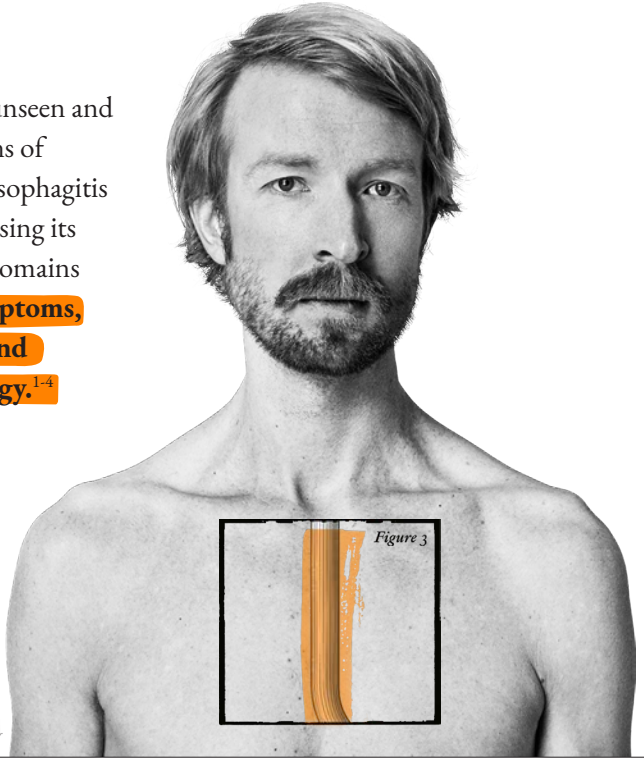
For U.S. Healthcare Professionals

EOSINOPHILIC ESOPHAGITIS IS ANYTHING BUT OBVIOUS[1]

Uncover the unseen and unspoken signs of eosinophilic esophagitis (EoE) by assessing its 3 diagnostic domains together: **symptoms, endoscopy, and histopathology.**[1-4]



SEE™
SEE EOSINOPHILIC ESOPHAGITIS (EoE)

Takeda

WHAT IS EoE?

Eosinophilic esophagitis is a **chronic,** relapsing immune-mediated, **inflammatory disease** localized in the esophagus that is rising in prevalence.[4-7]

THE PREVALENCE OF EoE IS RISING[5-7]

1 IN 2000

Approximately **1 in 2000 people** in the U.S. live with EoE[6-10]

The majority of EoE cases are in **children, adolescents, and adults** ages 50 or younger, but it can affect all ages[1,4,9,11,12]

2x

EoE is **approximately twice as common in men vs women** and more common among Caucasians, but can affect all sexes and races[9,11,12]

EoE is a leading cause of **dysphagia and food impaction** for children and young adults[4]

Mean diagnostic delay is up to 3.5 years in children and 8 years in adults.[11]

Investigate all **3 diagnostic domains** of EoE to **reduce delays** in diagnosis and **help manage** EoE over time.[2,4]

3 DIAGNOSTIC DOMAINS OF EoE

Symptoms

Identify adaptive behaviors and clinical presentations of EoE[1,2]

Endoscopy

Uncover endoscopic findings of EoE with EGD and biopsy[1,2]

Histopathology

Confirm ≥15 eos/hpf on a histologic examination and rule out non-EoE disorders[1,2]

Eosinophilic Esophagitis

According to the 2018 updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis from the AGREE Conference,

PPIs are no longer a tool to diagnose EoE.[2]

EGD=esophagogastroduodenoscopy, eos/hpf=eosinophils per high-power field, AGREE=A Working Group on Proton Pump Inhibitor Responsive Esophageal Eosinophilia, PPI=proton pump inhibitor.

SEE EoE BEYOND SYMPTOMS

In a 2018 cross-sectional U.S. online survey of 31,129 people, 1 in 6 adults reported experiencing **dysphagia (difficulty swallowing).***[13] In adults with EoE, dysphagia is the most frequently reported symptom.[1,13,14] Beyond dysphagia, EoE presents with a variety of symptoms across all ages *(Figure 1.1-1.3)*.†[1,11]

Other common symptoms in:[15]

Adults	Children	Infants & Toddlers
• Difficulty or pain when swallowing	• Difficulty or pain when swallowing	• Food aversion
• Food getting stuck in esophagus	• Choking sensation	• Vomiting
• Heartburn that does not respond to medicine	• Food getting stuck in esophagus	• Choking while eating
• Swallowed food coming back up	• Abdominal, chest, or throat pain	• Disruptive sleep
• Abdominal, chest, or throat pain	• Nausea and vomiting	
• Avoiding certain foods that trigger symptoms	• Disrupted sleep	
	• Loss of appetite	

