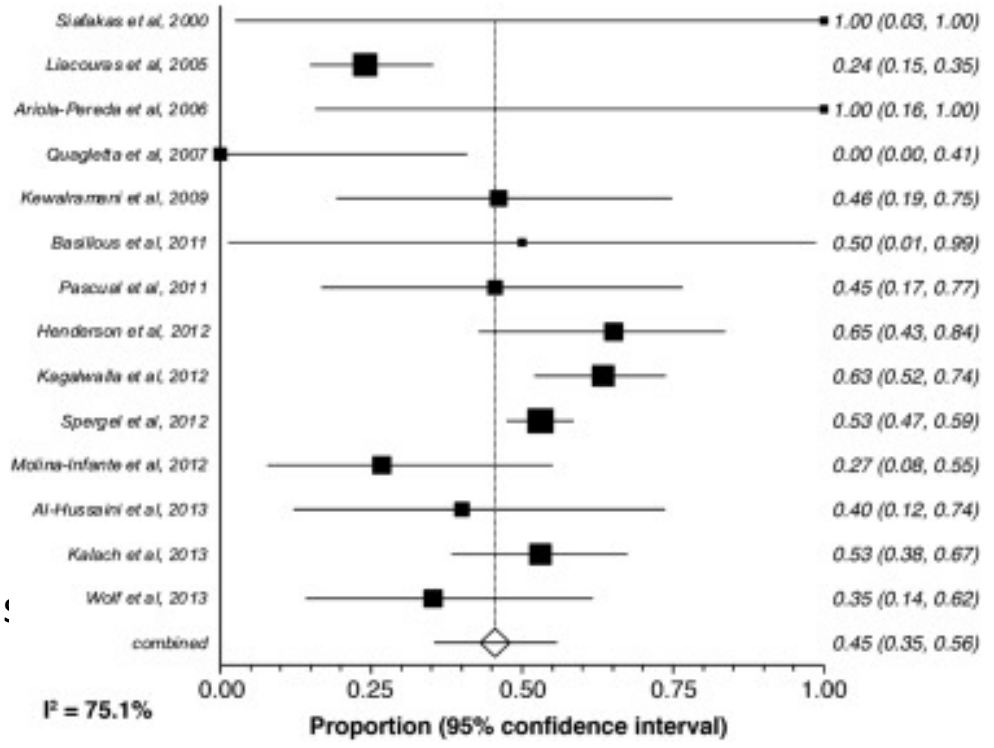
Obstacles:

- Bad taste
- Limited diet
- Expensive
- Difficulty with adherence, may require tube feeding
- Younger children may have oral motor/sensory delays

Kelly KJ, et al. Gastroenterology 1995;109(5):1503-1512.
Rank MA, et al. Gastroenterology. 2020;158(6):1789–1810.e15. doi: 10.1053/j.gastro.2020.02.039

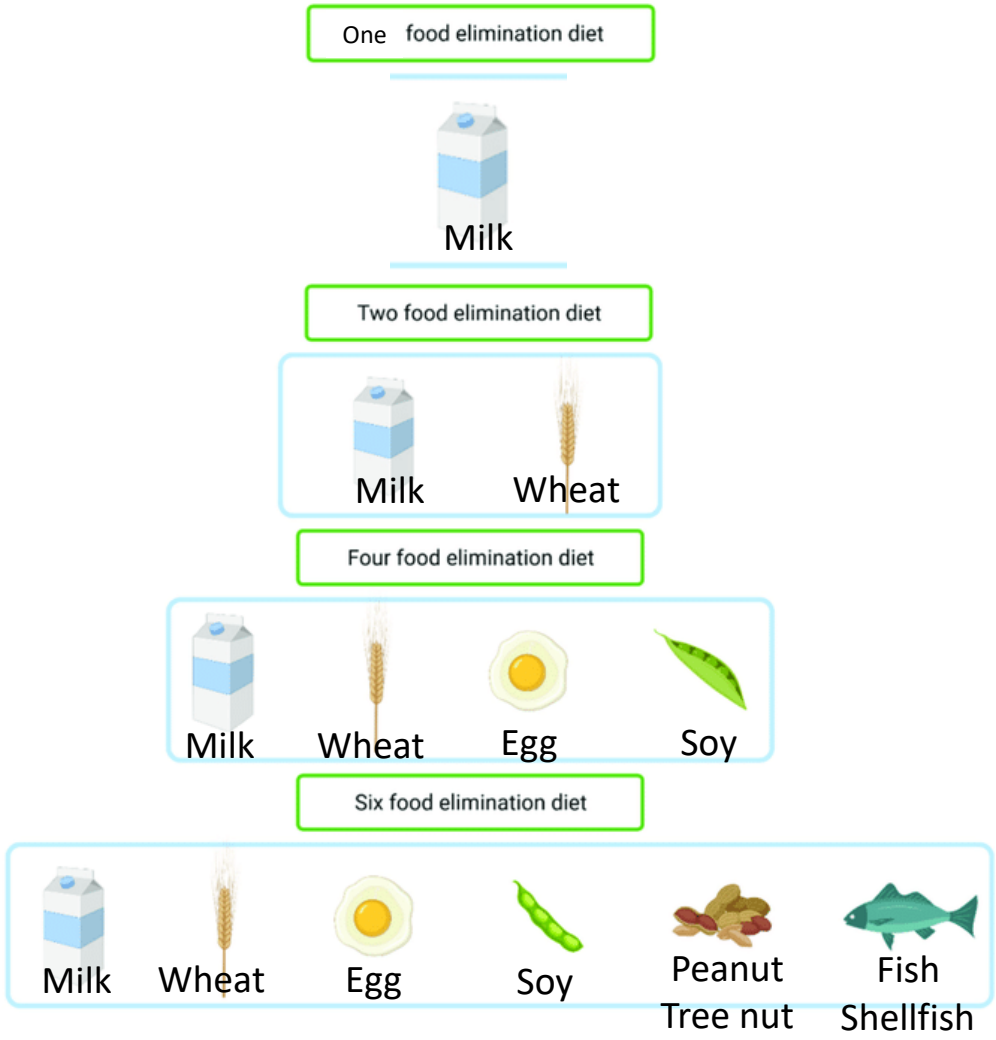
Allergy Testing-Directed Elimination Diet

- Uses a combination of skin prick tests, atopy patch tests, and serum IgE
- Wide variability of response:
  - Initial pediatric studies were favorable
  - Significantly lower response rate in adults
  - ***Overall efficacy 45.5%***
- Obstacles:
  - Testing is not very successful in identifying triggering foods
  - Time consuming, requires testing many foods
- Testing IS useful when reintroducing foods



Spergel JM et al. JACI 2002;109(2): 363-368.
Arias A et al. Gastroenterology 2014; 146: 1639–1648

Empiric Elimination Diets



Empiric Elimination Diets

Report From the AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters:

Meta-analysis of 14 observational studies:

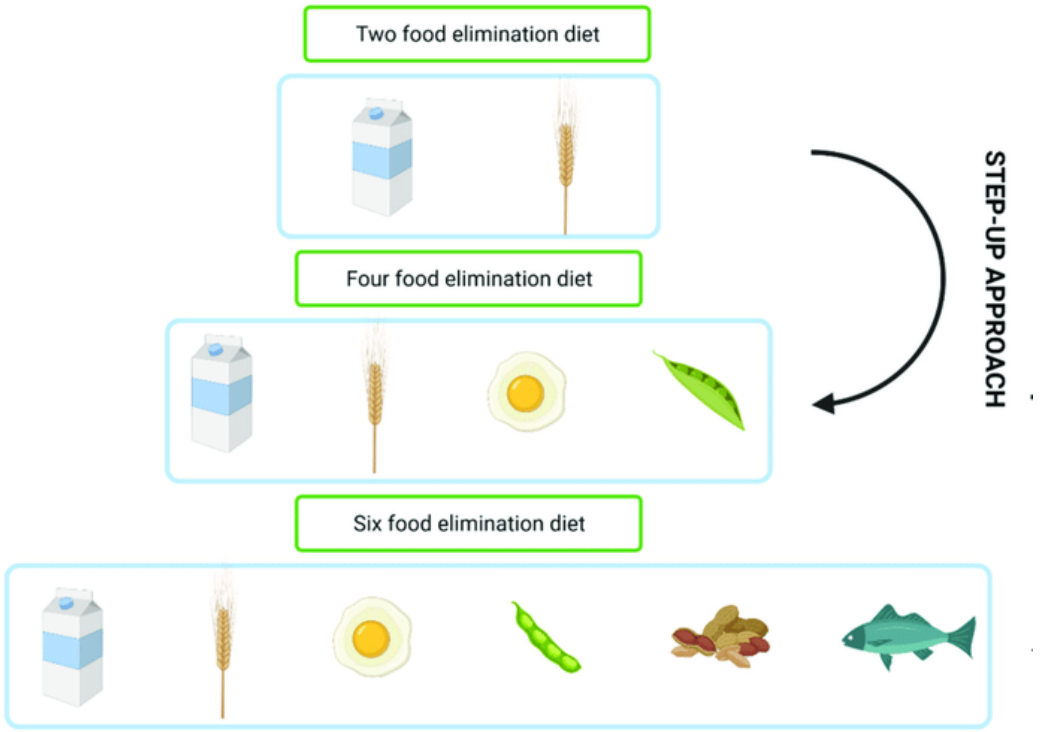
- 6 FED: 33% failure rate
- 4 FED: 43% failure rate
- 2 FED: 58% failure rate
- 1 FED: 46% failure rate

Comparing 6 FED to 1 FED:

- 129 patients (62 in 6 FED, 67 in 1 FED) for 6 weeks
- **Histological remission (<15 eos/hpf):** 25 (40%) patients in 6 FED v. 23 (45%) in 1 FED, p=0.58
- **Complete remission (<1 eos/hpf):** p=0.031
- Similar QOL scores
- *Milk elimination is an acceptable initial dietary therapy*

Rank MA et al. Gastroenterology. 2020 May;158(6):1789-1810.e15
Kliewer KL et al. Lancet Gastroenterol Hepatol. 2023 May;8(5):408-421.

- 130 patients (25 pediatric)
- Start on 2 FED – 43% remission
- Then step-up to 4 FED – 60% remission
- Then step-up to 6 FED – 79% remission
- Step-up approach can reduce endoscopic procedures by 20%



Molina-Infante J et al. J Allergy Clin Immunol. 2018 Apr;141(4):1365-1372.

Advantages and disadvantages of different dietary interventions for eosinophilic esophagitis

Consideration	Dietary intervention		
	Testing-directed elimination	Empiric elimination	Elemental formula
Therapeutic success rate	50 to 70%	50 to 70%	>90%
Number of foods avoided	Typically <6 foods eliminated	Typically 6 foods/food groups eliminated from diet	All food eliminated
Available data	Multiple centers Retrospective Pediatric	Multiple centers Prospective and retrospective Pediatric and adult	Multiple centers Prospective and retrospective Pediatric and adult
Cost	Requires purchase of specific specialty foods	Requires purchase of specific specialty foods	USD ≥$50 per can Not always covered by insurance unless via tube feeding

Role of the Allergist

Management of other allergic conditions

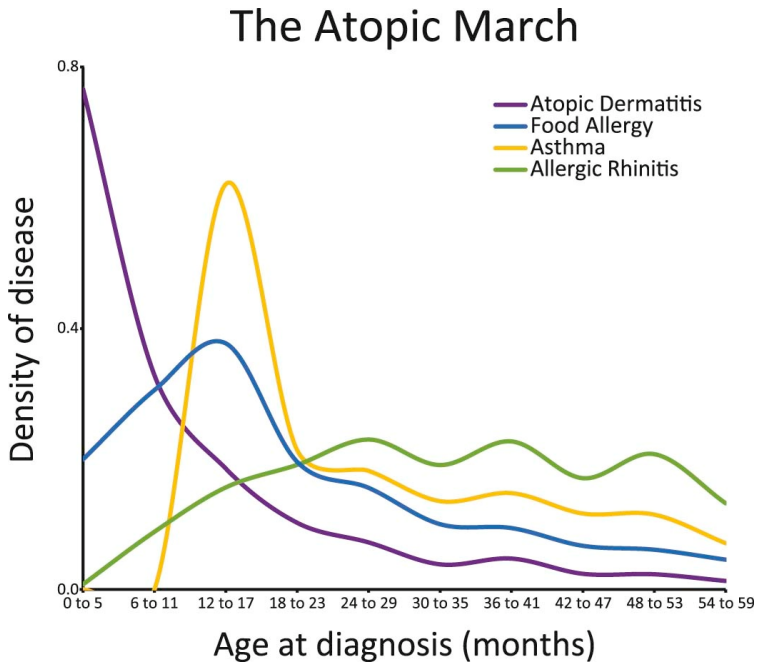
Participate in shared decision making with dietary therapy & changes in dietary therapy

Assist with reintroduction of foods and concerns for IgE mediated food allergies

Assist with seasonal symptom variations in EoE

EoE and Atopy

Pediatrics:	20% have atopic dermatitis
	60% have food allergy
	30-50% have asthma
	50-75% have allergic rhinitis
Adults:	5-10% have atopic dermatitis
	51% have food pollen allergy syndrome
	30-50% have asthma
	50-75% have allergic rhinitis



Assa'ad AH et al. J Allergy Clin Immunol. 2007 Mar;119(3):731-8

Furuta AT et al. Gastroenterology. 2007 Oct;133(4):1342-63.

Plaza-Martin AM et al. Allergol Immunopathol (Madr). 2007 Jan-Feb;35(1):35-7

Spergel JM et al. J Pediatr Gastroenterol Nutr. 2009 Jan;48(1):30-6

Liacouras CA et al. Clin Gastroenterol Hepatol. 2005 Dec;3(12):1198-206.

Guajardo JR. J Pediatr. 2002 Oct;141(4):576-81

Hill DA. J Allergy Clin Immunol Pract. 2017 Mar-Apr;5(2):369-375

Risk of IgE mediated food allergy?

Case series:

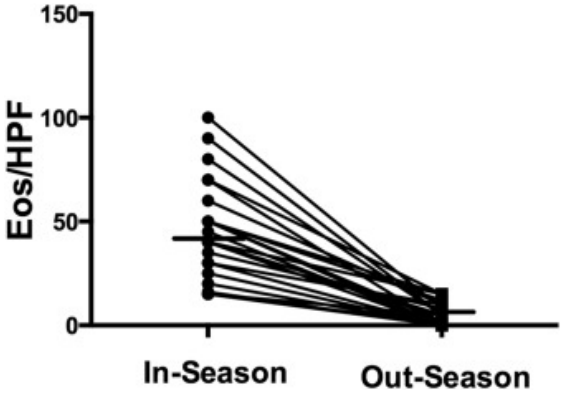
- 5 patients initially consuming cow's milk products with negative SPT
- Dietary elimination therapy
- 2 clinical reactions, 3 sensitized

Consideration:

- Children with atopic dermatitis (especially severe) – consider allergy testing before food reintroduction

Association with Environmental Allergies

- Directly impacting the esophagus from swallowed inhaled allergens or post-nasal drip?
- Systemic response causing eosinophils to traffic to the esophagus?
- Controversial: There are studies both supporting and refuting this association
- 1,180 patients with EoE
  - 160 (14%) reported aeroallergen triggers
    - 32/160 (20%) had biopsy confirmed variation of aeroallergen triggers



Ram G et al. Ann Allergy Asthma Immunol 2015 Sep;115(3):224-228

OIT (Oral Immunotherapy) associated EoE

- Is EoE during OIT a pre-existing, subclinical disease? Or is it new onset of EoE due to OIT?
- ~5% (range 0.5%-30%) of food allergic patients develop EoE

Summary of Safety Data From OIT Studies of Patients With Egg, Milk, or Peanut Allergy[a]

Rate	Discontinuation (any reason), %	SPR-EoE, %			EoE (biopsy), %	Discontinuation cause, %	
		Organ system	Specific symptom			SPR-EoE	EoE or SPR-EoE
		GI symptoms	Abdominal pain	Vomiting			
Overall	14	34	32	12	5.3	4.7	5.6
Egg	11	ND[b]	28	17	4.2	2.7	3.1
Milk	12	18	30	1	5.4	3.9	4.6
Peanut	16	56	40	20	5.2	6.7	8.5

Abbreviations: AE, adverse event; EoE, eosinophilic esophagitis; GI, gastrointestinal; ND, not determined; OIT, oral immunotherapy; SPR-EoE, symptoms possibly related to EoE.

