Approach to Diagnosis and Management of Eosinophilic Esophagitis (EoE)

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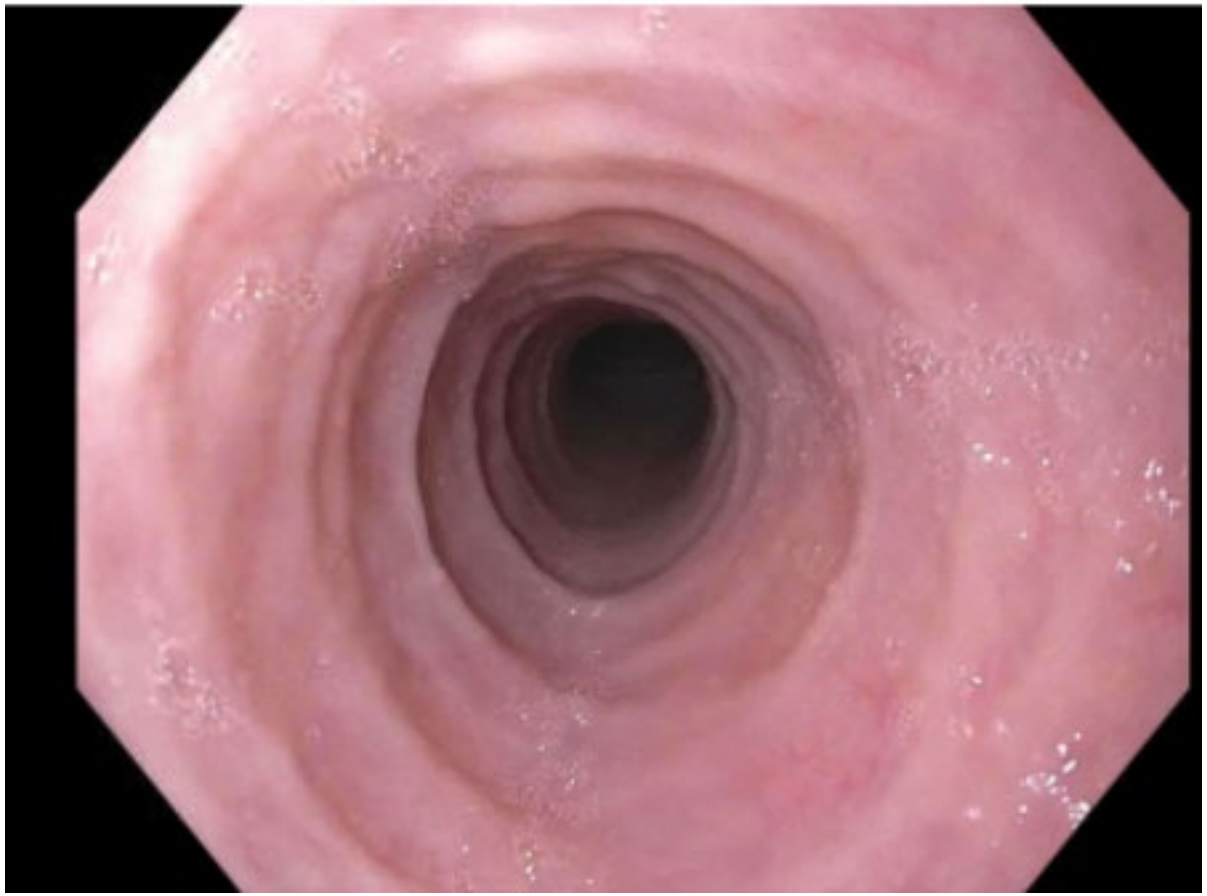
Disclosures

- None

Objectives

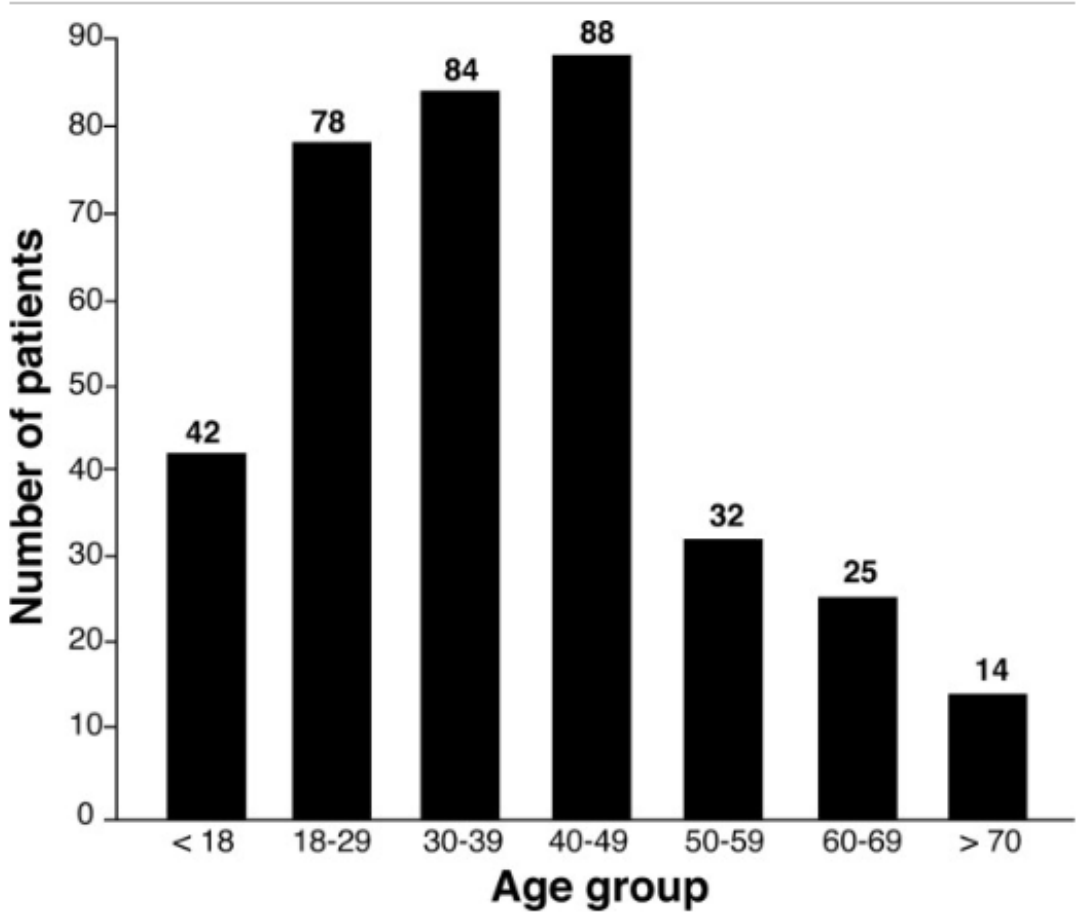
- Review the algorithm for establishing a diagnosis in this patient population
- Discuss the guidelines for treatment and management of Eosinophilic Esophagitis (EoE)

42M with history of EoE



Epidemiology

- Epidemiology:
  - Male predominance 3:1
  - Usually dx at younger age but affects all age groups
  - Association with asthma, allergies



Kapel et al. Gastro 2008.

Table 2

Descriptive data for EE cases

Variable	Adult cases (n=55)	Pediatric cases (n=23)
Age (mean ± SD)	37 ± 11	10 ± 6
Male Gender (n,%)	29 (52.7%)	15 (65.2%)
Dysphagia (n,%)	51 (92.7%)	14 (60.9%)
Food Impaction (n,%)	23 (41.8%)	5 (21.7%)
Heartburn (n,%)	30 (54.5%)	4 (17.4%)
Acid Regurgitation (n,%)	21 (38.2%)	5 (21.7%)
Abdominal Pain (n,%)	12 (21.8%)	7 (30.4%)
Nausea (n,%)	3 (5.4%)	3 (13.0%)
Vomiting (n,%)	10 (18.2%)	10 (43.5%)
Seasonal allergies (n,%) (data available on 30 adult and 13 pediatric patients)	15 (50.0%)	7 (53.8%)
Food allergies (n,%) (data available on 30 adult and 14 pediatric patients)	11 (36.7%)	8 (57.1%)
History of asthma (n,%) (data available on 28 adult and 11 pediatric patients)	11 (39.3%)	7 (63.6%)
Family History $^{\$}$(n,%) (data available on 39 adult and 16 pediatric patients)	9 (23.1%)	6 (37.5%)

Prasad et al. Clinical Gastroenterology and Hepatology, 2009.

Making the Diagnosis

- Symptoms + Endoscopic Appearance + Histologic Confirmation

EoE is clinicopathologic disorder diagnosed by clinicians taking into consideration both clinical and pathologic information without either of these parameters interpreted in isolation, and defined by the following criteria:

- Symptoms related to esophageal dysfunction
- Eosinophil-predominant inflammation on esophageal biopsy, characteristically consisting of a peak value of ≥15 eosinophils per high-power field (eos/hpf)
- Mucosal eosinophilia is isolated to the esophagus and persists after a PPI trial
- Secondary causes of esophageal eosinophilia excluded (**Table 2**)
- A response to treatment (dietary elimination; topical corticosteroids) supports, but is not required for, diagnosis. (Strong recommendation, low evidence)

Aceves et al. Gastrointestinal Endoscopy, 2022.
Dellon et al. Gastroenterology, 2018.

Diagnostic Criteria

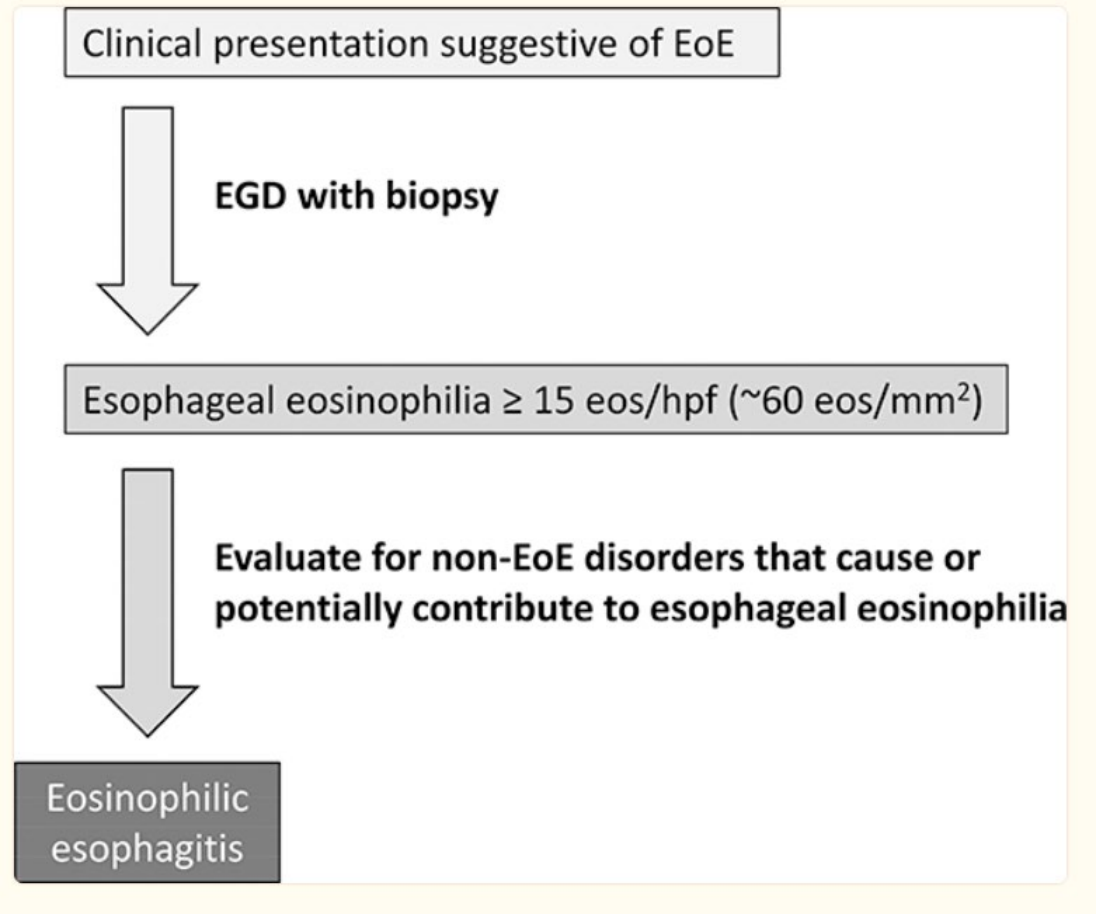
Table 2:

EoE diagnostic criteria

- Symptoms of esophageal dysfunction
  - Concomitant atopic conditions should increase suspicion for EoE
  - Endoscopic findings of rings, furrows, exudates, edema, stricture, narrowing, and crepe-paper mucosa should increase suspicion for EoE
- ≥15 eos/hpf (~60 eos/mm^2) on esophageal biopsy
  - Eosinophilic infiltration should be isolated to the esophagus
- Assessment of non-EoE disorders that cause or potentially contribute to esophageal eosinophilia

Dellon et al. Gastroenterology, 2018.

Diagnostic Algorithm



Dellon et al. Gastroenterology, 2018.

Symptoms

Table 2. Indications for Upper Endoscopy in Adult Cases (n = 321)

Indication[a]	Number	Frequency	95% confidence interval
Dysphagia	225	70.1%	64.8–75.1
GERD/heartburn	87	27.1%	22.3–32.3
Abdominal pain/dyspepsia	42	13.1%	9.6–17.3
Odynophagia	17	5.3%	3.1–8.3
History of stricture or narrowing[b]	13	4.1%	2.2–6.8
Chest pain	11	3.4%	1.7–6.1
Nausea and/or vomiting	8	2.5%	1.1–4.9
Food impaction	7	2.2%	0.9–4.4
Failure of GERD medical therapy	7	2.2%	0.9–4.4
Barrett's follow-up evaluation	3	0.9%	0.2–2.7
History of Schatzki ring	2	0.6%	0.1–2.2
Iron-deficiency anemia	1	0.3%	0.0–1.7
Other	15	4.7%	2.6–7.6

Prasad et al. Clinical Gastroenterology and Hepatology, 2009.

EoE Endoscopic Reference Score (EREFS)

- First described in 2013 and looks at endoscopic features of EoE
  - Used for diagnosis and to follow response to treatment

Major features

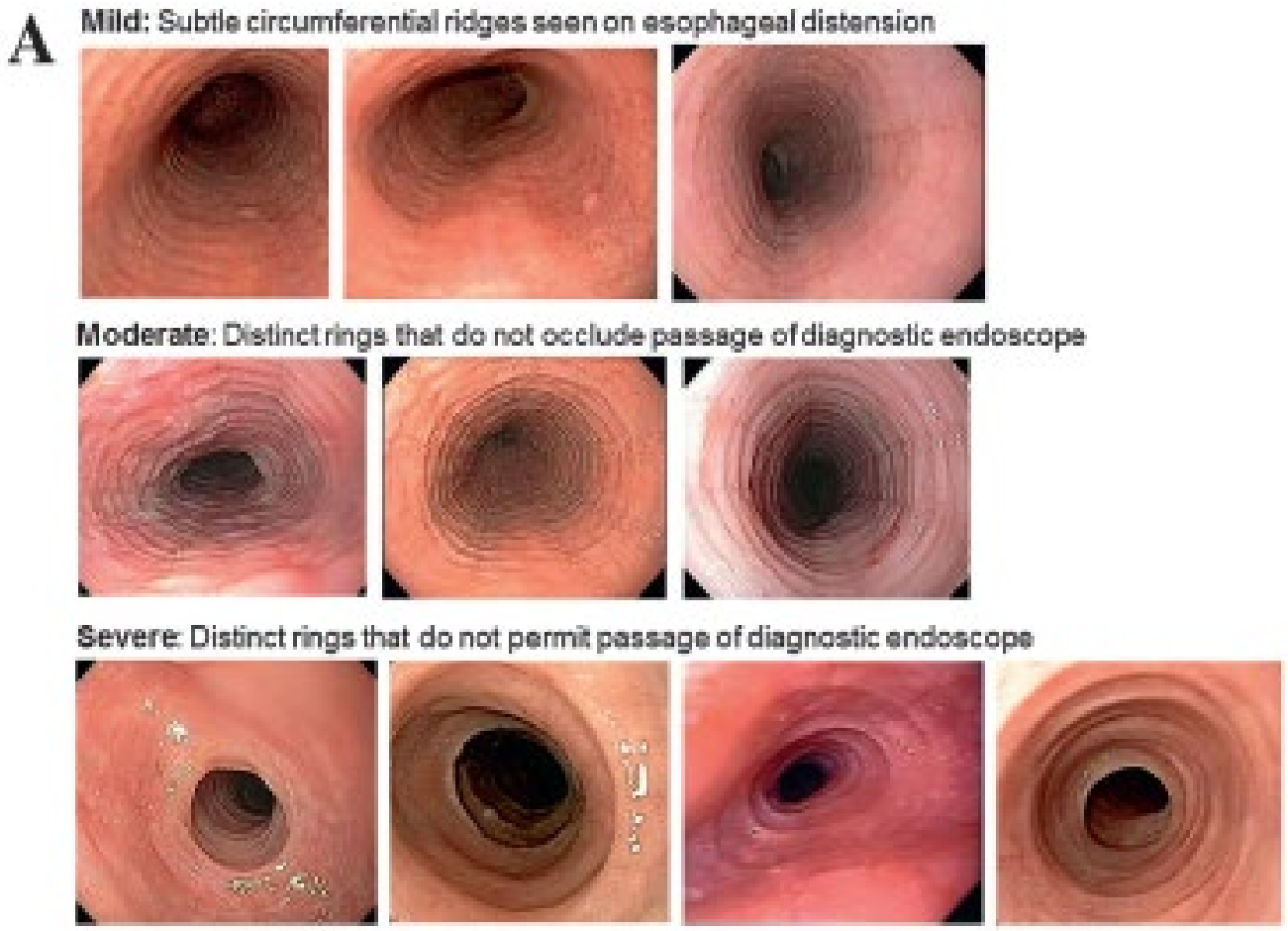
- **Fixed rings** (also referred to as concentric rings, corrugated oesophagus, corrugated rings, ringed oesophagus, trachealisation)
  - Grade 0: none
  - Grade 1: mild (subtle circumferential ridges)
  - Grade 2: moderate (distinct rings that do not impair passage of a standard diagnostic adult endoscope (outer diameter 8—9.5 mm))
  - Grade 3: severe (distinct rings that do not permit passage of a diagnostic endoscope)
- **Exudates** (also referred to as white spots, plaques)
  - Grade 0: none
  - Grade 1: mild (lesions involving <10% of the oesophageal surface area)
  - Grade 2: severe (lesions involving >10% of the oesophageal surface area)
- **Furrows** (also referred to as vertical lines, longitudinal furrows)
  - Grade 0: absent
  - Grade 1: present
- **Oedema** (also referred to as decreased vascular markings, mucosal pallor)
  - Grade 0: absent (distinct vascularity present)
  - Grade 1: loss of clarity or absence of vascular markings
- **Stricture**
  - Grade 0: absent
  - Grade 1: present

Minor features

- **Crepe paper oesophagus** (mucosal fragility or laceration upon passage of diagnostic endoscope but not after oesophageal dilation)
  - Grade 0: absent
  - Grade 1: present

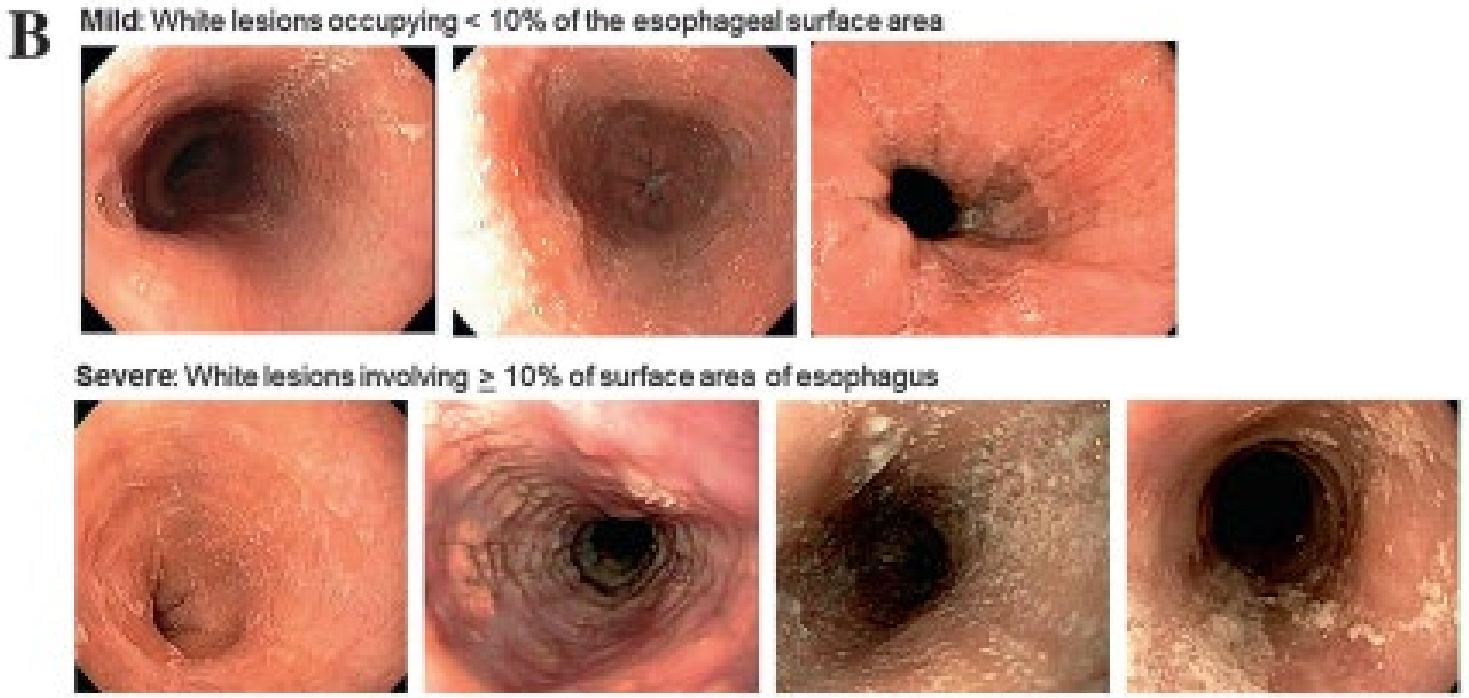
Hirano et al. Gut, 2012.
Dellon et al. Clinical Gastroenterology and Hepatology, 2016.

