**Eosinophilic Esophagitis (EoE)**

- Eosinophilic esophagitis represents a chronic, immune/antigen mediated, esophageal disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation.
- Diagnosed is based on clinical-pathologic findings on biopsy with greater than 15 eosinophils/HPF.
- Exclude other causes of esophageal eosinophilia:
  - GERD
  - Celiac
  - IBD
  - Allergic Rhinitis
- EoE is a lifelong chronic condition.

**Gastrointestinal Eosinophils**

Normal values, per 400x microscopic field:
- Esophagus (0)
- Gastric antrum (2-20)
- Duodenum (2-20)
- Colon (10-50)

**World Map of EoE**

**Review of EoE**

Endoscopic findings

- Normal
- Rings
**Review of EoE**

Endoscopic findings

- White plaques
- Furrows

**Review of EoE**

EoE – Histology

- Esophageal eosinophilia
- Abscess

**Other Causes of Eosinophilia**

- GERD
- Celiac
- IBD
- Fungal Infection
- Allergic Rhinitis
- Drug Allergy

**Rise of EoE-Philadelphia**

Spergel et al., JPGN 2009

**Manuscripts on EoE**

Lee et al., JPGN 2008, Franciosi et al. 2009

**True Rise?**

Lee et al., JPGN 2008, Franciosi et al. 2009
Is more endoscopy or more disease?


EoE Estimates in Europe and US

- Ronkainen and colleagues – performed EGD in random sample of adult Swedish population (no indication!)
- 411,000 subjects with ≥ 20 eosinophils/HPF
- 113,000 subjects with ≥ 15 eosinophils/HPF
- Prevalence of 110/10,000
- Estimates based on community prevalence
- 50/100,000 in Cincinnati, OH and Rochester, MN
- Estimates based on questionnaire
- 52.2/100,000 in the US


Management

- Serial Endoscopies
- Clinical Follow
  – Barium Swallow

Symptoms of EoE

EoE - Clinical manifestations
- Symptoms similar to those of GERD
- Histology does not respond to PPIs.
- Age related differences in symptoms
- Symptoms may be intermittent
- Male > Female
- May progress to esophageal fibrosis and esophageal dysfunctions if not managed appropriately.

Symptom Progression in EoE

Symptom Progression in EoE

Common Symptoms

- Infant: Food refusal, FTT, feeding intolerance/aversions
- Children: Vomiting, dysphagia, abdominal pain, heartburn, regurgitation, feeding refusal/feeding aversions
- Adult: Dysphagia, food impaction, heartburn, reflux

Symptom Progression in EoE

Symptom Progression in EoE

Chronic EoE: Adults

Strassmann et al, Gastroenterology 2003

Treatment Options

Pharmacologic Therapy

Systemic Steroids – effective at improving symptoms and histology of EoE in 95% of pts
- Upon discontinuation, 90% had recurrence of symptoms
- (Long term use) Side effects: bone abnormalities, poor growth, adrenal suppression
- May be needed short term for extreme cases

Topical/swallowed Steroids – less toxic to pt while still 85-90% effective
- A mainstay of EoE treatment in adults and children.
- Upon discontinuation almost all patients have a recurrence of symptoms
- Often, large doses needed
- Side effects: esophageal candidiasis

Pharmacologic Therapy

Liacouras et al, J Clin Gastroenterol 2005
Furuta et al, Gastroenterology 2007

Corticosteroid Therapy

DBPC trial:
- 15 OVB
- 5 placebo patients
- 1 mg BID (Children <5ft) and 2 mg BID (>5ft)
- Significant improvement in symptoms and bx
- 85% response rate

Dohil et al Gastroenterology 2010 139:418

Budesonide Study

Pharmacologic Therapy

Liacouras et al, Gastroenterology 2003
Furuta et al, Gastroenterology 2007

Corticosteroid Therapy

Liacouras et al, Oral steroids 2003

Furuta et al, Gastroenterology 2007

Furuta et al, Clin Gastroenterol Hepatol 2007

Dohil et al, Gastroenterology 2010

Food Avoidance Therapy
**Link Between Food Allergy and EoE**

- **Dobbins (1977):** 51 yo with GERD, food allergy and esophageal eosinophilia.
- **Kelly and Sampson (1995):**
  - 10 patients (5 yr range: 8 mo-12.5 yr)
  - Given amino-acid based formula (> 6 weeks)
  - Neocate® or Neocate®+
  - 6 prior Nissen fundoplication
  - Endoscopy pre- & post-trial.

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**Dietary Management**

**Amino Acid-Based Formula**

- 172 patients (128 nasogastric tubes, 32 oral, 4 failed, 8 noncompliant)
- Patients evaluated 4-6 weeks after starting diet

<table>
<thead>
<tr>
<th>Eosinophils/HPF</th>
<th>Pre-Diet</th>
<th>Post-Diet</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>38.7 ± 10.3</td>
<td>1.1 ± 0.6</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

**Dysphagia**

- 30
- 1
- <0.01

**GERD Symptoms**

- 134
- 3
- <0.01

---

**Oral Immunotherapy induces EoE**

- Seen after egg, milk and peanut OIT
- Incidence about 5-20%
- Indicates foods causes EoE and is not TH2 mechanism

---

**Selective Diet: Guess**

- 60 children
  - 35 children on elimination diet of milk, soy, wheat, egg, peanut and seafood
  - 25 children on elemental diet
- Repeat endoscopy 6 weeks later
- 74% of six-food diet had < 10 eos/hpf
- 88% of elemental diet had <4 eos/hpf