[a]Rates were derived from separate sample populations based on data availability and AE reporting.

[b]Rate of GI symptoms could not be determined for egg OIT because no studies of egg OIT reported AEs per patient by organ system.

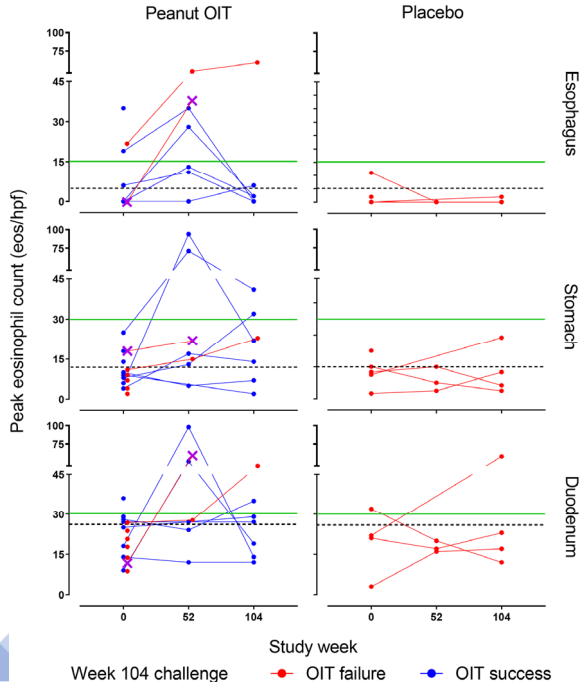
Petroni D et al. Ann Allergy Asthma Immunol. 2018 Mar;120(3):237-240.

OIT (Oral Immunotherapy) associated EoE

Summary of other studies:

- Gastrointestinal eosinophilia is present in a subset of food allergic patients
- In peanut OIT, GI eosinophils fluctuate over time and typically DO NOT correlate with GI symptoms

- Esophagus:
  - > 5 eos/hpf: N=5 (24%)
  - > 15 eos/hpf: N=3 (14%)
- Stomach (gastric antrum):
  - > 12 eos/hpf: N=5 (24%)
- Duodenum:
  - > 26 eos/hpf: N=6 (29%)



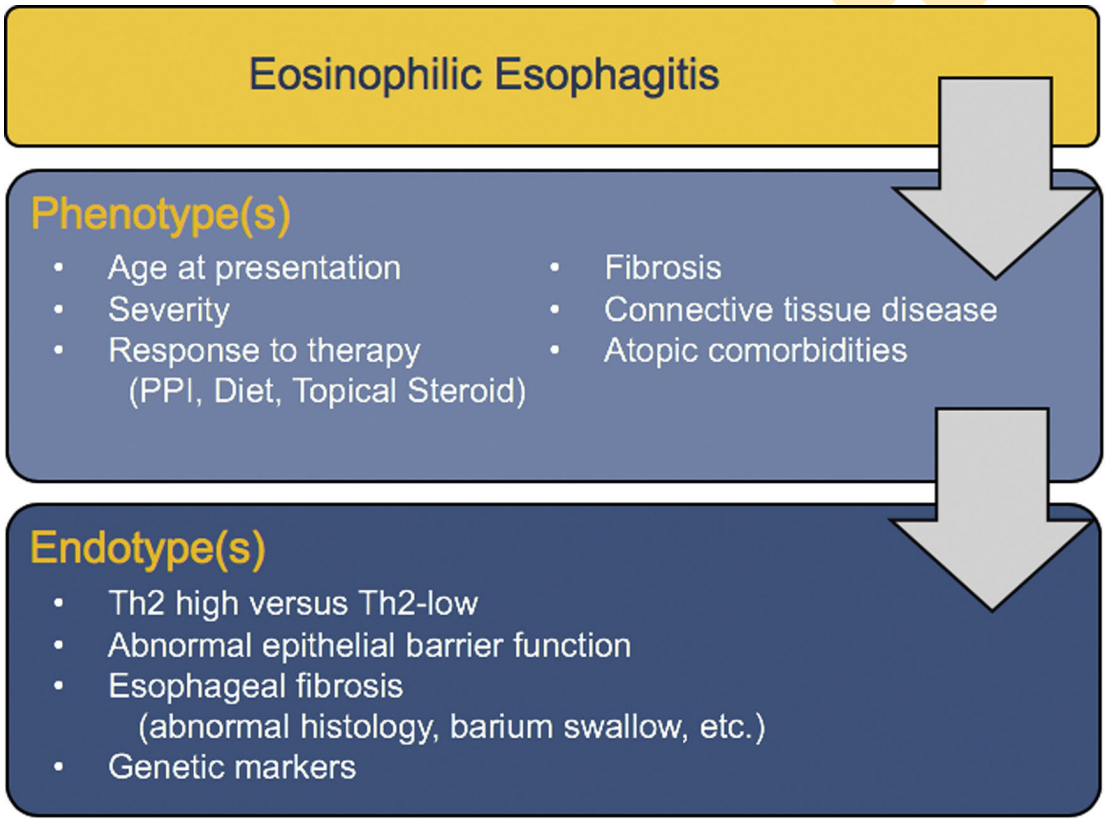
- Treatment considerations:
  - Continue OIT while treating GI symptoms
    - Addition of PPI
    - Topical steroids
    - Pause dosing or resume OIT at a lower dose
  - Stop OIT

Wright BL et al. Front Immunol. 2018;9:2624.
Wright BL et al. Clin Gastroenterol Hepatol. 2021 Jun;19(6):1151-1159.e14

- EoE is heterogeneous in its presentation, history, and response to treatment

➢ Better understanding phenotypes and endotypes can help individualize future care

- Multidisciplinary approach with shared decision making

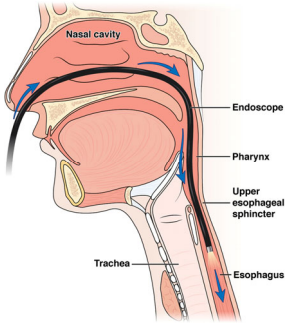


Innovations in EoE:

A Collaborative Effort at Children's Hospital Colorado

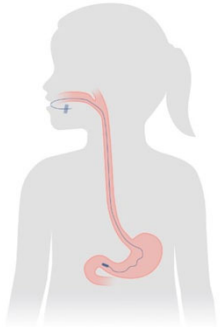
1

Transnasal Endoscopy



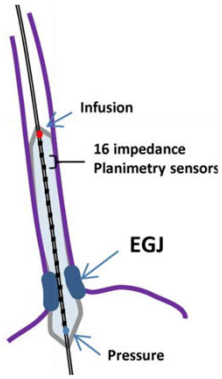
2

Esophageal String Test



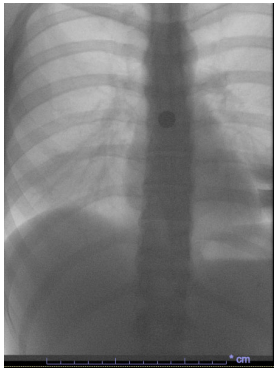
3

EndoFlip



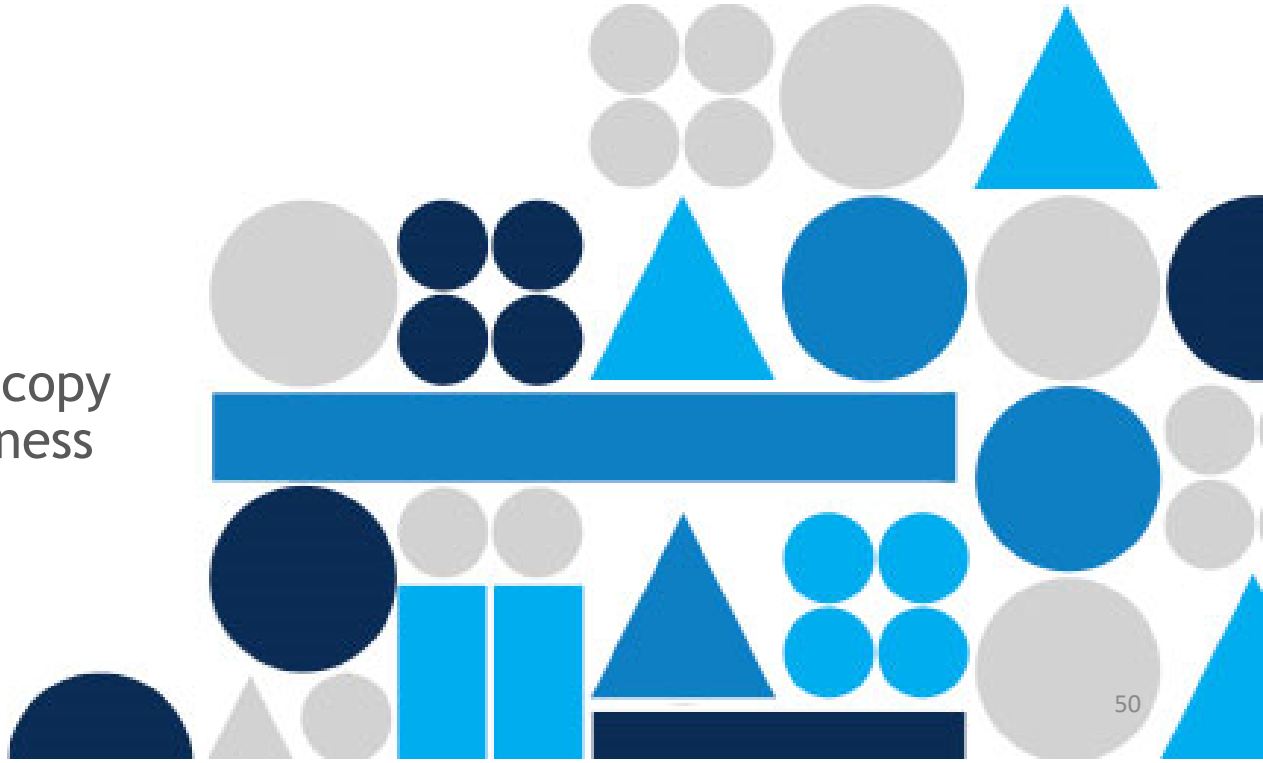
4

Barium Pill Esophagram



Innovations: Unsedated Transnasal Endoscopy

Barrier: Need for serial endoscopy to assess treatment effectiveness



Unsedated Transnasal Endoscopy:

Development from a multidisciplinary collaboration

- Aerodigestive Program: Working together with pulmonology and ENT; routinely use bronchoscopes to intubate nasal passages in children

- Led to the development of unsedated TNE in pediatrics at Children's Hospital Colorado in 2014

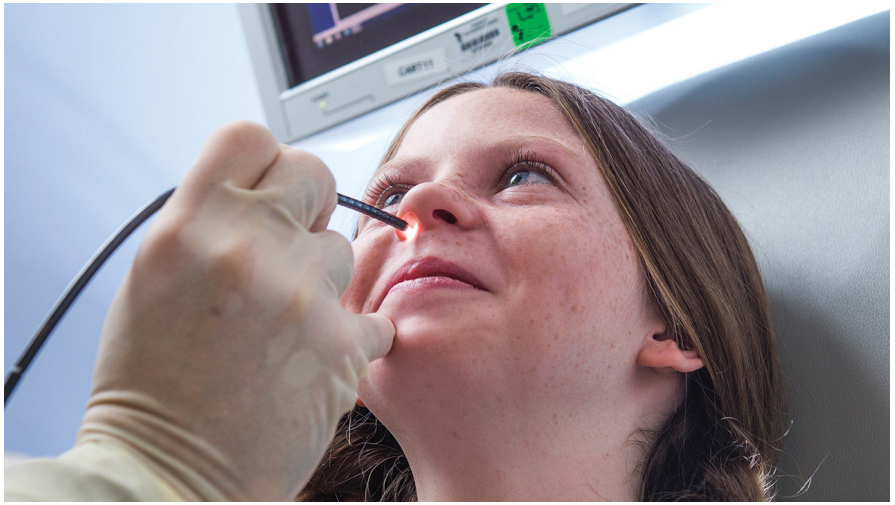


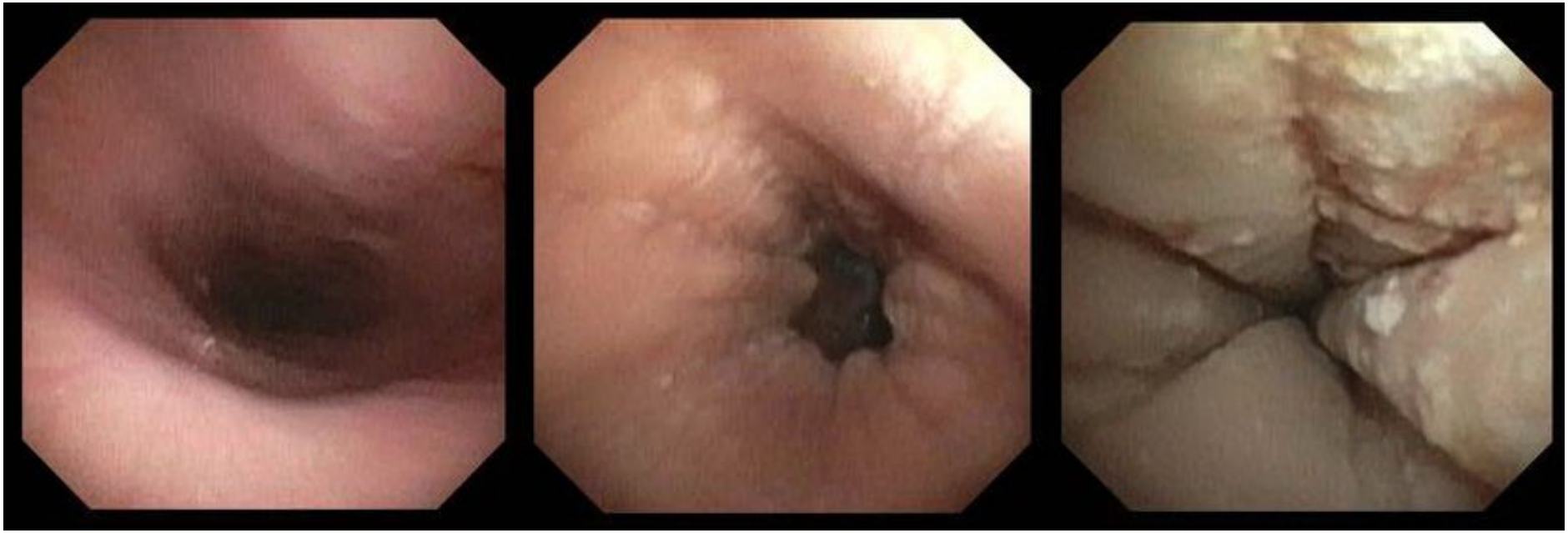
Photo from Children's Hospital Colorado Foundation

Unsedated Transnasal Endoscopy in Children with EoE

- 190 children and young adults underwent TNE from Jan 2015-Feb 2018
- Ages 3 years-22 years
- 98% success rate (294 TNEs performed, 300 attempts)
- Average total time spent in the clinic (front desk check-in to check-out) in 2018 was 71 min
  - TNE now takes 3-7 min, total time spent in clinic is 30-40 min

Nguyen et al. Clinical Gastroenterology and Hepatology 2019.