*In an online April 2018 Takeda-sponsored self-administered health survey of 31,129 people, 4998 people reported dysphagia. Of these people, 399 confirmed an EoE diagnosis.[13]

†Symptoms may vary among patients.[1,11]

THE LIMITATIONS OF ASSESSING SYMPTOMS ALONE

Patients may unknowingly develop adaptive behaviors to cope with these symptoms, making EoE difficult to diagnose by symptoms alone.[3,4,14,16]

Symptoms can be masked by adaptive behaviors that vary by patient.[1-4] Some patients may present with symptoms of EoE that can overlap with other conditions.[1,2,4]

SOME ADAPTIVE BEHAVIORS YOU MAY WANT TO DISCUSS AND UNCOVER IN YOUR PATIENTS INCLUDE:

- Cutting food into small pieces[1,17]
- Drinking with most bites of food[15,16,18]
- Chewing food excessively[4,15,18]
- Eating slowly[14,15,18]
- Substituting solids with blended or pureed foods[18,19]
- Poor acceptance of new foods[18,19]
- Avoiding social settings involving food[18,20]

Listen to patients speak about their adaptive behaviors before they were diagnosed with EoE by scanning the QR code on the back cover.

Learn how to identify adaptive behaviors at SeeEoE.com

Symptoms and adaptive behaviors vary by patient and not all patients with these symptoms and/or adaptive behaviors have EoE.

SEE EoE BEYOND ENDOSCOPY

In patients with EoE, esophageal remodeling driven by chronic inflammation can manifest as various endoscopic features that vary by age.[4,21] ***(Figures 2.1-2.5)***

In adults, esophageal remodeling can manifest as **fibrostenotic complications,** such as strictures, which can lead to **food impactions.**[21-23]

In children, endoscopic features like edema and exudates are more commonly seen.[21-23]

There are 5 key features that can help assess the severity of endoscopic complications of EoE:[4,9,15,24,25]

Edema

Figure 2.1

Rings

Figure 2.2

Exudates

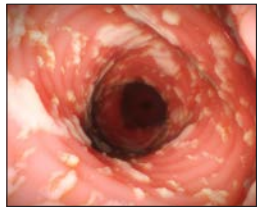


Figure 2.3

Furrows

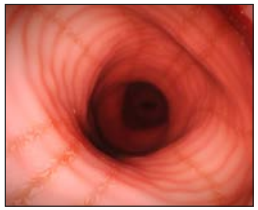


Figure 2.4

Strictures

Figure 2.5

Internal images of the body are artistic representations. Endoscopic features will vary by patient.

THE LIMITATIONS OF ASSESSING ENDOSCOPY ALONE

Endoscopic findings in EoE

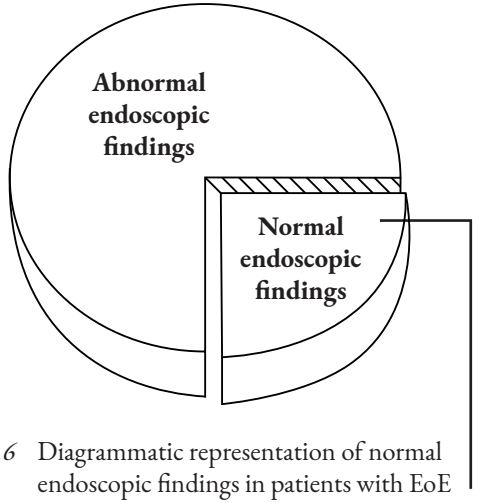


Figure 2.6 Diagrammatic representation of normal endoscopic findings in patients with EoE

Due to the patchy nature of the disease, some patients with EoE can present with normal endoscopic findings. In a 2007 retrospective study of 117 adults and children, **nearly 1 in 4 patients with EoE had normal endoscopic findings.**‡[26] *(Figure 2.6)*. Therefore, EoE should not be ruled out based on endoscopic findings alone.[26]

Diagnostic delays may increase the likelihood of fibrostenotic complications.[9,27]

‡In a retrospective study of 117 patients (108 adults and 9 children) with EoE, the esophageal mucosa was regarded as normal in 24.8% of the patients.[26]

SEE EoE BEYOND HISTOPATHOLOGY

The International Consensus Diagnostic Criteria for EoE from the 2017 AGREE Conference indicate that an **eosinophil count of ≥15/hpf** *(Figure 3.1)* in at least one of multiple esophageal biopsy samples taken from different locations is clinically indicative of EoE.[2,4]

