Eosinophilic Esophagitis: Diagnosis, Clinical Implications, and Treatment

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The University of California, San Diego has a financial interest in Meritage Pharma, the University of California may financially benefit (patent royalties) from this interest if the company is successful in developing and marketing its own product related to oral viscous budesonide. Dr Aceves is a co-inventor of OVB to which UCSD owns the patent. The terms of this arrangement have been reviewed and approved by the University of California, San Diego in accordance with its conflict of interest policies.

- Research funding from GlaxoSmithKline
- Some slides are from CDHNF, TIGERS and received funding from Takeda
Eosinophilic Esophagitis (EoE): A Clinicopathological Diagnosis

- Histologic Features
- Endoscopic Features
- Clinical Features
- Distinctions from GERD
Making the Diagnosis

Clinical Features
## Incidence of Atopic Symptoms

<table>
<thead>
<tr>
<th>Feature</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinoconjunctivitis</td>
<td>57.4</td>
</tr>
<tr>
<td>Wheezing</td>
<td>36.8</td>
</tr>
<tr>
<td>Food allergy*</td>
<td>46</td>
</tr>
<tr>
<td>Family history atopy</td>
<td>73.5</td>
</tr>
<tr>
<td>Family history EoE</td>
<td>6.8</td>
</tr>
</tbody>
</table>

*H/O positive skin-prick, RAST, or clinical response

# Prevalence of Atopy

<table>
<thead>
<tr>
<th>Author/population</th>
<th>Number of patients with EoE</th>
<th>Asthma</th>
<th>Allergic Rhinitis</th>
<th>Atopic Dermatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atopy in the General Population</td>
<td></td>
<td>8.5%</td>
<td>25%</td>
<td>10%</td>
</tr>
<tr>
<td>Spergel, et al; Philadelphia</td>
<td>620</td>
<td>50%</td>
<td>61%</td>
<td>21%</td>
</tr>
<tr>
<td>Assa’ad, et al; Cincinnati</td>
<td>89</td>
<td>39%</td>
<td>30%</td>
<td>19%</td>
</tr>
<tr>
<td>Sugnanam, et al; Australia</td>
<td>45</td>
<td>66%</td>
<td>93%</td>
<td>55%</td>
</tr>
<tr>
<td>Guajardo, et al; World wide registry</td>
<td>39</td>
<td>38%</td>
<td>64%</td>
<td>26%</td>
</tr>
</tbody>
</table>

EoE Presentation by Age

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

Age (Years)
Fraction of Pop.

Presenting Symptoms of EoE in Adults

Frequency of Indication

<table>
<thead>
<tr>
<th></th>
<th>Male (n=270)</th>
<th>Female (n=93)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysphagia (p&gt;0.2*)</td>
<td>71%</td>
<td>67%</td>
</tr>
<tr>
<td>GERD/Heartburn (p&gt;0.2*)</td>
<td>27%</td>
<td>26%</td>
</tr>
<tr>
<td>Abdominal Pain, Dyspepsia, N/V (p&gt;0.2*)</td>
<td>14%</td>
<td>15%</td>
</tr>
</tbody>
</table>

* P value for χ² comparing the proportion of males vs. females
Atypical EoE Presenting Symptoms

- Cough
- Hoarseness
- Post-tussive emesis

“Anaphylaxis” to every food
# Age of Onset of EoE

## Summary

<table>
<thead>
<tr>
<th>Mean age (N=30)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>At first diagnosis</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>6-65</td>
</tr>
<tr>
<td>At first manifestation</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>6-52</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mean age (N=31)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>At first diagnosis</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>14-77</td>
</tr>
<tr>
<td>Years &quot;incorrect diagnosis&quot;</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>2-12</td>
</tr>
</tbody>
</table>

*Age at first symptom:*
- < 3 to 4 years
- < 30 years

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Making the Diagnosis

Endoscopic Features
Endoscopic Features

- Pallor
- Lichenification
- Linear Furrows
- White Plaques
- Concentric Rings
- Strictures and Narrowings

Furuta et al, Gastroenterology 2007
Fox et al, GI Endoscopy 2005
Symptoms

- Feeding Disorder: 13%
- Vomiting: 50%
- Abdominal Pain: 50%
- Dysphagia: 30% (Pediatric), 97% (Adults)
- Food Impaction: 13% (Pediatric), 51% (Adult)
- Esophageal Stricture: 10% (Pediatric), 37% (Adult)

