Management of EoE

• Why should I give my patient with suspected EoE a trial of PPI therapy?
• How can I best assess disease activity?
• What are the pros and cons of drug and diet therapies?
Case: Patient MH

- 18 yo M with 5 year h/o progressive dysphagia now occurring on a daily basis with monthly, self limited food impactions
- One ER visit for food impaction
- Denies heartburn, refluxate or chest pain
- PMH Allergic rhinitis

What is the patient’s diagnosis?

- pH study OFF medications: Distal acid exposure 3.7%
- Allergy evaluation. SPT reactive to sweet potato, peas, squash, tomato, corn, chicken, rye, wheat, oat, barley. APT negative to same foods. APT equivocal to milk.
Case: Patient MH

- EGD 6/08 lansoprazole 30 mg BID. No dysphagia.
- Rings. No exudates.
- Path: 6 eos/hpf

- EGD 1/12 lansoprazole 30 mg QD. No dysphagia. 7 eos/hpf

Does this patient have EoE or GERD?

- EGD 1/12 lansoprazole 30 mg QD. No dysphagia. 7 eos/hpf
Prospective studies have demonstrated a 33-50% histologic response to PPI therapy in patients with suspected EoE

Can GERD cause or contribute to the pathogenesis of EoE?

PPI Response = GERD

Spechler Am J Gastro 2007; 102:1301-1306
GERD vs PPI responsive EoE??

“PPI responsive esophageal eosinophilia (PPIREE)”

Why patients with suspected EoE should be given a course of PPI therapy

1. It works. Reduces symptoms and esophageal eosinophilia in 30-50% of patients
2. PPIs are safe
3. pH testing is cumbersome and subject to significant false positive and negative results
4. Experimental evidence that GERD may contribute to allergic inflammation in EoE (Paterson) *Am J Physiol 1998; Rhijn Brendenoord DDW 2013*)
5. PPIs may have anti-inflammatory properties beyond acid suppression (Cheng,Souza Gut 2013; DDW13)
Management of EoE

• What do I need to know about PPIREE?
• How can I best assess disease activity?
• What are the pros and cons of drug and diet therapies?

EoE Disease Outcomes:
More than just counting eosinophils
Activity = Inflammation
Are we just scratching the surface?
*Do the effects of EoE extend beyond the mucosa?*

Muscularis Propria

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Esophageal Subepithelial Fibrosis
Demonstrated in majority of EoE patients

Straumann et al., Gastroenterology 2003.
Aceves J Allergy Clin Immunol 2007 ‡
Chehade J Pediatric Gastro Nutr
Lucendo J Allergy Clin Immunol 2011 †
EoE Disease Activity: More than just counting eosinophils!

Activity = Inflammation + Tissue Remodeling

Methods to detect esophageal remodeling in EoE

- Endoscopy
- Upper GI radiologic examination
- Endoscopic ultrasonography (EUS)
- Functional luminal imaging (FLIP)
- Pathology- subepithelial fibrosis
- Biomarkers of fibrogenesis and remodeling (EMT, TGF B, MBP etc)
Complications of EoE:
*Narrow caliber esophagus*

Classification and grading of endoscopically detected esophageal features in EoE

**EoE Endoscopic Reference Score (EREFS)**

- **Edema** (pallor)
- **Rings** (“trachealization”)
- **Exudates** (plaques)
- **Furrows** (vertical lines)
- **Stricture**

- Mucosal fragility
- Narrow caliber esophagus

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Vasilopoulos, Murphy, Auerbach, Massey, Shaker, Stewart, Komorowski, Hogan. Gastro Endosc 2002


Research supported by CURED.
Classification and grading of endoscopically detected esophageal features in EoE

EoE Endoscopic Reference Score (EREFS)

- Edema (pallor)
- Rings (“trachealization”)
- Exudates (plaques)
- Furrows (vertical lines)
- Stricture

Inflammatory

- Mucosal fragility
- Narrow caliber esophagus

Fibrostenotic

EoE Reference Score for Endoscopic Abnormalities (EoE-EREFS)

