

EoE Diagnosis

CDDW

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Conflict of Interest Disclosure

(over the past 24 months)

Advisory Board for Avir Pharma

CanMEDS Roles Covered

	Medical Expert (as <i>Medical Experts</i> , physicians integrate all of the CanMEDS Roles, applying medical knowledge, clinical skills, and professional values in their provision of high-quality and safe patient-centered care. <i>Medical Expert</i> is the central physician Role in the CanMEDS Framework and defines the physician's clinical scope of practice.)
	Communicator (as <i>Communicators</i> , physicians form relationships with patients and their families that facilitate the gathering and sharing of essential information for effective health care.)
	Collaborator (as <i>Collaborators</i> , physicians work effectively with other health care professionals to provide safe, high-quality, patient-centred care.)
	Leader (as <i>Leaders</i> , physicians engage with others to contribute to a vision of a high-quality health care system and take responsibility for the delivery of excellent patient care through their activities as clinicians, administrators, scholars, or teachers.)
	Health Advocate (as <i>Health Advocates</i> , physicians contribute their expertise and influence as they work with communities or patient populations to improve health. They work with those they serve to determine and understand needs, speak on behalf of others when required, and support the mobilization of resources to effect change.)
	Scholar (as <i>Scholars</i> , physicians demonstrate a lifelong commitment to excellence in practice through continuous learning and by teaching others, evaluating evidence, and contributing to scholarship.)
	Professional (as <i>Professionals</i> , physicians are committed to the health and well-being of individual patients and society through ethical practice, high personal standards of behaviour, accountability to the profession and society, physician-led regulation, and maintenance of personal health.)

Objectives

- How has the diagnostic criteria for EoE changed?
 - AGREE 2018
 - Understand some of the rationale for changes
- What advances have been made with regards to non / less invasive ways to diagnose EoE

Journey through time



AGA INSTITUTE

Eosinophilic Esophagitis in Children and Adults: A Systematic Review and Consensus Recommendations for Diagnosis and Treatment

Sponsored by the American Gastroenterological Association (AGA) Institute and North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition

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PHIL E. PUTNAM,# PETER BONIS,** ERIC HASSALL,†† ALEX STRAUMANN,§§ MARC E. ROTHENBERG,||| and Members
of the First International Gastrointestinal Eosinophil Research Symposium (FIGERS) Subcommittees##

Furuta GT, Liacouras CA, Collins MH, et al. Eosinophilic esophagitis in children and adults: a systematic review and consensus recommendations for diagnosis and treatment. *Gastroenterology*. 2007 Oct;133(4):1342-63.

2007:

- Clinicopathological disorder characterized by esophageal eosinophilia
- Ruling out other causes of Esophageal eosinophilia

Table 1. Differential Diagnosis of Esophageal Eosinophilia

Gastroesophageal reflux disease

Eosinophilic esophagitis

Eosinophilic gastroenteritis

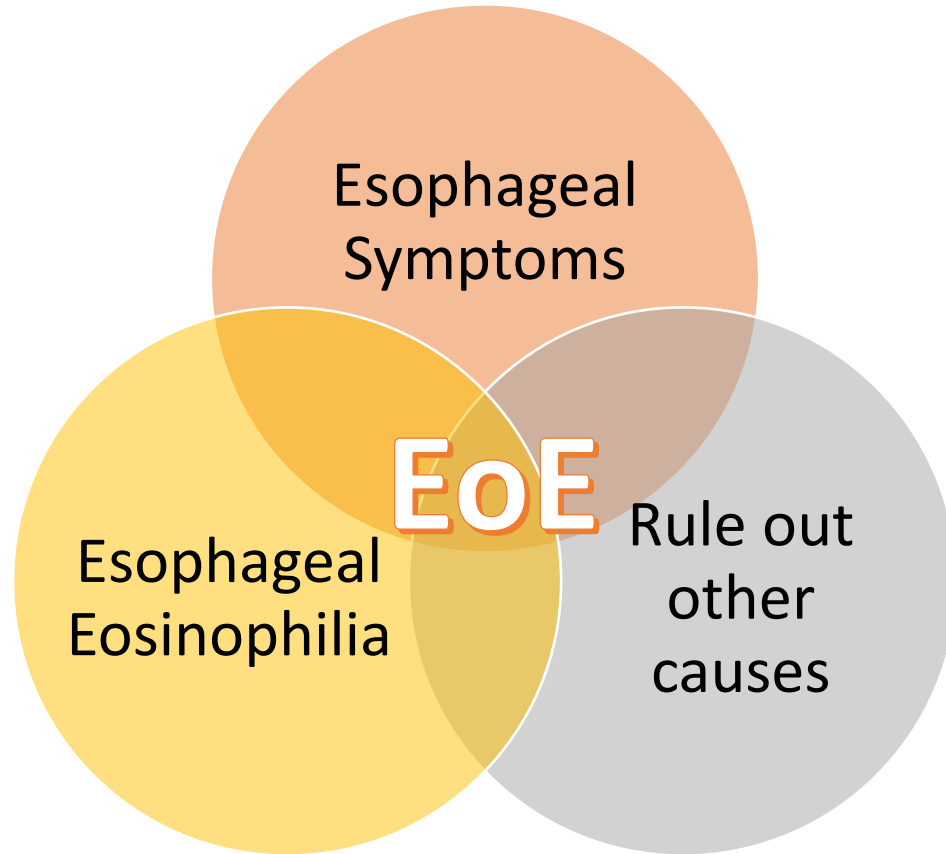
Crohn's disease

Connective tissue disease

Hypereosinophilic syndrome

Infection

Drug hypersensitivity response



2007

Table 2. Diagnostic Guidelines

Clinical symptoms of esophageal dysfunction

≥15 Eosinophils in 1 high-power field

Lack of responsiveness to high-dose proton pump inhibition (up to
2 mg/kg/day) or

