Eosinophilic Esophagitis
What’s New in 2013

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Esophageal Eosinophilia and Dysphagia

- 12 patients (10M, 32 yrs) with >20 eosinophils/HPF
  3 -1986-88 and 9 between 1988-1990
- All had dysphagia with normal endoscopy
- 7 hypersensitivity: 3 asthma and 1 peripheral eosinophilia
- Esophageal manometry/pH- nonspecific EMD in 10 ,
  LES normal in all, and 1 abnormal pH
- Treatment- all required frequent dilations
  one resolved with oral steroids

Attwood SE Dig Dis Sci 1993
New Cases of EoE at University of North Carolina 2000 to 2007

Estimated prevalence: 43-52 cases per 100,000 persons

Demographics of Eosinophilic Esophagitis

74% males
80% white

50% of patients with food impactions

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Increase in EoE Diagnosis at TUH from 2000 to 2009

Bohm M et al. J Clinical Gastroenterology 2012

Racial Differences in Symptom Presentations

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Racial Differences in Endoscopic Findings

Seasonal Distribution of New Cases of Eosinophilic Esophagitis

Aeroallergens and EoE

More Pieces to the Puzzle

• **Influence of climate (1)**
  Prevalence differs between climate zones with highest prevalence in cold/arid zones

• **Relationship with H pylori (2)**
  Inverse association with “dose” response
  >15 eos/hpf—OR, 0.79; CI 0.70-0.88
  >45 eos/hpf---OR, 0.75; CI 0.61-0.93
  >90 eos/hpf---OR, 0.52; CI 0.31-0.87

2) Dellon ES et al. Gastroenterology 2011
Eosinophilic Esophagitis - Rings

Eosinophilic Esophagitis

Furrows

Microabscesses
Prevalence and Diagnostic Utility of Endoscopy Features in EoE
A Meta-Analysis

- 4678 EoE patients and 2742 controls
- Pooled prevalence of endoscopic features
  - rings—44%
  - strictures—21%
  - furrows—48%
  - narrowed esophagus—9%
  - white plaques—27%
- All studies—normal EGD—17%
- Prospective studies—normal EGD—7%

Kim HP et al. Clinical GI and Hepatology 2012

Histology of Eosinophilic Esophagitis
> 15 eosinophils/hpf

Odze RD. Am J Gastroenterology 2009
Eosinophilic Esophagitis
Number of Biopsies to Make Diagnosis

Gonsalves N, et al. GIE 2006

Patchy Nature of EoE

Pathology

- 12/12/2011
  - Distal -- no eos
  - Proximal -- 8 eos/hpf
- 1/16/2012
  - Maximum of 10 eos/hpf
- 2/6/2012
  - Maximum of 15 eos/hpf

42 yo white male
More than Just Counting Eosinophils

- 23 cases of EoE and 20 cases of GERD with distal/proximal biopsies and eosinophils
- Proximal biopsies
  - 83% EoE cases vs 0% in GERD cases
  - 4 cases distal only biopsies would miss dx
- Subepithelial sclerosis
  - 74% EoE cases vs 5% in GERD cases

Lee s et al. J Clinical Pathology 2010

EoE: An Epiphany for Pathologists

Pathology reports from 27 patients with suspected EoE
Pathophysiology of Eosinophilic Esophagitis
Inflammatory Phase

Ferguson DD. Diseases of Esophagus 2007

Tissue Remodeling in Eosinophilic Esophagitis

Eosinophilic Esophagitis: Inflammation vs Fibrosis with Remodeling

• Separating the two disorders into distinct diseases may be too simplistic

• Possible relationships:
  - GERD causes esophageal injury with eosinophilia
  - GERD and EE co-exist, but are unrelated
  - EE causes or contributes to GERD
  - GERD causes or contributes to EE

• A trial of PPIs even when diagnosis of EE is clear-cut is recommended

Dilated Intercellular Spaces are a Feature of GERD

Healthy Subject

GERD Patient

Evolution of Eosinophilic Esophagitis

GERD

Dietary or Airborne Allergens

Eosinophilic Esophagitis with Chronic Inflammation

Fibrosis

Rings

Diffuse Scarring

Early

Children

Late

Adults
Treatments of Eosinophilic Esophagitis

- Elemental diet
- Systemic corticosteroids
- Inhaled topical steroids (fluticasone)
- Oral viscous budesonide
- Leukotriene receptor antagonists
- Immunomodulators
- PPIs and careful esophageal dilation

6 Food Elimination Diet (SFED)

- Milk
- Soy
- Eggs
- Wheat
- Peanuts/tree nuts
- Shellfish/fish
Six Weeks of 6 Food Elimination Diet

Eosinophil Response to Reintroduction of Foods

Common food triggers
- Wheat—60%
- Milk—50%
- Soy—10%
- Nuts—10%
- Egg—5%

Gonsalves N et al Clin Gastro and Hepatology 2012
Endoscopic Features Before and After SFED

Three Year Follow-up of Topical Steroids for EoE – Frequency of Dysphagia

First EoE Study in Adults with Fluticasone vs Placebo

- Fluticasone 220 micrograms—4 puffs BID for 6 weeks vs Placebo
- Initially 21 EoE patients in each group