---

**How to Select the foods?**
SFED follow-up

- Single Food Reintroduction in 36 children
- 74% to milk
- 26% to wheat
- 37% to egg
- 10% to soy
- 6% to peanut
- Single food in 72%, 2 foods in 8% and 3 foods in 8%

Kagalwalla et al. JPGN 2011

Most Common Foods in EoE

<table>
<thead>
<tr>
<th>Food</th>
<th>EoE by Rx</th>
<th>IgE Reactions</th>
<th>EoE by Symptoms</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>168</td>
<td>25</td>
<td>145</td>
<td>338</td>
</tr>
<tr>
<td>Egg</td>
<td>43</td>
<td>44</td>
<td>81</td>
<td>168</td>
</tr>
<tr>
<td>Soy</td>
<td>41</td>
<td>10</td>
<td>74</td>
<td>215</td>
</tr>
<tr>
<td>Wheat</td>
<td>55</td>
<td>2</td>
<td>64</td>
<td>121</td>
</tr>
<tr>
<td>Peanuts</td>
<td>16</td>
<td>44</td>
<td>42</td>
<td>102</td>
</tr>
<tr>
<td>Beef</td>
<td>27</td>
<td>0</td>
<td>61</td>
<td>88</td>
</tr>
<tr>
<td>Corn</td>
<td>31</td>
<td>0</td>
<td>51</td>
<td>82</td>
</tr>
<tr>
<td>Chicken</td>
<td>25</td>
<td>1</td>
<td>51</td>
<td>72</td>
</tr>
<tr>
<td>Potato</td>
<td>19</td>
<td>0</td>
<td>33</td>
<td>52</td>
</tr>
<tr>
<td>Pork</td>
<td>16</td>
<td>0</td>
<td>30</td>
<td>46</td>
</tr>
</tbody>
</table>

Predictive Values

- All pts had > 20 eos/hpf on GERD and AR medication and had
  - Removal of a single food leading to normal esophageal biopsy (eosinophils/HPF).
  - Addition of a single food leading to increased esophageal eosinophils on biopsy after a previously normal biopsy.

- 104 Children
  - 64 male, 30 female
  - Age: 6.4 ± 4.2 (2 to 18 years)
  - Redo the analysis currently on a larger n (200 patients)

Predictive Values: Combination of SPT and APT

<table>
<thead>
<tr>
<th>Food</th>
<th>PPV</th>
<th>Combined SPT and APT</th>
<th>Specificity</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk (n = 99)</td>
<td>93.0%</td>
<td>32.4%</td>
<td>84.0%</td>
<td>52.9%</td>
</tr>
<tr>
<td>Egg (n = 38)</td>
<td>65.5%</td>
<td>86.6%</td>
<td>86.7%</td>
<td>85.7%</td>
</tr>
<tr>
<td>Wheat (n=37)</td>
<td>73.7%</td>
<td>99.1%</td>
<td>80.8%</td>
<td>85.7%</td>
</tr>
<tr>
<td>Soy (n = 25)</td>
<td>43.2%</td>
<td>92.6%</td>
<td>76.9%</td>
<td>67.9%</td>
</tr>
<tr>
<td>Beef (n=21)</td>
<td>48.4%</td>
<td>96.2%</td>
<td>84.9%</td>
<td>65.2%</td>
</tr>
<tr>
<td>Chicken (n=20)</td>
<td>46.3%</td>
<td>99.0%</td>
<td>83.3%</td>
<td>84.0%</td>
</tr>
<tr>
<td>Corn (n=17)</td>
<td>92.5%</td>
<td>86.6%</td>
<td>81.7%</td>
<td>85.0%</td>
</tr>
<tr>
<td>Potato (n=13)</td>
<td>97.8%</td>
<td>92.2%</td>
<td>91.5%</td>
<td>81.8%</td>
</tr>
<tr>
<td>Rice (n=11)</td>
<td>93.6%</td>
<td>96.9%</td>
<td>92.5%</td>
<td>90.5%</td>
</tr>
<tr>
<td>Pork (n = 11)</td>
<td>38.5%</td>
<td>97.5%</td>
<td>93.1%</td>
<td>62.5%</td>
</tr>
</tbody>
</table>

Spergel et al, JACI 2007 and unpublished data

Specific IgE

- 53 adult patients
- 80% had positive sIgE to food or aeroallergens
- sIgE was most sensitive

Erwin et al, J Allergy Clin Immunol 2010
What method is best?

<table>
<thead>
<tr>
<th>Method</th>
<th>SPT/APT</th>
<th>MILK</th>
<th>Milk, Egg, Wheat</th>
<th>SFED</th>
<th>SPT/APT + MILK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rate of Resolution</td>
<td>57%</td>
<td>30%</td>
<td>48%</td>
<td>60%</td>
<td>77%</td>
</tr>
</tbody>
</table>

- Retrospectively examined all patients with defined food identified
- Excluded patients on ICS or anti-IL5
- Examined which diet method lead to normalization of histology

What have we learned in 28 years?  
Katz, Flores, Twarog SPR 1983

- Positive on Skin tests: highly atopic
- Response to Diet and Steroids
- pH probe negative
- Basal cell hyperplasia

Summary: Treatment in EoE

- Pharmacologic therapy has been shown effective but long term use and possible side effects must be considered
- Elimination diet is effective - keeping in mind nutrient deficiencies may occur
- Elemental diet is the most effective nutrition therapy. Compliance/cost may be an issue for some patients

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“Dietary therapy should be considered as an effective therapy in all children diagnosed with EoE.”