Key Updates in Eosinophilic Esophagitis

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Topics for today

• Historical perspective
• Presentation & pathogenesis
• How to make the diagnosis
• Treatment options
• Key changes in the past 24 months
• Key updates for the near future
Eosinophilic Esophagitis
History

- First described in 1977\(^1\)
- Initial report given no attention & subsequent papers in the 1980s linked eosinophilia with GERD\(^2\)
- First viewed as distinct clinical entity in 1993/1994 with publication of two case series\(^3,4\)

Dobbins JW. Gastroenterology 1977
Attwood SE. Dig Dis Sci 1993
Straumann A. Schweiz Med Wochenschr 1994
Publications by Decade

Number of publications

- Number of publications

Decades:
- 1970s
- 1980s
- 1990s
- 2000s
- 2010s
Epidemiology

• Is the incidence increasing or is this just newly recognized?
  – Arguments in favor of increasing incidence:
    (1) Barium radiography available for decades
    (2) Population-based studies showing increase in regions with fixed practice patterns
Incidence & Prevalence

• Incidence (systematic review, 2018)¹
  – 1376 articles identified; 47 on incidence/natural history
  – Increase in incidence:
    • Denmark: 20-fold (1997 – 2006)
    • Canada: 5.1-fold (2004 – 2008)

• Prevalence
  – Sweden, estimated to be 1% population²
  – Walter Reed, 6.5% of all patients undergoing endoscopy³

• Economic burden: estimated $1.36 billion/year in U.S. alone⁴

1. Shaheen NJ. Dis Esophagus 2018
2. Ronkainen J. Gut 2007
4. Jensen ET. Am J Gastroenterol 2014
Clinical Presentation

• In adults
  – Men > Women (76%)
  – Average age 30-50 (mean 38, range 0.5-89)
  – Industrial countries
  – Strong association with atopic disorders
  – Familial clustering (5% siblings/7% parent)
  – Possible seasonal variation
Clinical Presentation

• Adults
  – Most common
    • Dysphagia
    • Food impaction
  – Less common
    • GERD-like symptoms (7%-100%)
    • Chest pain (1%-58%)
    • Abdominal pain (3%-25%)
    • Diarrhea and weight loss rarely reported

• In children, GERD-like symptoms, nausea and food aversion are much more common & dysphagia is rare
Pathogenesis

• Exact mechanisms largely unknown
• Clearly linked with food allergies & potentially environmental allergens
• Recent data support potential role for:
  – Impaired barrier function
  – Microbiome derangements
Diagnosis

• Clinicopathologic diagnosis
  – Symptoms (dysphagia primarily)
  – Endoscopic findings associated with inflammation and/or fibrosis
  – Histology with eosinophil deposition (> 15 eos/hpf)

Straumann A. Gastroenterology 2018
Dellon ES. Am J Gastroenterol 2013
Liacouras CA. J Allergy Clin Immunol 2011
Endoscopy

- Endoscopic findings
  - Furrows (80%)
  - Concentric rings (64%)
  - Small caliber (28%)
  - White plaques (16%)
  - Strictures (12%)
  - Normal (10-20%)

Gonsalves N. Neurogastroenterol Motil 2009
Radiography

- Characteristic findings of strictures & rings can be seen on barium esophagram
- Given need for biopsies, barium studies are of limited clinical utility
- Caveat: in extreme dysphagia the length & caliber of a stricture may be of utility
Allergy Testing

• Rationale
  – Allergy strongly implicated as potential cause
  – Majority of patients have atopy (50-80%)
• Because of this, the AGA recommends allergy testing for all patients diagnosed with EoE
• Data supporting this recommendation is controversial

Furuta G. Gastroenterology 2007
Treatment

• Goals of therapy
  – Symptom control
  – Control of esophageal eosinophilia/inflammation
  – Prevention/reversal of fibrosis
Treatment

- General approaches
  - PPI use/acid suppression
  - Dietary modification
  - Topical steroids
  - Dilation
Proton Pump Inhibitors & EoE

• 2011 consensus & 2013 ACG guidelines both recommend a PPI trial for 8 weeks to exclude PPI-responsive esophageal eosinophilia (PPI-REE)
• Confusion:
  – Approximately 1/3 of patients will resolve with PPI therapy
  – PPI-REE and EoE cannot be distinguished based on gene expression, pathology or cytokines
  – A subset of patients resolve following PPI even in the documented absence of GERD
  – PPIs also have anti-inflammatory effects separate from their role in acid suppression
• Recent expert panel recommended not use PPI responsiveness in the diagnosis (AGREE Consensus)

