Key Updates in Eosinophilic Esophagitis

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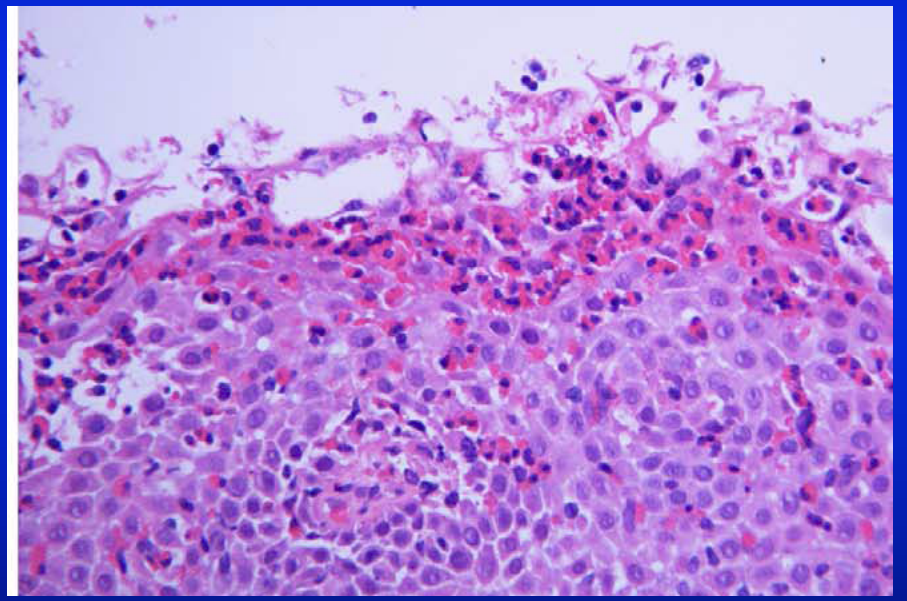
Topics for today

