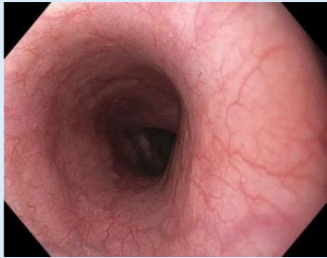


Epicentral: Epithelial Cytokines EoE infographic

Disease Overview and the Role of Epithelial Cytokines

EoE is a **chronic and progressive inflammatory disease** of the esophageal mucosa, characterized by inflammation, dysfunction, and remodeling of the esophageal epithelial layer^{1,2}

Endoscopic Presentation

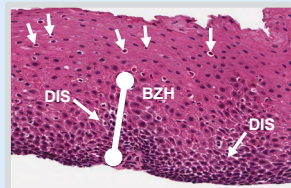


Healthy Esophagus³

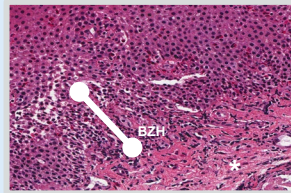


Endoscopic appearance of EoE, showing **edema, rings with presence of stricture**^{4,a}

Histological Presentation^{1,5-7}



Basal zone hyperplasia (BZH), eosinophil infiltration (arrows) and dilated intercellular spaces (DIS)^b



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

Clinical manifestations^{2,8,c}

- **Dysphagia^d**
- **Food impaction^d**
- Nausea/ Vomiting
- Heartburn
- Chest pain or discomfort
- Adaptive eating behaviors

EoE: Global Epidemiology



The prevalence of EoE rose from 8.2 cases/100k in 1976–2001 to about **74.4/100k** in 2017–2022⁹



The pooled global prevalence of EoE is up to **68 cases/100,000 population**^{9,10}



Higher incidence in North America (~51/100,000 inhabitant-years) **and Europe** (~42–43/100,000) compared to pooled Serbia, China, and Brazil (~14.2/100,000)⁹



EoE diagnosis is often delayed¹¹⁻¹³ untreated disease may progress; longer **diagnostic delay is associated with higher stricture prevalence**: 17.2% at <2 years vs 70.8% at >20 years¹⁴

EoE: Comorbidities



EoE is **five** times more likely to occur in people with atopy¹⁵



60%-80% of patients with EoE have a history of comorbidities of varying severity, such as food allergies, asthma, allergic rhinitis, or atopic dermatitis^{2,9}

EoE: Burden of Disease and Current Challenges



- Medical resource utilization is high in patients with EoE compared to healthy controls¹⁶⁻¹⁸
- The economic burden of EoE is likely to increase as incidence rises¹⁹



Impact On Daily Life

- Meal-triggered dysphagia, food impaction, heartburn, or chest pain, and adaptive eating behaviors²
- 75% of patients feel embarrassed by their condition^{2,16,20}
- More than 1 in 7 children/adolescents with EoE were reported to have anxiety and/or depression²⁰; approximately 1 in 3 adults with EoE were reported to have a comorbid psychiatric illness^{12,20}
- 45% of caregivers and 20% of adults report they've had to stop working^{16,21}



Current Treatment Challenges

Diet: Strict and burdensome dietary restrictions and need for close dietitian input^{1,2,18,20,22,23}

Medication: Poor adherence to current treatment options, with inconvenient dosing of some treatments and concerns about cumulative long-term effects^{2,18,22}

- Two thirds of patients on PPIs and one third of patients on STCs fail to achieve histologic remission¹⁸

Assessment of Response: Reliable predictors of treatment response remain unidentified¹⁸

- Repeated endoscopies for invasive monitoring of treatment response^{18,23}

Diagnosis: Three-Step Criteria

Step 1: Identification of Esophageal Dysfunction Symptoms^{2,3,d}



Dysphagia



Food impaction



Heartburn



Chest pain or discomfort



Adaptive eating behaviors (**IMPACT**)

IMPACT: Imbibe fluids, Modify foods, Prolong mealtimes, Avoid hard texture foods, Chew excessively, Turn away tablets/pills.

Step 2: Assessment of Endoscopic and Histological Findings^{2,3,22}

Endoscopy

- Findings (e.g., 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

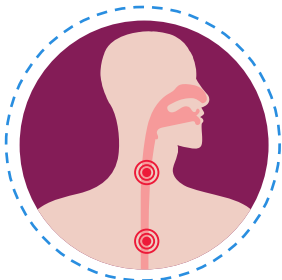
Step 3: Exclusion of non-EoE disorders^{2,3}

- 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

^aThe EREFS scoring system is used to characterize endoscopic findings in EoE, which classifies five key EoE features by severity: edema, rings, exudates, furrows, and strictures; ^bImages provided by courtesy of Dr Evan Dellon from his own research; ^cSymptom vary by age; ^dSymptoms of esophageal dysfunction, such as dysphagia to solid foods and food impaction are hallmark indicators of the disease.