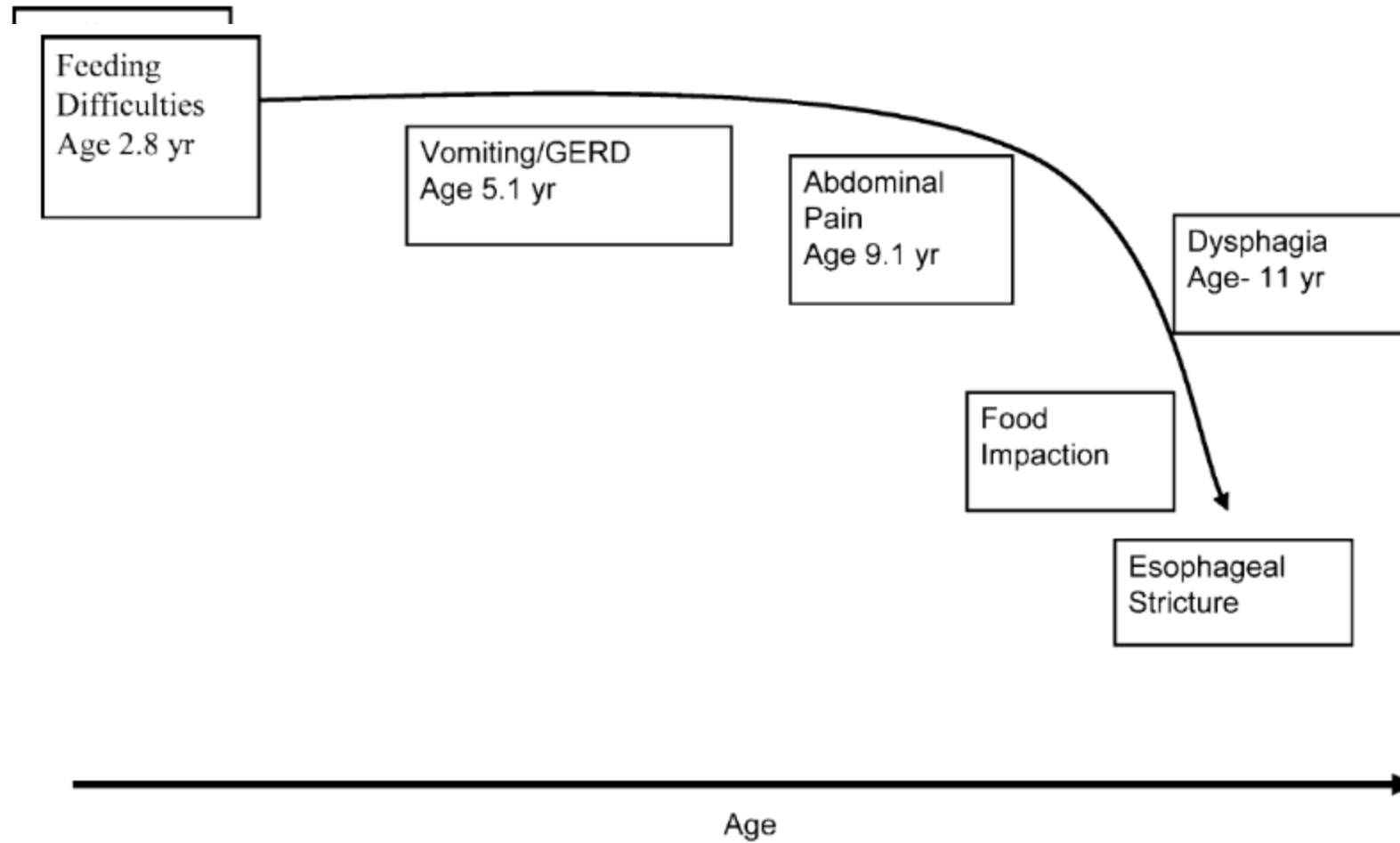
Normal pH monitoring of the distal esophagus

Clinical Symptoms

- Not a single symptom

Table 3. Symptoms Suggestive of Eosinophilic Esophagitis

Children	Adult
Feeding aversion/intolerance	Dysphagia
Vomiting/regurgitation	Food impaction
“GERD refractory to medical management”	“GERD refractory to medical management”
“GERD refractory to surgical management”	
Food impaction/foreign body impaction	
Epigastric abdominal pain	
Dysphagia	
Failure to thrive	



Spergel JM, Brown-Whitehorn TF, Beausoleil JL, et al. 14 years of eosinophilic esophagitis: clinical features and prognosis. *J Pediatr Gastroenterol Nutr.* 2009 Jan;48(1):30-6.

