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*Special Edition ACG Virtual Grand Rounds*  
**WHAT PRIMARY CARE AND ER PHYSICIANS NEED TO KNOW ABOUT EOE:  
ADVICE FROM 2 GASTROENTEROLOGISTS**



Kristle L. Lynch, MD




Amanda B. Muir, MD MSTR

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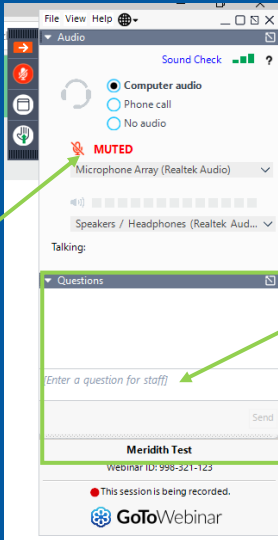
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## Faculty



### Kristle L. Lynch MD

Associate Professor of Clinical Medicine  
Director, GI Physiology Laboratory  
Director, Advanced Esophageal Fellowship  
Division of Gastroenterology  
The University of Pennsylvania

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## Faculty

## Amanda B. Muir, MD MSTR

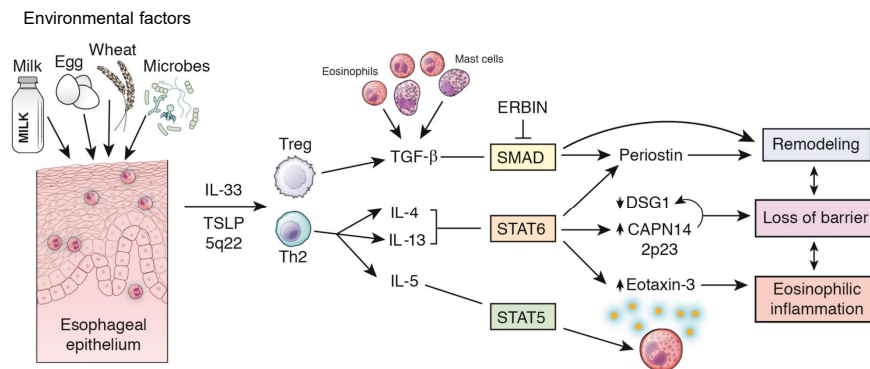


Assistant Professor of Pediatrics  
 Co-Director of the Gastrointestinal Epithelial Modeling Program, GEM  
 Associate Director of Fellowship Research  
 Division of Gastroenterology, Hepatology, and Nutrition  
 Perelman School of Medicine at the University of Pennsylvania

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## Eosinophilic Esophagitis

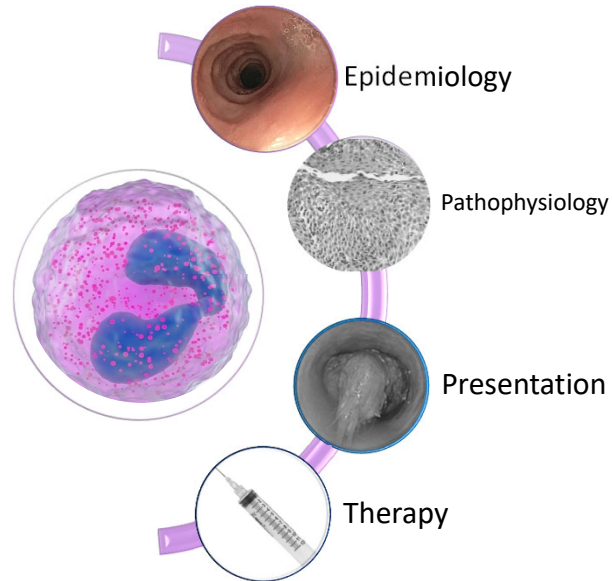
- Chronic immune-mediated allergic condition
- Characterized by eosinophilic infiltration of esophageal mucosa



O'Shea KM et al. Gastroenterology 2018

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# Eosinophilic Esophagitis



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## EoE: A Rare Disease?

*Digestive Diseases and Sciences, Vol. 38, No. 1 (January 1993), pp. 109-116*

### Esophageal Eosinophilia with Dysphagia A Distinct Clinicopathologic Syndrome

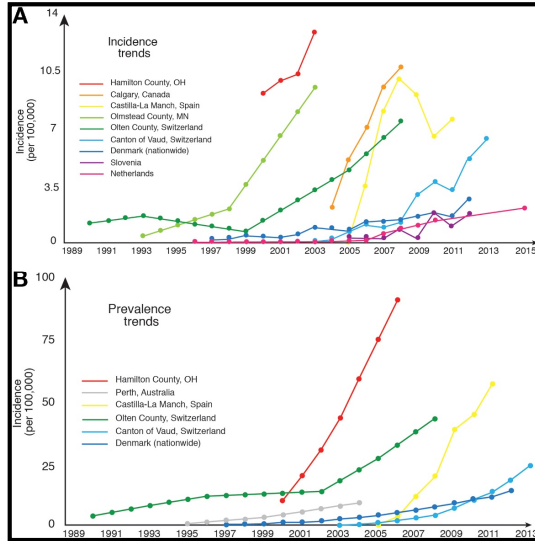
STEPHEN E.A. ATTWOOD, MB, FRCS, THOMAS C. SMYRK, MD, TOM R. DEMEESTER, MD,  
and JAMES B. JONES, PharmD

*Small numbers of intraepithelial esophageal eosinophils (IEE) may be seen in 50% of patients with gastroesophageal reflux disease and occasionally in normal volunteers. High concentrations of IEE are rarely seen in either setting. During a two-year period we identified 12 adult patients with very dense eosinophil infiltrates in esophageal biopsies (defined as >20 IEE/high-power field). Dysphagia was the presenting complaint in each, but no evidence of anatomical obstruction could be found. Endoscopic esophagitis was absent, but biopsy showed marked squamous hyperplasia and many IEE. Eleven patients had normal esophageal acid exposure on 24-hr pH monitoring. Esophageal manometry showed a nonspecific motility disturbance in 10 patients. For comparison, 90 patients with excess esophageal acid exposure on 24-hr pH monitoring were studied. Thirteen (14%) had motility disturbance, and 21 (23%) had dysphagia. Esophageal biopsies were devoid of IEE in 47 patients; none of the 43 with IEE had infiltrates as dense as those seen in the 12 study patients. The presence of high concentrations of IEE in esophageal biopsies from patients with dysphagia, normal endoscopy, and normal 24-hr esophageal pH monitoring represents a distinctive clinicopathologic syndrome not previously described.*

**KEY WORDS:** dysphagia; eosinophils; esophagitis; motility disorder; allergic gastroenteritis.

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# EoE: Incidence and Prevalence