Age
Making the Diagnosis

Histologic Features
Histology

- >15 eosinophils per hpf especially with acid blockade

- Typical Accompanying Features:
  - Basal Zone Hyperplasia
  - Dilated Intercellular Spaces
  - Eosinophil Clusters, Degranulation
  - Subepithelial Fibrosis

Furuta et al, Gastroenterology 2007
Making the Diagnosis

Distinguishing Features from GERD
## Diagnostic Comparison

<table>
<thead>
<tr>
<th></th>
<th>EoE</th>
<th>GERD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>Intermittent</td>
<td>Persistent</td>
</tr>
<tr>
<td>pH Probe</td>
<td>Normal</td>
<td>Abnormal</td>
</tr>
<tr>
<td>Acid blockade</td>
<td>Unresponsive</td>
<td>Responsive</td>
</tr>
<tr>
<td>Endoscopy</td>
<td>Often repeated needed</td>
<td>Typically none or once</td>
</tr>
<tr>
<td>Pathology</td>
<td>&gt; 15 eos/hpf</td>
<td>1-5 eos/hpf</td>
</tr>
</tbody>
</table>
### Symptom Comparison

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Not at all</th>
<th>Mild: No interference with daily activities, Meds as needed</th>
<th>Severe: Regularly interferes with daily activities or requires daily meds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does your child ever have burning in the chest?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does your child ever feel food coming back up into his/her throat?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does your child complain about stomach pains?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is your child often irritable for no apparent reason?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How often does your child complain about feeling like throwing up?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How often does your child complain about eating too little or getting full before finishing his/her meal?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How often does your child wake up during the night from belly pain?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How often has your child noticed blood in his/her stool in the last 3 months?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Does your child have difficulty swallowing?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Not at all=0, Mild=1, Severe=2

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**Figure:**
- Score graph showing comparisons of symptoms among different groups.
- Normal
- Allergy NonEE
- GERD
- EE

---

**Legend:**
- Normal
- Allergy NonEE
- GERD
- EE

---

**Reference:**
Aceves et al, Ann of Allergy 2009
# Eosinophils and GERD

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)/sex</td>
<td>14/M</td>
<td>25/M</td>
<td>13/F</td>
</tr>
<tr>
<td>Presentation</td>
<td>Pain</td>
<td>Food impaction</td>
<td>Dysphagia</td>
</tr>
<tr>
<td>Environmental Allergies</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Treatment</td>
<td>Omeprazole 10 mg BID</td>
<td>Omeprazole 20 mg BID</td>
<td>Omeprazole 20 mg QD</td>
</tr>
<tr>
<td>Eosinophils/hpf</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before treatment</td>
<td>37</td>
<td>21</td>
<td>59</td>
</tr>
<tr>
<td>After treatment</td>
<td>1</td>
<td>3</td>
<td>0</td>
</tr>
</tbody>
</table>

Number of Biopsies to Diagnose Pediatric EoE

% Positive Diagnosis

≥15 eos/hpf
Diagnostic Threshold

Making The Diagnosis

Other Distinguishing EoE Features
Epithelium
Eotaxin-3

53-fold increase in Eotaxin-3 gene expression in EE versus GERD pediatric patients

Thymic Stromal Lymphopoietin

- Increased TSLP expression in EoE
- Genetic variants in TSLP and Eotaxin-3 associate with EoE

Rothenberg et al, Nature Genetics 2010
Adaptive Immune System

- B Cells
- T Cells
B Cells and Local IgE Production

Increased B cells in:
- Epithelium
- Vascular Papillae
- Lamina Propria

Increased IgE Class Switch Genes

Vicario et al, Gut 2009
T Cells

- Increased CD3+
- Increased CD8+
- Murine EoE Induction Relies on T cells

Lucendo et al, 2007
Mishra et al, 2007
Zhu et al, 2009
Interleukins

IL-5
IL-13
IL-15
IL-5

- EoE patients have Increased IL-5
- IL-5 Deficient Mice are Protected from EoE
- IL-5 miniosmotic pump promotes murine EoE