Diagnosis

- “Endoscopic appearance should be documented and photographed.
- “Biopsy specimens should be obtained *regardless of the gross appearance of the mucosa* and multiple biopsy specimens should be obtained from different esophageal locations along the length of the esophagus. “

Figure 1. Endoscopy findings typical of eosinophilic esophagitis: *Multiple concentric rings (white arrows), linear furrows (black arrows), and small white exudates (eosinophilic microabscesses) (circled).*

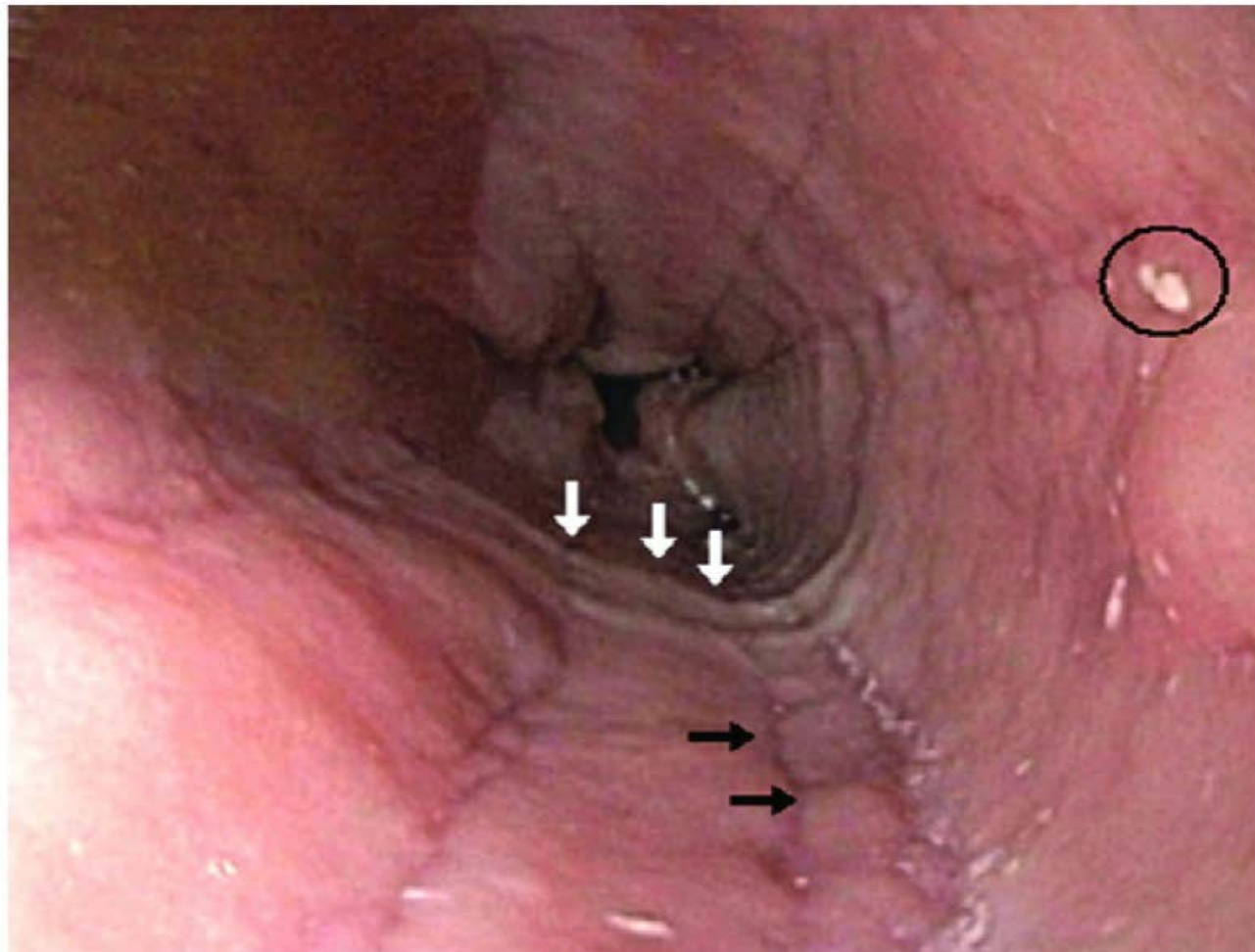


Image used with patient's permission.

Table 5. Histologic Features Associated With EE

≥15 Intraepithelial eos/HPF (peak count)

Eosinophil microabscess

Superficial layering of eosinophils

Basal zone hyperplasia

NOTE. None of the features are pathognomonic of EE.

- When the diagnosis of GERD vs EE is not apparent despite endoscopy and biopsy, **intraesophageal pH monitoring may be of use** in excluding pathologic reflux as either the primary or a concomitant cause for esophageal eosinophilia.
- Alternatively, an upper endoscopy **after 6 – 8 weeks of high-dose PPI treatment** can help determine the etiology of esophageal eosinophilia

Eosinophilic esophagitis: Updated consensus recommendations for children and adults