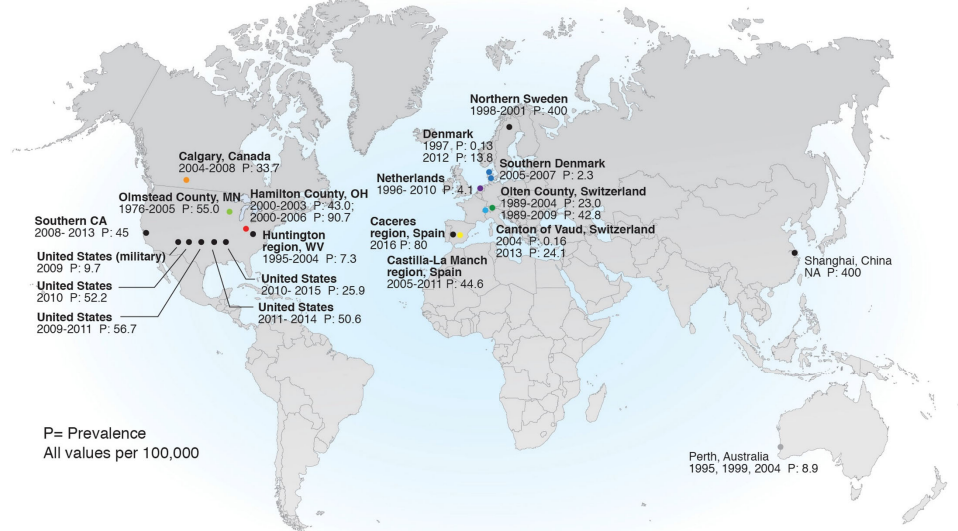


- Incidence and prevalence both increasing worldwide
- Overall prevalence estimate is 0.5-1 cases / 1000 persons

Dellon et al. Gastroenterology, 2018.

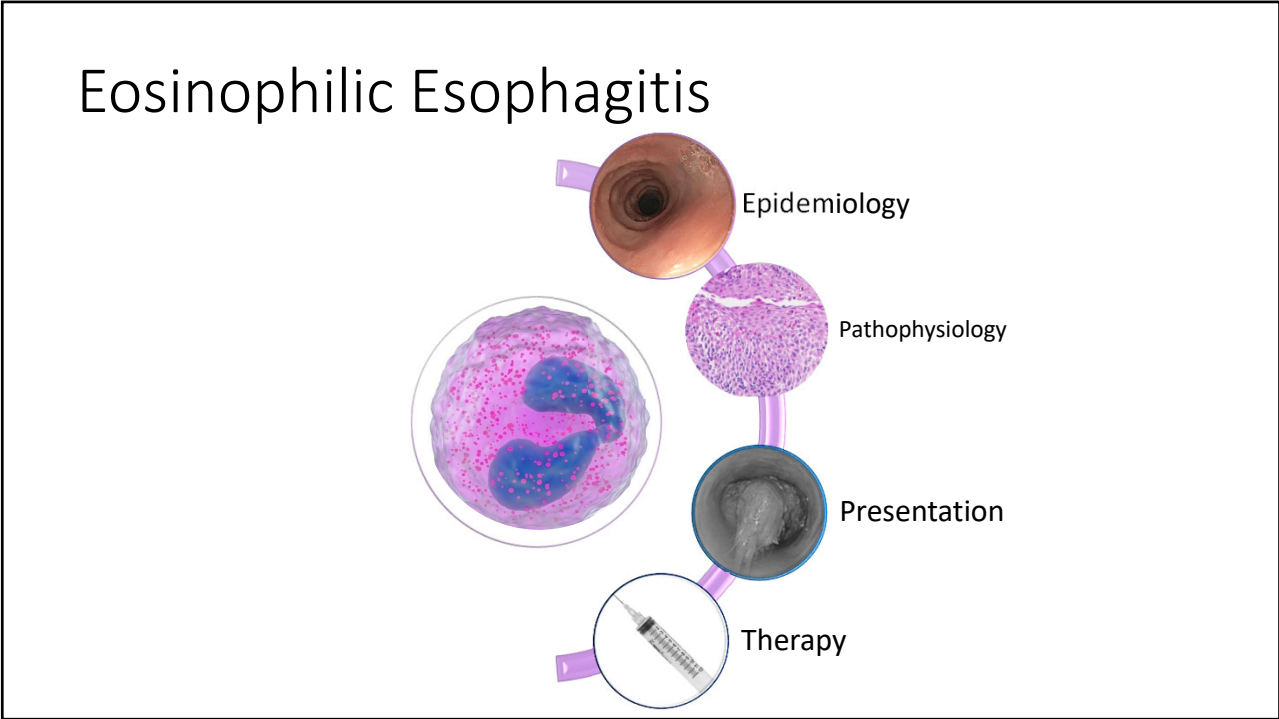
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# EoE: A Global Disease

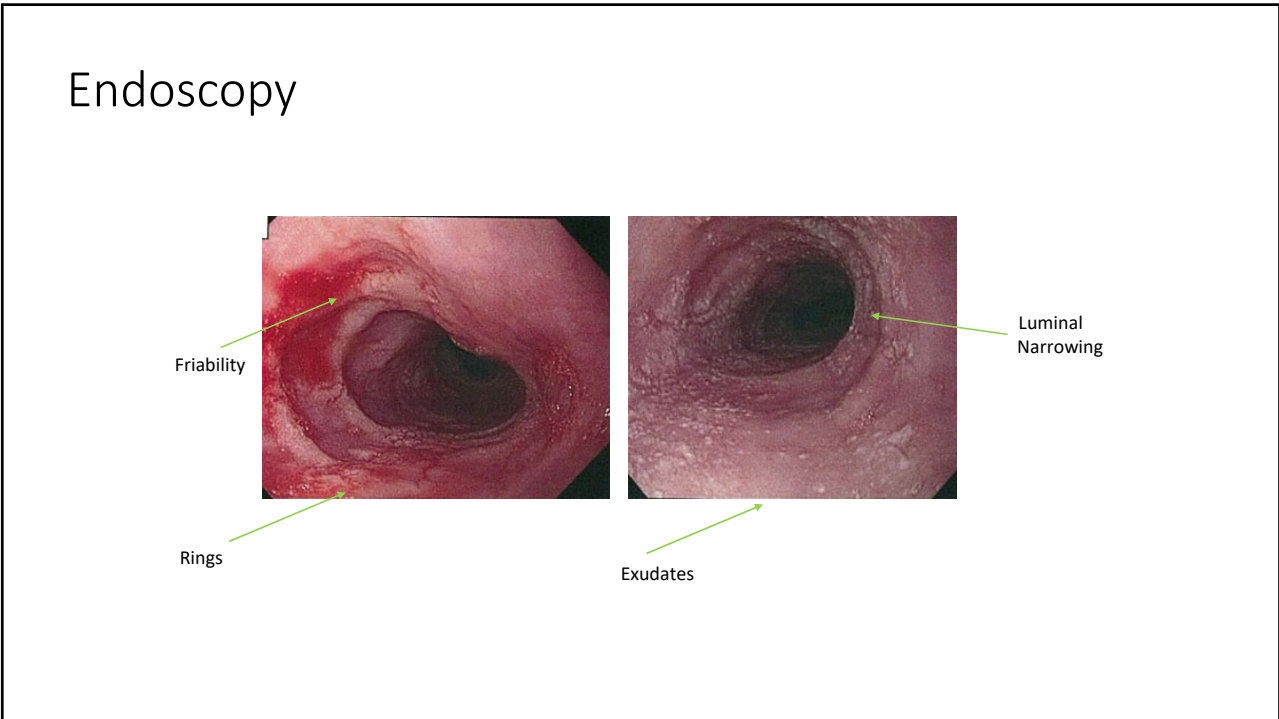


Dellon et al. Gastroenterology, 2018.