Straumann et al, JACI 2001
Mishra et al, 2008
**IL-13**

- Instilling IL-13 Causes Murine EE
- Resolved with anti-IL-13 Antibody

Mishra & Rothenberg, Gastroenterology 2003
Blanchard et al, Clin Exp Allergy 2005

- IL-13 treatment promotes EoE transcriptome
- IL-13 induces the Eotaxin-3 promoter
IL-15

- Increased IL-15 on EoE Gene Chip
- IL-15Rα Deficient Mice: Protected from experimental EoE
- IL-15 Increased in Human Esophageal biopsies

Rayapudi et al, Gastroenterology 2010
Mast Cells
Mast Cells

- Increased Mast Cells:
  - Epithelium
  - Smooth muscle
- Increased degranulated Mast Cells in EE versus GERD

Lucendo, 2007
Aceves, 2009

Kirsch et al, JPGN 2007
Konikoff et al, Gastroenterology 2006
Subepithelium

Lamina Propria: Esophageal Remodeling
Esophageal Remodeling: Fibrosis

- Human subjects have increased fibrosis

- Animal EE Models have increased fibrosis

Aceves et al, JACI 2007
Mishra et al, Gastroenterology 2008
Esophageal Remodeling: Pro-Fibrotic Factors

Esophageal Remodeling: Pro-Fibrotic Factors

- Eosinophils produce TGFβ1

- Animals that lack eosinophils are protected from fibrosis

Aceves, J All Clin Immunol 2007
Mishra, Gastroenterology 2008
## Inflammation Correlates with Endoscopy and Symptoms

<table>
<thead>
<tr>
<th>Inflammation</th>
<th>Endoscopy</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Epithelial:</strong></td>
<td>Thickened/Furrows ( r=0.82^* )</td>
<td>Dysphagia + Anorexia/Early Satiety ( r=0.32^* )</td>
</tr>
<tr>
<td>Average Epithelial Score</td>
<td>White Plaques, ( r=0.64^* )</td>
<td></td>
</tr>
<tr>
<td>Prox+Mid+Distal</td>
<td>Pallor ( r=0.62^* )</td>
<td></td>
</tr>
<tr>
<td><strong>Lamina Propria:</strong></td>
<td>Thickened/Furrows ( r=0.64^* )</td>
<td>Dysphagia</td>
</tr>
<tr>
<td>Fibrosis + Eosinophils</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

• Severity of Eosinophilic Inflammation in the epithelium and LP can correlate with Endoscopic and Symptom Findings

• Severity of Fibrosis can correlate with Endoscopic and Symptom Findings

Aceves et al, Annals of All Immunol 2009
Blood Vessels

Angiogenesis
Vascular Activation
Esophageal Remodeling: Vascularity

**vWF Positive Vessels**

- Normal
- GERD
- EE

**VCAM-1 Positive Vessels**

- Normal
- GERD
- EE

**Normal GERD EE**
Diagnosing EoE: More Than Eosinophil Numbers?

Eosinophil peroxidase footprint in absence of intact eosinophils meeting diagnostic criteria
Protheroe et al, CGH, 2009
Prevalence and Epidemiology
Distribution of EoE

- Canada
- United States
- Mexico
- Brazil
- Switzerland
- Spain
- Belgium
- England
- Netherlands
- Italy
- Germany
- France
- Israel
- Japan
- Australia
### Incidence and Prevalence of EoE

<table>
<thead>
<tr>
<th>Region</th>
<th>Incidence*</th>
<th>Prevalence*</th>
<th>Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ohio</td>
<td>↑</td>
<td>1.3</td>
<td>6.9</td>
</tr>
<tr>
<td>(Pediatrics)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minnesota</td>
<td>↑</td>
<td>.9</td>
<td>10.5</td>
</tr>
<tr>
<td>(Mixed)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Australia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pediatrics</td>
<td>↑</td>
<td>.09</td>
<td>'95-'04</td>
</tr>
<tr>
<td>Adults</td>
<td>↑</td>
<td>.6</td>
<td>1.5</td>
</tr>
<tr>
<td>Switzerland</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td>↑</td>
<td>.15</td>
<td>2.9</td>
</tr>
</tbody>
</table>

Disease Chronicity
Clinical Implications

- Triggers
- Chronicity
- Complications
EoE and Allergy: Causal Link or Coincidence
Indoor Allergen Sensitization

Rayapaudi et al, J Leuko Biol 2010
Aerollergens and EoE: Causal Link

- Instillation of:
- Intranasal Aspergillus
- Intranasal HDM
- Intranasal Cockroach
- Drives Murine EoE

Mishra et al., J Clin Invest 2001
Rayapaudi et al, J Leuko Biol 2010
Aerollergens and EoE: Causal Link

- EE during pollen season
- Spontaneous disease resolution

Fogg et al., JACI 2003
Seasonal EoE?

