



Eosinophilic Esophagitis- Recognition, Management, and Misperceptions

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Objectives



- Recognize the signs and symptoms of eosinophilic esophagitis (EoE) in different age groups
 - Appreciate the change in our understanding of the pathophysiology of EoE
 - Understand how EoE is diagnosed
 - Discuss the treatment options for EoE
-
- No financial or other disclosures

- 7yo male with difficulty swallowing x 1 year
 - Occurs when eating
 - Solids worse than liquids
 - Occasional heartburn
 - No choke/gag/cough
 - “Feels food go down”

Differential Diagnosis- Dysphagia



- Esophagitis
 - GERD
 - Eosinophilic Esophagitis (EoE)
 - Infectious
- Anatomic/vascular anomaly
- Traumatic injury
- Psychosomatic
- Crohn's Disease
- Motility (i.e. achalasia)
- Mediastinal mass
- Neurologic
- Connective tissue disease

Additional History...



- Washes food down with water
- Slow eater
- Fine in between episodes
- Weight gain slowed
- IgE mediated food allergy to peanuts
- Father with chronic dysphagia, food impaction age 20s; “has not gotten it checked”

What is Eosinophilic Esophagitis (EoE)?



- Chronic inflammation of esophagus
 - Eosinophil dominant
- Immune-mediated
- Food (?aeroallergen) trigger

So what?

Why EoE Matters



- #2 cause esophagitis
- Leading cause of dysphagia and food impaction in kids and adults
- Complications
- Incidence rising

Symptoms Vary by Age



- ***Abdominal pain, vomiting, dysphagia***
- **Infants/Toddlers**
 - Feeding difficulties (gag/choke/refusal), vomiting
- **Children**
 - Vomiting/GER, nausea, abdominal pain, chest pain, poor growth
- **Adolescents/adults**
 - Dysphagia, food impaction, chest pain

Epidemiology



- Incidence 1/10,000¹
- Prevalence 5-10/10,000
- Young men (3:1)²
- Age 30-50yo
- High rate atopy
 - 2/3- allergic rhinitis, asthma, eczema
 - IgE mediated food allergy common (15-40%)
 - Up to 75% have personal or family history³

¹Noel R, et al. N Engl J Med 2004; **351**:940-1.

²Orenstein S, et al. Am J Gastroenterol 2000; **95**: 1422-30.

³Furuta GT, et al. Gastroenterology 2007; **133**:1342-63.

Why the Rise?



- Environmental
 - Hygiene hypothesis
 - Dietary changes (antioxidants, fats, Vitamin D)
 - Food processing
 - Delayed oral exposure to foods
- Early antibiotics
- C-section
- Prematurity
- Microbiome
- Infectious- HSV, Mycoplasma; H. pylori (inverse)
- Oral/sublingual immunotherapy
- PPI, low Vit D

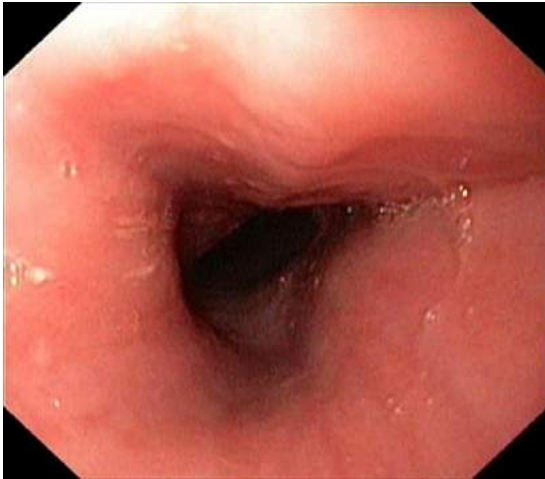
Evaluation & Diagnosis

- **Physical exam– no diagnostic findings**
 - Allergic shiners
 - Rhinitis
 - Reactive airways
 - Atopic dermatitis
- **Laboratory– no diagnostic tests**
 - Mild peripheral eosinophilia in <50% with EoE¹
 - Allergy testing (skin prick, IgE)
 - No direct correlation with non-IgE mediated disease