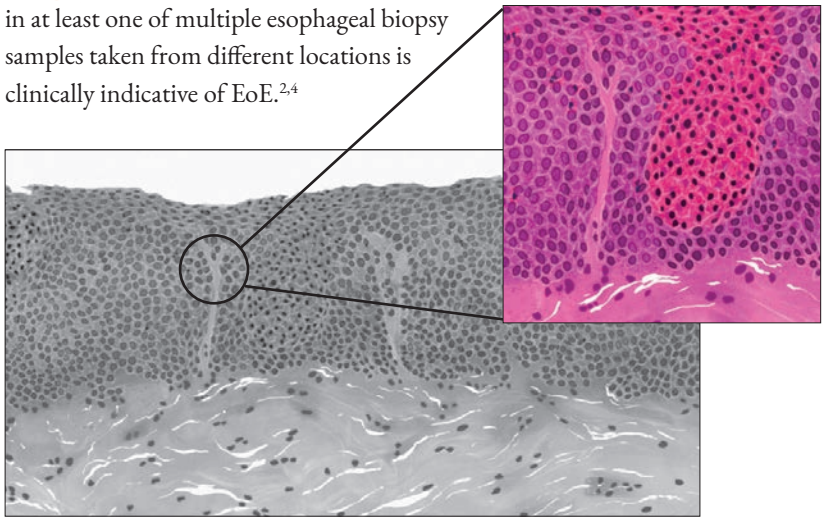


Figure 3.1

CONSIDER:

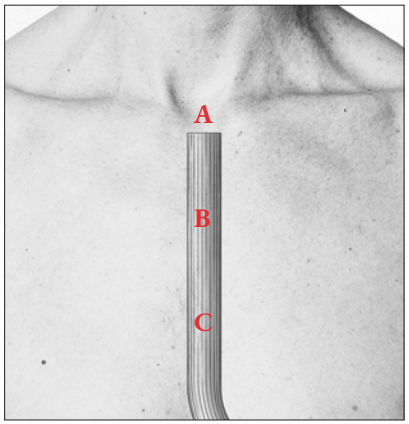
The presence of **esophageal eosinophilia alone, however, cannot establish an EoE diagnosis** without further investigation of symptoms and endoscopy.[2-4]

THE LIMITATIONS OF ASSESSING HISTOPATHOLOGY ALONE

Histopathology may help confirm a suspected diagnosis, but esophageal eosinophilia can be a sign of various esophageal-related diseases besides EoE, like eosinophilic gastritis and gastroesophageal reflux disease (GERD).[2]

Moreover, due to patchy infiltration of eosinophils along the esophagus in EoE, **multiple biopsies should be taken from distal, mid, and proximal locations.** *(Figure 3.2)*[2,4,28]

Though histopathology is an important part of the 3 diagnostic domains and an effective method of evaluating the severity of esophageal inflammation, **assessing this domain alone cannot provide an effective diagnosis** and should be evaluated in the context of symptoms and endoscopic features.[2,4,29]



A **Proximal esophagus**

B **Mid-esophagus**

C **Distal esophagus**

Figure 3.2

UNTREATED, PERSISTENT CHRONIC INFLAMMATION CAN LEAD TO ESOPHAGEAL REMODELING

Esophageal remodeling driven by inflammation can manifest as endoscopic features that can vary by age.[4,21] Diagnostic delays may increase the risk of fibrostenotic complications.[22,27]

In adults, esophageal remodeling can manifest as fibrostenotic complications, such as strictures, which can lead to food impactions.[21-23]

For infants and toddlers, inflammation can lead to food avoidance, vomiting, nausea, abdominal pain, and food refusal.[1,4]

In children, endoscopic features like edema and exudates are more commonly seen.[21-23]

UNDERSTAND CHRONIC INFLAMMATION & FIBROSIS

Data in adults suggest that there's potential for **inflammation to progress into strictures** in some EoE patients with untreated disease.[30-31]