Visual Findings in TNE



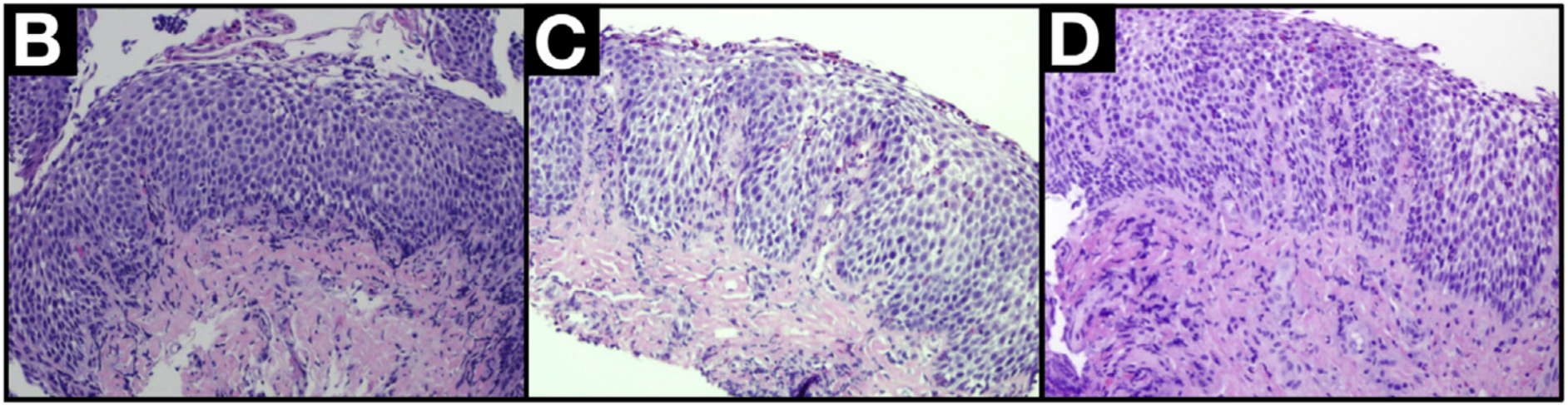
Nguyen et al. Clin Gastroenterol Hepatol 2019.

Unsedated Transnasal Endoscopy in Children with EoE

Average Charge per visit	
EGD with biopsy	$9444
Transnasal endoscopy with biopsy	$4394
Average Charge Reduction per visit	**$5050**

Nguyen et al. Clin Gastroenterol Hepatol 2019.

Unsedated Transnasal Endoscopy in Children with EoE



Nguyen et al. Clin Gastroenterol Hepatol 2019.

Adverse Events during TNE, N=178

All adverse events during TNE were grade 1; No adverse events classified as grade 2 or higher

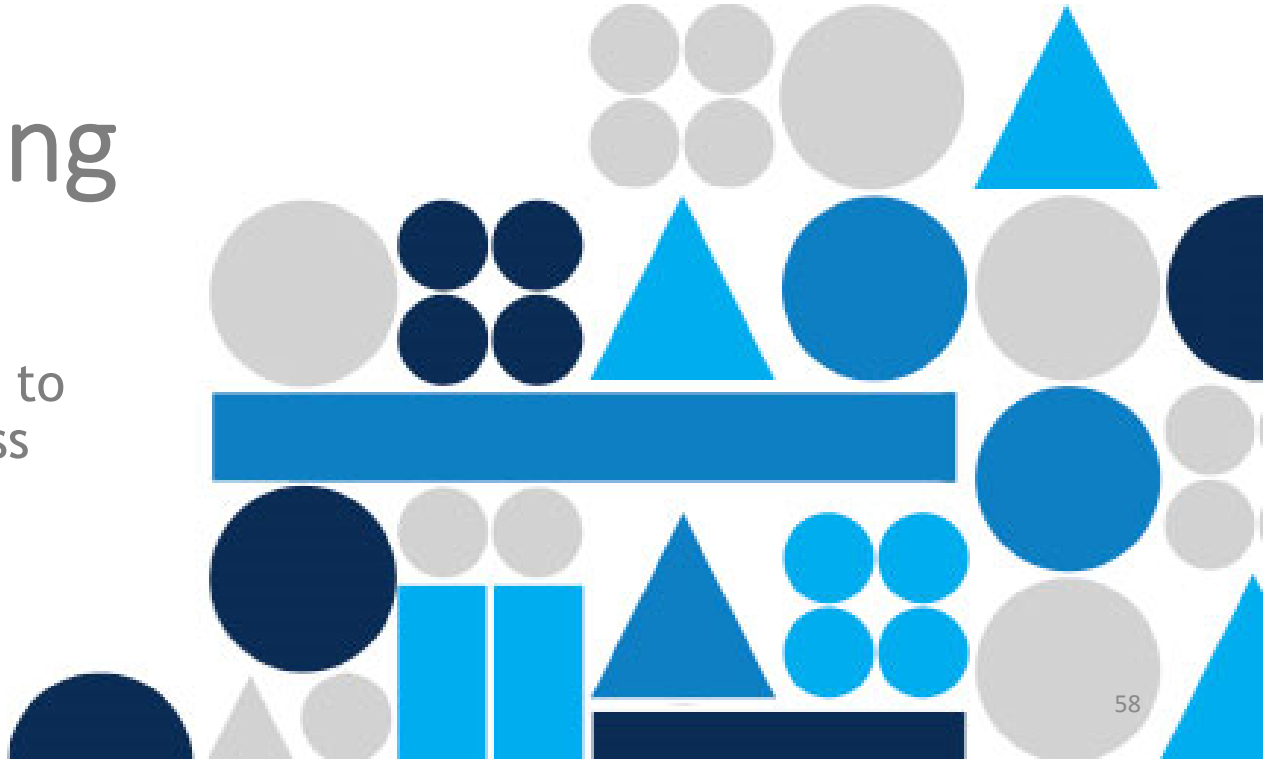
Adverse Event	Number of Subjects (%)
Vomiting	8 (4.5%)
Spit up	6 (3.4%)
Nasal Irritation	4 (2.2%)
Epistaxis	2 (1.1%)
Pre-syncope	1 (0.6%)
Anxiety	1 (0.6%)
Procedure Suspended	1 (0.6%)
No Events	155 (87%)

Nguyen et al. Clin Gastroenterol Hepatol 2019.