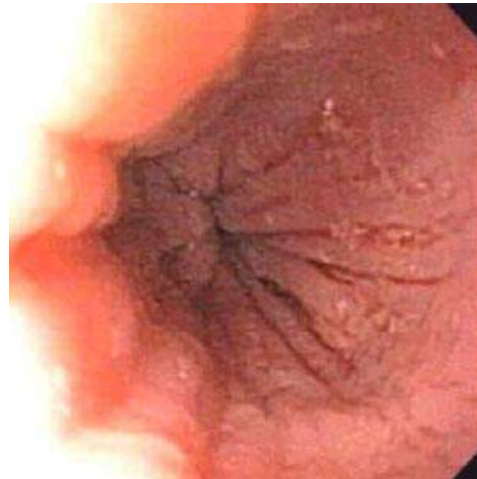
¹Putnam, PE. Immunol and All Clin N Amer 2009; **29**: 1-10.

- **Other questions to ask:**
 - Onset with introduction of solids?
 - Slow eater?
 - Drink to wash down food?
 - Particular food avoidance?
 - Excessive chewing?
 - Other atopy-patient, family?
 - Growth failure?

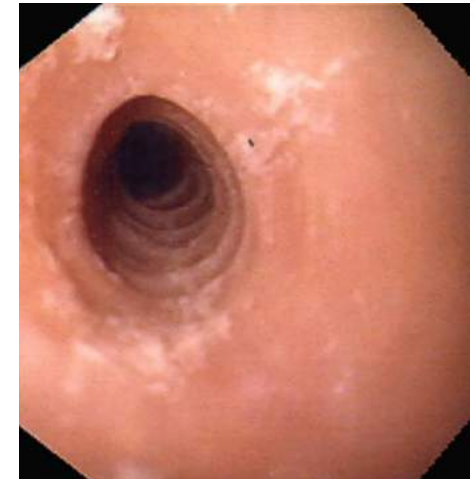
Endoscopy



Normal



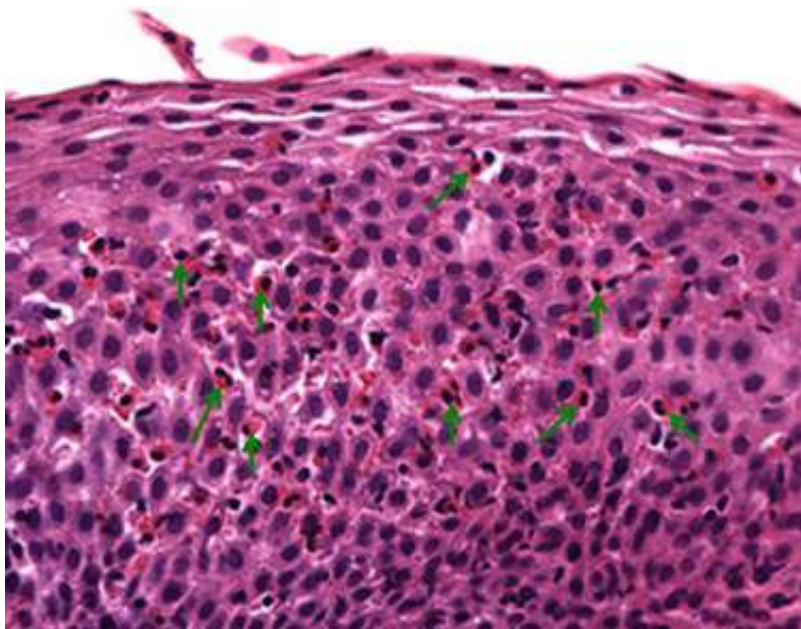
**Longitudinal
furrowing**



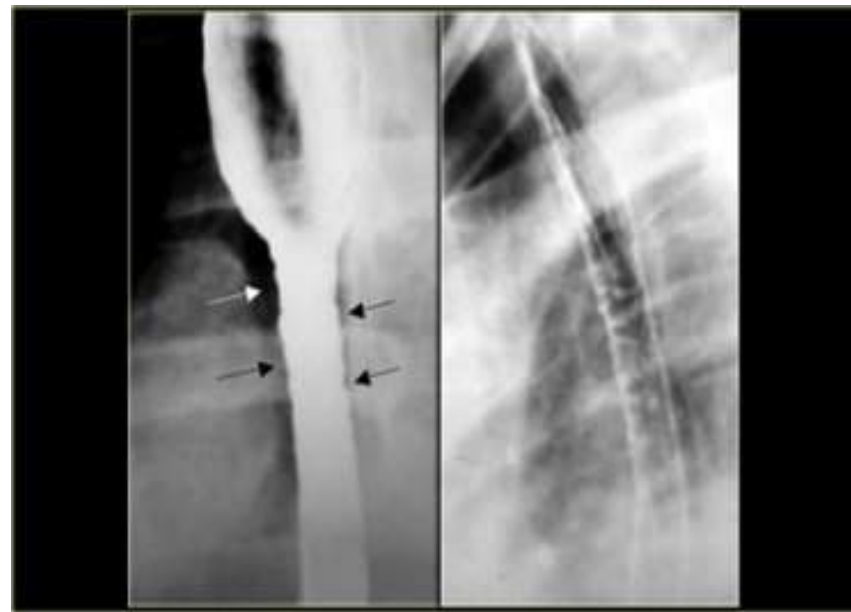
**Concentric
rings,
exudate**

-Up to 30% who have histologic EoE have endoscopically normal mucosa¹

¹Potter J, et al. Gastrointest Endosc 2004; **59**:355-61.



- Increased eos/HPF, microabscesses, superficial layering, basal zone hyperplasia



Concentric rings in esophagus

Diagnostic Criteria Has Changed



- **2007¹**
 - ≥ 15 eos/HPF, PLUS
 - Characteristic symptoms which do not respond to high dose PPI therapy, OR normal pH monitoring¹
- **2011-Proton Pump Inhibitor-responsive Esophageal Eosinophilia (PPI-REE)²**
 - ≥ 15 eos/HPF, PLUS
 - Symptoms of esophageal dysfunction, PLUS
 - Improvement/resolution of symptoms and eosinophilia after high dose PPI

¹Furuta GT, et al. Gastroenterology 2007.

²Liacouras CA, et al. J Allergy and Clin Immun. 2011.

Assumptions



1. GERD and EoE distinct
2. GERD is the only esophageal condition that responds to PPI¹

¹Dellon et al. Gastroenterology Vol 155 2018

New Understanding



- AGREE (**A** Working **G**roup on PPI-**REE**)¹
- ***GERD and EoE may overlap***
 1. EoE → GERD? (dysmotility)
GERD → EoE? (impaired mucosal barrier)
 2. EoE and PPI-REE similar histologically
 3. RNA expression profiles similar