Straumann A. Gastroenterology 2018
Molina-Infante J. Gut 2016
Odiase E. Gastroenterology 2018
Dellon ES. Gastroenterology 2018
Dietary Modification

• Strong evidence that dietary approaches work
• Three basic approaches
  – Elemental diet
  – Elimination/restricted diet
  – Allergy test-based diet
## Dietary Modification

![Graph showing histologic remission rates for different dietary modifications.](image)

**FIG 1.** Histologic remission rates broken down by age group and shown by different modalities of dietary therapy (elemental diet, empiric elimination diet, and allergy testing-guided elimination diet) for EoE. *Indirect data from prospective studies on 4-FEDs and 2-FEDs. Efficacy of milk elimination diets in children ranges from 33% to 56%.*

Molina-Infante J. J Allergy Clin Immunol 2018
Medical Therapy

• Medical therapy
  – Corticosteroids (topical or systemic)
  – Montelukast
  – Immunomodulators
  – Biologics
## Corticosteroids

### Fluticasone RCTs
- **Konikoff, 2006**
  - n = 21 MDI
  - n = 15
  - ≤ 1 eos/hpf
  - a/s
  - 3 mos

- **Alexander, 2012**
  - n = 21 MDI
  - n = 15
  - > 90% decrease in eosinophils
  - No
  - 6 wks

- **Butz, 2014**
  - n = 28 MDI
  - n = 14
  - ≤ 1 eos/hpf
  - No
  - 3 mos

### Budesonide RCTs
- **Dohil, 2010**
  - n = 15 OVB
  - n = 9
  - ≤ 6 eos/hpf
  - Yes
  - 3 mos

- **Straumann, 2010**
  - n = 18 NEB
  - n = 16
  - < 5 eos/hpf
  - Yes
  - 19 days

- **Gupta, 2011**
  - n = 51 OVB
  - n = 18
  - ≤ 1 eos/hpf
  - No
  - 12 wks

- **Mehlka, 2014**
  - n = 19 BRI
  - n = 19
  - < 16 eos/mm^2
  - No
  - 14 days

### Comparative RCTs
- **Schaffer, 2006**
  - n = 40 MDI
  - n = 40 Prednisone
  - Response in biopsy grade
  - Yes
  - 12 wks

- **Dellon, 2012**
  - n = 23 OVB
  - n = 12 NEB
  - < 1 eos/hpf
  - No
  - 8 wks
Dilatation
Key Updates in the past 24 months

• AGREE consensus (2018):
  – A PPI trial is no longer required to make a diagnosis of EoE
  – PPIs are a treatment option

• Multisociety guideline (2020):
  – Joint guideline of AAAAI, ACAAI and AGA
  – Published in April
  – Key updates:
    • Topical steroids are now recommended as first-line
    • PPIs, diet therapy & dilation also recommended as treatment options in selected patients
    • More research is needed before biologic therapy can be recommended
New Developments

• Key updates in pathophysiology:
  – Microbiome
  – Esophageal barrier

• New diagnostic tests:
  – Functional lumen imaging probe
  – Mucosal impedance
  – Cytosponge
  – Endoscopic allergy testing
  – Biomarkers (urine/blood)
  – Gene expression profiling

• New treatment options
  – Biologic therapies in development: IL-4, IL-5, IL-13
  – Oral dissolvable steroids
Acute EPT response
Stanford Esophageal Center

- **GI (esophagus)**
  - John Clarke
  - Nielsen Fernandez-Becker
  - Patricia Garcia
  - Afrin Kamal
  - Monica Nandwani
  - Linda Nguyen
  - Shelly Orloff
  - Irene Sonu
  - George Triadafilopoulos
  - Tom Zikos

- **GI (therapeutics)**
  - Shai Friedland
  - Joo Ha Hwang

- **Surgery (Minimally-invasive)**
  - Dan Azagury
  - Mary Hawn
  - James Lau

- **Surgery (Thoracic)**
  - Mark Berry
  - Natalie Lui
  - Joe Shrager

- **ENT**
  - Ed Damrose
  - Karuna Dewan
  - Heather Starmer
  - Kwang Sung

- **Research Coordinator**
  - Divya Pathak
Thank you