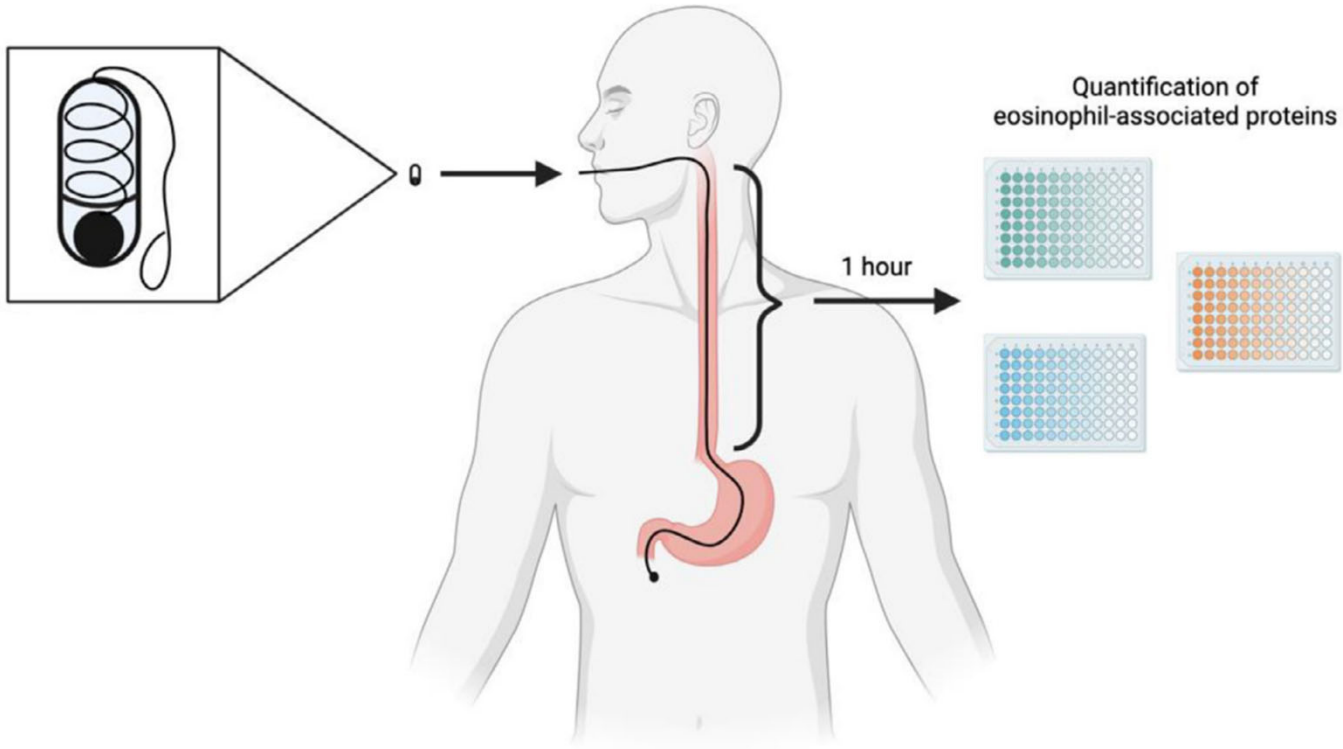
TNE in 2023

Innovations: Esophageal String Test (EST)

Barrier: No biomarkers, need to assess treatment effectiveness



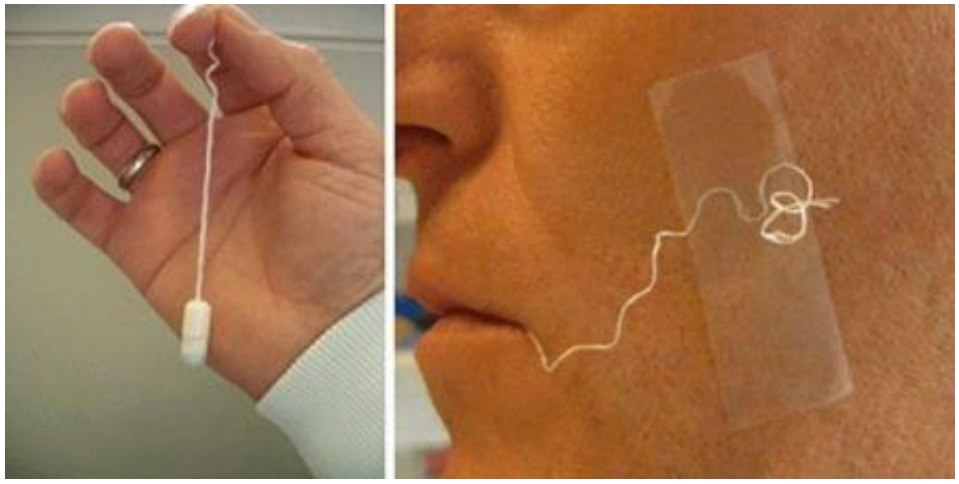
Esophageal String Test



McGowan et al. Ann Allergy Asthma Immunol 2022.

Esophageal String Test

- Esophageal dwell time of 1 hour and subjects underwent endoscopy
- Eosinophil-associated protein levels were compared between EST effluents and esophageal biopsy extracts



Furuta et al. Gut, 2013.
Ackerman et al. Am J Gastroenterol, 2019.

Esophageal String Test

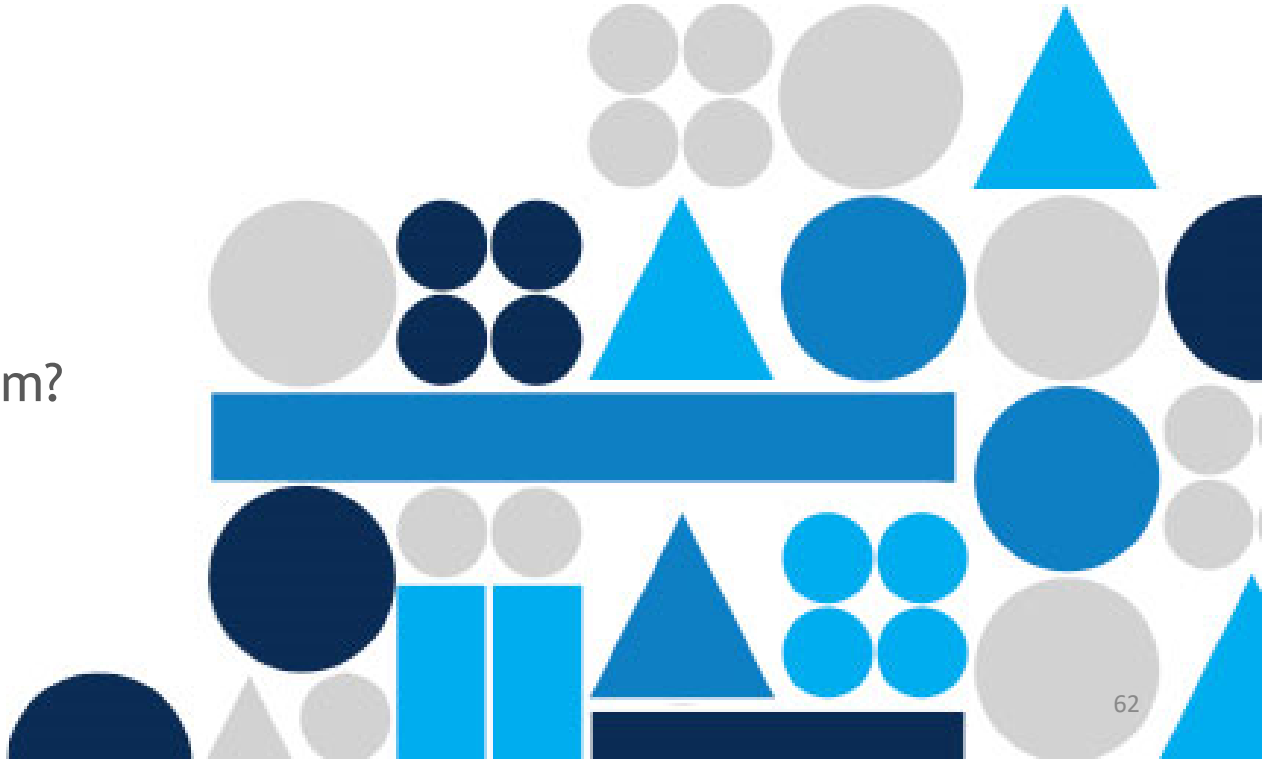
- EST was able to capture eosinophil-associated biomarkers
- Biomarkers (MBP and eotaxin-3) correlate with peak eosinophil count and endoscopic visual scoring

The 1-hour EST distinguishes active from inactive EoE in children and adults and can facilitate monitoring of disease activity in a safe and minimally invasive fashion

Furuta et al. Gut, 2013.
Ackerman et al. Am J Gastroenterol, 2019.