 4. Atopy present in EoE and PPI-REE
 5. PPI-REE responds to EoE treatment (topical steroids, dietary elimination)

¹Dellon ES, et al. Gastroenterology 2018.

PPIs-More Than Gastric Acid Inhibition



Non-acid related mechanisms

- Antioxidant
- Blocks secretion of eosinophil trafficking molecule (eotaxin-3)
- Proton pumps in inflammatory cells and non-gastric cells
- Patients with normal pH probe can respond to PPI therapy

Management

Goals



- Symptom control
- Histologic normalization
- Reversal of remodeling
- Avoidance of complications

Treatment Options



- 2011
 - Elimination Diet
 - Swallowed Topical Steroid

- 2019
 - *PPI*
 - Elimination Diet
 - Swallowed Topical Steroid

Dietary Therapy

Classification of Food Allergy



- IgE mediated
 - Acute (anaphylaxis, oral swelling)
- Cell mediated (Delayed/chronic)
 - Delayed/chronic (FPIES, food protein proctitis)
- **Mixed IgE/cell mediated**
 - Delayed/chronic (eosinophilic GI disease, eczema)
 - Serum IgE and Skin Prick Testing → ***not helpful in EoE!***

Dietary Options



1. **Elemental**
2. **Empiric 6, 4, 2, 1 elimination**
3. **Directed elimination**

Determining dietary modification



IgE Mediated

- Cow's Milk
- Egg
- Peanut
- Tree nuts
- Fish
- Shellfish
- Wheat, soy
- Sesame

EoE

- Cow's milk
 - 40-90%
 - 50% only trigger¹
- Wheat
- Egg
- Soy

¹Kagalwalla AF et al. Clin Gastroenterol Hepatol 2017.

Elimination Diets for EoE



- Elemental
 - 90% remission¹
- 6 Food: Dairy, wheat, soy, egg, nuts, fish/shellfish
 - 50-75% remission²
- 4 Food: Dairy, gluten, egg, legumes
 - 50-65% remission²
- 2 Food: Dairy, gluten
 - 43% remission³

¹Aria A et al. Gastro 2014.