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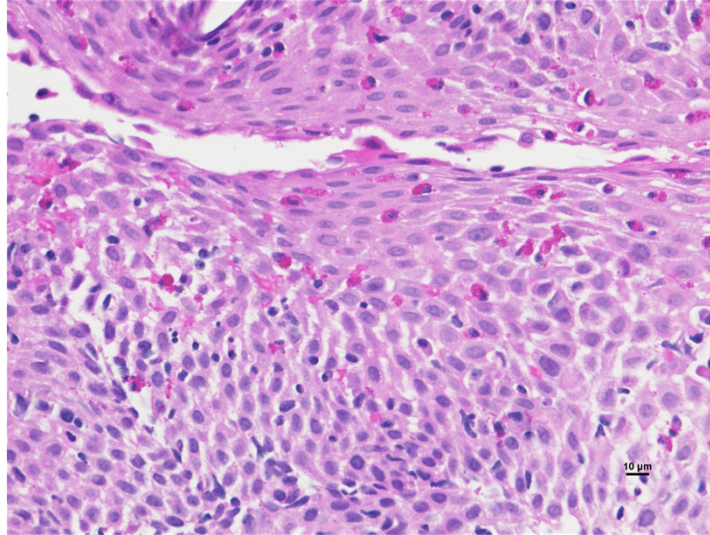
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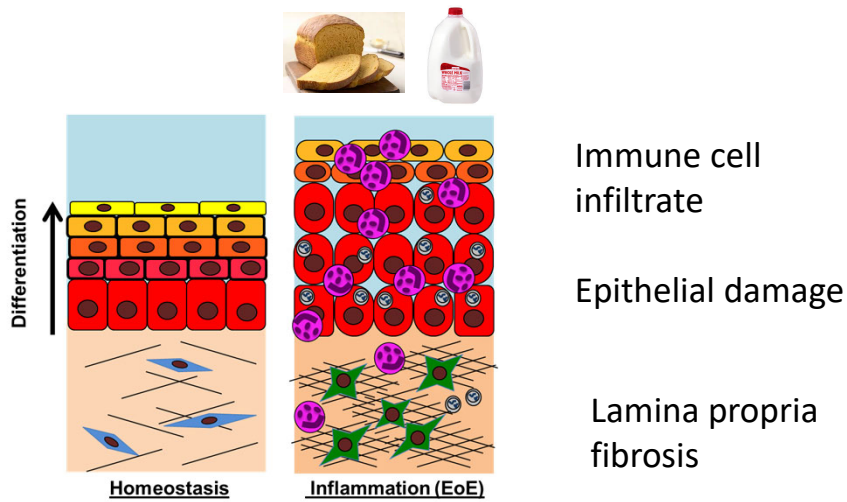


# Pathology



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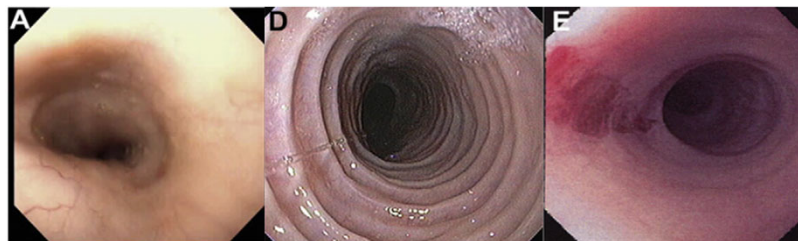
# Pathophysiology: Simplified



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## Fibrosis: Leads to esophageal narrowing

- Natural response to injury
- Excessive collagen deposition leads to tissue stiffness and esophageal stricture



Normal esophagus

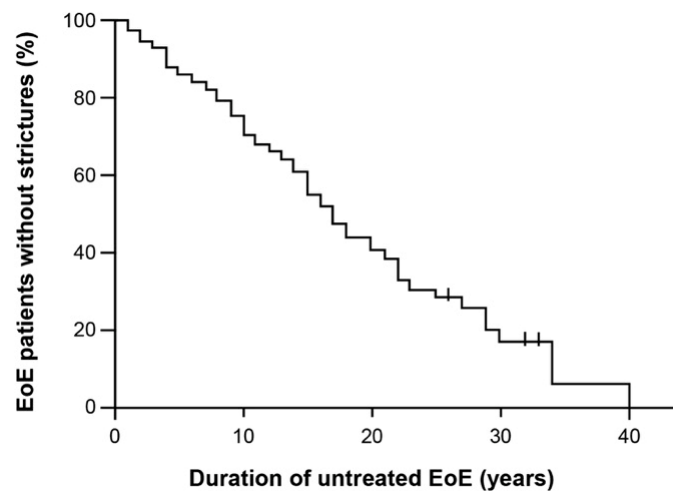
Trachealization

Stricture

Liacouras et al. JACI. 2011

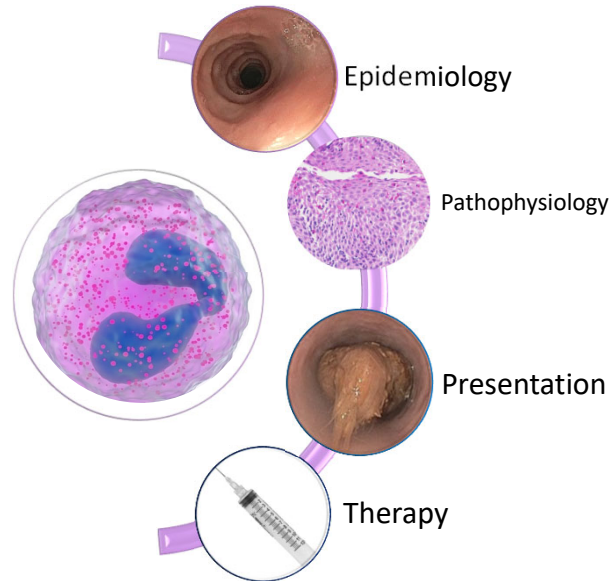
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## Natural history of EoE

Schoepfer et al, *Gastroenterology*, 2013

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## Eosinophilic Esophagitis



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## Symptoms of esophageal dysfunction

Dysphagia

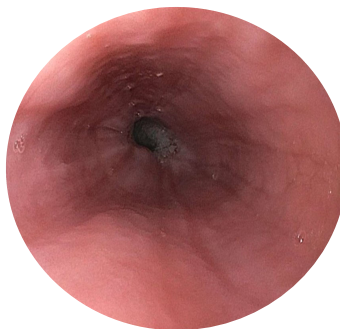
Regurgitation

Food impaction

Vomiting

Heartburn

Chest pain



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## Diagnostic Updates

Clinical  
Presentation  
Suggestive of EoE

EGD w/biopsies

Esophageal  
eosinophilia  
≥15/hpf

No other cause for findings identified

Eosinophilic  
Esophagitis

Dellon ES, et al. Gastroenterology. 2018

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## Symptoms of esophageal dysfunction

