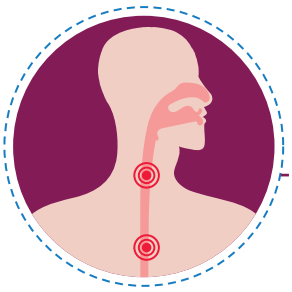
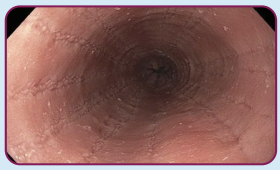


Eosinophilic Esophagitis (EoE):

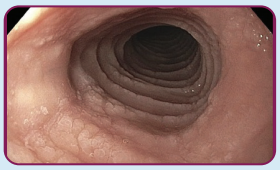
Disease Overview and the Role of Epithelial Cytokines

EoE is a **chronic and progressive inflammatory disease** of the esophagus, characterized by inflammation, remodeling, and dysfunction of the esophageal epithelial layer[1,2]

Endoscopic Presentation[2,*]



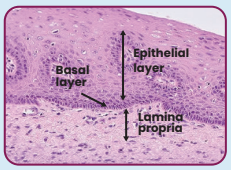
Mild rings in the absence of stricture[2]



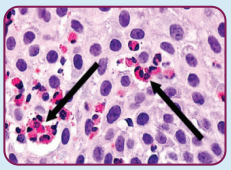
Esophageal remodeling: Moderate rings with presence of stricture[2]

*The EREFS scoring system is used to characterize endoscopic findings in EoE, which classifies 5 key EoE features by severity: edema, rings, exudates, furrows, and strictures.

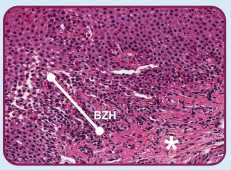
Histological Presentation[1,3-5]



Healthy esophagus[3]



Eosinophil infiltration with eosinophilic abscesses (arrows)[4]



Fibrosis (asterisk) in the lamina propria and basal zone hyperplasia (BZH)

EoE: Epidemiology (US)

- **1 in 700 people** are impacted by EoE[6]
- **Five-fold increase in prevalence** since 2009[6]
- **Higher prevalence among males** vs females (204.45/100,000 vs 122.06/100,000)[6]
- **Increasing incidence** outpaces increased recognition and improved diagnostic procedures[6-9]
- **EoE diagnosis is often delayed**[10-12]; untreated disease may progress, with the risk of stricture increasing by 26% for every year of gaps in care[13]

EoE Comorbidities

- EoE is **five** times more likely to occur in people with atopy[14]
- **60%–80%** of patients with EoE have a history of comorbidities, such as food allergies, asthma, allergic rhinitis, or atopic dermatitis[2]

Challenges With Diagnosis of EoE

Economic burden and healthcare utilization

- US EoE–associated costs ≈ $1.32 billion (2024)[6,†]
- ED visit costs nearly tripled from 2009 to 2019[15]
- Diagnostic delays and frequent visits to HCPs or ED exert ongoing burden[7-9]

Impact on daily life

- Meal-triggered dysphagia, food impaction, heartburn, or chest pain[2]
- Adolescents and adults reported symptoms of anxiety/depression to a greater extent than the general population[7]
- 75% feel embarrassed by their condition[16]
- 45% of caregivers and 20% of adults have had to stop working[16,17]

Challenges with current treatments

Dietary Modifications: Strict dietary restrictions and need for close dietitian input[2,18,19]

Medication: Poor adherence to current treatment options, with inconvenient dosing of some treatments and concerns about cumulative long-term effects[2,18,19]

- Two thirds of patients on PPIs and one third of patients on STCs fail to achieve histologic remission[18]

Assessment of Response: Reliable predictors of treatment response remain unidentified[18]

- Repeated endoscopies for invasive monitoring of treatment response[18]

Diagnosis: Three-Step Criteria

Step 1: Identification of Esophageal Dysfunction Symptoms[2,20,‡]

- Dysphagia
- Food impaction
- Heartburn
- Chest pain or discomfort
- Adaptive eating behaviors **(IMPACT)**

IMPACT: Imbibe fluids, **M**odify foods, **P**rolong mealtimes, **A**void hard texture foods, **C**hew excessively, **T**urn away tablets/pills.

Step 2: Assessment of Endoscopic and Histological Findings[2,20,21]

Endoscopy

- Findings (eg, edema, rings, exudates, furrows, and strictures) evaluated using **EREFS**

Histology

- EoE diagnosis requires esophageal biopsy specimens demonstrating **≥ 15 eos/hpf**
- Six or more biopsies from at least two esophageal levels are recommended

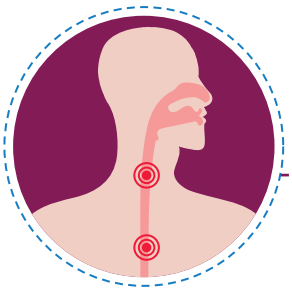
Step 3: Exclusion of non-EoE disorders[2,20]

- Other disorders that can potentially cause or contribute to esophageal eosinophilia should be excluded
  - Such disorders include HES, achalasia, Crohn's disease, pill esophagitis, drug hypersensitivity reactions, infections, and connective tissue or autoimmune diseases, among others

†Total costs adjusted for inflation. ‡Symptoms vary by age.