Esophageal Rings (trachealization)



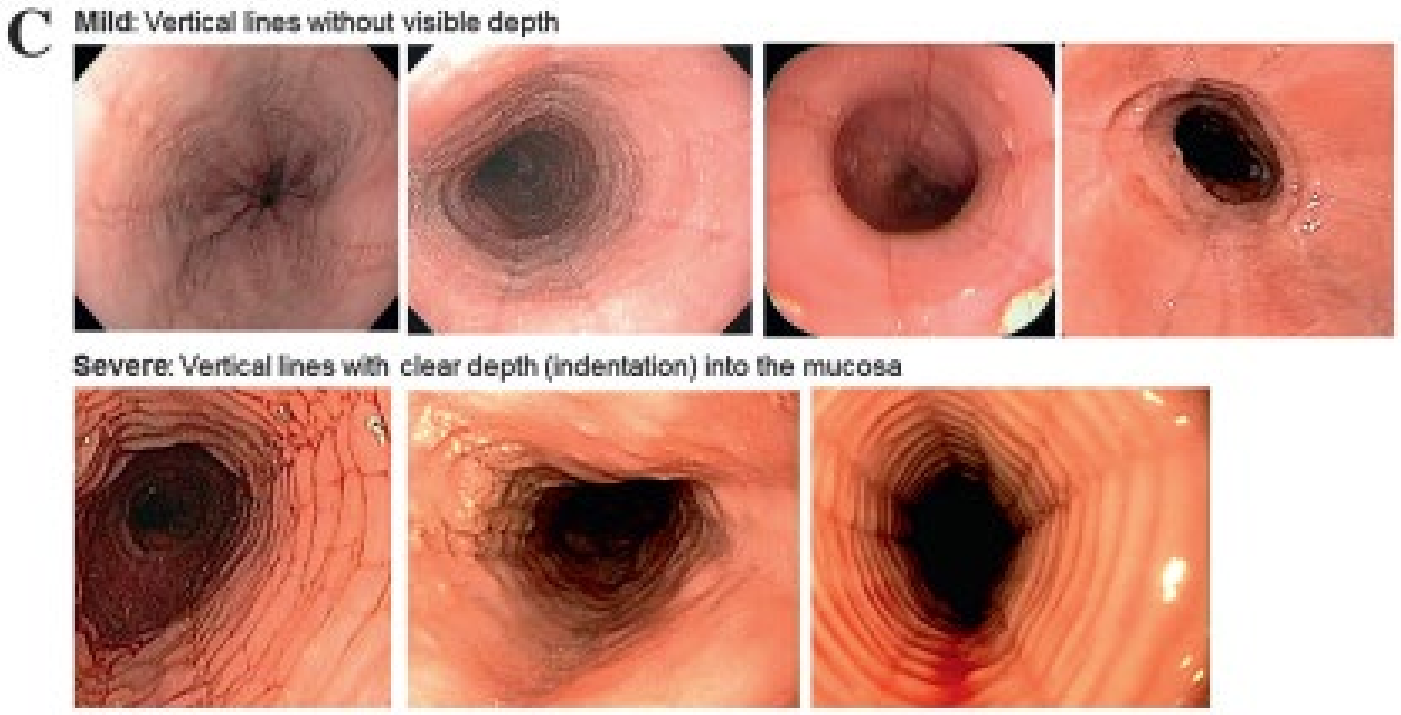
Hirano et al. Gut, 2012.

Exudates (plaques)



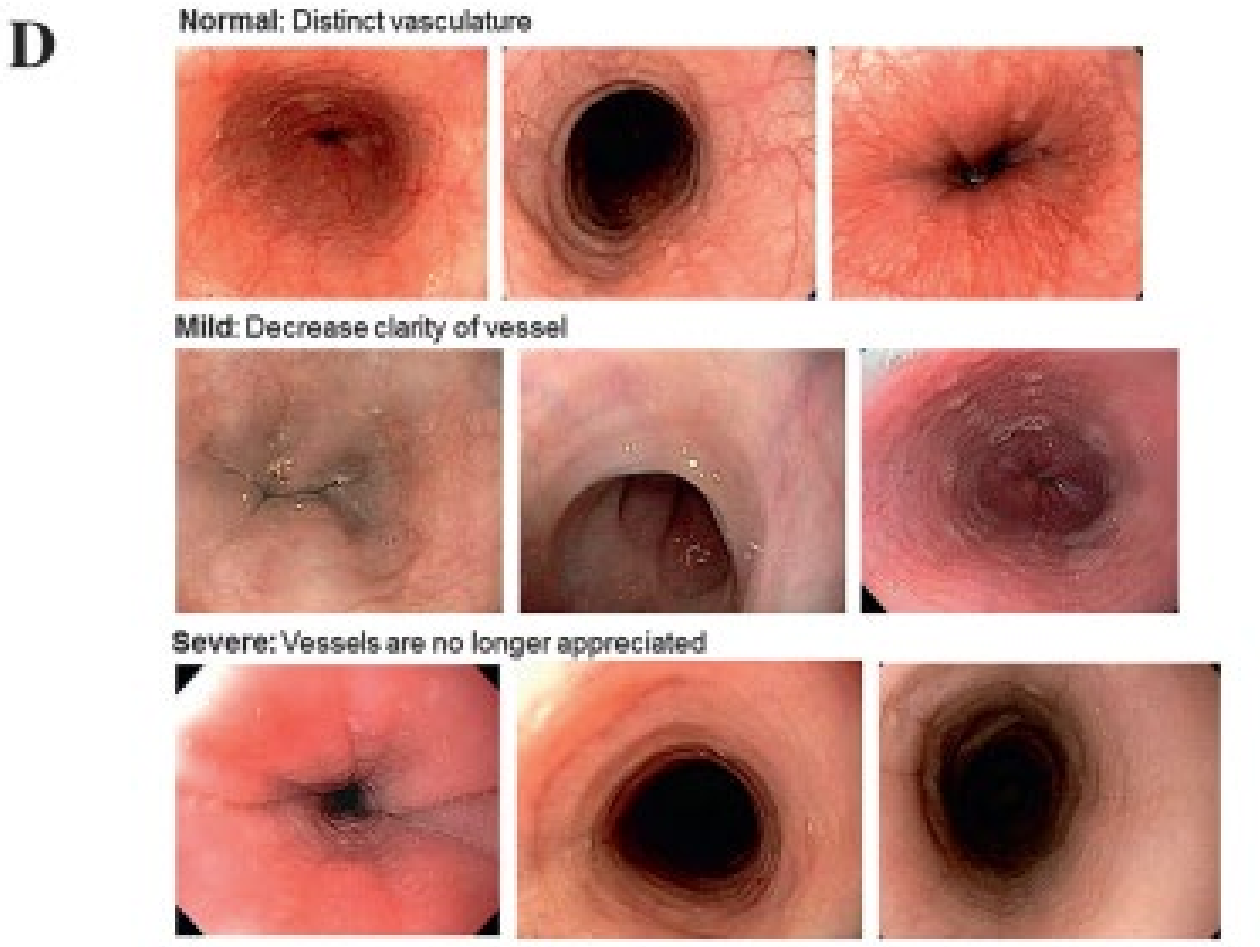
Hirano et al. Gut, 2012.

Furrows (vertical lines)



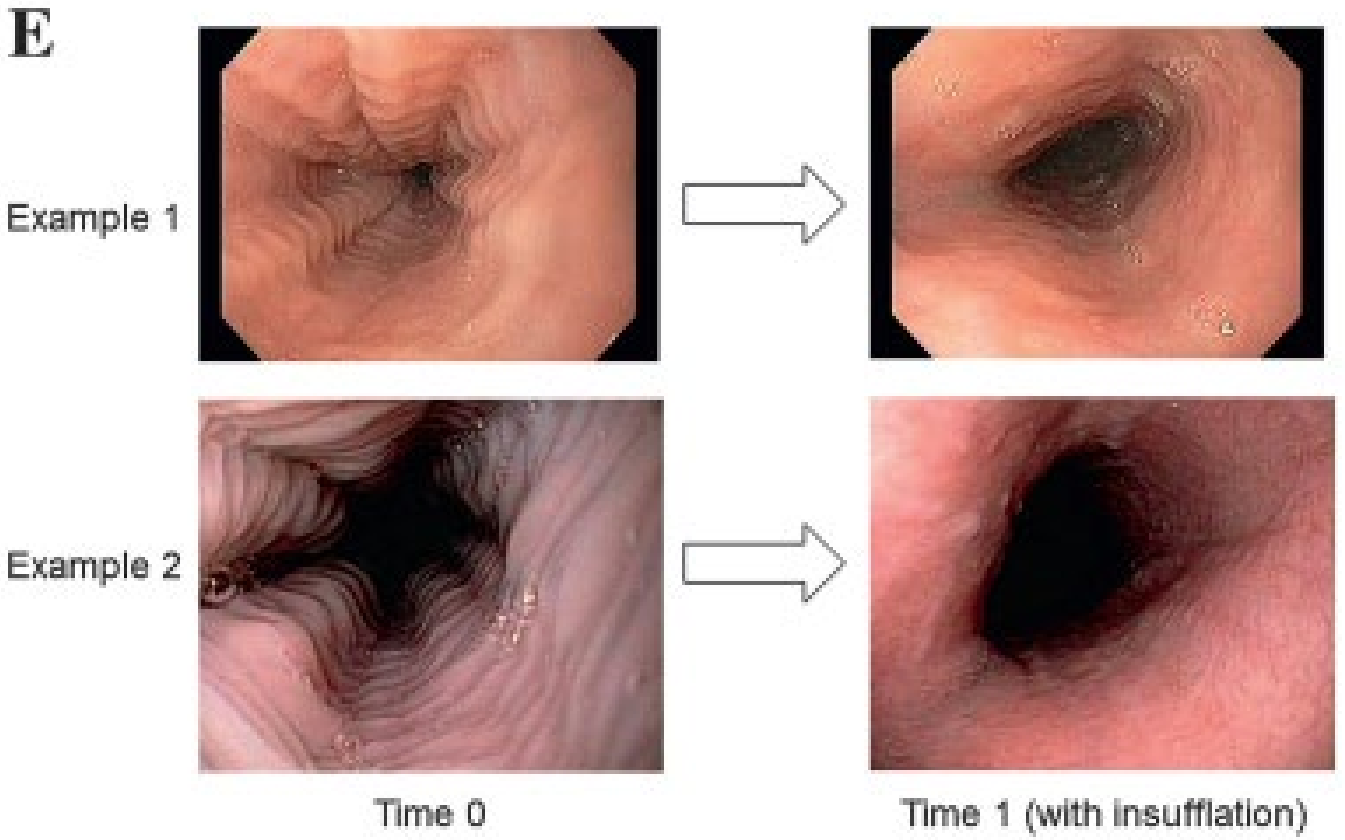
Hirano et al. Gut, 2012.