Moawad et al. Alim Pharm Ther 2009
Almansa et al. Am J Gastro 2009

Figure 3. Newly diagnosed cases of eosinophilic esophagitis (EoE) during two distinct periods of time.
Triggers: Foods
Six Food Elimination in Adult EoE

• Prospective study
  - 27 adults completed SFED (diet eliminating milk, soy, egg, wheat, nuts, seafood) for 6 weeks. Those that resolved started reintroduction process (11 patients)

• EGD and symptom score completed before and after SFED
  - Total resolution of EoE defined as peak number of esophageal eosinophils \( \leq 5 \) eos/hpf
  - Near complete resolution: peak eosinophils \( \leq 10 \) eos/hpf
  - Partial resolution: > 50% reduction in peak eos/hpf

Effect of Diet on Esophageal Eosinophilia

median

Diet and Dysphagia Symptom Score

Median Score

Pre 12 → Post 3.5

* P < 0.01

Food Reintroduction and Esophageal Eosinophilia

Endoscopic Improvement

Pre Diet

Post Diet

Reintroduction of Wheat

Chronicity
Pediatric EoE

Patients with EE diagnosed at Cincinnati Children’s Hospital
n=57
Duration of Follow up: Median 2.58 years (range 0.18-5.61)

Resolved EE
n=38

Resolved EE, No Relapse
N=8
Duration of follow-up: Median 0.8 years (range 0.2-3.1)
21% Resolved

Resolved EE, Subsequent Relapse
N=30
Duration of follow up: Median 3.2 years (range 0.5-5)
79% Relapsed

Persistent EE
N=19
Duration of follow up: Median 1.3 (range 0.3-5.7)
33% No Resolution

Assa‘ad et al, JACI 2007
Adult EoE

Dysphagia or inflammatory intensity vs. time between diagnosis and follow-up (years).
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.
Complications

Remodeling

Strictures
IL-13 induces eosinophilia, esophageal thickness, and collagen accumulation

Zou et al, J Immunol 2010
IL-13, TGFβ1, and Periostin

Increased periostin expression induced by TGFβ

Periostin increases eosinophil trafficking and adhesion

Blanchard et al, Mucosal Immunol 2008
Complications
Smooth Muscle Dysfunction

- Thickened muscular bundles in EE
- Muscular dysfunction with poor relaxation
- Increased motility correlates with episodes of dysphagia

Fox et al GI Endoscopy 2003
Korsapati et al Gastro 2009
Nurko et al, Am J Gastro 2009
Esophageal Mast Cells Make TGFβ1
Mast Cells and Smooth Muscle Function

Aceves et al, JACI, in press
Distal Esophageal Stricture
Food Impaction and Iatrogenic Complications

- Food Impactions: 35%
- Flexible endoscopic bolus removal: 93%
- Rigid endoscopic bolus removal: 7%
- Transmural Perforation:
  - 20% Rigid Endoscopy
  - Spontaneous rupture in 1 patient

Straumann et al, Clin Gastroenterol Hepatol 2008
Small Caliber Esophagus
Pill Impaction
Treatment
Foods

- Elimination diets resolve EE
  - Empiric: 50% (adults)-74% (pediatric)
  - Targeted: 70%

- Elemental formula resolves EE
  - >90%

- Addition of foods causes EE

- Animal models using ovalbumin cause EE/EG

Kagalwalla et al, Clin Gastro Hepatol 2006
Hogan et al, Nature Immunology 2001
Song et al, Clin Exp Allergy 2009
Liacouras et al, Clin Gastro Hepatol
Spergel et al, JACI 2008
Diet and Eosinophilic Esophagitis

• After elemental diet:
  – Symptom resolution in 8 patients, improvement in 2
  – Improvement occurred within 3 weeks
  – Biopsies improved as well