Dysphagia

Regurgitation

Food impaction

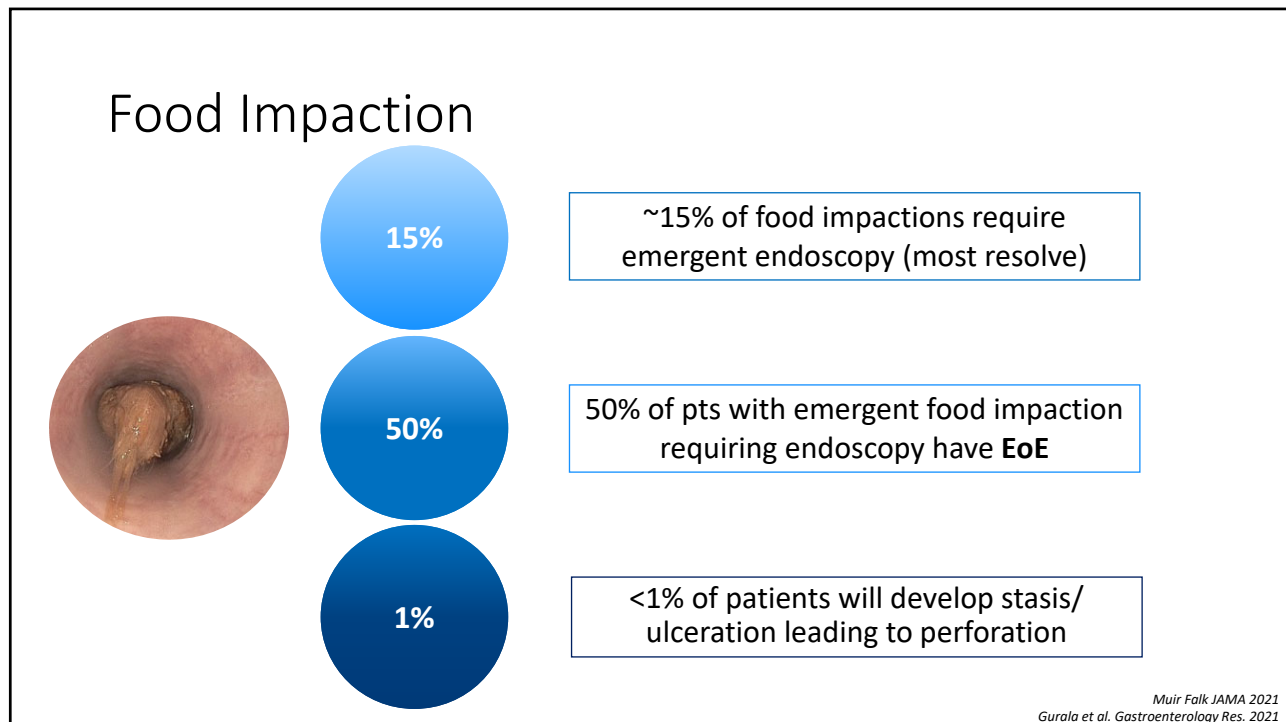
Vomiting

Heartburn

Chest pain




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## Food Impaction: Glucagon



- Frequently used for emergent food impaction as a smooth muscle relaxant
- Success rates vary: reported range 12% - 50%
- Higher doses are not more effective in reducing LES pressure
- Less effective in patients with structural abnormalities
- Studies do show glucagon can shorten door to scope time

Gurala et al. Gastroenterology Res. 2021

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## Emergent Endoscopy

- Timing: Typically within 24 hours, unless the patient is unable to manage secretions
- Airway Management is essential



*Gurala et al. Gastroenterology Res. 2021*

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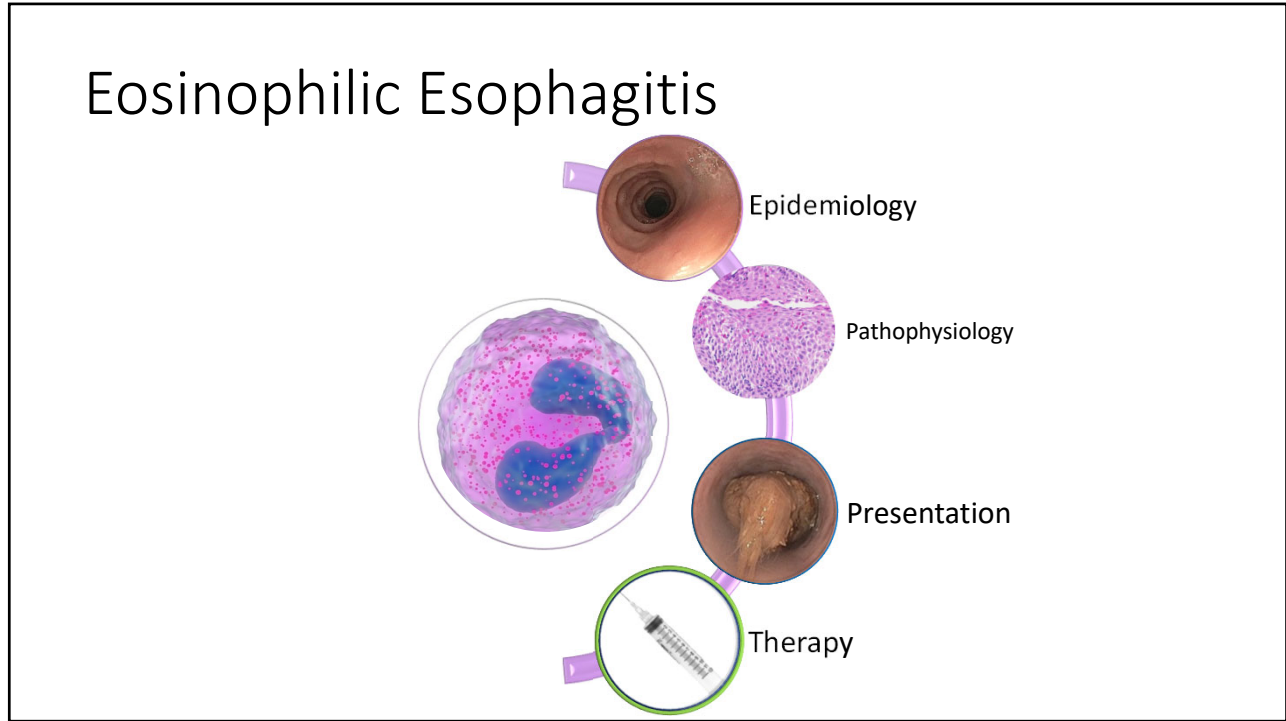
## Emergent Endoscopy

- Various techniques are used for endoscopic intervention (Roth net, graspers, push technique, pull technique, etc)
- Biopsies are essential
  - not yet routinely performed in 80% of cases(!)
- Dilations are performed on an as-needed basis