Edema



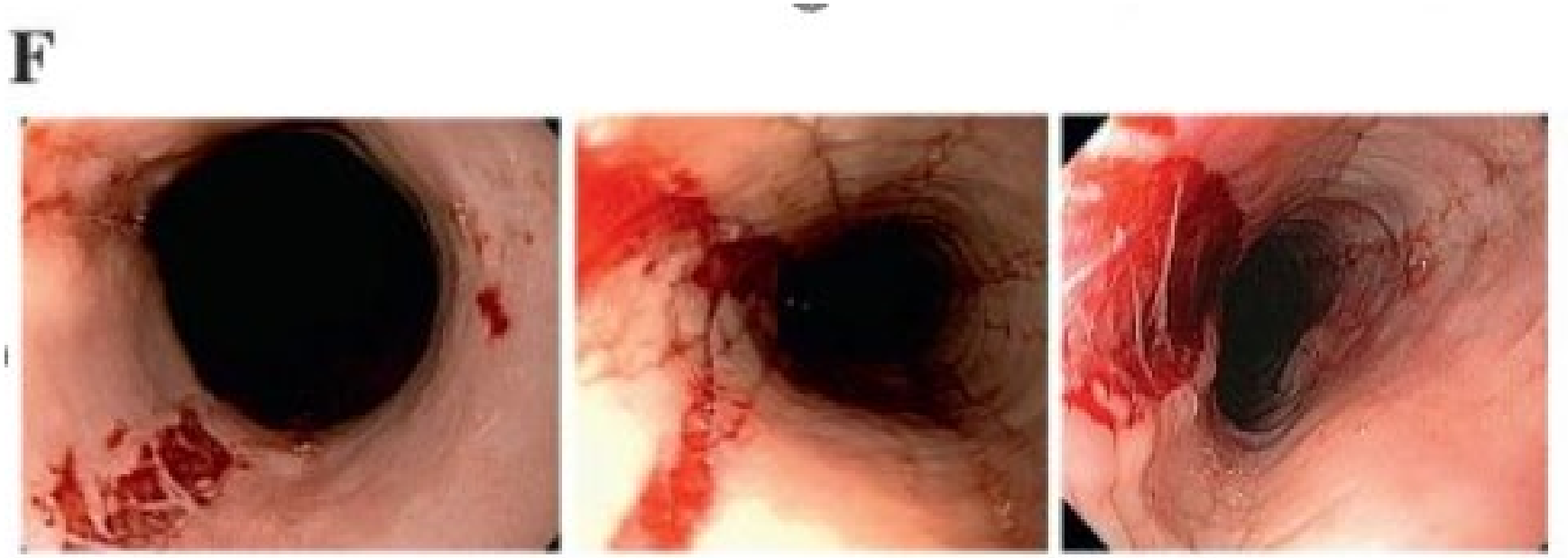
Hirano et al. Gut, 2012.

Transient Esophageal Rings (feline esophagus)



Hirano et al. Gut, 2012.

Crepe Paper Esophagus (friability)



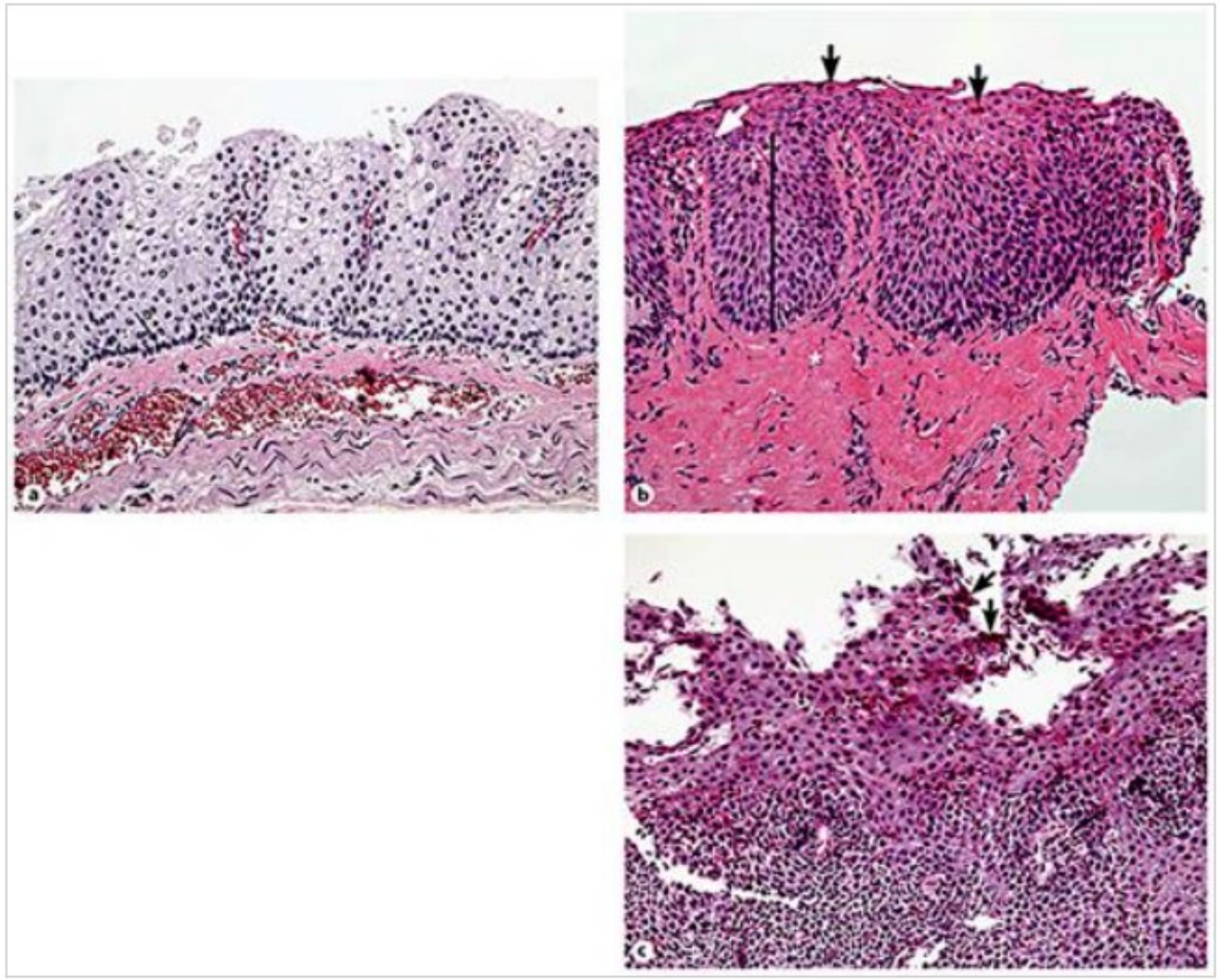
Hirano et al. Gut, 2012.

Endoscopic Evaluation

- ASGE Guidelines:
  - Take at least 6 biopsies from the esophagus
  - Biopsies should be taken from the distal and proximal esophagus
  - In a patient with suspected EoE, biopsy samples should be obtained from the esophagus regardless of endoscopic appearance
  - Should also take biopsies of the duodenum and stomach to assess for eosinophilic gastroenteritis at index endoscopy
  - Esophageal biopsies should be taken at the time of food impaction

Aceves et al. Gastrointestinal Endoscopy, 2022.

Histology



Collins. Digestive Diseases, 2014.

Other Causes of Esophageal Eosinophilia

Table 3:

Conditions associated with esophageal eosinophilia

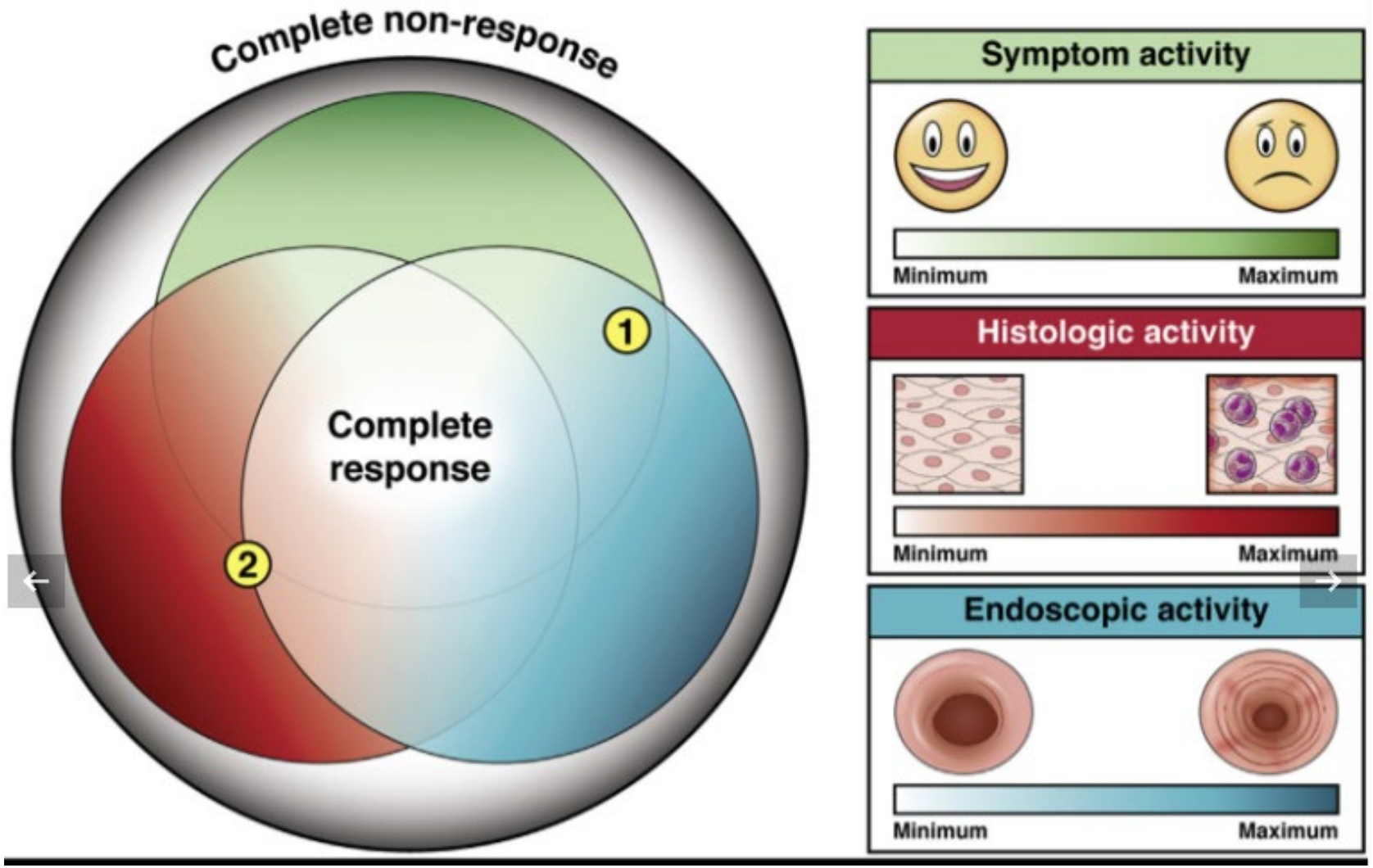
- Eosinophilic esophagitis
- Eosinophilic gastritis, gastroenteritis, or colitis with esophageal involvement
- Gastroesophageal reflux disease
- Achalasia and other disorders of esophageal dysmotility
- Hypereosinophilic syndrome
- Crohn's disease with esophageal involvement
- Infections (fungal, viral)
- Connective tissue disorders
- Hypermobility syndromes
- Autoimmune disorders and vasculitides
- Dermatologic conditions with esophageal involvement (i.e. pemphigus)
- Drug hypersensitivity reactions
- Pill esophagitis
- Graft vs host disease
- Mendelian disorders (Marfan Syndrome Type II, Hyper-IgE Syndrome, PTEN Hamartoma Tumor Syndrome, Netherton's Syndrome, Severe Atopy Metabolic Wasting Syndrome)

Dellon et al. Gastroenterology, 2018.