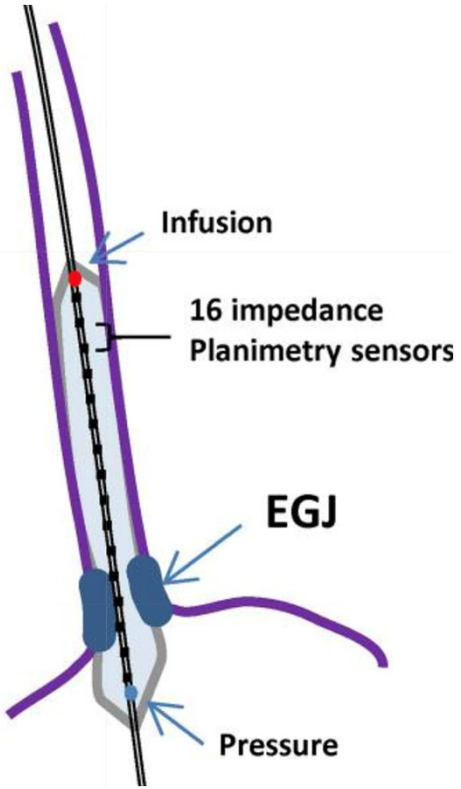
Innovations: EndoFLIP

Barrier: Beyond the epithelium?



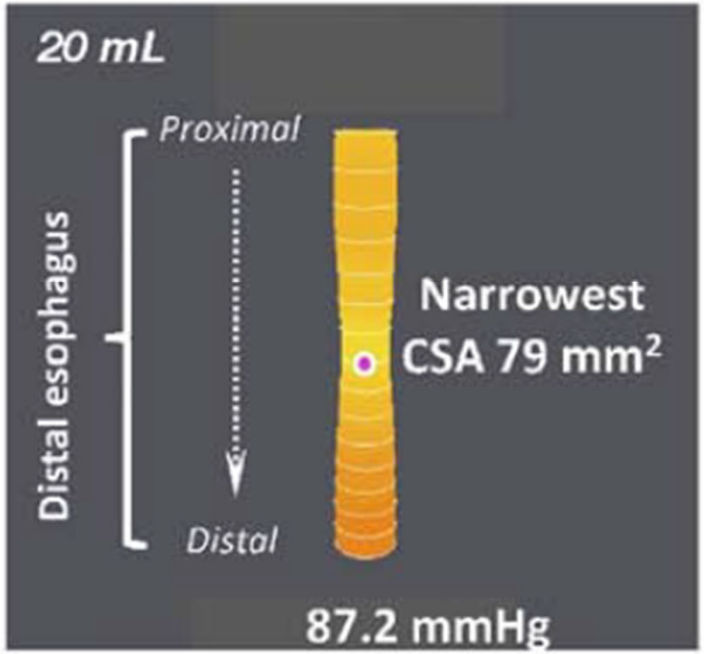
Functional Luminal Imaging Probe (EndoFLIP)

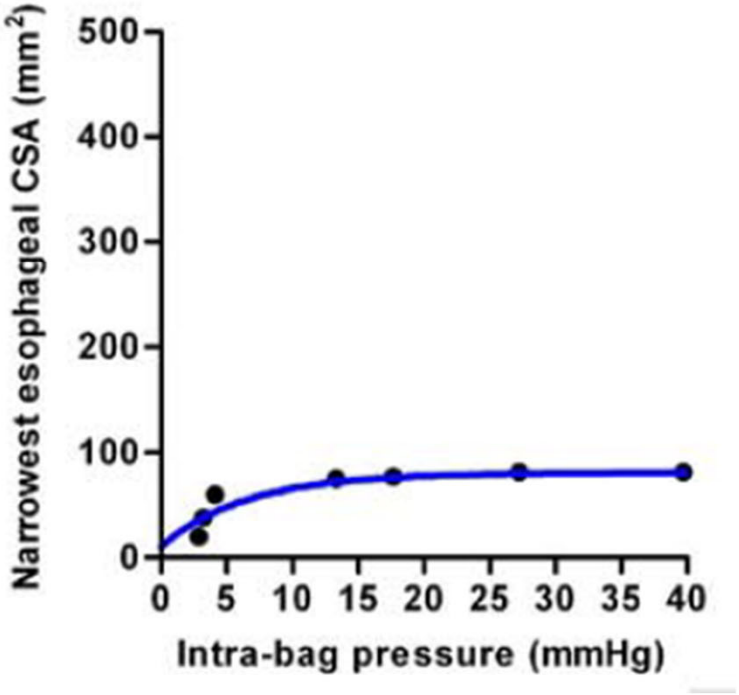
- Catheter inserted into the esophagus during endoscopy
- Measures distensibility of the esophagus
- Esophageal distensibility is decreased in EoE patients
- Patients with increased disease activity have decrease distensibility



Kwiatek et al. Gastroenterology 2011.
Menard-Katcher et al. Am J Gastroenterol 2017.

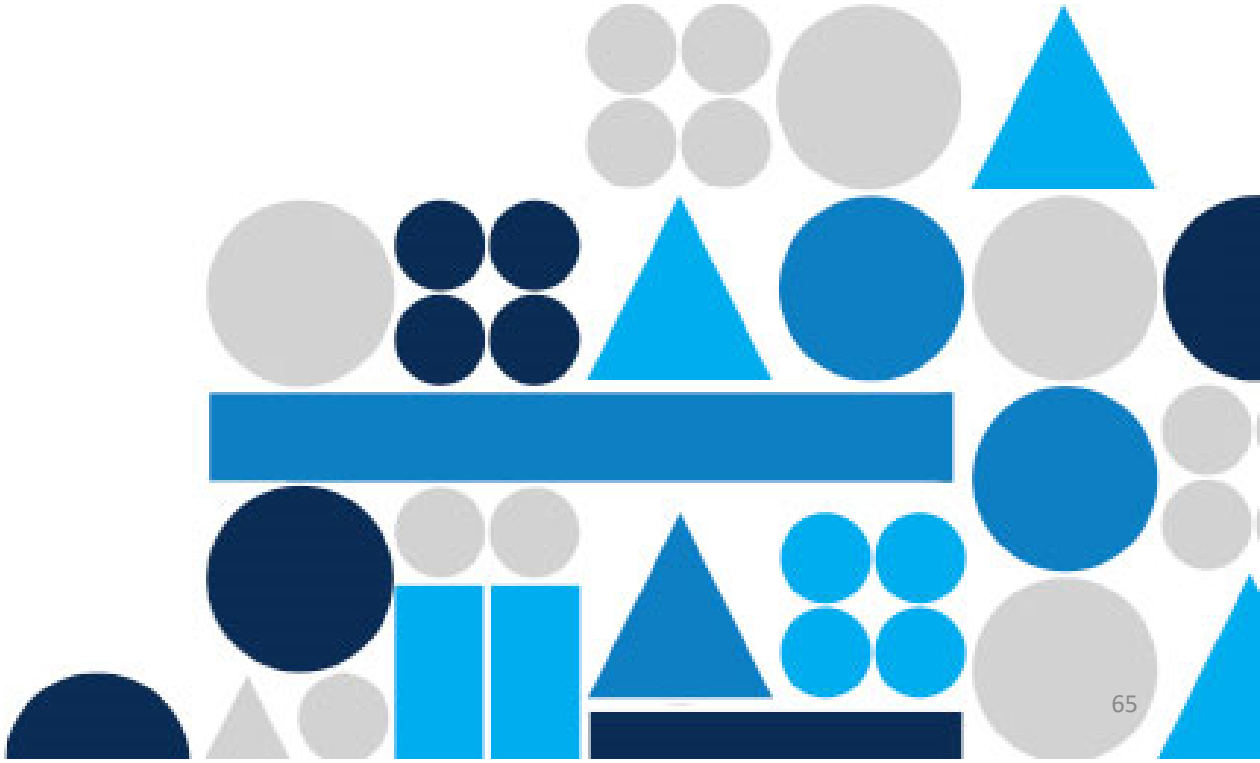
EoE patient with narrowed distal esophagus





Kwiatek et al. Gastroenterology 2011.
Menard-Katcher et al. Am J Gastroenterol 2017.