²Molina Infante J et al. J Allergy Clin Immunol 2018

³Molina-Infante J et al. [Expert Rev Gastroenterol Hepatol](#). 2017

Dietary Options



- Directed Elimination:
 - 12 single arm studies → 50% remission¹
 - Testing techniques varied
 - Not effective

¹Hirano I et al. AGA Clinical Guidelines 2019.

Pharmacotherapy

PPI



- 1-2 mg/kg/day divided BID
- Max dose- Lansoprazole 30mg BID, Omeprazole 40mg BID
- 23 observational studies → 40% histologic improvement¹
 - Heterogeneous studies

¹Hirano I et al. AGA Clinical Guidelines 2019.

- **Swallowed topical steroids**
 - Fluticasone
 - Budesonide slurry
 - 8 double-blind placebo controlled studies
 - 66% remission vs. <15% placebo¹
- TRY TO AVOID: Systemic steroids
- NOT: Mast cell stabilizers (Cromolyn), leukotriene antagonists (Montelukast), biologics (Anti-TNF α , Anti-IL5, Anti-IL13)

¹Hirano I et al. AGA Clinical Guidelines 2019

Swallowed Topical Steroids



- **Fluticasone**
 - 1-4yo: 44 mcg, two sprays twice daily
 - 5-10yo: 110 mcg, two sprays twice daily
 - ≥ 11 yo: 220 mcg, two sprays twice daily
- **Budesonide**
 - < 10 yo: 1 mg daily
 - > 10 yo: 2 mg daily

Limitations in Current Data



- No prospective, double-blind, randomized trial to compare PPI to diet or steroid
 - Small studies, retrospective
 - Inconsistent study design
 - PPI duration, dose
 - PPI responder vs. non-responder
 - Lack consistent definition re: clinical or histologic response

Risks/benefits: PPI vs. Diet vs. Topical Steroid

- **PPI**
 - Long term safety concerns
- **Diet**
 - QOL
 - Developmental feeding & social skills
 - Cost
 - Possible NG/Gtube
- **Topical steroid**
 - Local infection
 - Adrenal suppression
 - Growth?

Natural History



- Esophageal subepithelial remodeling
- Increased angiogenesis
- Vascular activation
 - conduits for inflammatory cell trafficking
 - collagen deposition, accumulation of matrix proteins
 - eosinophil accumulation

EoE Is Chronic, Progressive



- 2003- Straumann A et al
- 30 adults, 7 year follow-up
 - No medical therapy
 - Dysphagia
 - 40% better, 40% stable, 25% worse
 - *Subepithelial fibrosis- worse 86%*
- Limitations:
 - 1/3 s/p dilation
 - 50% altered eating habits

Do Not Delay Diagnosis



- Symptom as outcome: *lack of significant progression*
 - Dysphagia children → adult: 30-50%
 - Patients adapt
- Histology as outcome: *significant progression of fibrosis*

#1 risk factor fibrostenotic disease =
delay in diagnosis

Challenges



- **Natural history of EoE still not fully understood**
 - Variable symptoms– different phenotypes?
 - Outcomes in asymptomatic patients
 - Consistent symptom, histologic endpoints
- **Distinguishing EoE from GERD**
- **Non-invasive methods for assessing disease**
 - Less invasive diagnostic modalities
 - Histologic biomarkers
 - Genetic markers

- **Treatment**
 - Loss of therapeutic efficacy
 - Role of rescue therapy for “flares”
 - Biologic therapy
 - Need clinical trials comparing therapies

Take Home



- Symptoms differ by age
- Symptoms do not correlate with histology
- Food allergy testing not reliable
- Need upper endoscopy with biopsies to diagnose
- EoE and PPI-REE same entities
 - PPI, dietary elimination, and topical steroids
- Avoid delay in diagnosis

EoE Referrals



- **Pediatric Specialists of Virginia**
Fairfax, VA
703.876.2788
 - Jaime Wolfe, MD & Darlene Mansoor, MD
 - Otto Louis-Jacques, MD
- **Children's National Health System**
Friendship Heights
202.476.3032
 - Seema Khan, MD & Hemant Sharma, MD