Progression of Inflammation & Fibrosis in EoE

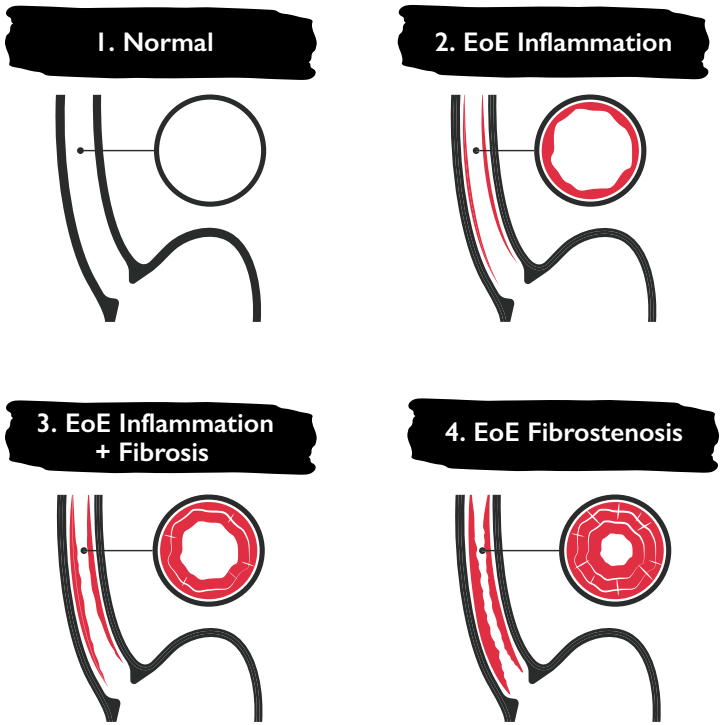


Illustration adapted from Dellon ES, Hirano I. *Gastroenterology*. 2018;154(2):319-332.e3.

MANAGING EoE

Chronic inflammation in eosinophilic esophagitis can be managed by **medical and/or dietary therapy.**[30]

2020 AGA and JTF Clinical Guidelines for the Management of EoE		
Therapeutic Approach	**Strength of Recommendation[§]**	**Quality of Evidence[§]**
Proton Pump Inhibitors (vs no treatment)	Conditional	Very Low
Topical Glucocorticosteroids (vs no treatment)	Strong	Moderate
Topical Glucocorticoids (vs Systemic [Oral] Glucocorticosteroids)	Conditional	Moderate
Esophageal Dilation (vs no dilation)	Conditional • Recommended for adult patients with dysphagia from a stricture associated with EoE Esophageal dilation does not address the esophageal inflammation associated with eosinophilic esophagitis.	Very Low
Anti-Interleukin-13, Anti-Interleukin-5, and Anti-Interleukin-4 receptor α (only in clinical trials)	No Recommendations	Knowledge Gap
Anti-IgE Therapy	Conditional recommendation against the use of anti-IgE therapy for EoE	Very Low
Montelukast, Cromolyn Sodium, Immunomodulators, or Anti-TNF Therapy (only in clinical trials)	No Recommendations	Knowledge Gap

The 2020 AGA and JTF guidelines conditionally recommend PPI, diet therapy, and esophageal dilation in the management of EoE. Topical glucocorticosteroids versus no treatment received strong recommendation.[30]

Dietary Approach	Strength of Recommendation[§]	Quality of Evidence[§]
Elemental Diet (vs no treatment)	Conditional • Patients who put a higher value on avoiding the challenges of adherence to an elemental diet and the prolonged process of dietary reintroduction may reasonably decline this treatment option	Moderate
Empiric 6-Food Elimination Diet (vs no treatment)	Conditional • Patients who put a higher value on avoiding the challenges of adherence to diet involving elimination of multiple common food staples and the prolonged process of dietary reintroduction may reasonably decline this treatment option	Low
Allergy Testing-Based Elimination Diet (vs no treatment)	Conditional • Due to the potential limited accuracy of currently available, allergy-based testing for the identification of specific food triggers for EoE, patients may prefer alternative medical or dietary therapies to an exclusively testing-based elimination diet	Very Low

The 2020 guidelines for management of EoE published by the AGA and JTF did not evaluate dupilumab, which has since been approved by the FDA for EoE.

[§]An assessment/analysis was made of current treatment approaches and published by the AGA and the JTF using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE). Using the GRADE methodology, the AGA and JTF categorize the strength of their recommendations as either "strong" or "conditional." These recommendations are based on evidence that is categorized as "high," "moderate," "low," or "very low."[30]

IgE=immunoglobulin E, TNF=tumor necrosis factor, AGA=American Gastroenterological Association, JTF=Joint Task Force on Allergy-Immunology Practice Parameters.

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The following are coding reference guides that may be useful when diagnosing or when ordering diagnostic tests for suspected cases of EoE in your patients.[32,33]

The listed symptoms are commonly found in EoE. This is not a complete list of symptoms.[1,15]

Diagnosis	ICD 10 Code	ICD 11 Code
Eosinophilic esophagitis	K20.0	DA24.1
Symptom	**ICD 10 Code**	**ICD 11 Code**
Dysphagia	R13.10	MD93
Food impaction	T18.128A	DA0E.4
Vomiting	R11.10	MD90.1

Visit SeeEoE.com to learn more

Scan to watch an adaptive behavior story about living with EoE