**Edema** (Also referred to as decreased vascular markings, pallor or edema)

**Normal (Grade 0):** Distinct vascular markings
EoE Reference Score for Endoscopic Abnormalities (EoE-EREFs)

**Edema** *(Also referred to as decreased vascular markings, pallor or edema)*

**Normal (Grade 0):** Distinct vascular markings

**Decreased (Grade 1):** Loss of clarity or absence of vascular markings

**Rings** *(Also referred to as esophageal rings, corrugated esophagus or trachealization)*

**Mild (Grade 1):** Subtle circumferential ridges seen on esophageal distension
EoE Reference Score for Endoscopic Abnormalities (EoE-EREFs)

**Rings** *(Also referred to as esophageal rings, corrugated esophagus or trachealization)*

**Mild (Grade 1):** Subtle circumferential ridges seen on esophageal distension

**Moderate (Grade 2):** Distinct rings that do not occlude passage of diagnostic (8-10 mm) endoscope

**Severe (Grade 3):** Distinct rings that do not permit passage of diagnostic (8-10 mm) endoscope
EoE Reference Score for Endoscopic Abnormalities (EoE-EREFs)

**Exudates** *(Also referred to as white exudates, plaques or punctate white spots)*

**Mild (Grade 1):** White lesions involving < 10% of the surface area of the esophagus

**Severe (Grade 2):** White lesions involving ≥ 10% of the surface area of the esophagus
**EoE Reference Score for Endoscopic Abnormalities (EoE-EREFs)**

**Furrows** *(Also referred to as vertical lines or longitudinal furrowing)*

![Images of furrows](image1.png)

**Stricture** *(Estimate luminal diameter)*

![Images of strictures](image2.png)
Risk of food impaction correlated with EREFS ring severity score

EREFS:
- Allows for uniform characterization
- Provides information regarding fibrostenosis
- Complements assessment of therapeutic outcomes

Management of EoE

- What is PPIREE and do I need any?
- How can we best assess disease activity?
- What are the pros and cons of drug and diet therapies?

Treatment Options for EoE

- **Endoscopic Therapy**
- **Medical Therapy**
  - Topical steroids
  - Systemic steroids
  - Leukotriene antagonists (montelukast)
  - Mast cell stabilizers (cromolyn sodium)
  - Immunomodulators (CRTH2 antagonist, azathioprine)
  - Biologics (anti IL5, anti IL13, anti TNF, anti IgE)
- **Dietary Therapy**
  - Empiric elimination diet
  - Allergy testing directed elimination diet
  - Elemental diet
Topical steroids

- Swallowed - not inhaled
  - Fluticasone 220ug 2-4 puffs BID
  - Budesonide 0.5-1 mg BID
- Liquid formulations are mixed with substance (sucralose) to increase viscosity
- Patients instructed to fast for 30 minutes after administration
- Mouth rinse after administration to reduce risk thrush may reduce effectiveness

Randomized, Double-Blind Placebo Controlled Trials Budesonide

36 Adults with EoE Placebo or budesonide 1 mg BID x 15 days
24 Children with EoE: Placebo or budesonide 0.5-1 mg BID x 3 months

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<td>Budesonide</td>
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Fluticasone in EoE: What dose?

- Konikoff Rothenberg 2006
  - 36 Peds; Fluticasone 440 mcg BID x 3 mos vs placebo
  - 55% with < 6 eos/hpf
- Schaefer Gupta 2008*
  - 80 Peds; RCT fluticasone 220-440 mcg QID vs prednisone x 8 weeks
  - 67% with < 6 eos/hpf post fluticasone
- Peterson Fang 2009
  - 26 Adults; Fluticasone 440 mcg BID vs Esomeprazole x 8 weeks
  - 15% with < 5 eos/hpf
- Alexander Talley 2012
  - 42 Adults; Fluticasone 880 mcg BID x 6 weeks vs placebo
  - 71% with < 5 eos/hpf
- Moawad Wong 2012
  - 42 Adults; Fluticasone 440 mcg BID vs esomeprazole x 8 weeks
  - 19% with < 7 eos/hpf