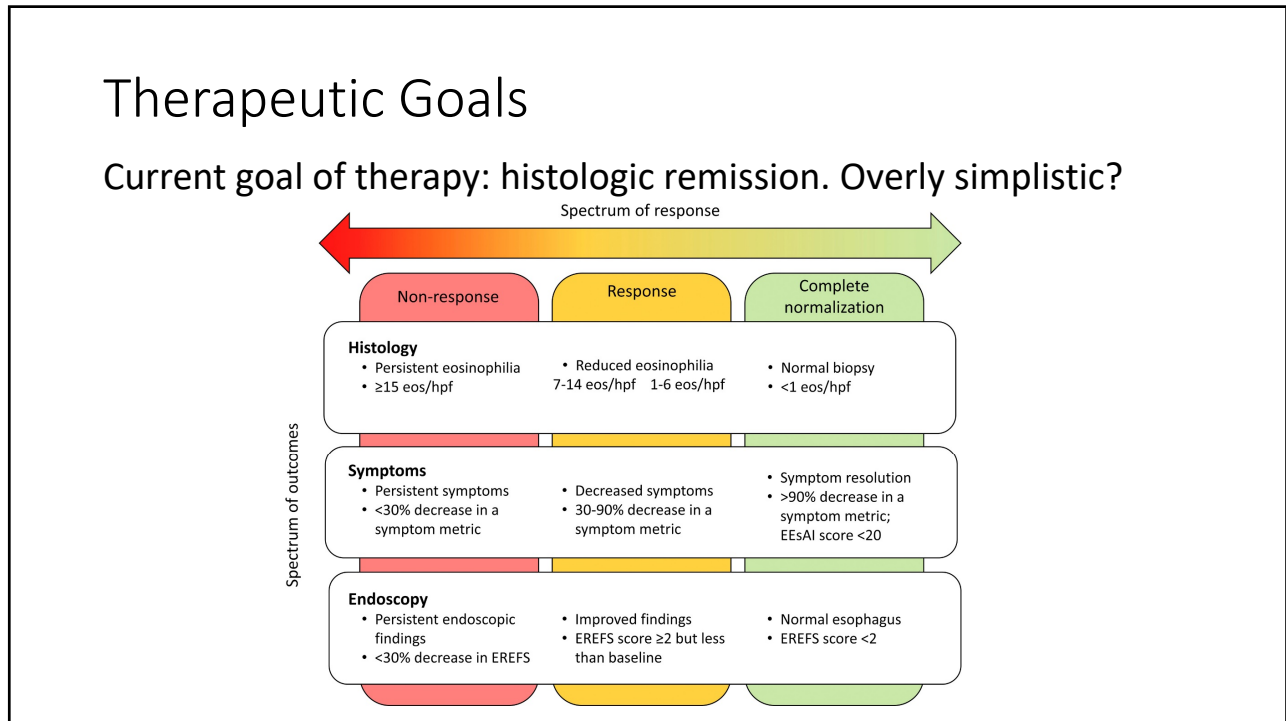


*Gurala et al. Gastroenterology Res. 2021*

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## Clinical Severity Index

Points per features	1 point	2 points	4 points	15 points
<b>Symptoms</b>	Weekly	Daily	Multiple x per day	
<b>Complications</b>		Food impaction with ER visit or endoscopy	Hospitalization due to EoE	Esophageal perforation, BMI <5 <sup>th</sup> %ile, Elemental formula, systemic steroids
<b>Inflammatory (edema, furrows, exudates)</b>				
<b>Endoscopy</b>	Localized	Diffuse		
<b>Histology</b>	15-60 eos/hpf	>60 eos/hpf		
<b>Fibrotic (rings, strictures)</b>				
<b>Endoscopy</b>	Present, but scope passes	Present but snug fit or requires dilation		Cannot pass standard upper endoscope, repeat dilations
<b>Histology</b>		BZH or LPF (or DEA/SEA)		

**Total Score: <1: Inactive EoE; 1-6: Mild Active EoE;  
7-14: Moderate Active EoE; ≥15: Severe Active EoE**

Dellon Khoury Muir et al. J Allergy Clin Immunology 2022

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## EoE: Therapies



Diet



Medications

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## Dietary Therapy for EoE



- Allergy Testing Guided Diet

- Limited to single-arm observational studies
- Heterogeneous testing: skin-prick testing, serum-specific IgE testing, atopy patch testing, or combinations

Diet limitation based on IgE mediated testing is not currently recommended

*Simon D et al. Allergy. 2016*

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## Dietary Therapy for EoE



- Elemental Diet

- Elemental formulas are comprised of macronutrients broken down to their simplest forms including monosaccharides (carbs), medium chain triglycerides (fat), and amino acids (proteins)
- They are formulated to meet full nutritional needs without supplementation

*Peterson KA et al. Am J Gastroenterol. 2013  
Warners MJ et al. Aliment Pharmacol Ther. 2017*

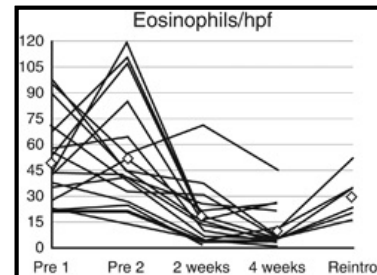
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## Dietary Therapy for EoE

### • Elemental Diet

- Limited prospective data in adults
- 21 adults, 4 weeks
  - 17 adhered to diet
  - 71% histologic response  $\leq 15$  eos/hpf at 4 weeks
- 29 adults, 4 weeks
  - 3 adults adhered to diet
  - 8 adults with histologic response  $\leq 10$  eos/hpf at 4 weeks
  - 72% histologic response  $\leq 10$  eos/hpf at 4 weeks
  - After resuming a normal diet, eos  $\uparrow\uparrow$  in 3-7 days

The elemental diet is  
efficacious but difficult to  
maintain



Peterson KA et al. *Am J Gastroenterol.* 2013  
Warners MJ et al. *Aliment Pharmacol Ther.* 2017