Chris A. Liacouras, MD, Glenn T. Furuta, MD, Ikuo Hirano, MD, Dan Atkins, MD, Stephen E. Attwood, MD, FRCS, FRCSI, MCh, Peter A. Bonis, MD, A. Wesley Burks, MD, Mirna Chehade, MD, Margaret H. Collins, MD, Evan S. Dellon, MD, MPH, Ranjan Dohil, MD, Gary W. Falk, MD, MS, Nirmala Gonsalves, MD, Sandeep K. Gupta, MD, David A. Katzka, MD, Alfredo J. Lucendo, MD, PhD, Jonathan E. Markowitz, MD, MSCE, Richard J. Noel, MD, Robert D. Odze, MD, FRCP, Philip E. Putnam, MD, FAAP, Joel E. Richter, MD, FACP, MACG, Yvonne Romero, MD, Eduardo Ruchelli, MD, Hugh A. Sampson, MD, Alain Schoepfer, MD, Nicholas J. Shaheen, MD, MPH, Scott H. Sicherer, MD, Stuart Spechler, MD, Jonathan M. Spergel, MD, PhD, Alex Straumann, MD, Barry K. Wershil, MD, Marc E. Rothenberg, MD, PhD,* and Seema S. Aceves, MD, PhD* *Aurora and Denver, Colo, Milwaukee, Wis, Cincinnati, Ohio, Rochester, Minn, Philadelphia, Pa, Basel and Lausanne, Switzerland, Chapel Hill and Durham, NC, Boston, Mass, Chicago, Ill, San Diego, Calif, New York, NY, Indianapolis, Ind, Tomelloso, Spain, Greenville, SC, and North Shields, United Kingdom*

“TIGER” = The International Gastrointestinal Eosinophil Researchers

Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. J Allergy Clin Immunol. 2011 Jul;128(1):3-20 e6; quiz 1-2.

2011

- Principal of PPI- REE
 - Proton Pump Inhibitor Responsive Esophageal Eosinophilia
 - Part of EoE, Part of Reflux, own entity?

AGREE 2018

Dellon et al.

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Updated international consensus diagnostic criteria for eosinophilic esophagitis: Proceedings of the AGREE conference

Dellon ES, Liacouras CA, Molina-Infante J, et al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. *Gastroenterology*. 2018 Oct;155(4):1022-33 e10.

AGREE 2018

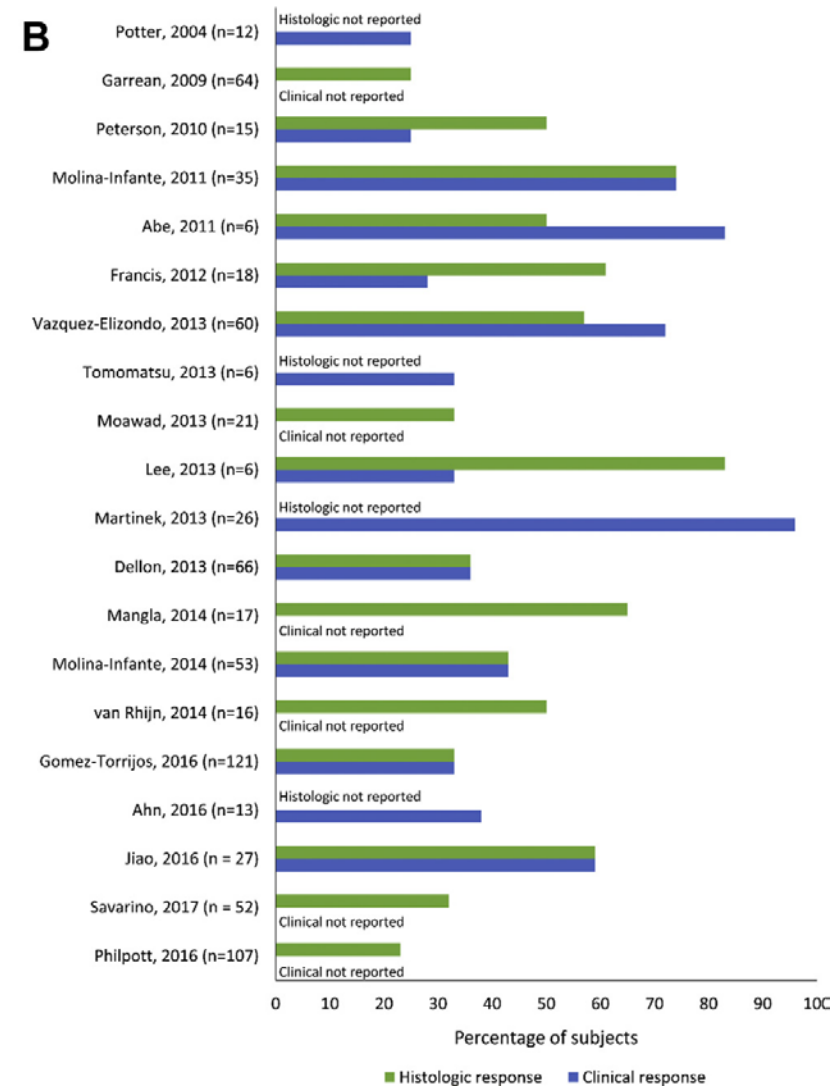
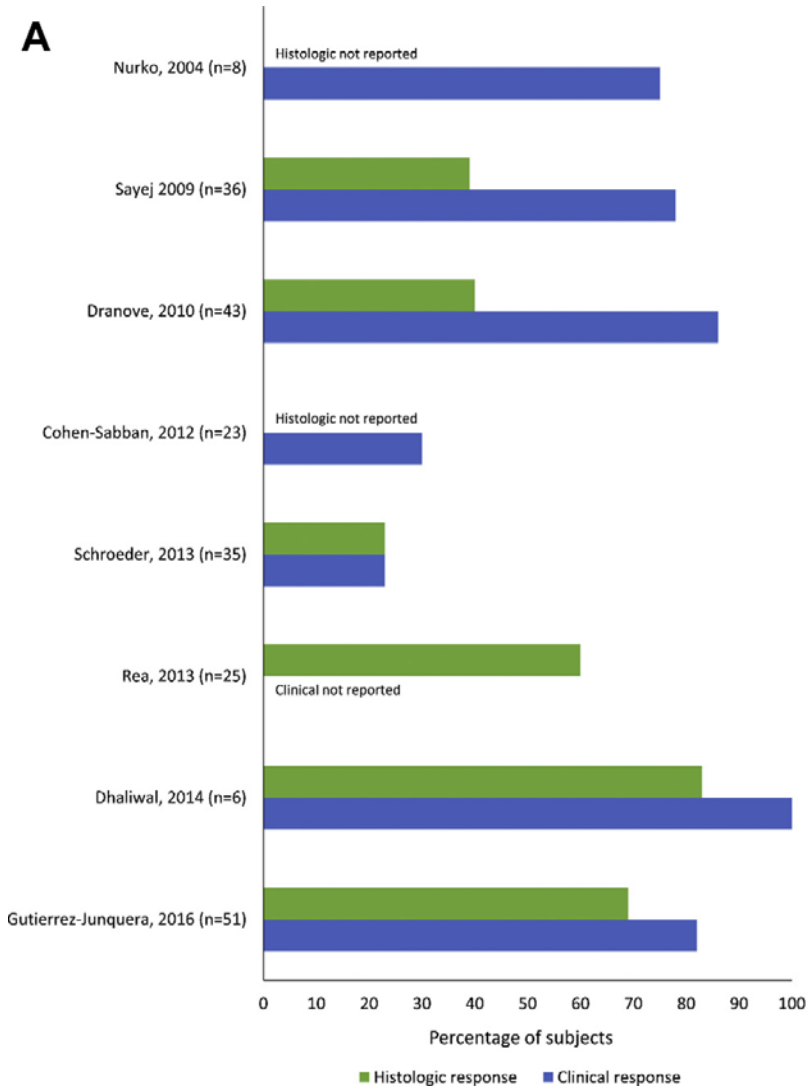
Conclusions: EoE should be diagnosed when there are symptoms of esophageal dysfunction and at least 15 eosinophils per high-power field (or ~60 eosinophils per mm²) on esophageal biopsy, and after a comprehensive assessment of non-EoE disorders that could cause or potentially contribute to esophageal eosinophilia. The evidence suggests that PPIs are better classified as a treatment for esophageal eosinophilia that may be due to EoE than as a diagnostic criterion, and we have developed updated consensus criteria for EoE that reflect this change.