*GERD systematically excluded
**Eosinophilic Esophagitis: Dietary Treatment**

- **Elemental diet**: Amino acid, carbohydrate, lipid, vitamin/mineral based formula *(Kelly Sampson Gastroenterology 1995)*

- **Directed elimination diet**: Exclusion of specific food allergens based on the results of allergy testing (skin prick & patch) *(Spergel, Liacouras Ann Allergy Asthma Immunol 2005)*

- **Non-directed elimination diet**: Empiric exclusion of common food allergens *(Kagalwalla, Li Clin Gastro Hep 2006)*

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**Six Food Elimination Diet (SFED)**

*Prospective Study in Adults (n=50)*

6 wk elimination (milk, soy, nuts, eggs, wheat, seafood/shellfish)

*Before Diet*

*After Diet*

*Gonsalves, Ritz, Yang, Ditto, Hirano. Gastroenterology 2012*
Effect of SFED on Esophageal Eosinophilia

Proximal Esophagus  Distal Esophagus

Eos/hpf

Pre  Post

* P <0.05

Median  Pre  Post

34  8

48  13
Effect of SFED on Esophageal Eosinophilia

64% achieved histologic response defined by < 5 eos/hpf

Effect of SFED on Dysphagia Score

* P <0.01
Effect of Reintroduction of Foods on Esophageal Eosinophilia

Proximal Esophagus  Distal Esophagus

<table>
<thead>
<tr>
<th>Eos/ hpf</th>
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ACG Regional Postgraduate Course - St. Louis, MO
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Effect of Reintroduction of Foods on Esophageal Eosinophilia

Proximal Esophagus  Distal Esophagus

Food triggers identified by reintroduction: Wheat (60%), milk (50%), soy (10%), egg (5%)

15% of patients with more than one food trigger

SPT accurately predicted 13% of food triggers.

67% of patients with food trigger had negative SPT
Empiric Elimination Dietary Treatment for EoE in Adults

- Prospective Spanish study of 67 adults with EoE
- Diet avoidance of wheat, milk, egg, seafood, legumes, peanuts, soy, rice, corn for 6 weeks (modified SFED)
- Disease remission defined as < 15 eos/hpf
- 73% response (48 to 3.5 eos/hpf in responders)
- Single food trigger in 36%; 2 foods 31%; 3+ foods 33%
- Most common triggers: milk (62%), wheat (29%), egg (26%), legumes (24%)
- 2 year follow up in 15 pts. Sustained symptom and histologic response
Diet therapy in EoE: PROS

- No FDA approved medical therapies for EoE
- Many patients would prefer a dietary alternative rather than chronic steroids
- Conceptual appeal of removing disease trigger rather than suppress inflammatory consequences
- Elimination diets can be a healthy alternative to conventional Western diets
- Goal of diet therapy is the identification of specific food trigger(s), not elimination of all potential food groups

Provides an important proof of concept regarding the role of dietary allergens in the pathogenesis of EoE

- Goal of diet therapy is the identification of specific food trigger(s), not elimination of all potential food groups
Suggested Algorithm for Management Of Eosinophilic Esophagitis

**Suspected EoE**

- Symptom relief & Normal histology
- PPI x 8 wks

**EGD with Bx**

- "PPI Responsive Esophageal Eosinophilia" (EoE vs GERD)
- Persistent Symptoms and Pathology

**EoE**

- Topical steroid
- Dietary therapy

**EGD with Bx**

- Persistent dysphagia with stricture
- Esophageal dilation

- Consider Maintenance Therapy

---

Management of EoE

- **What do I need to know about PPIREE?**
  
  *PPI therapy is a safe and an effective means of recognizing the potential contribution of acid reflux in suspected EoE.*

- **How can I assess disease activity?**
  
  *Symptoms and histology are important but endoscopic findings complement assessment of esophageal remodeling and provides basis for decision for dilation*

- **What are the pros and cons of drug and diet therapies?**
  
  *Elimination diets are an effective alternative for motivated children and adults*

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ACG Clinical Guideline: Evidenced Based Approach to the Diagnosis and Management of Esophageal Eosinophilia and Eosinophilic Esophagitis 2013