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## Dietary Therapy for EoE

### • Six Food Elimination Diet (SFED)

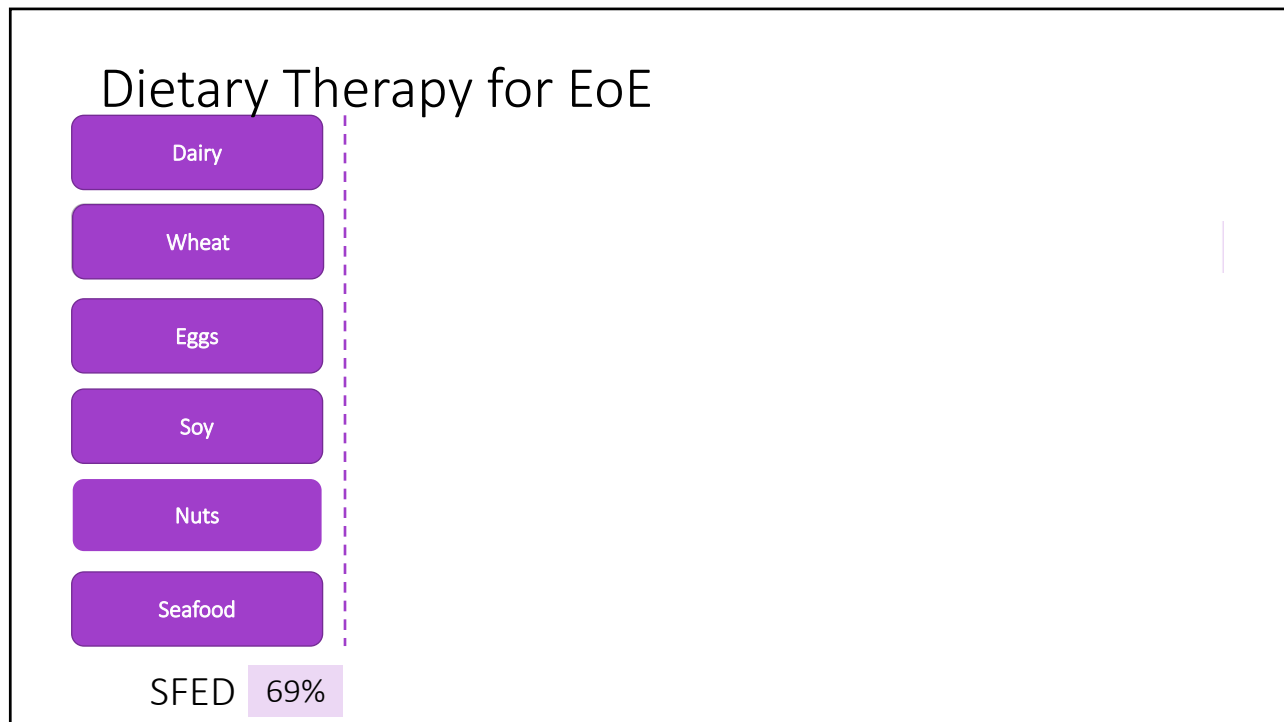
- Wheat
- Dairy/Cow's Milk
- Eggs
- Nuts
- Soy
- Seafood/Shellfish



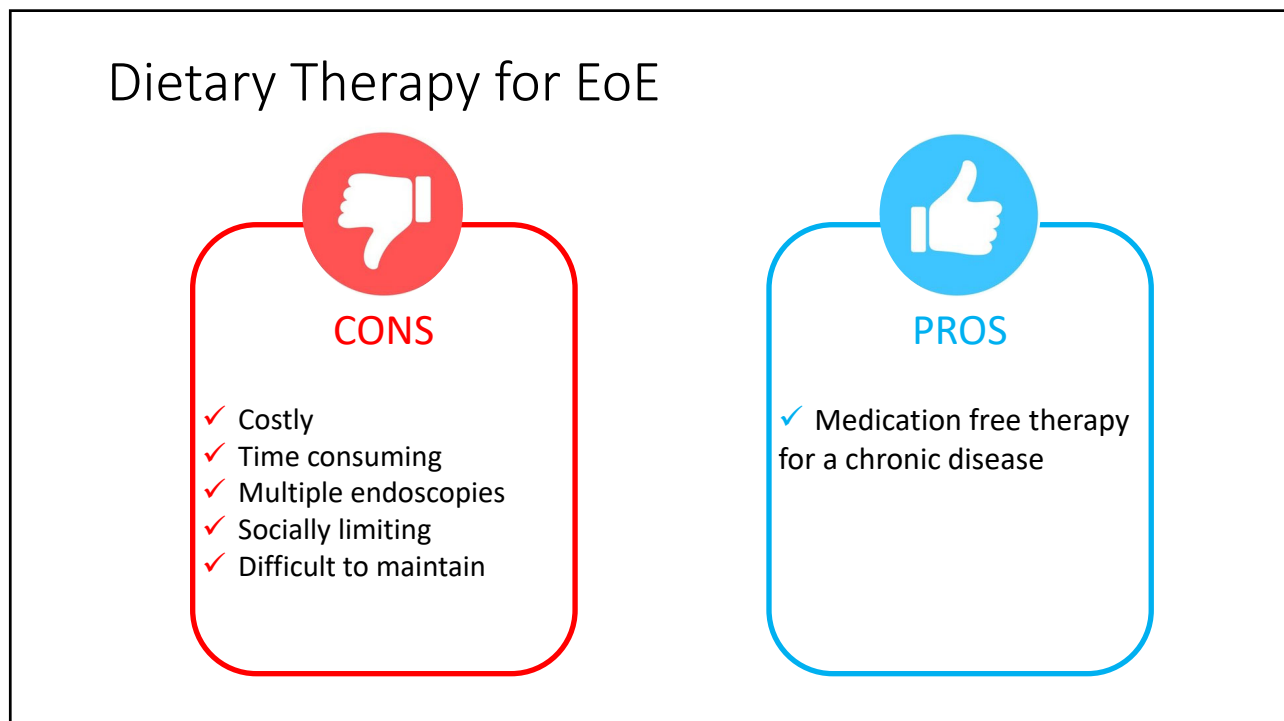
- SFED for 6+ weeks, followed by an endoscopy with biopsies
- If successful, reintroduce 1-2 food groups back in 6+ week intervals followed by an endoscopy each time

Kagalwalla AF et al. *Clin Gastroenterol Hepatol.* 2006

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## EoE: Therapies



Diet



Medications

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## Medical Therapy for EoE: Response

Table. Current Treatment Options for Eosinophilic Esophagitis

Treatment approach	Dose or methods	Pooled histologic response	Adverse effects	Other considerations
Proton pump inhibitors <sup>9</sup>	Omeprazole or equivalent, 20 mg, twice daily Pantoprazole, 40 mg, twice daily Lansoprazole, 30 mg, twice daily Rabeprazole, 20 mg, twice daily	41.7% in a systematic review of observational data of 1051 participants compared with a historical placebo comparison group of 13.3% <sup>32</sup>	Acute: Headache <5% <sup>33</sup> Diarrhea <5% <sup>33</sup> Enteric infections (1.4% in 53 152 patient-years of follow-up) <sup>34</sup> Proposed chronic <sup>35</sup> : Chronic kidney disease (0.1%-0.3%/patient/y) Bone fracture (0.1%-0.5%/patient/y) Dementia (0.07%-1.5%/patient/y)	Low cost Readily available Ease of administration Well tolerated
Topical corticosteroids	Fluticasone, 440-880 µg, twice daily Budesonide, 1-2 mg, twice daily	64.9% in 8 randomized clinical trials of 437 patients compared with 13.3% treated with placebo <sup>32</sup>	Esophageal candida (12%-16%) Oral thrush (2%-3%) <sup>36</sup>	Off-label use of asthma medications results in need to repurpose as slurry for budesonide and swallow instead of inhale for fluticasone Cost may be considerable because it is not always covered by insurance

\*An upper endoscopy is necessary to assess histologic response

Muir *Falk JAMA* 2021

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## Pharmacologic therapy

### Topical swallowed steroids

Fluticasone (Inhaler)



Budesonide (Slurry)