- 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

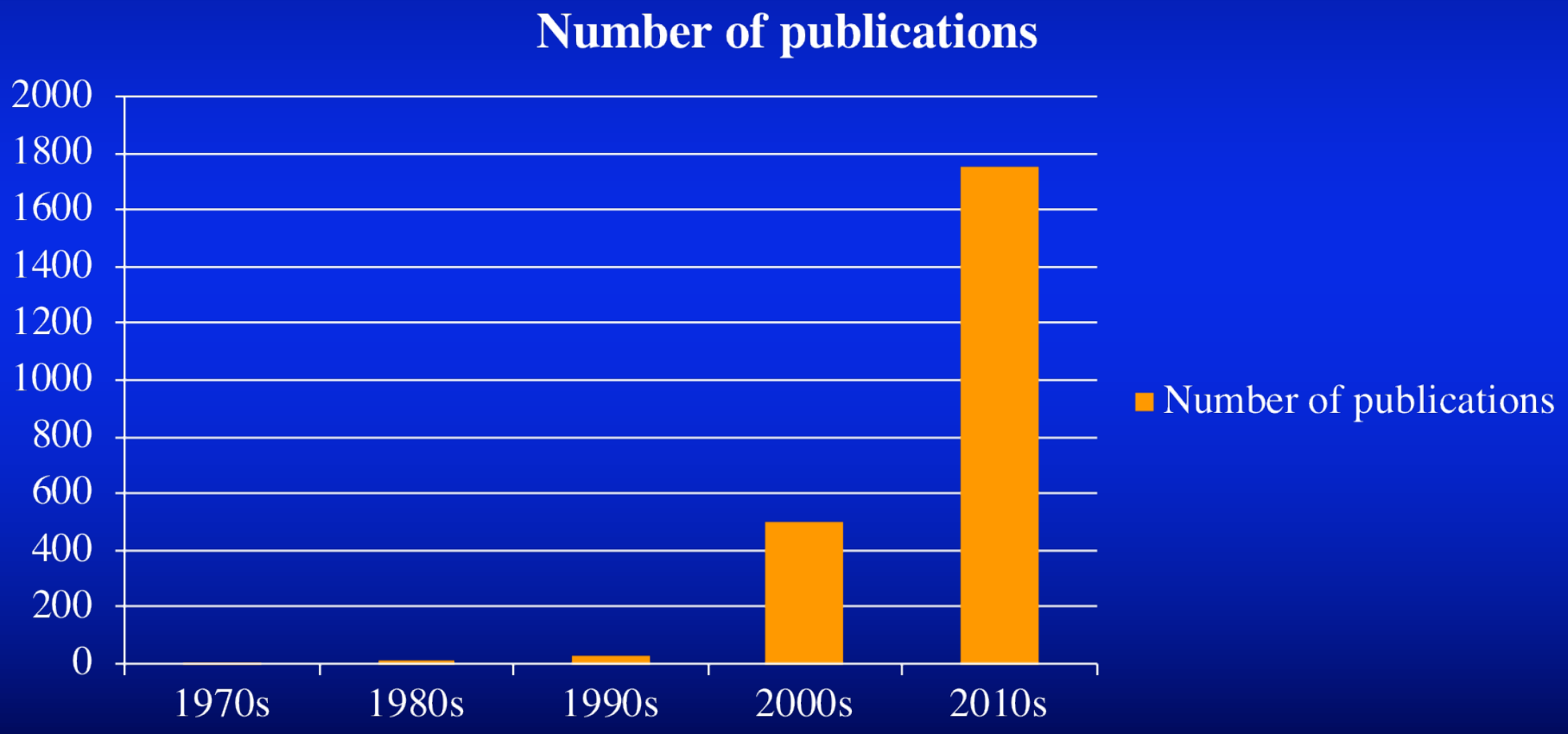


History

- 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
Brown LF. Am J Surg Pathol 1984
Attwood SE. Dig Dis Sci 1993
Straumann A. Schweiz Med Wochenschr 1994

Publications by Decade



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:
    - Netherlands: 131-fold (1996 – 2010)
    - Denmark: 20-fold (1997 – 2006)
    - Canada: 5.1-fold (2004 – 2008)
- Prevalence
  - Sweden, estimated to be 1% population[2]
  - Walter Reed, 6.5% of all patients undergoing endoscopy[3]
- Economic burden: estimated $1.36 billion/year in U.S. alone[4]

1. Shaheen NJ. Dis Esophagus 2018
2. Ronkainen J. Gut 2007
3. Moawad FJ. Dig Dis Sci 2009
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

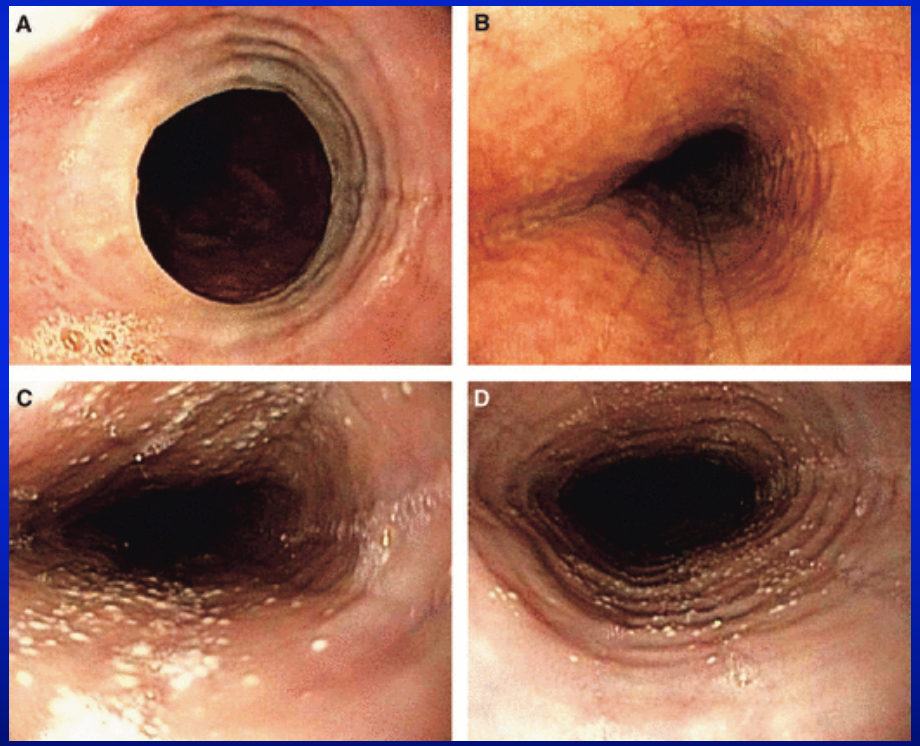
- Exact mechanisms largely unknown
- Clearly linked with food allergies & potentially environmental allergens
- Recent data support potential role for:
  - Impaired barrier function
  - Microbiome derangements