Table 1:

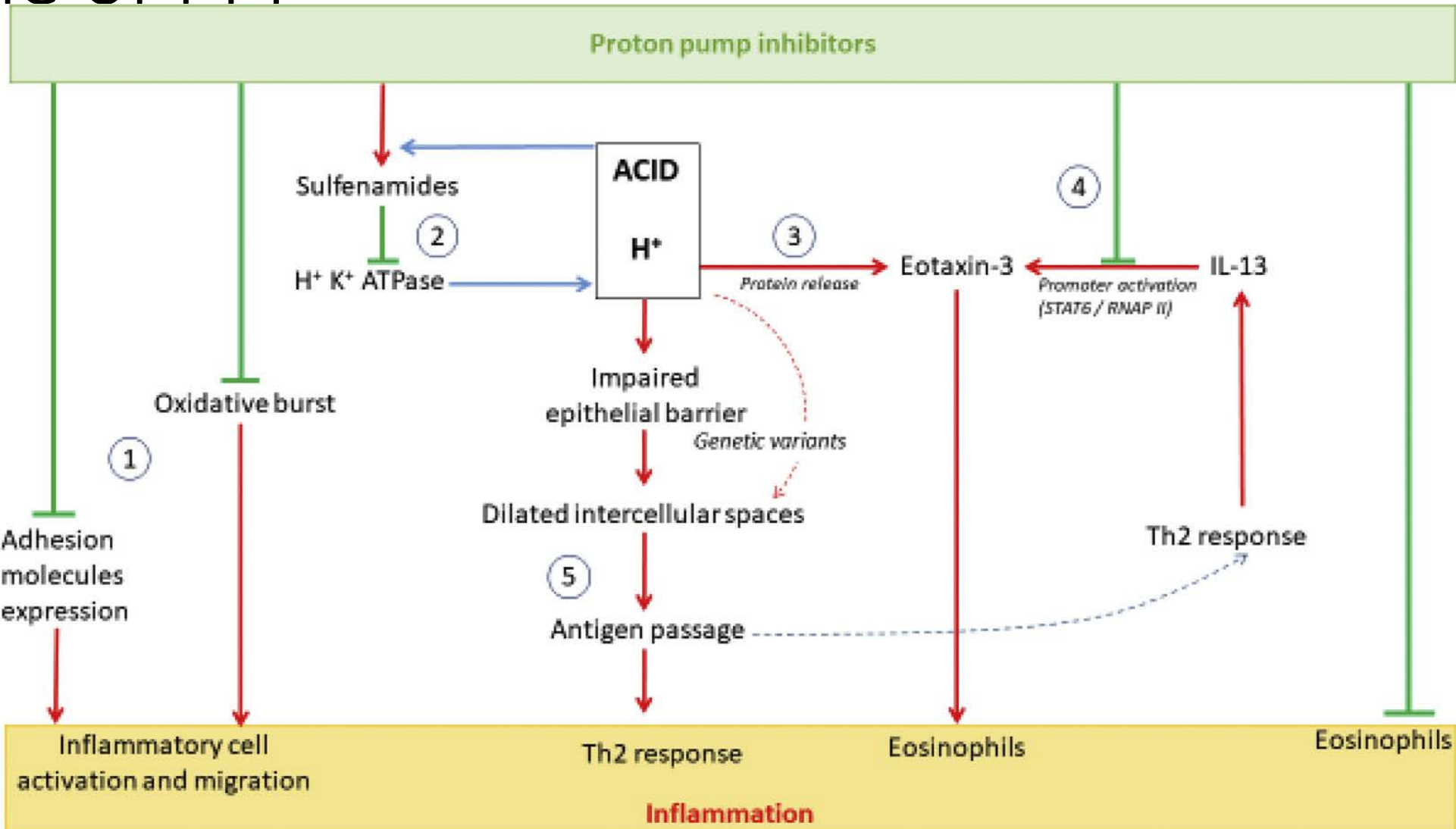
Rationale for changing the EoE diagnostic criteria and removing the PPI trial

