Eosinophilic Esophagitis (EoE) Diagnosis and Treatment

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Disclosures

• I have no conflict of interest with the topic discussed
• I have no financial interest in the topic or its treatments
• I will discuss non-FDA-approved therapies as supported in peer reviewed research on the topic.
Overview

• Definition
• Epidemiology
• Proposed Pathophysiology
• Diagnosis
  – Clinical
  – Radiologic
  – Endoscopic
  – Histologic
• Treatment
“Eosinophilic esophagitis represents a chronic immune/antigen mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation.”

Gastrointestinal Eosinophils

Normal eosinophil values, per high power field (hpf):

- Esophagus (0)
- Gastric antrum (2-10)
- Duodenum (10-20)
- Colon (15-30)

Average accepted values

Esophageal Eosinophilia

Differential Diagnosis
- Eosinophilic Esophagitis
- Gastroesophageal Reflux Disease
- PPI-responsive esophageal eosinophilia
- Celiac Disease
- Eosinophilic gastroenteritis
- Crohn’s Disease
- Hypereosinophilic syndrome
- Achalasia
- Vasculitis, pemphigus, connective tissue disease
- Infection
- GVHD
### Age of Onset of EoE

#### Average age at diagnosis

- **5 to 10 years**
- **30 years**

#### Mean age (N=30) and Range

<table>
<thead>
<tr>
<th>At first diagnosis</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>33</td>
<td>6-65</td>
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<tr>
<td>At first manifestation</td>
<td>29</td>
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#### Mean age (N=31) and Range

<table>
<thead>
<tr>
<th>At first diagnosis</th>
<th>Range</th>
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<tr>
<td>34</td>
<td>14-77</td>
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<td>Years “incorrect diagnosis”</td>
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</tr>
</tbody>
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Potential Pathogenesis

Intraluminal allergen exposure

Induction of Th2 response

Mucosal production of eosinophilic chemoattractants

Influx of eosinophils

Release of inflammatory mediators

Rothenberg ME, Gastro 209;1371238-1249.
Clinical Features

• Male predominance (about 3:1)
• Multiple reports of familial clustering (within and across generations)
• Association with food allergy and atopy
• Chronic condition in adults and children

Furuta et al. Gastroenterology. 2007; 133:1342-1363.
Clinical Symptoms

- Dysphagia
- Food impaction
- Abdominal pain
- Vomiting
- Failure to thrive
- Reflux symptoms refractory to therapy

- Age-related differences exist:
  - Younger children - failure to gain weight
  - Older children/adults – food impaction and recurrent dysphagia
EoE Presentation by Age

- Feeding Disorder: 13%
- Vomiting: 26%
- Abdominal Pain: 26%
- Dysphagia: 27%
- Food Impaction: 7%

Radiologic

- Reflux
- Stricture
- Rings
- Dysmotility
- Impaction
Normal Endoscopy

- Smooth mucosa
- Visible blood vessels
Esophageal Furrowing
White Plaques
Esophageal Rings
Esophageal Fragility
Food Impaction
Histology
Normal Histology
EoE Histology

- Increased Basal Cell Layer
- Elongated papillae
- Degranulated eosinophils
EoE Histology
Histology of EoE

Eosinophilia is often patchy

Multiple biopsies are necessary

EoE currently determined by the number of eosinophils in most affected field
Number of Biopsies to Diagnose Pediatric EoE

Histologic Diagnosis

• Epithelial reaction
  – Basal cell hyperplasia
  – Elongation of papillae
  – Spongiosis

• Eosinophilic inflammation
  – One HPF with ≥ 15 eosinophils
  – All esophagus: Greater in mid/proximal esophagus

• Lamina propria fibrosis
2011 Consensus Report

Diagnostic Guideline

- EoE is a clinico-pathologic disease
- Clinically characterized by esophageal dysfunction
- Pathologically 1 or more biopsies show eosinophil predominant inflammation (15+ eosinophils in peak hpf)
- Isolated to esophagus (need for other GI biopsies)
- Other causes need to be excluded
  - Distinguish between “EoE” and “esophageal eosinophilia”
  - “PPI responsive esophageal eosinophilia”
- EoE diagnosis made by clinicians
- Rarely < 15 eos/hpf (if other path features are present)

Management/Treatment
Treatment Endpoints

• Improvements in clinical symptoms
  – Important but can’t always be used as reliable determinants of disease activity or response to therapy

• Improvement in esophageal eosinophilic inflammation
Treatment of EoE

• Why should we treat EoE?
  – Resolution of clinical symptoms
  – Prevention of nutritional deficiencies
  – Prevention of complications such as fibrosis and strictures
  – Improves quality of life
Treatment

• Pharmacologic
  – PPI
  – Steroids: systemic / topical
• Dietary
  – Elemental, targeted or empiric
• Endoscopic
  – dilation
PPI Responsive Esophageal Eosinophilia

• About 1/3 of patients with esophageal eosinophilia on biopsy respond to PPI therapy
• These patients should not be labeled with eosinophilic esophagitis
PPI Therapy and EoE

- Acid suppression with PPI’s
  - Important for making the diagnosis of EoE
  - Useful for treating symptoms associated with EoE that may be due to secondary GERD
  - Possible primary therapy for esophageal eosinophilia not related to acid suppression but instead to another, as yet identified, PPI related response
  - Proton pump inhibitor therapy alone, is insufficient for the treatment of EoE
Steroids