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

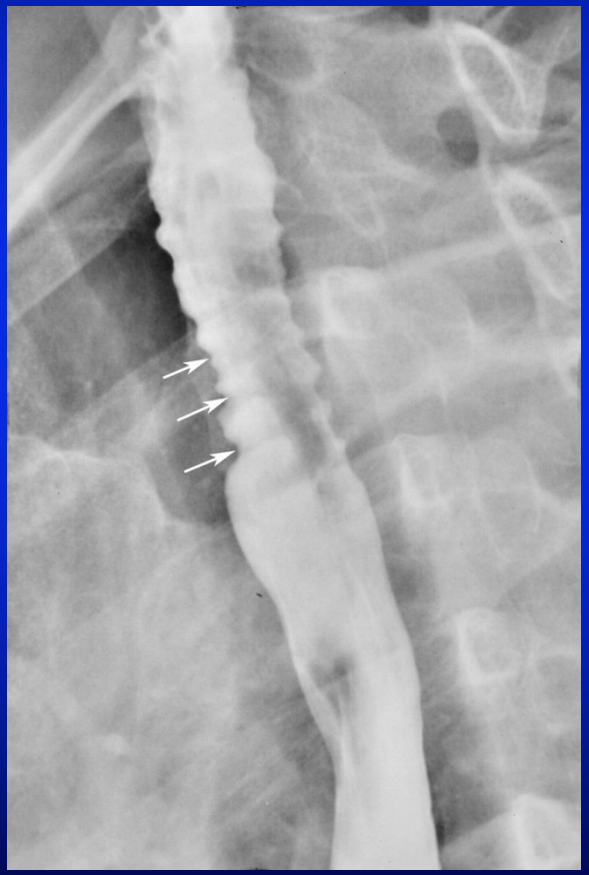


- Endoscopic findings
  - Furrows (80%)
  - Concentric rings (64%)
  - Small caliber (28%)
  - White plaques (16%)
  - Strictures (12%)
  - Normal (10-20%)