**Table 2. Dysphagia Response**

<table>
<thead>
<tr>
<th></th>
<th>Fluticasone</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT complete</td>
<td>42.9% (8/19)</td>
<td>26.6% (6/21)</td>
<td>.52</td>
</tr>
<tr>
<td>PP complete</td>
<td>47.4% (9/19)</td>
<td>40.0% (6/15)</td>
<td>.74</td>
</tr>
<tr>
<td>ITT partial or complete</td>
<td>57.1% (12/21)</td>
<td>33.3% (7/21)</td>
<td>.22</td>
</tr>
<tr>
<td>PP partial or complete</td>
<td>53.2% (12/19)</td>
<td>46.7% (7/15)</td>
<td>.49</td>
</tr>
<tr>
<td>PP complete 2 weeks</td>
<td>42.1% (8/19)</td>
<td>26.7% (4/15)</td>
<td>.47</td>
</tr>
<tr>
<td>PP complete 4 weeks</td>
<td>47.4% (9/19)</td>
<td>26.7% (4/15)</td>
<td>.30</td>
</tr>
</tbody>
</table>

**Table 3. Histologic Response**

<table>
<thead>
<tr>
<th></th>
<th>Fluticasone</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT complete</td>
<td>61.9% (13/21)</td>
<td>0% (0/21)</td>
<td>&lt;.001</td>
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<tr>
<td>PP complete</td>
<td>68.4% (13/19)</td>
<td>0% (0/15)</td>
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<tr>
<td>ITT partial or complete</td>
<td>81.0% (17/21)</td>
<td>4.8% (1/21)</td>
<td>&lt;.001</td>
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<tr>
<td>PP partial or complete</td>
<td>89.5% (17/19)</td>
<td>6.7% (1/15)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*Despite nearly eliminating eosinophils, symptom relief no better than placebo

Alexander JA et al. Clinical GI and Hepatology 2012

**Distribution of Nebulized vs Viscous Budesonide in Eosinophilic Esophagitis**

- Swallowed viscous budesonide
- Nebulized budesonide

Dellon ES et al. Gastroenterology 2012
Median Time to Symptom Relapse: Budesonide vs Placebo

Median time to relapse in days:
- Budesonide: >125 days
- Placebo: >95 days


Esophageal Wall Structure in EoE Patients and Healthy Controls

Most Adults with EoE Respond to PPIs

- 712 adults with UGI symptoms undergoing EGD
  35 (4.9%) EoE defined > 15 eos/HPF in proximal esoph
  55% allergies  70% food impactions/dysphagia
- Treatment: rabeprazole 20mg BID for 2 months
- Results:
  26 (75%) clinical and histologic remission (<5 eos/HPF)
  17 GERD profile—100%
  9 EoE profile—50%
  pH monitoring poorly predictive of PPI response
  normal (33%) pathological (80%)


Comparison of EoE Responsive and Nonresponsive to PPI Therapy

Why EoE May Respond to PPIs

• Healing disrupted epithelial barrier to prevent further immune activation
• Decrease eosinophil longevity
• Inherent anti-inflammatory properties of PPIs
  ---downregulation of IL-4 and IL-13 murine asthma model
  ---block IL-13 stimulated secretion of eotaxin 3 in EoE esophageal cell line

Kedika RR et al . Dig Dis Sciences 2009

Esophageal Dilation for Eosinophilic Esophagitis

• Three recent studies with 109 adult EoE patients
• Types of dilators: evenly divided between bougies and TTS balloons
• Mean # of sessions: 1.2 to 2 to get to 16-17 mm diameter
• Clinical improvement: 91%
• Average symptom relief: 22-23 months
• Mucosal eosinophil count did not change
• Complications: 3 mucosal tears, no perforations

Bohm M, et al Dis of Esophagus 2010
Dellon E, et al GIE 2010
Esophageal Dilation in EoE
Pain Frequency and Patient Acceptance


Natural History of EoE Treated with Esophageal Dilation over 13 Years

14 patients (11 men)—average age 32 Average follow-up 13 yrs (5-24 yrs)
Esophageal Tears and Perforations in EoE Patients

- Mucosal tears are common: 0% to 100%
  - Many are asymptomatic—some associated with chest pain
  - Risk of complications higher with (1):
    - longer symptoms
    - higher eosinophil count

- Esophageal perforations are very rare --0.1% (2)

- No deaths reported due to these complications

What Should Be the Endpoint of Therapy??

- Patient—symptom improvement
  no further fear of food impactions
- Gastroenterologist—normal esophageal exam
  minimize need to dilate
- Allergist—elimination of eosinophils

Proposed Treatment Algorithm for Eosinophilic Esophagitis

Endoscopic Findings

- Furrows / Plaques / Exudates
  - Swallowed / systemic steroids or budesonide
    - No response
    - Elimination diet
  - Allergy testing

- Rings / Strictures / Narrow lumen
  - Esophageal dilation and PPIs
  - Swallowed steroids or budesonide for 2-6 weeks
  - Maintenance therapy ??
  - Role of follow-up endoscopy?
Recommended Reading

Eosinophilic esophagitis: Updated consensus recommendations for children and adults
J Allergy Clin Immunol 2011