• Symptoms returned after food was reintroduced

• Conclusions:
  – EoE is an allergic phenomenon
  – EoE improves with food elimination
Elemental Formula Eliminates EoE

- Kelly 1993
- Liacouras 2005
- Markowitz 2003
- Spergel 2005
- Kagalwalla 2006
Empiric Elimination Diet

• Six food elimination diet (SFED)
• 60 EoE patients – retrospective review
  – 35 given diet without milk, soy, wheat, egg, peanut, nut and fish
  – 25 given amino acid formula
• Biopsies done at start compared with 6 weeks of diet therapy
• Improvement in restricted group 75% while amino acid group 90%

IgE Testing

- Use food extracts as for anaphylaxis
  - Most data is from Children’s Hospital of Philadelphia

- Food ImmunoCAP Testing: Limited data in EGIDs
  - Overall varying success with RAST based elimination diet
  - Paucity of data
Food Patch Test

- Delayed/Cellular Hypersensitivity
- Fresh foods or single item baby food
- Milk, egg, soy, wheat used as powders in saline
- Apply in large Finn chamber
- Remove at 48 hours
- Read at 72 hours
Atopy Patch Testing

- Milk
- Soy
- Corn
- Beef
- Chicken
- Wheat
- Potato
- Egg
- Oat
- Rice
- Saline
## Predictive Values: SPT + APT

### TABLE II. Predictive values for the combination of SPT and APT

<table>
<thead>
<tr>
<th>Food</th>
<th>PPV</th>
<th>NPV</th>
<th>Specificity</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>92.0%</td>
<td>40.9%</td>
<td>63.9%</td>
<td>81.8%</td>
</tr>
<tr>
<td>Egg</td>
<td>84.8%</td>
<td>87.5%</td>
<td>86.7%</td>
<td>85.7%</td>
</tr>
<tr>
<td>Soy</td>
<td>73.7%</td>
<td>92.9%</td>
<td>87.5%</td>
<td>83.9%</td>
</tr>
<tr>
<td>Wheat</td>
<td>76.5%</td>
<td>90.0%</td>
<td>81.3%</td>
<td>87.1%</td>
</tr>
<tr>
<td>Corn</td>
<td>63.4%</td>
<td>92.5%</td>
<td>86.7%</td>
<td>76.6%</td>
</tr>
<tr>
<td>Beef</td>
<td>85.2%</td>
<td>92.5%</td>
<td>82.1%</td>
<td>93.9%</td>
</tr>
<tr>
<td>Chicken</td>
<td>62.5%</td>
<td>98.6%</td>
<td>93.8%</td>
<td>88.5%</td>
</tr>
<tr>
<td>Apple</td>
<td>57.1%</td>
<td>97.7%</td>
<td>66.7%</td>
<td>96.6%</td>
</tr>
<tr>
<td>Rice</td>
<td>60.9%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>88.8%</td>
</tr>
<tr>
<td>Potato</td>
<td>61.1%</td>
<td>97.4%</td>
<td>84.6%</td>
<td>91.4%</td>
</tr>
<tr>
<td>Peanut</td>
<td>71.4%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>95.2%</td>
</tr>
<tr>
<td>Oat</td>
<td>50.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>89.4%</td>
</tr>
<tr>
<td>Barley</td>
<td>73.3%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>95.2%</td>
</tr>
</tbody>
</table>

Spergel et al, JACI 2007
Foods Causing EoE

- Foods found in single elimination or reintroduction with positive biopsies
  
  Milk > Egg, Soy > Corn, Wheat, Beef > Chicken > Peanuts, Rice, Potato > Oat, Barley, Turkey, and Pea

- Most EoE patients, average 4 to 5 foods

- Up to 25% have severe food allergies - unable to tolerate ANY food without symptoms and histologic changes
## Dietary Options: Pros and Cons