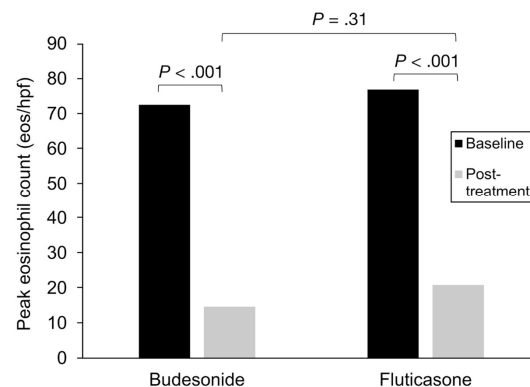


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## Pharmacologic therapy: Topical Steroids

RCT, 129 patients

- Budesonide (slurry) 1 mg BID vs.
- Fluticasone (inhaler) 880  $\mu$ g BID
- Post treatment max eos/hpf:
  - OVB: 15 eos/hpf
  - MDI: 21 eos/hpf
  - $p = .31$



Overall topical steroids are an effective primary therapeutic option

*Dellon ES, et al Gastroenterology. 2019*

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## Pharmacologic Therapy: Topical Steroids

### Emerging Therapies

- Novel Steroid Formulations
  - Budesonide Suspension – Dec 2021 not approved by the FDA
  - Fluticasone disintegrating tablet –studies ongoing
  - Budesonide orodispersible tablet- approved for use in Europe, Canada, and Australia

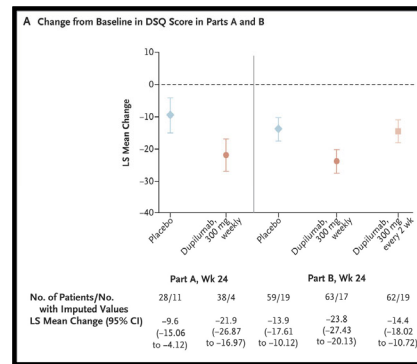
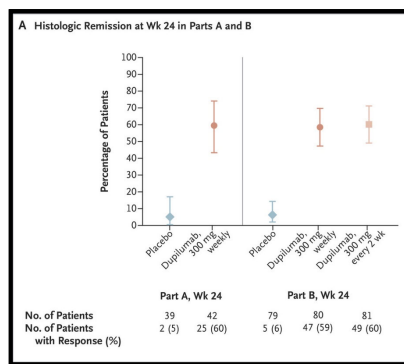


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## Pharmacologic Therapy: Dupilumab

First FDA-approved medication for EoE (2022)

- IL-4R $\alpha$  subunit receptor antagonist
- Phase 3 Study: Dupilumab 300 mg weekly (or Qoweeek) vs placebo
- Dysphagia score and peak eosinophil count were significantly lower in the dupilumab weekly group



Dellon et al. NEJM 2022

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# Pharmacologic Therapy: Dupilumab

Most sAEs were not considered related to the trial, except 1 sAE of systemic inflammatory response syndrome

Most common AEs involved injection site

**Table 2. Incidence of Adverse Events during the Treatment Period (Safety Analysis Set).<sup>2\*</sup>**

Event	Part A		Part B		Part A-C Group in Part C		
	Dupilumab, 300 mg weekly (N=42)	Placebo (N=39)	Dupilumab, 300 mg weekly (N=80)	Dupilumab, 300 mg every 2 wk (N=81)	Placebo (N=78)	Dupilumab-dupilumab (N=40)	Placebo-dupilumab (N=37)
number of patients (percent)							
Deaths	0	0	0	0	0	0	0
Adverse event	36 (86)	32 (82)	67 (84)	63 (78)	55 (71)	24 (60)	27 (73)
Serious adverse event†	2 (5)	0	5 (6)	1 (1)	1 (1)	0	1 (3)
Adverse event leading to discontinuation†	1 (2)	0	2 (2)	2 (2)	2 (3)	0	2 (5)
Adverse event occurring in ≥10% of patients in any group‡							
Injection-site reaction	7 (17)	4 (10)	16 (20)	18 (22)	16 (21)	4 (10)	8 (22)
Injection-site erythema	3 (7)	5 (13)	8 (10)	18 (22)	9 (12)	4 (10)	5 (14)
Injection-site pain	4 (10)	3 (8)	7 (9)	10 (12)	4 (5)	2 (5)	3 (8)
Injection-site swelling	3 (7)	1 (3)	10 (12)	7 (9)	2 (3)	2 (5)	0
Nasopharyngitis	5 (12)	4 (10)	2 (2)	4 (5)	3 (4)	1 (2)	3 (8)
Headache	2 (5)	4 (10)	6 (8)	5 (6)	9 (12)	3 (8)	2 (5)
Acne	0	1 (3)	0	2 (2)	3 (4)	0	4 (11)
Rash	0	4 (10)	2 (2)	4 (5)	0	1 (2)	0

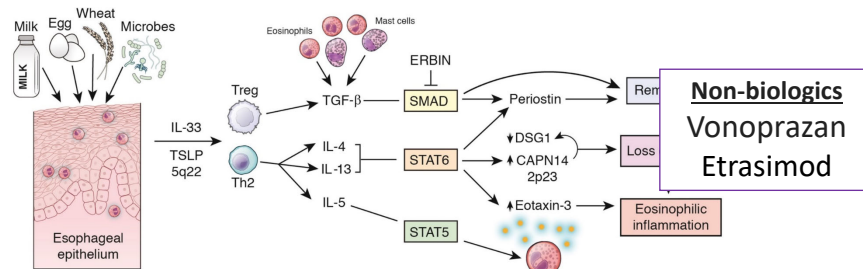
Dellon et al. NEJM 2022

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# Emerging Therapies

## Biologics

- Cendakimab
- Mepolizumab
- Lirentelimab
- Vedolizumab
- Tezepelumab
- Barzovolimab



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# Special Considerations in Pediatrics



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## Case Report #1

- 17 year old male presents to the ED with a food stuck in his throat
- He is unable to swallow his secretions and is spitting into a basin
- He is retching but only saliva is coming up
- He is able to speak and breath comfortably
- PMH: allergic rhinitis
- Exam: normal growth, allergic shiners, CTA
- He undergoes emergency endoscopy
- Biopsy reveals 60 eos/hpf in esophagus; normal antrum and duodenum



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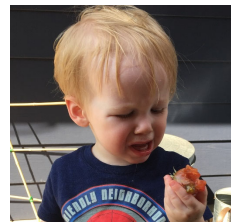
## Case Report #2

- 5 year old female with eczema, IgE mediated food allergy to egg and peanut, asthma, and allergic rhinitis presenting for allergy follow up.
  - She had outgrown her IgE milk allergy 2 years ago and eats yogurt and ice cream regularly.
- As an aside her mother reports that for the last 6 months she has daily abdominal pain, gastroesophageal reflux and regurgitation
- Allergist notices her weight percentiles decreased from 50<sup>th</sup> percentile to 30<sup>th</sup> percentile
- She is referred to GI for evaluation
  - Initially started on proton pump inhibitor and constipation addressed
  - Symptoms persisted and EGD revealed > 100 eos/hpf

