Pediatric Eosinophilic Esophagitis Research: Where are We Going?

North American Society of Pediatric Gastroenterology, Hepatology and Nutrition Annual Meeting October 26, 2014

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In the last year, have we,

• Identified Novel Therapeutic Targets?

• Improved Therapeutic Strategies?

• Developed New Assessment Tools?

What is pathophysiology of EoE?

Novenski et al Clev Clin J 2008

Does Helicobacter pylori Protect against Eosinophilic Esophagitis in Children?

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• Retrospective review of children’s first endoscopy

• 966 charts
  – 62 with EoE
  – 31 with HP

• Significant negative relationship between Hp and EoE
**Commensal bacteria protect against food allergen sensitization**


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*Editor* by Sue R. Litman, New York University Medical Center, New York, NY, and approved August 5, 2014 (accepted for review June 25, 2014)

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**Dilated Intercellular spaces in EoE**

Ravelli et al JPN 2014

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**Diminished Desmosomes in EoE**

Unpublished data

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**2 functional assessments**

- FITC flux
- TER

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**Effects of Topical Steroids on Tight Junction Proteins and Spongiosis in Esophageal Epithelia of Patients With Eosinophil Esophagitis**


*Division of Gastroenterology and Hepatology, and Division of Pathology, Mayo Clinic, Rochester, Minnesota*

- Adults with Active (10), Inactive (10) and controls (10)
- Immunohistochemical staining for junctional proteins

Clin Gastro Hepatol 2014
Desmoglein-1 is decreased in EoE

Loss of desmoglein-1 alters barrier

Barrier dysfunction may contribute to the pathogenesis of EoE
PhD and MD scientists
6 different academic institutions
almost 10,000 patients

miR 223

- Leukocyte proliferation and activation
- Cytokine production
- Target genes involved in adaptive immune system polarization
- Regulation of eotaxin-3

Lu TX et al JACI 2012

miR expression in EoE

Zahm AM, Menard-Katcher C et al Am J Physiol Gastrointest Liver Physiol 2014
Phospholamban is a protein associated with tissue contraction
- Required for cardiac contraction
- Present in gastric smooth muscle
- Associated with gallbladder contraction
- Reduced in colitis
The natural history of eosinophilic oesophagitis in the transition from childhood to adulthood

Conclusions
The majority of young adults diagnosed with EoE during childhood continue to require pharmacological treatment and/or dietary modification for EoE. A substantial proportion of this population experiences ongoing swallowing difficulties that a standard dysphagia questionnaire fails to capture. Dietary quality of life, but not total quality of life, appears to be adversely affected. These data suggest that EoE diagnosed during childhood remains a significant medical issue during early adulthood and that better EoE symptom measurement instruments are needed.
EoE can lead to fibrosis

<table>
<thead>
<tr>
<th>Diagnostic delay (years)</th>
<th>Normal esophagus</th>
<th>Inflammatory</th>
<th>Fibrotic</th>
<th>Inflammatory + fibrotic</th>
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EoE: eosinophilic esophagitis

• Retrospective study

• 206 patients with 5 year follow up

• 33 patients with 42 impactions

• Esophageal stricture-OR 2.666, 95% CI, 1.259-5.465, p=0.01

• Increased frequency of TCS reduced risk of FI

Endoluminal Functional Luminal Imaging (EndoFLIP)

Determination of esophageal pressure-volume relationships

Infinitely compliant cylindrical bag

17 receiver electrodes determine CSA

Intra-bag pressure Measurement

Kuwatek, Gastroenterology 2011

Allergy topical corticosteroids reduce the risk for long-lasting bolus impactions in eosinophilic esophagitis

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P = 0.007

P = 0.005 (trend test)

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Kuwatek, Gastroenterology 2011
Efficacy, Dose Reduction, and Resistance to High-Dose Fluticasone In Patients With Eosinophilic Esophagitis

- 22 treated, 13 placebo, 1760 mcg daily dose
- No differences in severity or frequency of symptoms
- 1 subject developed thrush
- 8 subjects with decreased cortisol

Reference for Endoscopic Abnormalities (EoE-EREFs)

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

- Mild (Grade 1): Scattered lesions occupying < 10% of the surface area of the

**Severe (Grade 2): Lesions involving ≥ 10% of the surface area of the**

The Enterotest

Developed in 1970’s for analysis of parasitic infections
Method - The Esophageal String Test (EST)

Cytosponge captures Eosinophil derived neurotoxin in adult EoE

Tethered capsule endomicroscopy enables less invasive imaging of gastrointestinal tract microstructure

Tethered confocal endomicroscopy capsule for diagnosis and monitoring of eosinophilic esophagitis
Characterization of eosinophilic esophagitis murine models using optical coherence tomography

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National institutes of Health, CTSA, FDA
American Gastroenterological Association, APFED, Pappas Foundation, CURED, FARE