Innovations: Barium Pill Esophagram



Clinical Barrier/ Observation

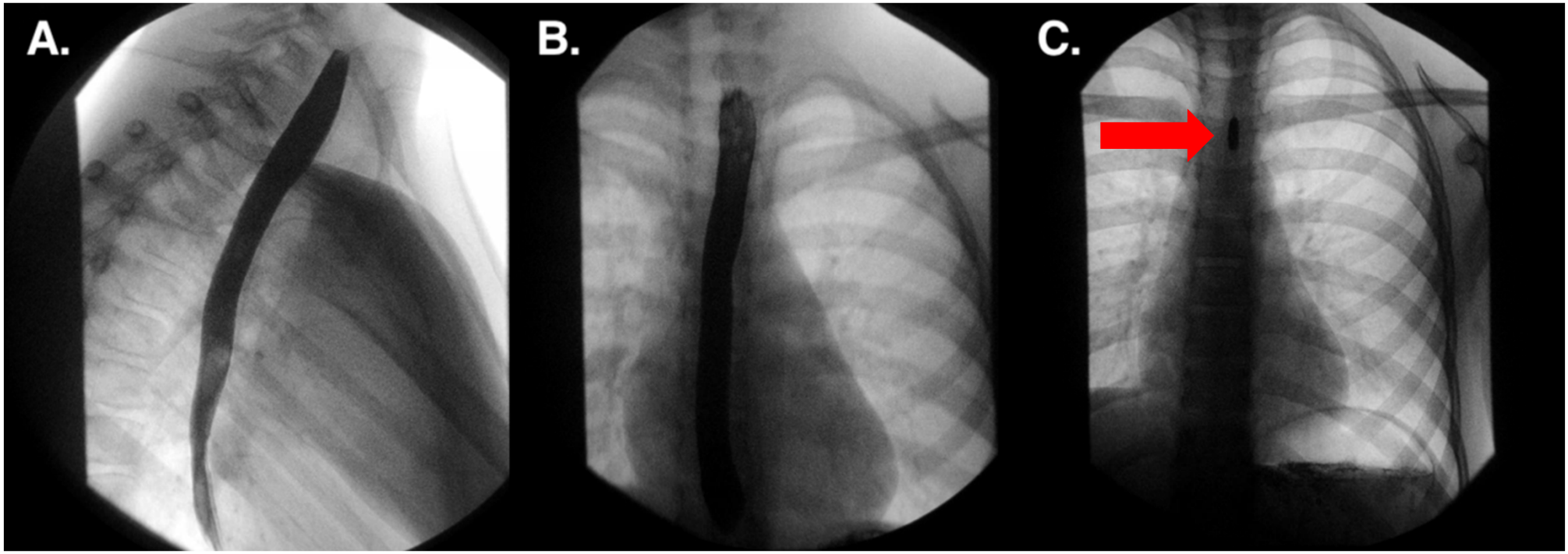
- Clinical conundrum: Patients with EoE continued to have dysphagia despite treatment for EoE and normal esophagram

- It is difficult to detect subtle narrowing in patients with EoE

- Identified patients with normal liquid barium esophagram who had retention of barium pill for > 5 minutes

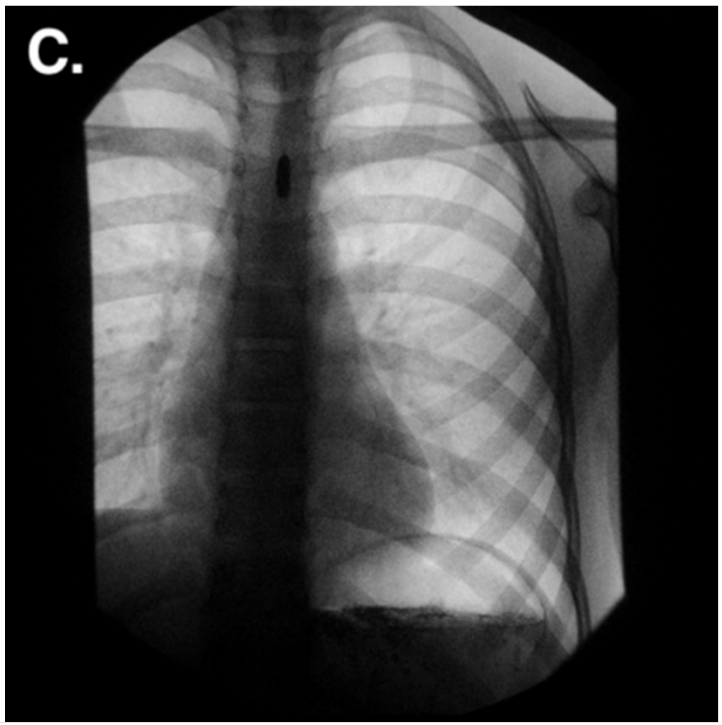
Nguyen et al. JPGN 2020.

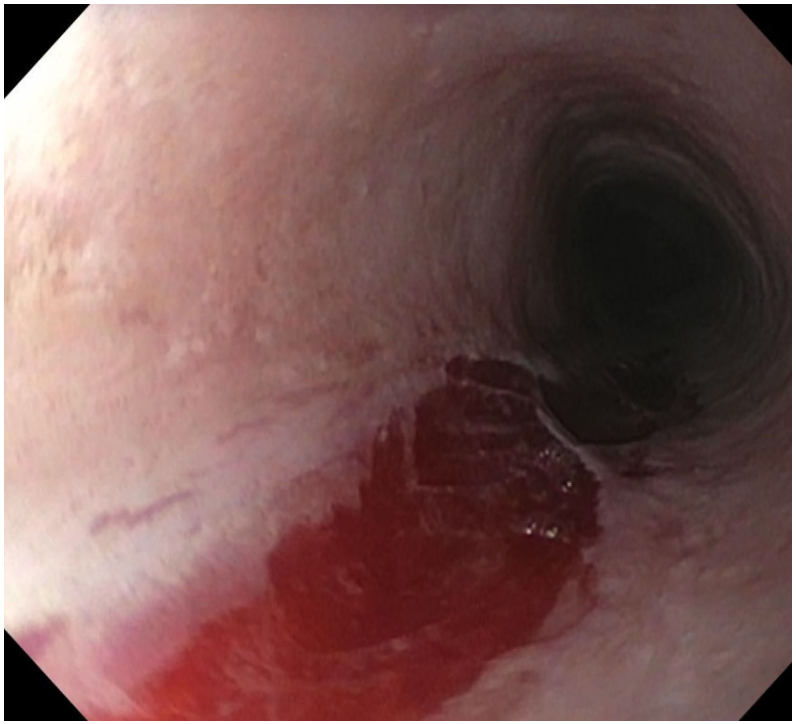
Barium Pill Esophagram



Nguyen et al. JPGN 2020.

Esophageal Dilation with Mucosal Tear





Nguyen et al. JPGN 2020.

Summary

- The clinical presentation of EoE can vary amongst different age groups and can be different for adults and children
- If clinical symptoms are suggestive of EoE, consider evaluation by GI for endoscopy
- Future directions include the development of new treatments and methods for disease monitoring in EoE
- Identifying barriers to care and collaboration is key to moving the field forward