- Topical steroids for an initial duration of 8 weeks are first line pharmacological therapy for treatment of Eosinophilic Esophagitis
- Prednisone may be useful to treat EoE if topical steroids are not effective or in patients that require rapid response
- Patients without symptomatic or histological improvement after steroids might benefit from longer course or other treatment modality

Steroids

• **Topical**
  – **First line treatment**
    • **Budesonide** (oral viscous solution) - once to twice a day
      – Randomized trial (vs. placebo) showed significant improvement in symptoms, endoscopic findings and esophageal eosinophilia
    • **Fluticasone** (swallowed) – twice a day
      – Randomized trial (vs. steroids and vs. placebo) showed approximately 50% complete and 95% partial response in eosinophils

• **Systemic**
  – **Topical steroids are not effective or rapid response needed**

Konikoff Mr, et al., Gastroenterology 2006;131:1381-91.
Oral Steroid Studies

Topical Steroids (Swallowed Fluticasone)

Design:  
- Konikoff: RCT (n=18)  
- Noel: Retrospective (n=20)  
- Teitelbaum: Prospective (n=13)  
- Schaefer: RCT (n=40)

Max Dose:  
- Konikoff: 880 mcg/day  
- Noel: 1320 mcg/day  
- Teitelbaum: 880 mcg/day  
- Schaefer: 1760 mcg/day

Eos/lpf

84.6  
43.4  
23  
33.3

Pre-treatment
Post-treatment

*Post treatment data on 16 patients.

Randomized, Double-Blind Placebo Controlled Trial Budesonide (BEE Trial)

36 Adults with EoE
Placebo or budesonide 1 mg BID x 15 days

- Before treatment
- After treatment

Eosinophils per hpf

Budesonide: 62.01
Placebo: 44.56
Budesonide: 3.83
Placebo: 43.85

Other Medications

• Leukotriene inhibitors (montelukast)
  – Case reports show symptomatic improvement only
  – Adult study: not effective for maintaining remission

• Immunomodulators
  – Adult case reports: improvement in steroid dependent; not recommended for routine use

• Interleukins
  – IL-5 antibody (mepolizumab) – reduced eosinophil counts but complete histological remission in only small percentage; no change in symptoms (adults)

Rothenberg ME, Gastroenterology 2009;137:1238-49.
Dietary Therapy
Dietary Therapy

- Dietary elimination can be considered as initial treatment of pediatric and adult EoE
- Specific dietary approach should be tailored to the individual patient
- Clinical improvement and endoscopy with biopsies should be used to assess response
- Consultation with allergist to identify and treat atopic conditions and help guide elimination diets
- Dietician support is important

Dietary Treatment

• Elemental Diet
  – Most effective; costly; affects quality of life
• Directed Elimination Diet
  – Based on skin prick testing or patch testing
• Empiric Six Food elimination Diet
  – milk, egg, soy, wheat, nuts and seafood

All three approaches have demonstrated symptomatic and histologic resolution

Historical Basis for Elemental Diet

• 1995: Eosinophilic esophagitis attributed to gastro-esophageal reflux: improvement with an amino-acid based formula
  – 10 patients with refractory reflux symptoms
  – 6 had received anti-reflux surgery with no change
  – All with marked esophageal eosinophilia

• Trial of elemental diet
  – Resolution of symptoms and tissue eosinophilic inflammation

Dietary Management  
Amino Acid-Based Formula

- 172 Patients (128 nasogastric tube, 32 oral, 4 failed, 8 noncompliant)
  - 160 patients completed therapy

- Patients evaluated 4-6 weeks after instituting diet

<table>
<thead>
<tr>
<th>160 Patients</th>
<th>Pre-diet</th>
<th>Post-diet</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eosinophils per hpf</td>
<td>38.7 ± 10.3</td>
<td>1.1 ± 0.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>30</td>
<td>1</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>GERD symptoms</td>
<td>134</td>
<td>3</td>
<td>&lt;.01</td>
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</tbody>
</table>

Selective Elimination Diet

- Limited number of foods removed
- Dietary restriction
  - Empiric: history of most likely culprits
    - Milk, soy, eggs, peanuts, wheat, fish, meat
  - Directed:
    - Allergy testing: skin prick or patch testing
    - Clinical symptoms
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Response of 3 Types of Dietary Restriction

Endoscopic Treatment

- Esophageal dilation, approached conservatively, may be used as an effective treatment in symptomatic patients with strictures that persist in spite of medical or dietary therapy.
- Patients should be well informed of the risks of esophageal dilation.

Endoscopic Treatment

• Complications of EoE
• Dilations – used as first line treatment in symptomatic patients
  – Mean duration of response is 1.5 years

Treatment Algorithm

EE diagnosis confirmed by biopsy after PPI
Allergy testing
Family Education/Decide on next treatment option

Pharmacotherapy with topical steroids
Follow up EGD in 3 months

Remission
- Continue Medication
  - F/u EGD in 12 months
No Remission
- Increase dose, systemic steroids or Start Elimination Diet
  - F/u EGD in 3 months

Elimination Diet: Directed or Six Food Elimination
Follow up EGD in 3 months

Remission
- Maintain Diet or Reintroduce Foods
  - F/u EGD if change in diet
No Remission
- Change Diet Or Pharmacotherapy
  - F/u EGD in 3 months

Elemental Diet
Follow up EGD in 3 months

Remission
- Maintain Diet or Reintroduce Foods
  - F/u EGD if change in diet
No Remission
- Introduce Pharmacotherapy
  - F/u EGD in 3 months
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