Abbreviations: ED, emergency department; EoE, eosinophilic esophagitis; eos/hpf, eosinophils per high-powered field; EREFS, Eosinophilic Esophagitis Endoscopic Reference Score; HCP, healthcare provider; HES, hypereosinophilic syndrome; PPI, proton-pump inhibitor; STC, swallowed topical corticosteroid; US, United States.

References: 1. Lucendo AJ, et al. *United European Gastroenterol J.* 2017;5:335-358. **2.** Dellon ES, et al. *Am J Gastroenterol.* 2025;120:31-59. **3.** von Arnim U, et al. *Allergo J Int.* 2024;33:1-8. **4.** Jevtić J, et al. *Diagnostics (Basel).* 2023;13:3445. **5.** Braunberger RC, et al. Accessed January 17, 2026. https://www.pathologyoutlines.com/topic/esophaguseosinophilic.html. **6.** Thel HL, et al. *Clin Gastroenterol Hepatol.* 2025;23:272-280.e8. **7.** Gold BD, et al. *Gastro Hep Adv.* 2024;3:1087-1097. **8.** Mukkada V, et al. *Clin Gastroenterol Hepatol.* 2018;16:495-503. **9.** Mathews SC, et al. *Clin Gastroenterol Hepatol.* 2022;20:1480-1487. **10.** Reed CC, et al. *Clin Gastroenterol Hepatol.* 2018;16:1667-1669. **11.** Navarro P, et al. *United European Gastroenterol J.* 2022;10:507-517. **12.** Warners MJ, et al. *Am J Gastroenterol.* 2018;113:836-844. **13.** Chang NC, et al. *Clin Gastroenterol Hepatol.* 2022;20:1701-1708.e2. **14.** Weir AA, et al. *Ann Allergy Asthma Immunol.* 2025;134:362-364. **15.** Lam AY, et al. *Clin Gastroenterol Hepatol.* 2023;21:3041-3050.e3. **16.** Pokrzywinski RM, et al. *Adv Ther.* 2020;37:4458-4478. **17.** Votto M, et al. *Minerva Pediatr.* 2020;72:424-432. **18.** Bredenoord AJ, et al. *Am J Gastroenterol.* 2022;117:1231-1241. **19.** Haasnoot ML, et al. *Am J Gastroenterol.* 2022;117:1412-1418. **20.** Farah A, et al. *Diagnostics (Basel).* 2025;15:240. **21.** de Bortoli N, et al. *Dig Liver Dis.* 2024;56:1173-1184.



Eosinophilic Esophagitis (EoE):

Disease Overview and the Role of Epithelial Cytokines

EoE is associated with **epithelial damage** and **T2 inflammation** in response to environmental and genetic factors[1]

Environmental

- **Ingested food allergens**[2]
- Seasonal allergens[3]
- Microbiome factors; exposure to certain infections[3]
- Environmental chemical exposures, including detergents, surfactants, pollutants, etc[3-5]