So how do we treat it?

- Diet:
  - Elemental diet, elimination diets
- Pharmacologic:
  - Proton pump inhibitors
  - Steroids: swallowed/topical or systemic
  - Biologics
- Endoscopic:
  - Dilation

Goals of therapy



Hirano et al. Gastroenterology, 2020.

Diet

- Elemental Diet
- Six Food Elimination Diet (SFED)
  - milk protein, soy, eggs, wheat, peanuts/tree nuts, and seafood
- Targeted Elimination
  - Skin and allergy testing

Gastroenterology 2014;146:1639–1648

CLINICAL—ALIMENTARY TRACT

Efficacy of Dietary Interventions for Inducing Histologic Remission in Patients With Eosinophilic Esophagitis: A Systematic Review and Meta-analysis

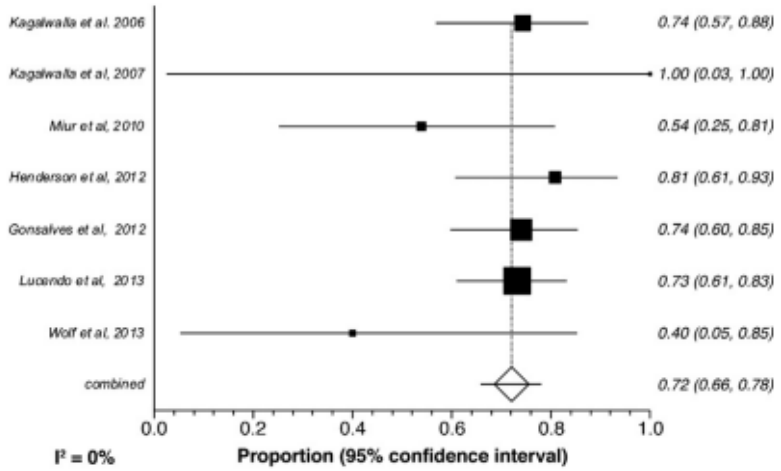
Ángel Arias,[1] Jesús González-Cervera,[2] José M. Tenias,[1] and Alfredo J. Lucendo[3]

[1]Research Unit, Complejo Hospitalario La Mancha Centro, Alcázar de San Juan, Ciudad Real, Spain; [2]Department of Allergy, Hospital General de Tomelloso, Tomelloso, Ciudad Real, Spain; and [3]Department of Gastroenterology, Hospital General de Tomelloso, Tomelloso, Ciudad Real, Spain

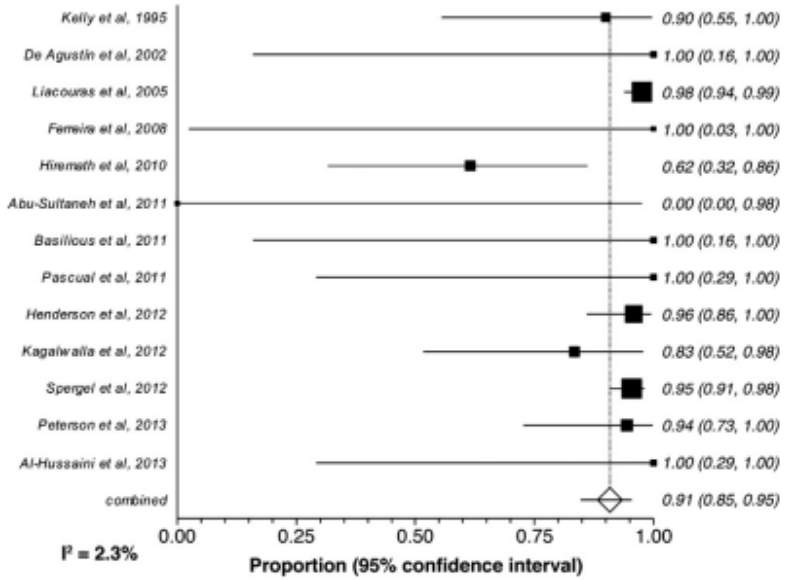
Arias et al. Gastroenterology, 2014.

Diet

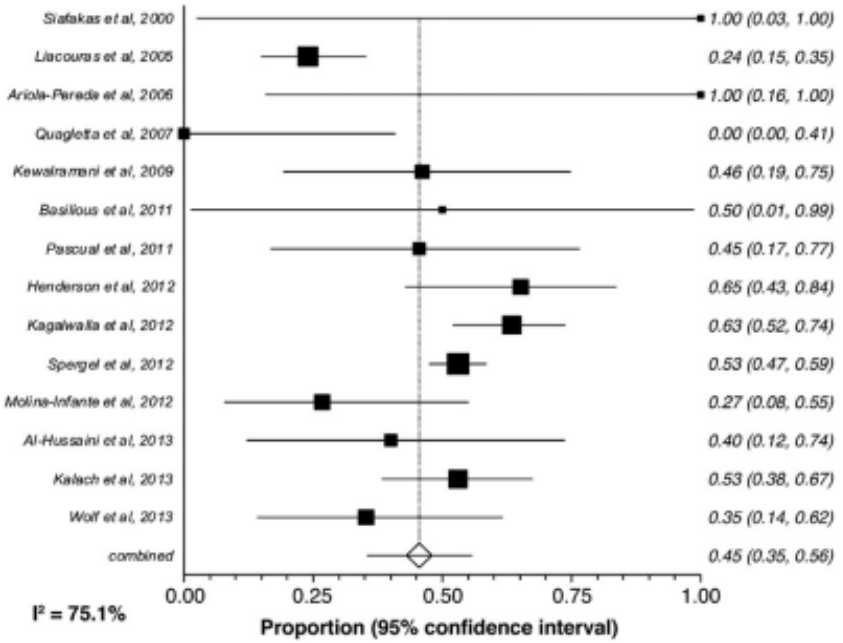
Six Food Elimination Diet- 72%



Elemental Diet- 91%



Targeted Elimination Diet- 46%



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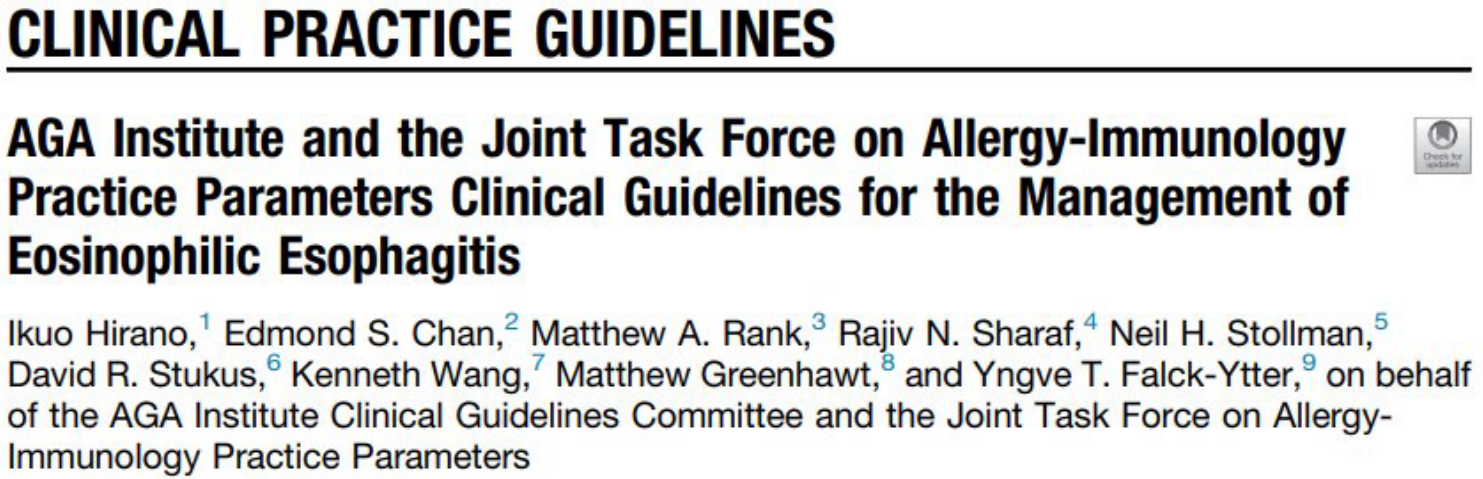
Arias et al. Gastroenterology, 2014.

So what do the guidelines say?