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## Symptoms of EoE

- Vomiting
- Feeding refusal
- Failure to thrive
- Abdominal pain
- Heart burn
- Dysphagia
- Food impactions



Younger children



Adolescents or Adults

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## Coping Mechanisms

- Overchewing
- Slow meal eating
- Lubrication
- Increased drinking
- Avoiding “tough” foods



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## Multi-disciplinary Approach

- Patient and family
- Allergy
  - Role of atopy
  - Recognition and treatment of other atopic conditions
- Gastroenterology
  - Concomitant reflux, constipation, delayed gastric emptying
  - Procedures
- Nutrition
  - Ensure proper nutrition micro and macronutrient level
- Feeding therapist
- Psychologist

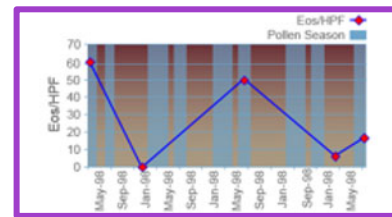


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## More common in patients with other forms of allergy

Author/population	IgE-Mediated Food Allergy	Asthma	Allergic Rhinitis	Atopic Dermatitis
General Population	3%	8.5%	25%	10%
EoE patients	5.7%	33-66%	30-90%	19-55%

- In terms of allergic rhinitis, seasonal variations may exist.
  - 30% of patients have environmental allergies contribute to EoE
  - Few patients where only cause



Spiegel et al JPN 2009;48(1):30-6. Asa'ad et al JACI 2007; 119(3):731-8.  
 Sugnanam et al. Allergy 2007;62(11):1257-60. Guajardo et al J Pediatr 2002;141(4):576-81, Roy-Ghanta et al  
 Clin Gastroent Hepatol 2008;6(5):531-5. Fogg, et al; JACI 2003; 112: 796-7. Ram et al, Ann Allergy Asthma  
 Immunol 2015; 115(3):224-228. Hill DA JACI Pract 2018;6:1528-33

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## Psychosocial and Quality of Life

- Recognize stressors on patient and family
  - Symptom standpoint
    - Are there ways to help
  - Treatment itself
  - Financial standpoint
- Seek ways to help with stressors
- APFED, CURED, ACAAI, AAAAI, EAACI



Klennert MD et al. JPN 2014;59: 308-316.

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## Therapy options

- Offer choices
  - Therapy that you pick now does not have to be your forever therapy
- What **therapy** are you going to be able to adhere to?
- If diet is already limited, can you feasibly limit any more?
  - Feeding disorders

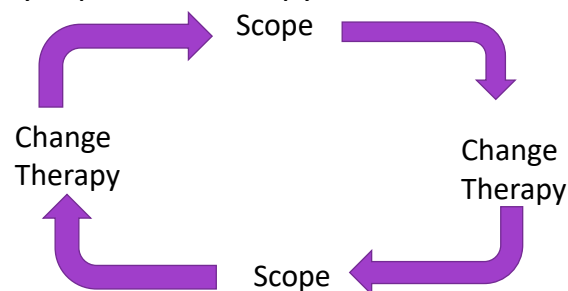


Dellon, *Gastroenterology* 2019

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## Monitoring

- Coping mechanisms make assessing symptoms difficult
- Non-response rates are 20 to 60%
- Need to assess by repeat endoscopy



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## Special patient groups

- Outside of patients with known atopy, other “higher risk groups”
  - Outgrowing IgE mediated food allergy
  - Outgrowing FPIES trigger foods
  - Undergoing oral immunotherapy



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## Monitoring for disease: transnasal endoscopy

- Retrospective study 190 patients (3 to 22 years)
- Underwent video goggle or virtual reality-based unsedated TNE
- 294 of 300 attempts successful
  - 54 underwent multiple TNE
- Reduced cost by 54% from \$9400 to \$4400
- Side effects:
  - 11 epistaxis, 9 spit up, 8 vomiting, 1 nausea, 1 sneeze (tracheal intubation)
  - 264 tolerated

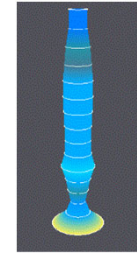
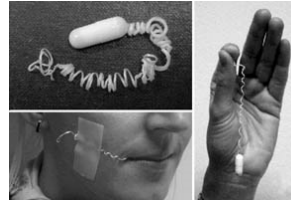


Nguyen, N et al. Clin Gastroenterology and Hepatology 2019.

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## The future

- Better monitoring
  - Esophageal String Test
  - Cytology sponge
  - Esophageal Brush
  - Endoflip
- Different treatment options
  - Medications directed against specific chemokines, cytokines and inflammatory mediators
- More research
  - Role of organoids and personalized medicine



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## Following up

- One must have a repeat endoscopy to truly know what is going on in esophagus
  - Whatever plan is patient must be following OR EGD will not answer question at hand
  - Can still have esophageal eosinophils without symptoms...
  - If a patient needs systemic steroids for any reason, typically wait a month before repeat EGD
  - Once there is a normal EGD, how often does one need to repeat it?



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## Case Report #1—what happened?

- 17 year old male presents to the ED with a food stuck in his throat
- Biopsy reveals 60 eos/hpf in esophagus; normal antrum and duodenum
- Initially placed on high dose PPI (compliant) and repeat endoscopy improved but still abnormal.
- Swallowed steroids started along with PPI led to remission
- Over time, may consider Dupilumab

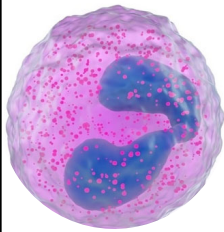
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## Case Report #2: what happened?

- 5 year old female with eczema, IgE mediated food allergy to egg and peanut (outgrew milk allergy), asthma, and allergic rhinitis presenting for allergy follow up.
- Endoscopy revealed >100 eos/hpf in esophagus while on PPI
- Variety of options offered but ultimately removed dairy with resolution in symptoms and normalization of esophageal eosinophils

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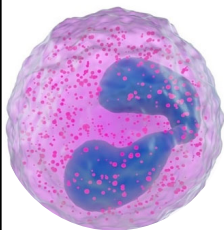
## Conclusions



- EoE is a chronic immune-mediated allergic condition
- It can affect people of all ages
- Over 60% of patients have comorbid atopic condition
- Presenting symptoms in adults include heartburn, dysphagia, and food impaction
- Small children have vomiting and failure to thrive

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## Conclusions

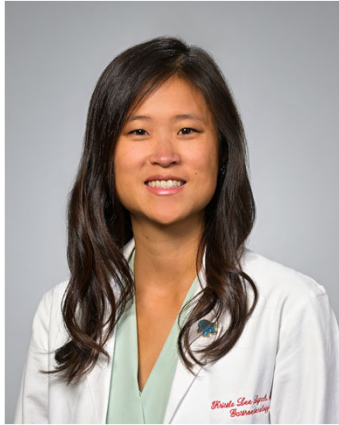


- 50% of pts with food impaction requiring EGD have EoE
- Medical therapy includes proton pump inhibitors, topical swallowed steroids, and dupilumab
- Elimination diets are the most common form of dietary therapy in adults
- Long-term therapy is recommended

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Questions?



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