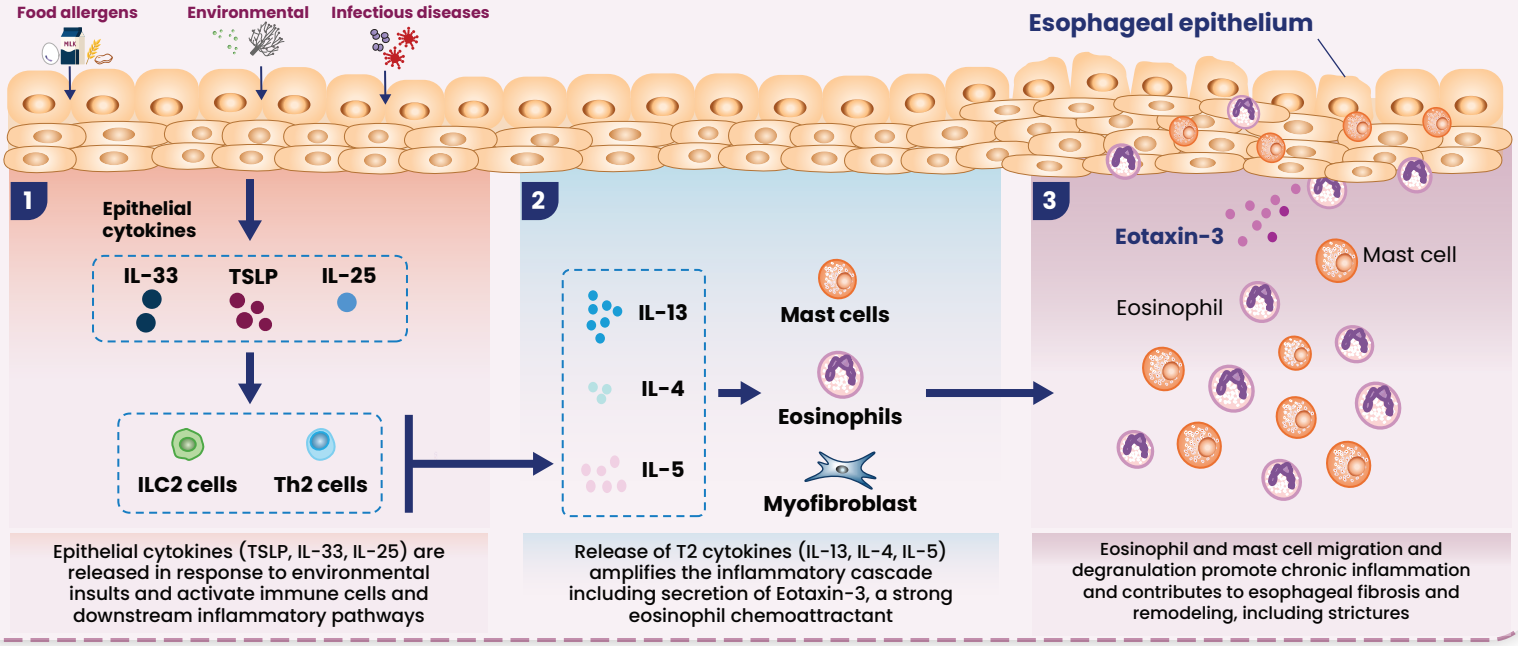
Immune System

- **Driven by epithelial cytokines and a T2 immune response**[4]
- Infiltration of eosinophils and mast cells[5]
- Epithelial inflammation[5]

Hereditary

- EoE has a **strong heritability pattern**[6]
- Genes contributing to EoE development include *TSLP, CAPN14, EMSY, STAT6, LRRC32, ANKRD27,* and *CCL26*[7]

EoE Pathogenesis[4,5,8-10]

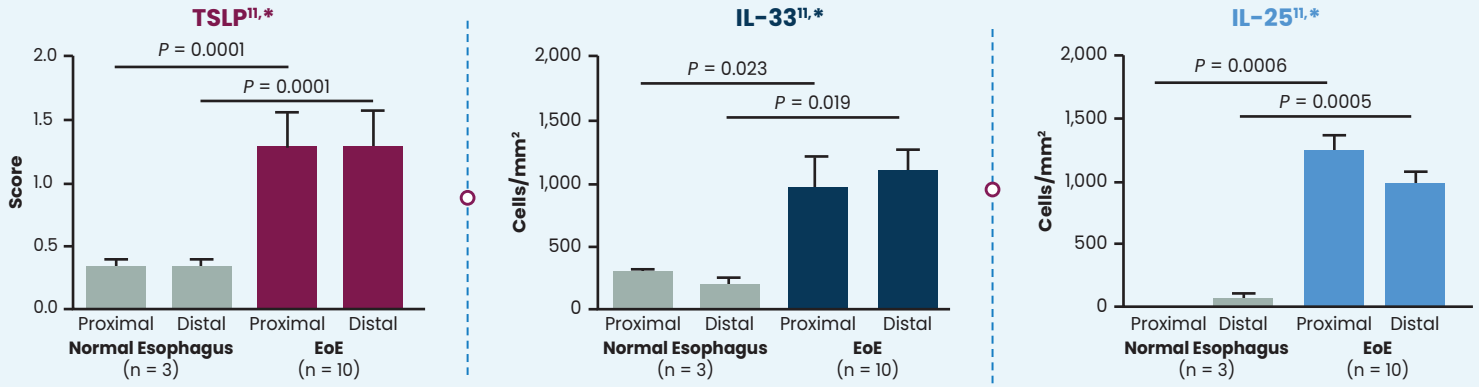


Epithelial cytokines (TSLP, IL-33, IL-25) are released in response to environmental insults and activate immune cells and downstream inflammatory pathways

Release of T2 cytokines (IL-13, IL-4, IL-5) amplifies the inflammatory cascade including secretion of Eotaxin-3, a strong eosinophil chemoattractant

Eosinophil and mast cell migration and degranulation promote chronic inflammation and contributes to esophageal fibrosis and remodeling, including strictures

Epithelial Cytokines Are Overexpressed in Patients With EoE[11-13]



- **Esophageal epithelial tissue of patients with active EoE demonstrated significantly higher epithelial cytokine expression (TSLP, IL-33, and IL-25) compared to healthy controls**[11]
- **Increased TSLP levels were associated with increased disease severity**[11,14]

*TSLP expression was calculated using an ordinal scoring system (0 = none, 1 = mild, 2 = medium, 3 = strong, 4 = very strong) to represent how widely the cytokine marker was expressed in tissue sections, while nuclear expression of IL-33 and IL-25 expression was calculated by counting the number of infiltrating cytokine-positive cells in the area.[11]

Abbreviations: EoE, eosinophilic esophagitis; IL, interleukin; ILC2, type 2 innate lymphoid cell; Th, T helper; TSLP, thymic stromal lymphopoietin.

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