<table>
<thead>
<tr>
<th></th>
<th>Elemental Formula</th>
<th>Directed Elimination</th>
<th>Empiric Elimination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compliance</td>
<td>Difficult</td>
<td>Better</td>
<td>Better</td>
</tr>
<tr>
<td>Cost</td>
<td>Expensive</td>
<td>Manageable</td>
<td>Manageable</td>
</tr>
<tr>
<td>Invasive?</td>
<td>Potentially (GT, NGT)</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Number of EGDs</td>
<td>Many</td>
<td>Fewer, every 1-2 foods</td>
<td>Fewer, every 1-2 foods (6 in total)</td>
</tr>
<tr>
<td>Tolerability</td>
<td>Low</td>
<td>Better</td>
<td>Better</td>
</tr>
<tr>
<td>Complications</td>
<td>Oral Aversion</td>
<td>Nutritional</td>
<td>Nutritional</td>
</tr>
<tr>
<td></td>
<td>Cost</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tube related</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Response Rate</td>
<td>&gt;95%</td>
<td>75%</td>
<td>75%</td>
</tr>
<tr>
<td>QOL</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
Medications

Topical Corticosteroids

Biologics
Oral Steroid Studies

![Bar chart showing eosinophils per high power field (Eos/hpf) pre-treatment and post-treatment for Liacouras (n=20) and Schaefer (n=40).]

- Liacouras (n=20): Pre-treatment 34.2, Post-treatment 1.5
- Schaefer (n=40): Pre-treatment 29, Post-treatment 1.3

1 mg/kg BID; max 30 mg BID

Topical Steroids

![Bar chart showing eosinophil counts before and after treatment with different studies.](image)

- **Konikoff** (n=18): Max Dose: 880 mcg/day (Pre-treatment: 84.6, Post-treatment: 19.7)
- **Noel** (n=20): Max Dose: 1320 mcg/day (Pre-treatment: 43.4, Post-treatment: 1)
- **Teitelbaum** (n=13): Max Dose: 880 mcg/day (Pre-treatment: 23, Post-treatment: 2.7)
- **Schaefer** (n=40): Max Dose: 1760 mcg/day (Pre-treatment: 33.3, Post-treatment: 4.8)

*Post treatment data on 16 patients.

References:
Fluticasone Lowers Eos in Esophagus

Proximal Esophagus

Distal Esophagus

Eosinophils per High Power Field

PRE-TREATMENT POST-TREATMENT PRE-TREATMENT POST-TREATMENT

Remedios, et al; Gastrointest Endosc 2006; 63:3.
Oral Viscous Budesonide

- Overall Response Rate to viscous budesonide: 87%
- Overall Response Rate to Placebo + PPI: 0%

Dohil et al, Gastroenterology 2010
Randomized, Double-Blind Placebo Controlled Trial Budesonide (BEE Trial)

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

Eosinophils per hpf

Before
After

Budesonide
Placebo

Anti-IL-5 Therapy in EoE

Mean (±SD) esophageal eosinophils (ECP staining)

P = 0.387

P = 0.001*

- 55.3%

Straumann et al, Gut 2010
Effects of Therapy on Complications
Topical Fluticasone Reverses Transcriptome Profile

Blanchard et al, JACI 2007
Treatment Resolves Pathology: Remodeling

LP Eosinophils

Fibrosis Score

Aceves et al, Allergy 2010
Treatment Resolves Pathology: Remodeling

C. TGFβ

D. pSmad2/3

Aceves et al, Allergy 2010
Decreased Vascular Activation

VCAM-1 Positive Vessels

Dilated Intercellular Spaces

Aceves et al, Allergy 2010
Treatment Strategy
EoE: >15 eosinophils per hpf despite acid blockade

Aeroallergen Testing: SPT
Food Testing: SPT
?APT

Institute Therapy

Elimination Diet
Empiric:
6 Food Elimination
Directed:
SPT, APT Based

Topical Corticosteroids
>7-10 years old: Fluticasone BID
Budesonide + Sucralose/Maltodextin

Food Reintroduction

Repeat EGD with Biopsy

Histologic/EGD/Symptom Response
Histologic/EGD Failure

Maintenance

Elemental Formula
Systemic corticosteroids
Biologics
Conclusions

- EoE is a chronic disease of children and adults
- Typical symptoms include dysphagia, abdominal pain, and anorexia/early satiety
- Prevalence is increasing
- Successful therapies are diet and topical corticosteroids
- Complications: Strictures, Remodeling
- Pathogenesis includes Eotaxin-3, IL-5, IL-13, IL-15, TGFβ1 and involves the Epithelium, Innate and Adaptive Immunity, Vascularity, and Smooth Muscle
- No surrogate disease markers