- Suggest elemental diet over no treatment
- Suggest empiric SFED over no treatment
- Suggest allergy-based testing over no treatment



CLINICAL PRACTICE GUIDELINES

AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis

Ikuo Hirano,[1] Edmond S. Chan,[2] Matthew A. Rank,[3] Rajiv N. Sharaf,[4] Neil H. Stollman,[5] David R. Stukus,[6] Kenneth Wang,[7] Matthew Greenhawt,[8] and Yngve T. Falck-Ytter,[9] on behalf of the AGA Institute Clinical Guidelines Committee and the Joint Task Force on Allergy-Immunology Practice Parameters

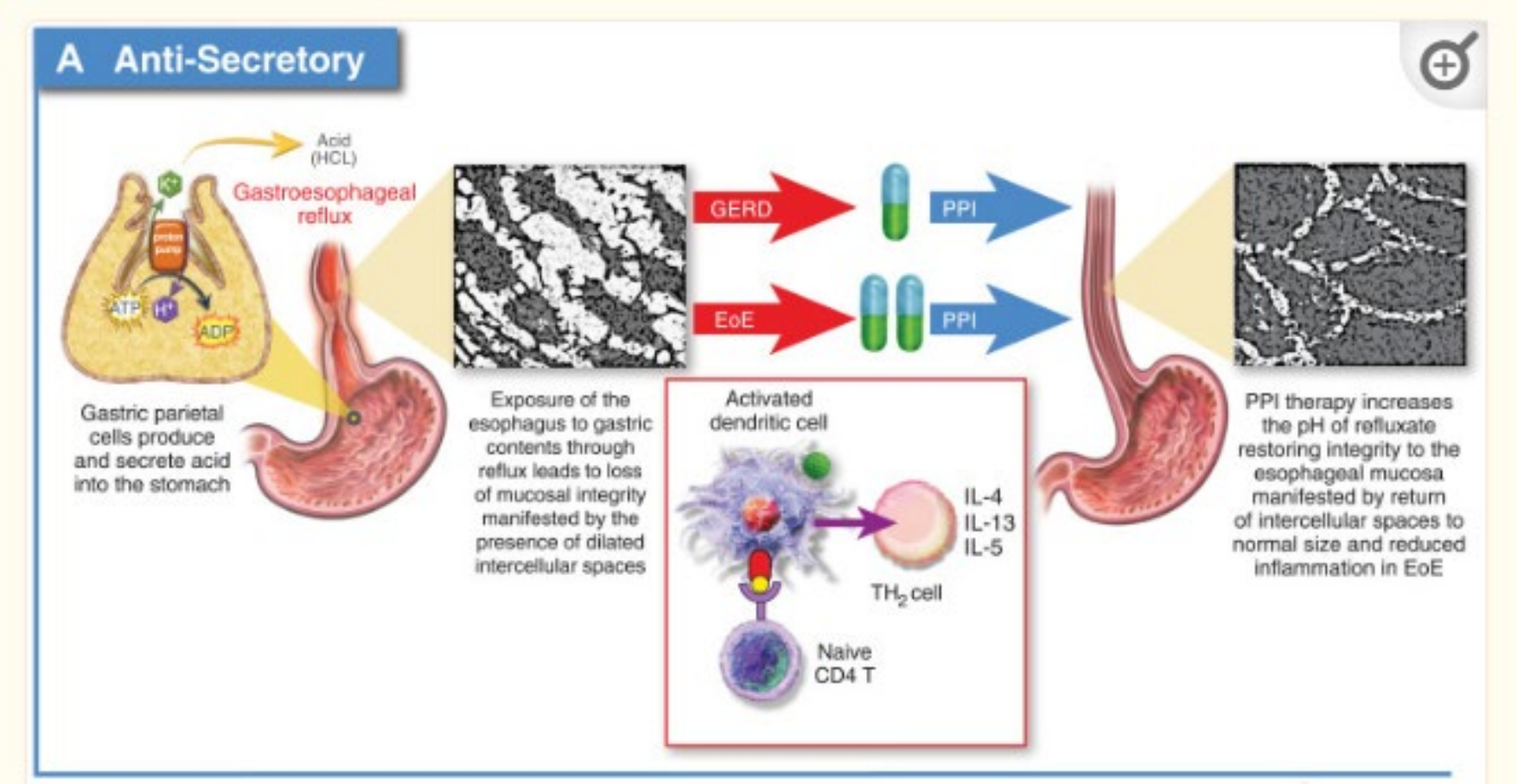
Hirano et al. Gastroenteroogy, May 2020.

Pharmacologic therapy

- Proton pump inhibitors
  - No longer used as part of the diagnostic criteria for EoE (formerly PPI-responsive EoE)
  - Now used as first line therapy
    - Consider BID dosing and wean as tolerated

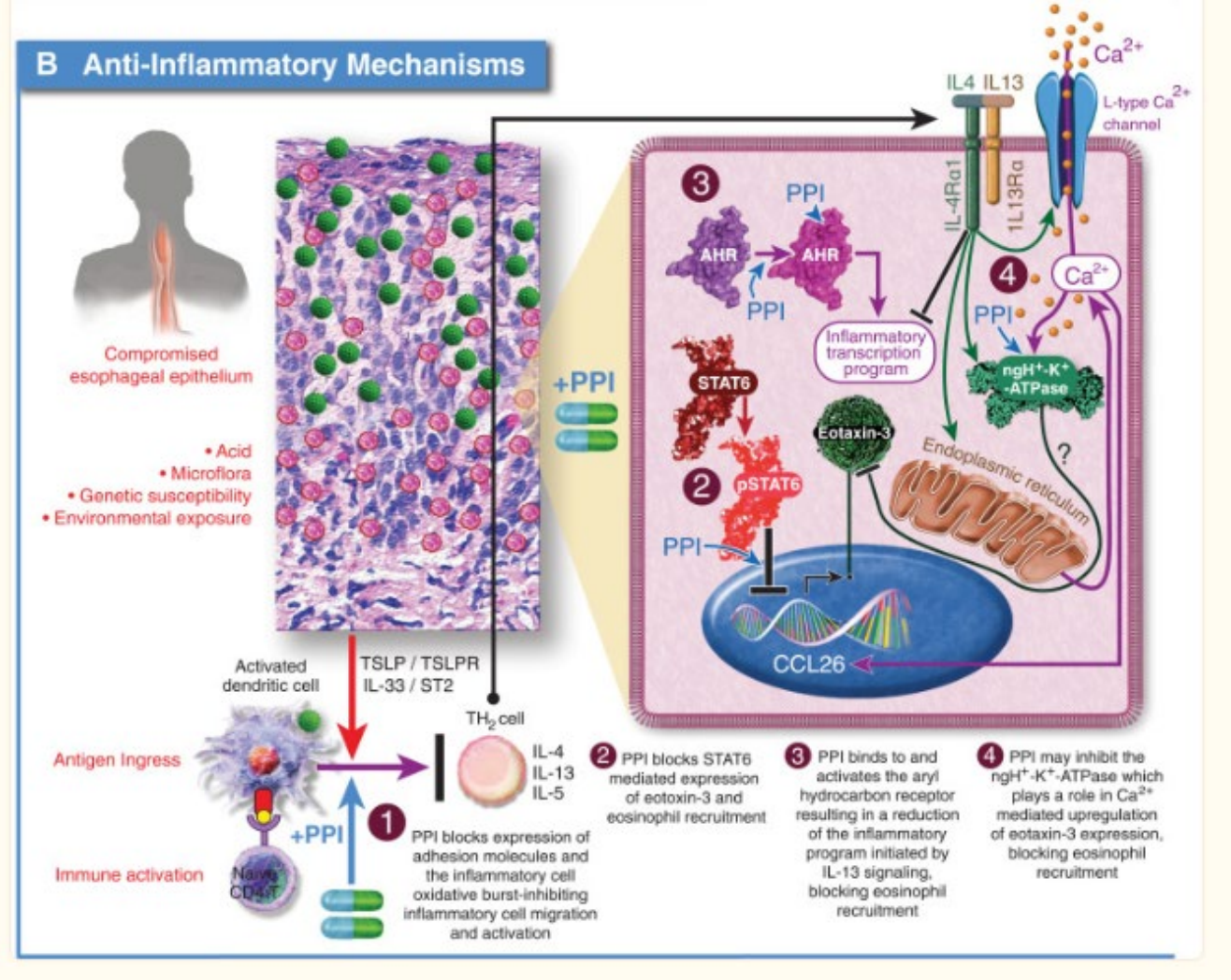
Hirano et al. Gastroenterology, May 2020.

PPI Mechanism of Action



Franciosi et al. Journal of Allergy and Asthma. 2022

PPI Mechanism of Action



Franciosi et al. Journal of Allergy and Asthma. 2022

Steroids

- AGA guidelines recommend topical steroids:
  - Eight double-blind placebo-controlled studies: compared budesonide or topical fluticasone to placebo x 8 weeks
- Recent FDA approval for budesonide formulation

Table 1

Doses of STS recommended in EoE.

Drug	Phase of Treatment	Children	Adults
Budesonide	Induction	1–2 mg/day	2–4 mg/day
	Maintenance	1 mg/day	2 mg/day
Fluticasone propionate	Induction	880–1760 mcg/day	1760 mcg/day
	Maintenance	440–880 mcg/day	880–1760 mcg/day

Glowczewski et al. Journal of Clinical Medicine, 2022.

Oral Budesonide

A Study in Adolescents and Adults With Eosinophilic Esophagitis (EoE) Measuring Histologic Response and Determine if Reduction in Dysphagia is Achieved

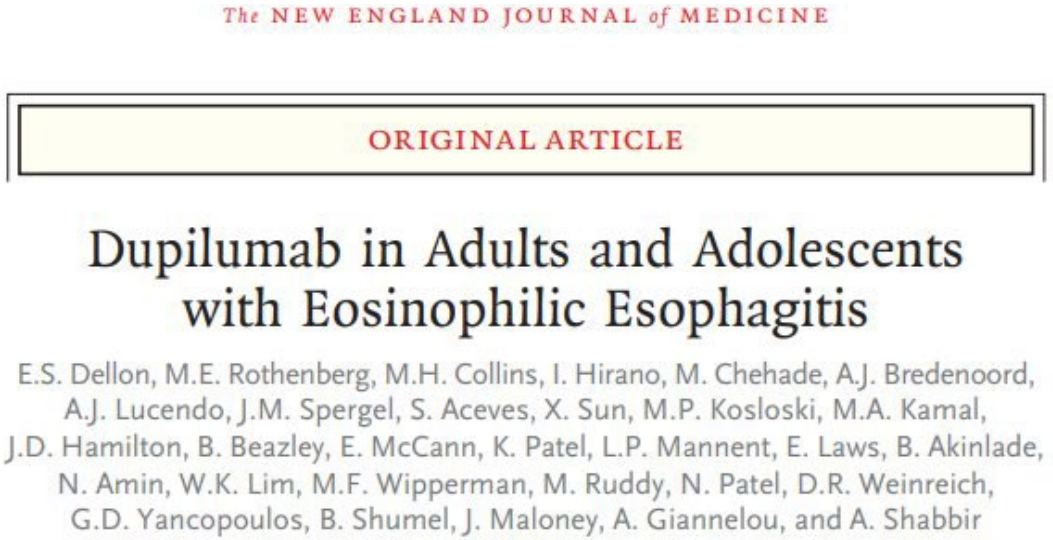
ClinicalTrials.gov Identifier: NCT02605837

OBS in Adolescent and Adults With EOE: A Phase II, Randomized, Double-Blind, Placebo Controlled, Study With an Open Label Extension

ClinicalTrials.gov ID NCT01642212

Gastroenterology and Endoscopy News, 2024.

Dupilumab


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dupilumab in Adults and Adolescents with Eosinophilic Esophagitis

E.S. Dellon, M.E. Rothenberg, M.H. Collins, I. Hirano, M. Chehade, A.J. Bredenoord, A.J. Lucendo, J.M. Spergel, S. Aceves, X. Sun, M.P. Kosloski, M.A. Kamal, J.D. Hamilton, B. Beazley, E. McCann, K. Patel, L.P. Mannent, E. Laws, B. Akinlade, N. Amin, W.K. Lim, M.F. Wipperman, M. Ruddy, N. Patel, D.R. Weinreich, G.D. Yancopoulos, B. Shumel, J. Maloney, A. Giannelou, and A. Shabbir

- Initially approved for atopic conditions: asthma, atopic dermatitis
- Inhibition of IL-4 and IL-13 cytokines:
  - Important in inflammation driven by T-Helper type 2 cells
- Dosing 300 mg subQ weekly
- Usually reserved for those who have failed other treatment options

Dellon et al. NEJM, 2022.