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



Zimmerman SL. Radiology 2005

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

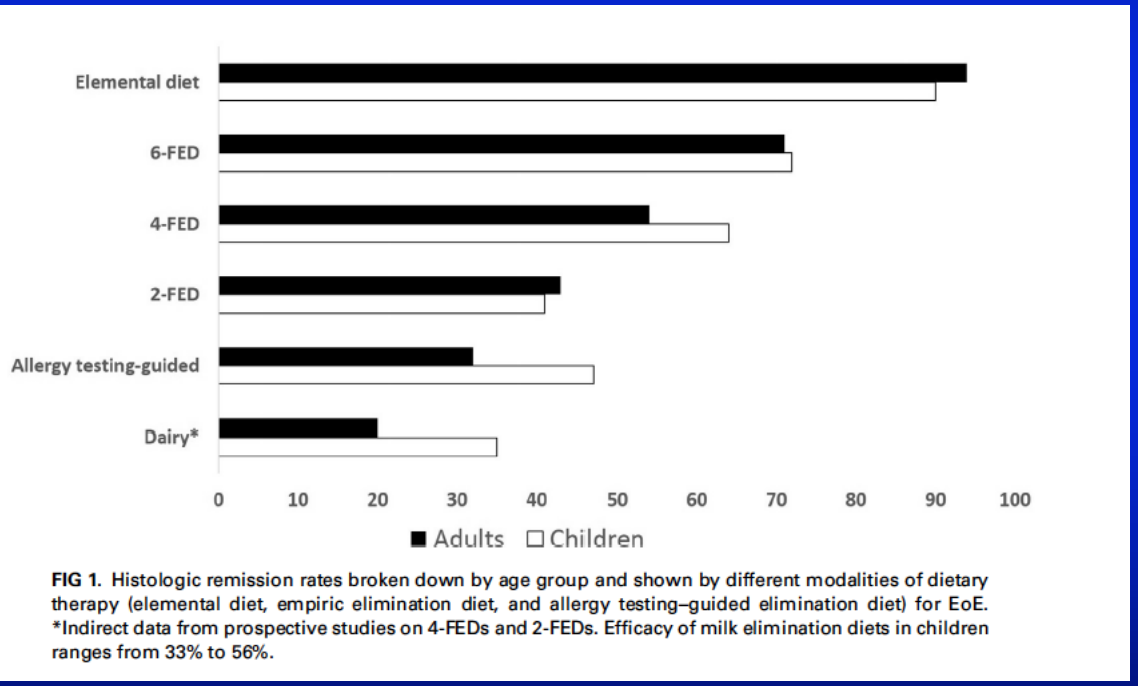


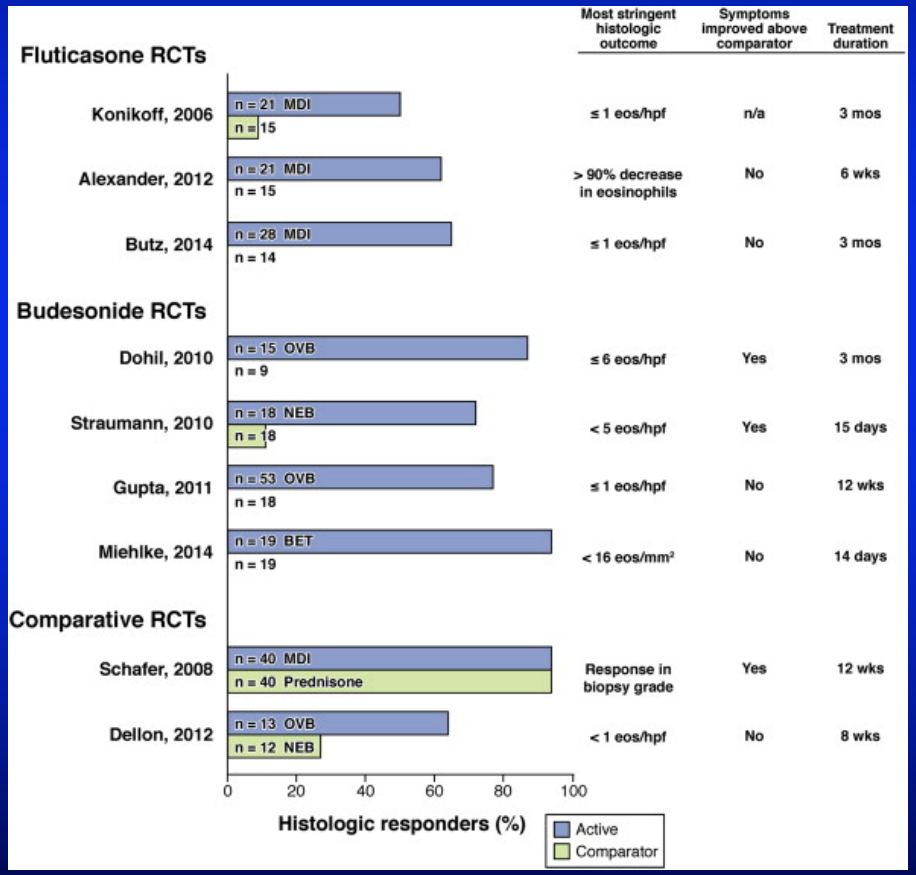
FIG 1. Histologic remission rates broken down by age group and shown by different modalities of dietary therapy (elemental diet, empiric elimination diet, and allergy testing–guided elimination diet) for EoE. *Indirect data from prospective studies on 4-FEDs and 2-FEDs. Efficacy of milk elimination diets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