BZH = basal zone hyperplasia; DIS = dilated intercellular spaces; eos/hpf = eosinophils per high-power field; EoE = eosinophilic esophagitis; EREFS = Eosinophilic Esophagitis Endoscopic Reference Score; HES = hypereosinophilic syndrome; PPIs = proton pump inhibitors; STCs = swallowed topical corticosteroids.

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Epicentral: Epithelial Cytokines EoE infographic: Disease Overview and the Role of Epithelial Cytokines

EoE is associated with **epithelial damage** and **T2 inflammation** in response to environmental and genetic factors¹

Environmental



- Ingested food allergens²
- Seasonal allergens³
- Microbiome factors; exposure to certain infections³
- Environmental chemical exposures, including detergents, surfactants, pollutants, etc³⁻⁵

Immune System

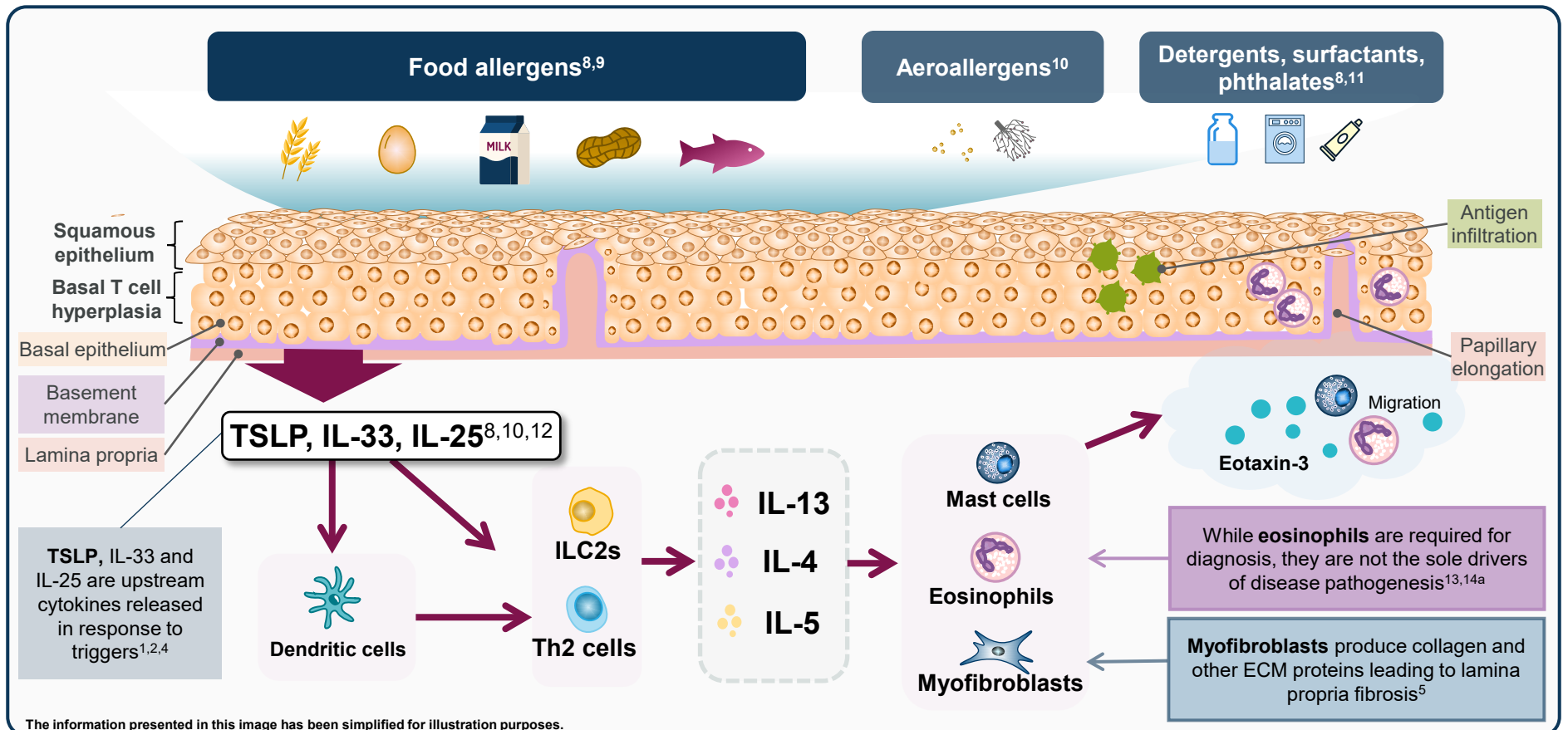


- Driven by epithelial cytokines and a T2 immune response⁴
- Infiltration of eosinophils and mast cells⁵
- Epithelial inflammation⁵