Rationale	Comment
Similarities between EoE and PPI-REE	EoE and PPI-REE share similar clinical, endoscopic, histologic, immunologic, and molecular features prior to PPI treatment, suggesting that distinguishing these entities with a medication trial is artificial, and the PPIs are better positioned as a treatment for EoE.
EoE and GERD are not necessarily mutually exclusive	An initial rationale for the PPI trial was to distinguish EoE from GERD, but it is now known that these conditions have a complex relationship and are not necessarily mutually exclusive.
Lack of a gold standard for GERD diagnosis	Without a definitive method for defining GERD, no single test (including a PPI trial) can exclude the presence of GERD.
Novel mechanisms of action of PPIs to explain response of eosinophilia	Mechanisms that support PPIs as a treatment for EoE and esophageal eosinophilia include acid-independent anti-inflammatory/anti-eosinophil activity and reversal of epithelial permeability.
Observation that PPI-REE could also respond to classic EoE treatments	Patients with PPI-REE can also have a response to dietary elimination or topical steroid therapy, further blurring the line between EoE and PPI-REE.
Concern about using a treatment response to define a disease	Few diseases are primarily defined by response to treatment, and doing so limits potential treatment options for patients with EoE and esophageal eosinophilia.

PPI and clinical and histologic response



Role of PPI



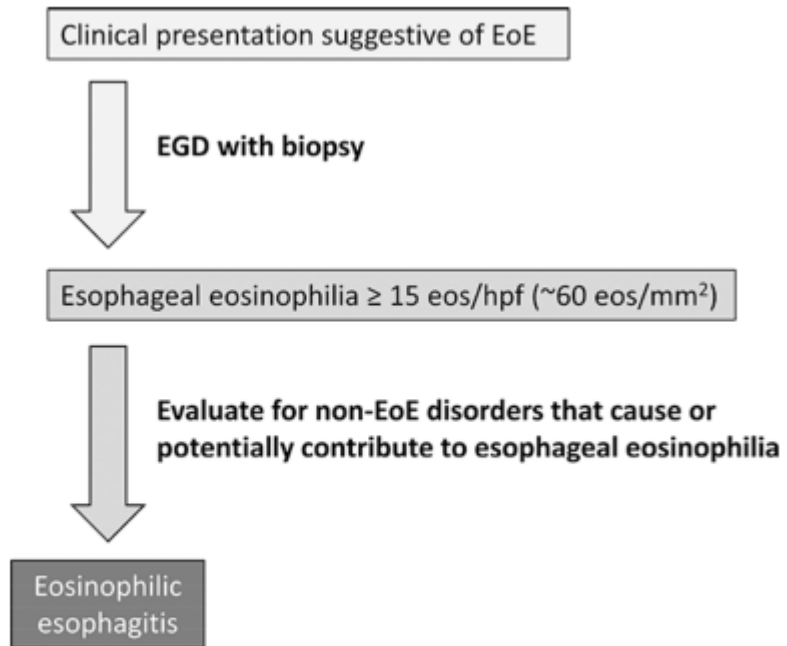


Figure 1.
Updated EoE diagnostic algorithm.

Spergel JM, Dellon ES, Liacouras CA, et al. Summary of the updated international consensus diagnostic criteria for eosinophilic esophagitis: AGREE conference. *Ann Allergy Asthma Immunol.* 2018 Sep;121(3):281-4.