Molina-Infante J. J Allergy Clin Immunol 2018

Medical Therapy

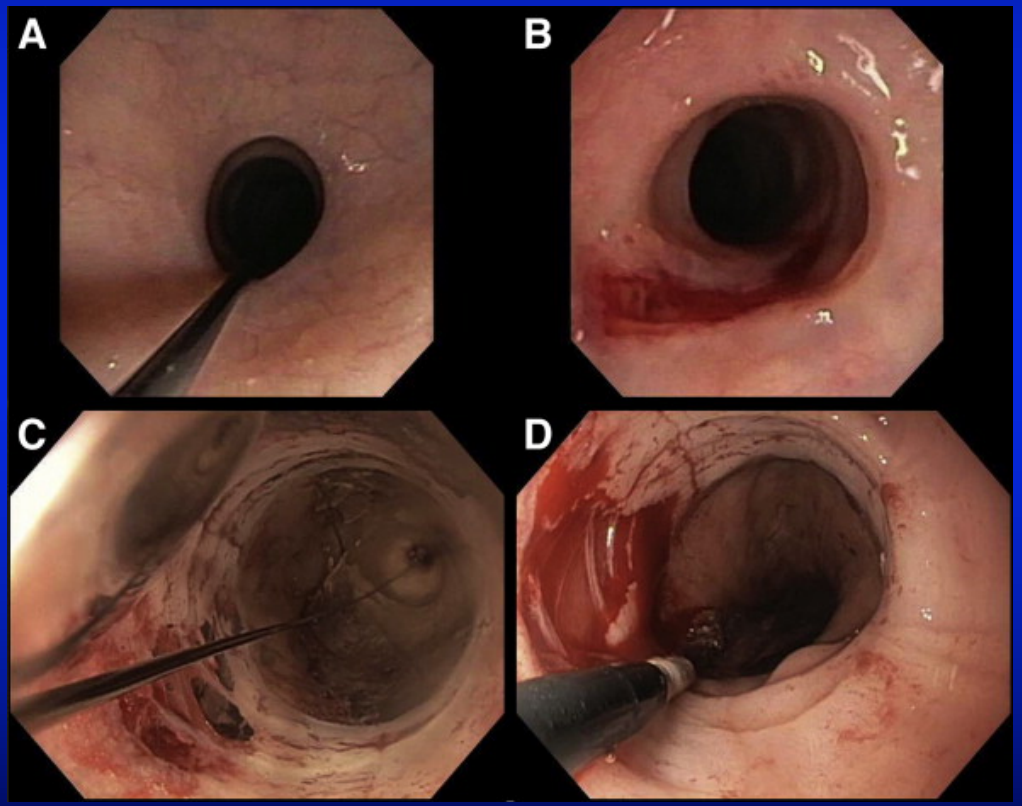
- Medical therapy
  - Corticosteroids (topical or systemic)
  - Montelukast
  - Immunomodulators
  - Biologics

Corticosteroids



Dellon ES. Gastroenterology 2014

Dilatation



Key Updates in the past 24 months

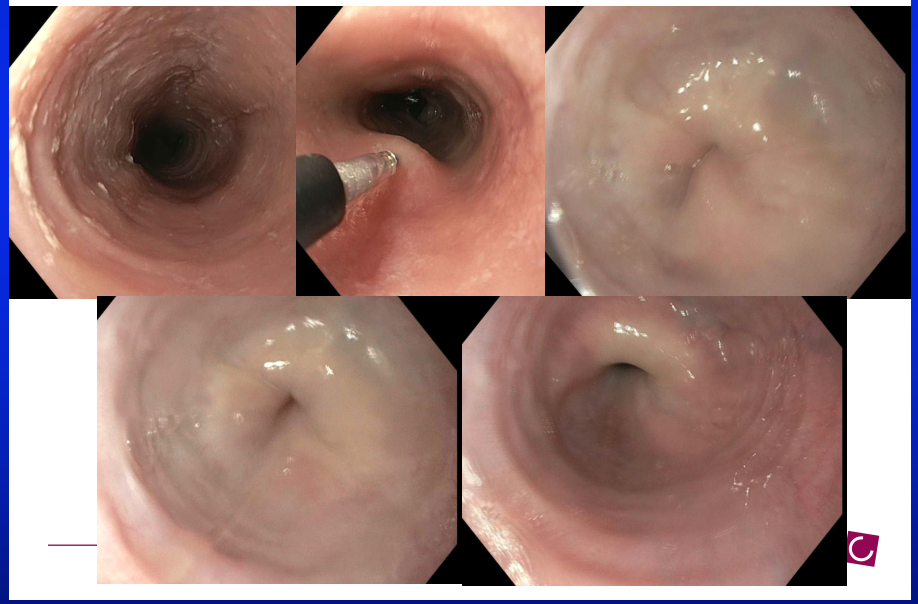
- AGREE consensus (2018):
  - A PPI trial is no longer required to make a diagnosis of EoE
  - PPIs are a treatment option
- Multisociety guideline (2020):
  - Joint guideline of AAAAI, ACAAI and AGA
  - Published in April
  - Key updates:
    - Topical steroids are now recommended as first-line
    - PPIs, diet therapy & dilation also recommended as treatment options in selected patients
    - More research is needed before biologic therapy can be recommended

Dellon ES. Gastroenterology 2018
Hirano I. Gastroenterology 2020

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

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  - George Triadafilopoulos
  - Tom Zikos
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  - Joo Ha Hwang
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  - Mary Hawn
  - James Lau
- Surgery (Thoracic)
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- ENT
  - Ed Damrose
  - Karuna Dewan
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Thank you