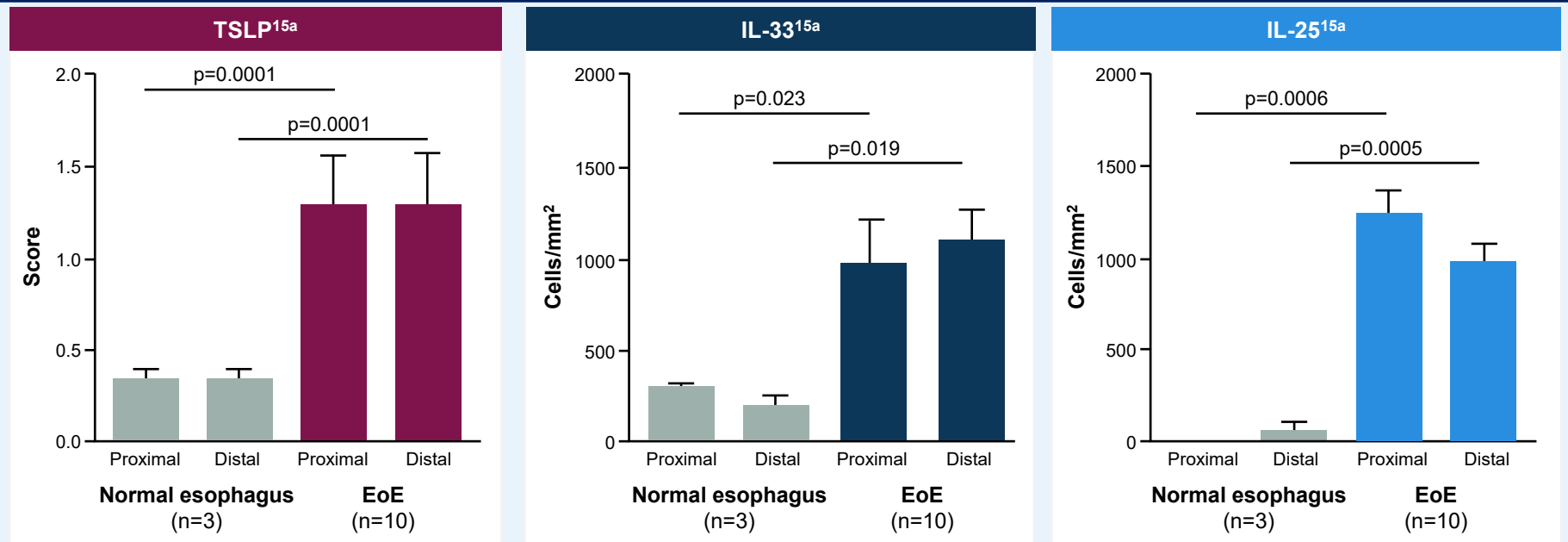
Genetic



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



Epithelial Cytokines Are Overexpressed in Patients With EoE¹⁵⁻¹⁷



- Esophageal epithelial tissue of patients with **active EoE** demonstrated significantly **higher epithelial cytokine expression (TSLP, IL-33 and IL-25)** compared to healthy controls¹⁵
- **Increased TSLP levels** were associated with **increased disease severity**^{15,18}

^aTSLP 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.¹⁵

ANKRD27 = ankyrin repeat domain-containing protein 27; CAPN14 = calpain 14; CCL26 = C-C motif chemokine ligand 26; ECM = extracellular matrix; EMSY = BRCA2-interacting transcriptional repressor EMSY; EoE = eosinophilic esophagitis; IL = interleukin; ILC = innate lymphoid cells; LRRC32 = leucine-rich repeat-containing protein 32; STAT6 = signal transducer and activator of transcription 6; T2 = type 2 inflammation; T cell = T lymphocyte; Th2 = type 2 T-helper cell; TSLP = thymic stromal lymphopoietin

1. Muir A et al. *JAMA*. 2021;326(13):1310-1318. 2. Dellon ES et al. *Gastroenterology*. 2018;154(2):319-332.e3. 3. Jensen ET et al. *J Allergy Clin Immunol*. 2018;142(1):32-40. 4. Underwood B et al. *Ann Allergy Asthma Immunol*. 2023;130(1):28-39. 5. Laky K et al. *J Allergy Clin Immunol*. 2024;153(6):1485-1499. 6. Dhar A et al. *Gut*. 2022;71(8):1459-1487. 7. O'Shea KM et al. *Gastroenterology*. 2018;154(2):333-345. 8. Berni Canani R et al. *Allergy*. 2024;79(6):1485-1500. 9. Gonsalves NP. *Gastroenterol Hepatol (N Y)*. 2021;17(1):35-38. 10. Farah A et al. *Diagnostics (Basel)*. 2025;15(3):240. 11. Doyle AD et al. *Allergy*. 2023;78(1):192-201. 12. Rothenberg ME et al. *Nat Genet*. 2010;42(4):289-91. 13. Dellon ES. *Dig Dis Sci*. 2013;58:1445-1448. 14. Rothenberg ME et al. *N Engl J Med*. 2024;390:2252-2263. 15. Simon D et al. *Allergy*. 2015;70(4):443-452. 16. Chandramouleeswaran PM et al. *PLoS One*. 2016;11(3):e0150968. 17. Travers J et al. *Sci Rep*. 2017;7:17563. 18. Rochman Y et al. *Sci Signal*. 2023;16:eadg6360.