AGREE conference (A Working Group on PPI-REE)

Table 2. EoE Diagnostic Criteria

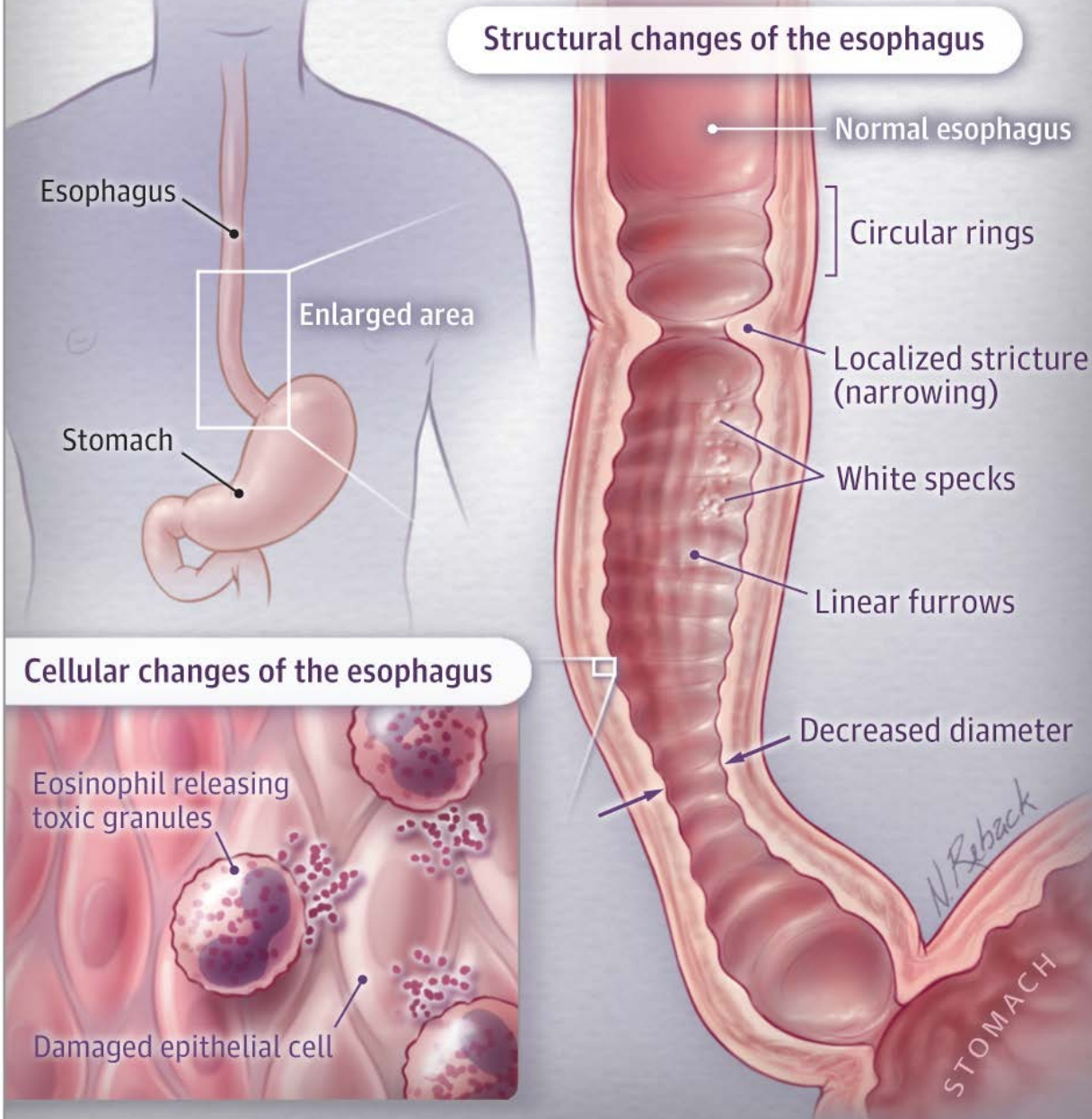
- Symptoms of esophageal dysfunction
 - Concomitant atopic conditions should increase suspicion for EoE.
 - Endoscopic findings of rings, furrows, exudates, edema, stricture, narrowing, and crepe paper mucosa should increase suspicion for EoE.
- ≥ 15 eos/hpf (~ 60 eos/mm²) on esophageal biopsy
 - Eosinophilic infiltration should be isolated to the esophagus.
- Assessment of non-EoE disorders that cause or potentially contribute to 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)
-

Eosinophilic Esophagitis is an allergic condition caused by the abnormal presence of eosinophils, a type of white blood cell, in the wall of the esophagus.



Peiris CD, Tarbox JA.
Eosinophilic Esophagitis
(Patient Education). JAMA.
2019 Apr 9;321(14):1418.