Dupilumab

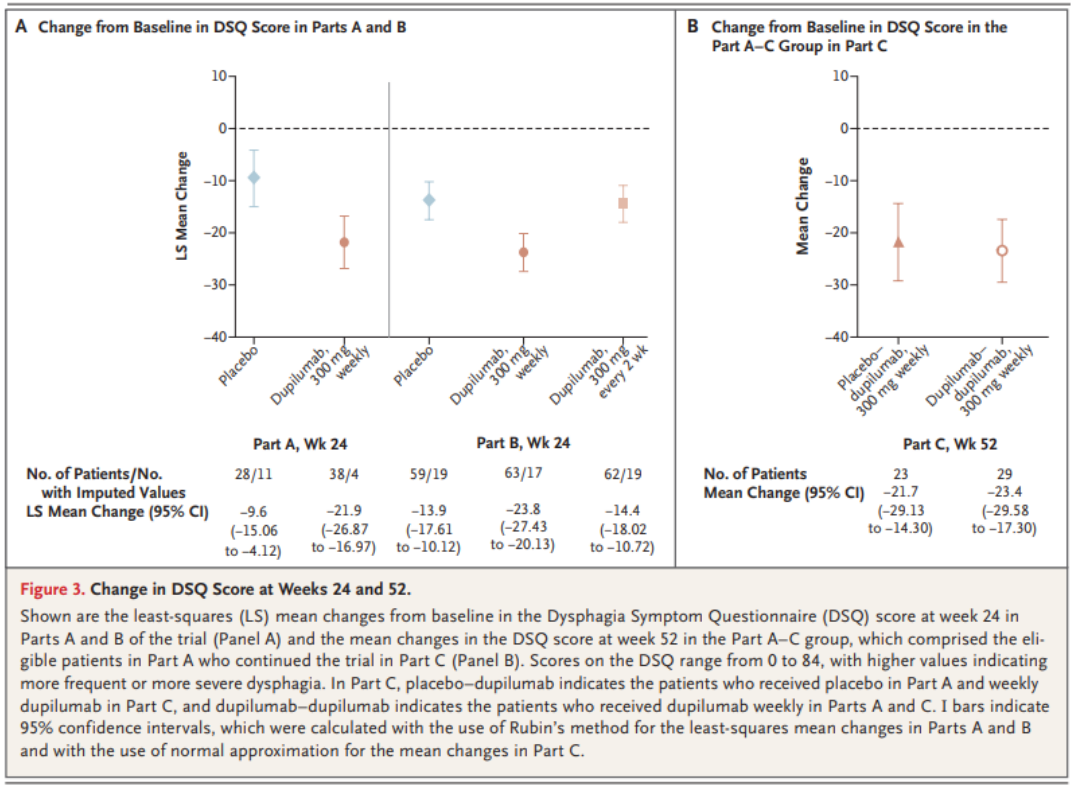


Figure 3. Change in DSQ Score at Weeks 24 and 52.

Shown are the least-squares (LS) mean changes from baseline in the Dysphagia Symptom Questionnaire (DSQ) score at week 24 in Parts A and B of the trial (Panel A) and the mean changes in the DSQ score at week 52 in the Part A–C group, which comprised the eligible patients in Part A who continued the trial in Part C (Panel B). Scores on the DSQ range from 0 to 84, with higher values indicating more frequent or more severe dysphagia. In Part C, placebo–dupilumab indicates the patients who received placebo in Part A and weekly dupilumab in Part C, and dupilumab–dupilumab indicates the patients who received dupilumab weekly in Parts A and C. I bars indicate 95% confidence intervals, which were calculated with the use of Rubin's method for the least-squares mean changes in Parts A and B and with the use of normal approximation for the mean changes in Part C.

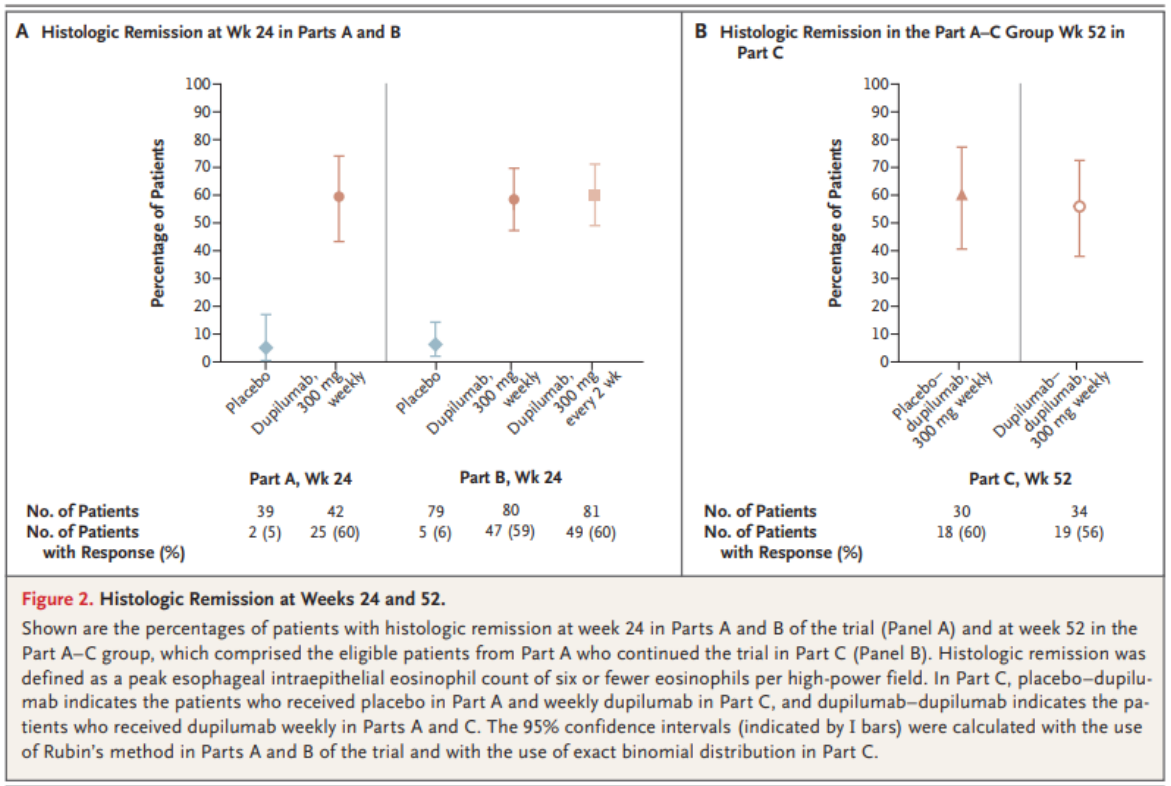


Figure 2. Histologic Remission at Weeks 24 and 52.

Shown are the percentages of patients with histologic remission at week 24 in Parts A and B of the trial (Panel A) and at week 52 in the Part A–C group, which comprised the eligible patients from Part A who continued the trial in Part C (Panel B). Histologic remission was defined as a peak esophageal intraepithelial eosinophil count of six or fewer eosinophils per high-power field. In Part C, placebo–dupilumab indicates the patients who received placebo in Part A and weekly dupilumab in Part C, and dupilumab–dupilumab indicates the patients who received dupilumab weekly in Parts A and C. The 95% confidence intervals (indicated by I bars) were calculated with the use of Rubin's method in Parts A and B of the trial and with the use of exact binomial distribution in Part C.

Dellon et al. NEJM, 2022.

Dupilumab

Table 2. Incidence of Adverse Events during the Treatment Period (Safety Analysis Set).*

Event	Part A		Part B			Part A–C Group in Part C	
	Dupilumab, 300 mg weekly (N=42)	Placebo (N=39)	Dupilumab, 300 mg weekly (N=80)	Dupilumab, 300 mg every 2 wk (N=81)	Placebo (N=78)	Dupilumab–dupilumab (N=40)	Placebo–dupilumab (N=37)
	number of patients (percent)						
Deaths	0	0	0	0	0	0	0
Adverse event	36 (86)	32 (82)	67 (84)	63 (78)	55 (71)	24 (60)	27 (73)
Serious adverse event†	2 (5)	0	5 (6)	1 (1)	1 (1)	0	1 (3)
Adverse event leading to discontinuation†	1 (2)	0	2 (2)	2 (2)	2 (3)	0	2 (5)
Adverse event occurring in ≥10% of patients in any group‡							
Injection-site reaction	7 (17)	4 (10)	16 (20)	18 (22)	16 (21)	4 (10)	8 (22)
Injection-site erythema	3 (7)	5 (13)	8 (10)	18 (22)	9 (12)	4 (10)	5 (14)
Injection-site pain	4 (10)	3 (8)	7 (9)	10 (12)	4 (5)	2 (5)	3 (8)
Injection-site swelling	3 (7)	1 (3)	10 (12)	7 (9)	2 (3)	2 (5)	0
Nasopharyngitis	5 (12)	4 (10)	2 (2)	4 (5)	3 (4)	1 (2)	3 (8)
Headache	2 (5)	4 (10)	6 (8)	5 (6)	9 (12)	3 (8)	2 (5)
Acne	0	1 (3)	0	2 (2)	3 (4)	0	4 (11)
Rash	0	4 (10)	2 (2)	4 (5)	0	1 (2)	0

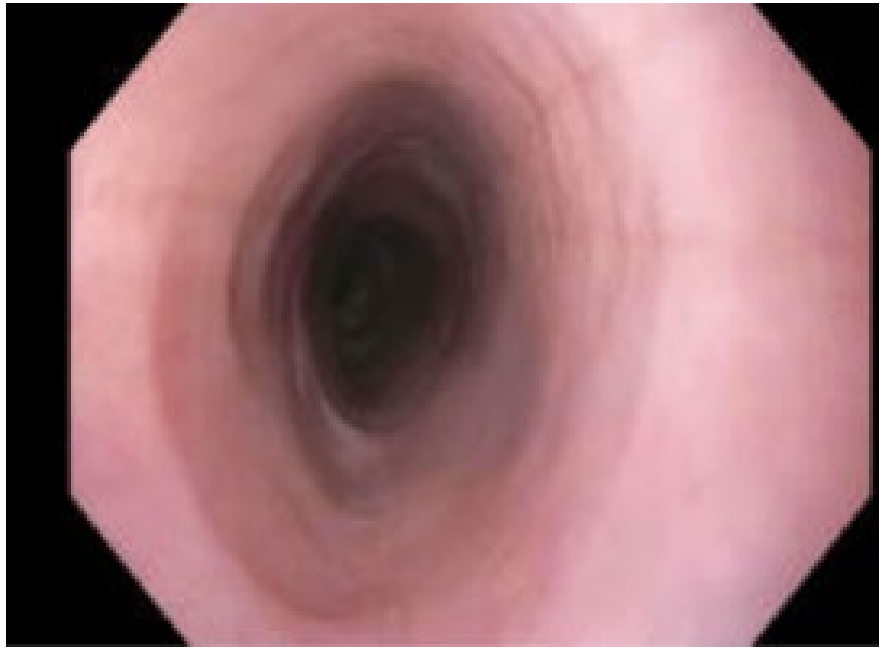
Dellon et al. NEJM, 2022.