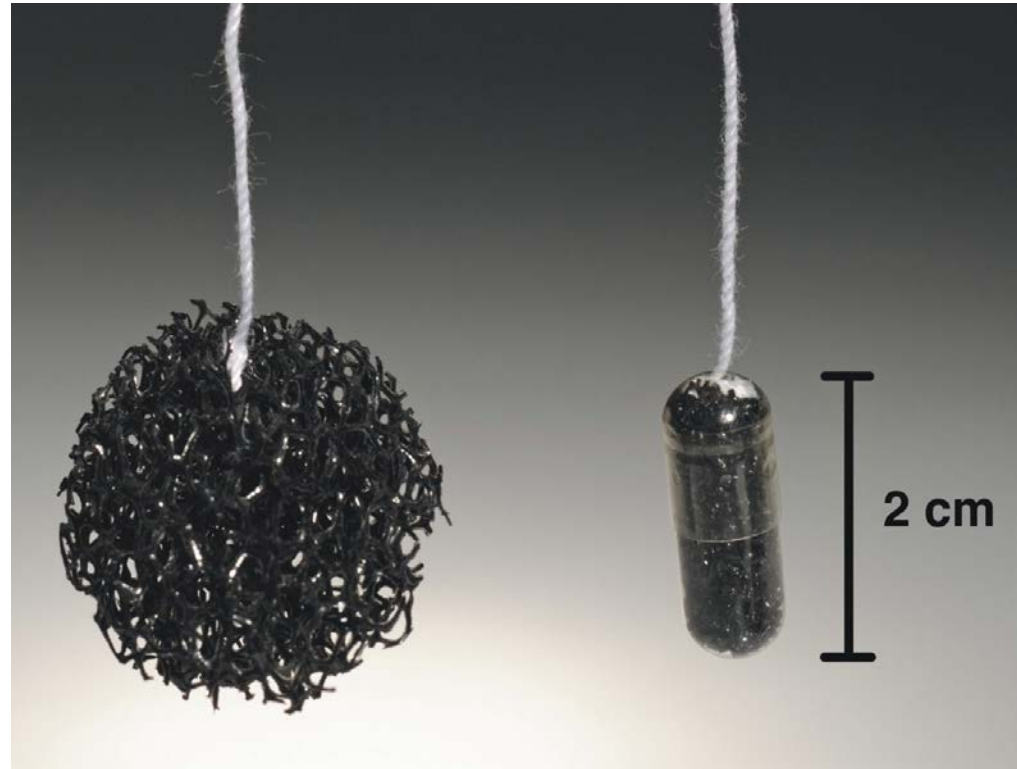
Systematic Review – Minimally Invasive

- 49 studies
- Blood 41
- Sponge or String 3
- Oral / Throat secretions 2
- Breath 2
- Stool 2
- Urine 2

Minimally Invasive

Cytosponge

- In capsule
- Pull back
- Some tissue



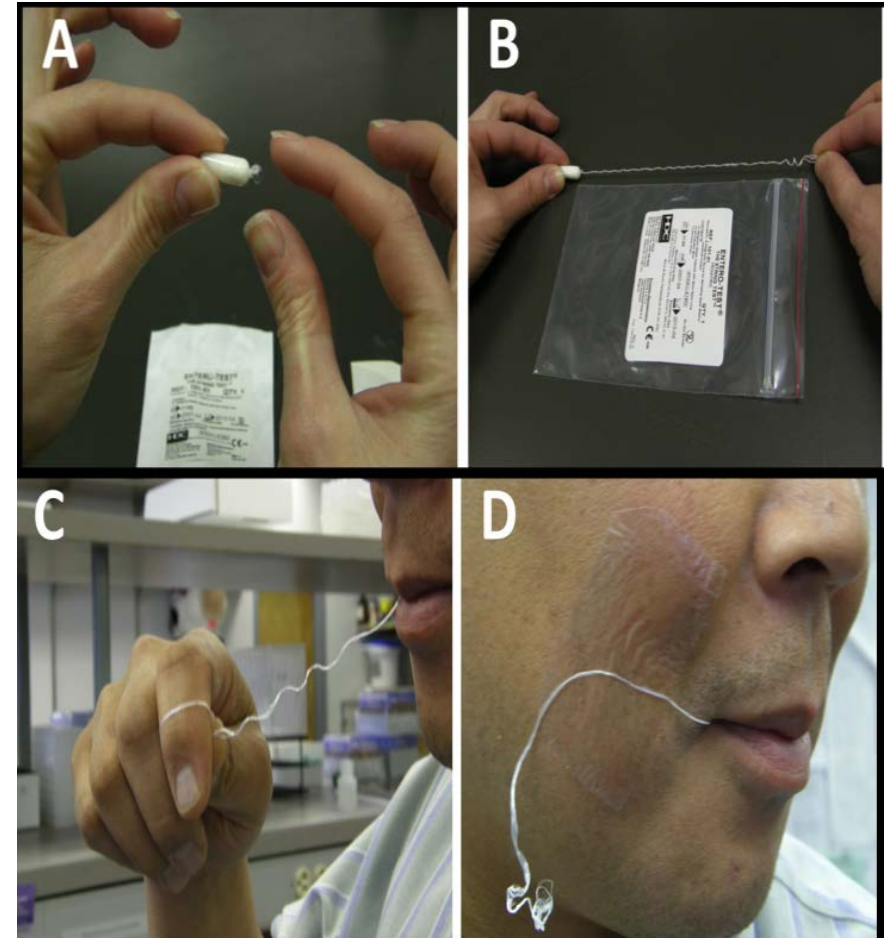
Katzka Am J Gastro 2017

Minimally Invasive

String Test

- Now shorter duration
- No tissue
- Looks at pattern
 - Active vs. not

Ackermann Am J Gastro
2019



Photos <https://www.emaze.com/@ATQTCLZ/EoE-Presentation>

Minimally invasive - TNE

- Transnasal Endoscopy
- Not new
- Validated (with VR) in children
 - Small risk nose bleeds
 - ~ 98% completion
- Costs down, for kids no anaesthetic, parents prefer

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