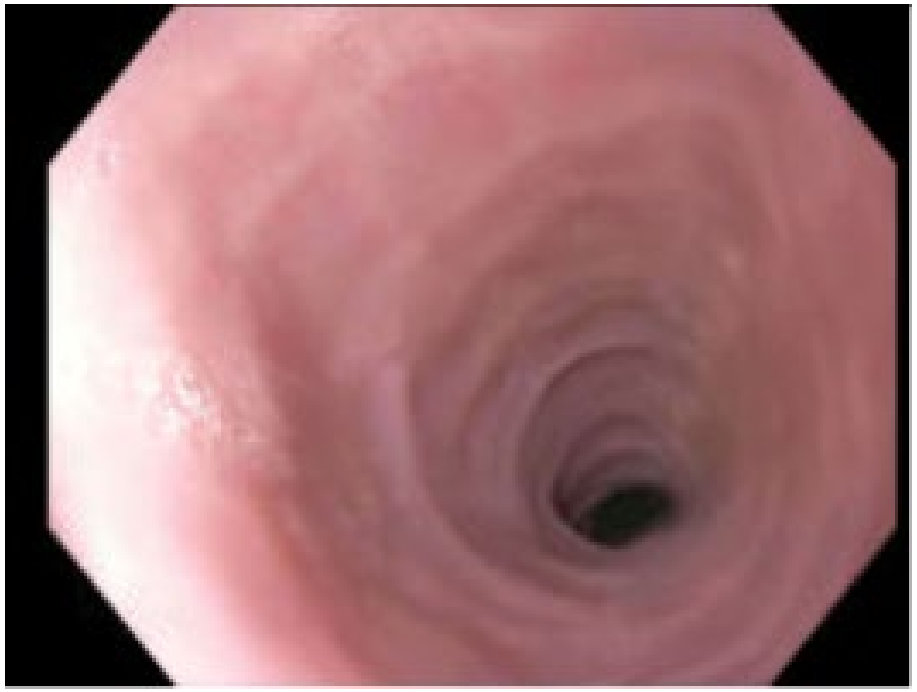
Endoscopic Dilation

- Endoscopic dilation can be considered for all patients with EoE and an esophageal stricture with dysphagia
  - Fibrostentotic versus inflammatory disease
- Goal of treatment is mucosal disruption
- Luminal diameter goal is 16 mm- may take a few sessions
- Important to control inflammation to decrease need for further dilations
- Dilation is considered safe in patients with inflammation and EoE

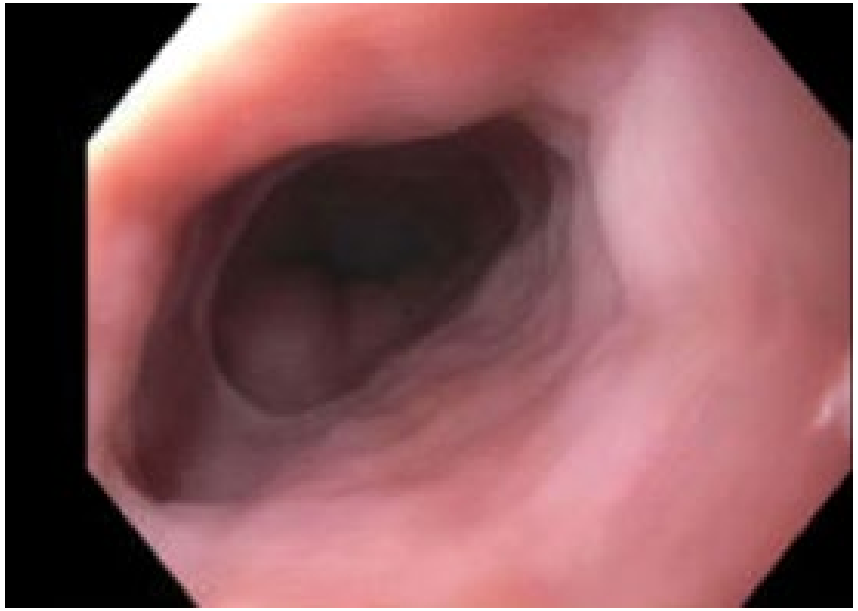
Aceves et al. Gastrointestinal Endoscopy, 2022.

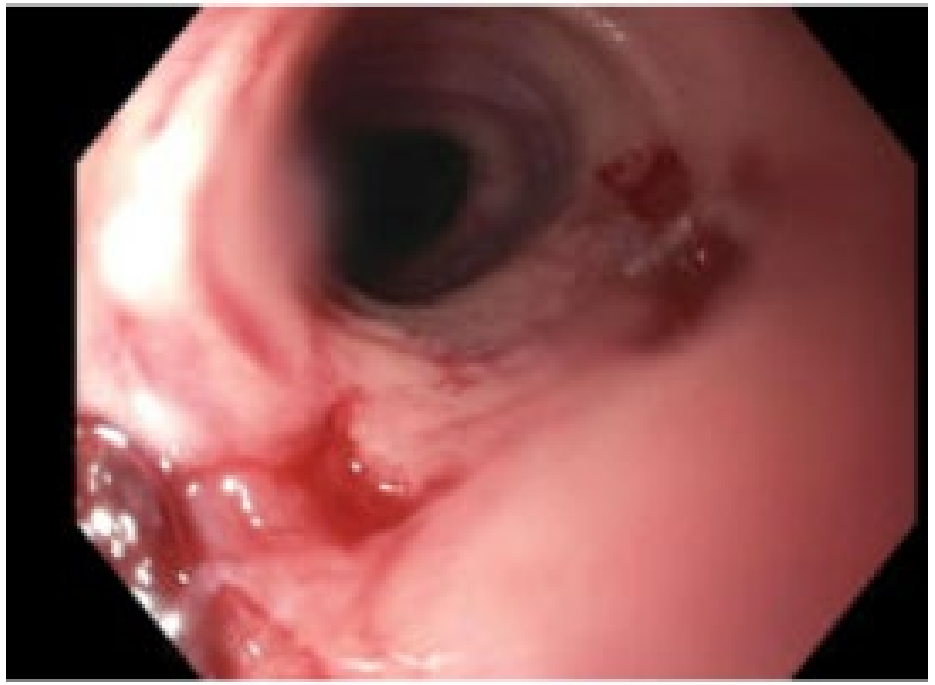
2 weeks later



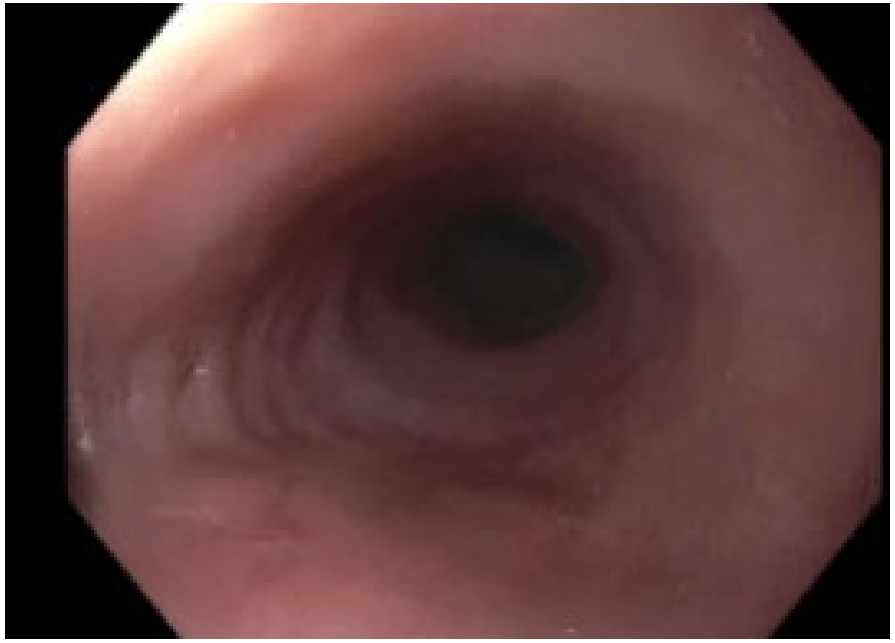


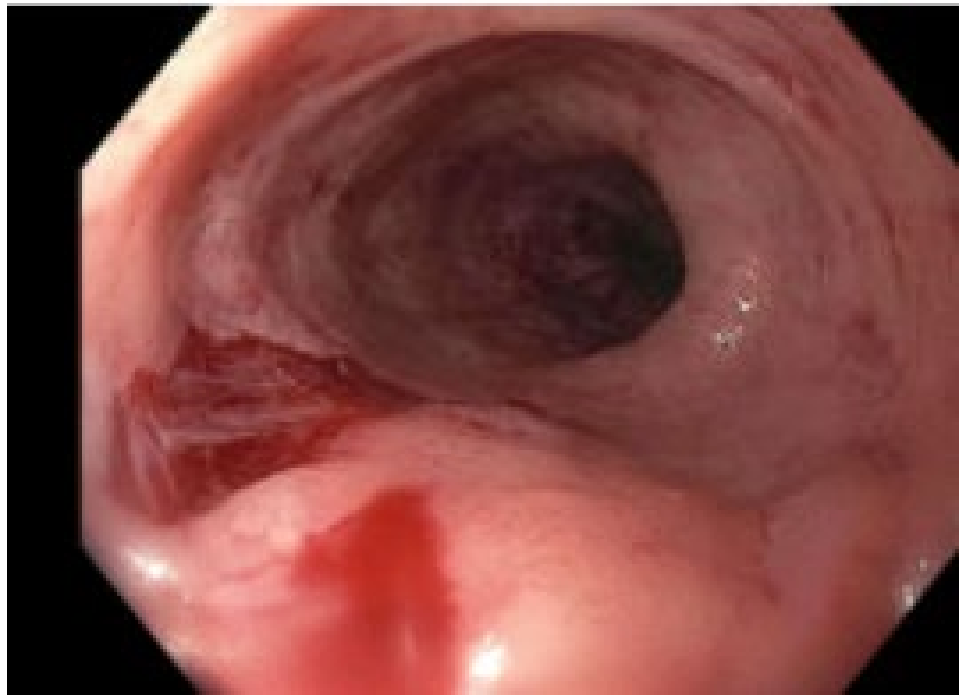
…2 More Weeks





… and yet another 2 weeks





Take Home Points

- The diagnosis of EoE is based on symptoms, endoscopic appearance, and histologic confirmation
- Use EREFS scoring system at the time of diagnosis to establish baseline and subsequently to evaluate response to therapy
- Diet, pharmacologic therapy, and endoscopic dilation are the mainstays of therapy

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