EOSINOPHILIC ESOPHAGITIS:

FREQUENTLY ASKED QUESTIONS

What is eosinophilic esophagitis (EoE)?

EoE is a chronic, progressive, inflammatory disease characterized by symptoms related to esophageal dysfunction and Type 2 inflammation driven by T helper 2 (Th2)–type responses.[1-3] EoE can lead to a variety of symptoms, including[2,4-8]:

- Dysphagia
- Chest pain (noncardiac)
- Fibrosis of the esophagus
- Food impaction requiring bolus removal
- Impaired quality of life (eg, social isolation, higher economic burden)

People living with EoE often require significant lifestyle modifications to reduce symptoms.[4,8] Approximately 1 in 2000 people have EoE in the United States, and diagnosis in adults can be delayed by ~10 years due to misdiagnosis or underdiagnosis.[9,10]

What type of inflammation drives EoE?

EoE is driven primarily by chronic Type 2 inflammation, characterized by epithelial barrier dysfunction, immune dysregulation, and enhanced Th2 cell activity.[2,11,12] Esophageal biopsies and blood samples of patients with active EoE show increased levels of hallmark Type 2 cytokines and chemokines. Type 2 inflammation in EoE encompasses[11,13]:

INFLAMMATORY CELL TYPES

- Th2 cells
- ILC2 cells
- Mast cells
- Basophils
- Eosinophils
- B cells

KEY TYPE 2 CYTOKINES

- IL-4
- IL-13
- IL-5

ILC2, type 2 innate lymphoid cells.

Does Type 2 inflammation drive any other diseases?

Yes. Chronic Type 2 inflammation can be a feature of certain allergic diseases, such as allergic rhinitis, asthma, atopic dermatitis, CRSwNP, food allergy, and a range of other inflammatory diseases.[13]

In all of these diseases, Type 2 inflammation can play a central role in pathogenesis and is associated with the key cytokine mediators IL-4, IL-13, and IL-5.[13]

~75% of patients with EoE have at least 1 additional Type 2 inflammatory disease[10,13-16]

CRSwNP, chronic rhinosinusitis with nasal polyposis.

What is the impact of Type 2 inflammation on EoE?

Chronic Type 2 inflammation in EoE results in histologic and endoscopic changes that reflect symptom progression[6,11-13,17-22]:

B-CELL CLASS SWITCHING

IL-4 and IL-13 promote B-cell class switching and production of IgE and IgG4

MAST CELL AND BASOPHIL ACTIVATION

IL-4 and IL-13 contribute to the activation of mast cells and basophils, leading to degranulation of several inflammatory mediators

EPITHELIAL BARRIER DYSFUNCTION

IL-4 and IL-13 increase epithelial permeability and promote barrier disruption, leading to increased exposure to allergens and pathogens and leukocyte infiltration

REMODELING AND FIBROSIS

IL-13 contributes to tissue remodeling and fibrosis (such as furrows, rings, and strictures) and increased smooth muscle contraction

EOSINOPHILIC INFLAMMATION

IL-4, IL-13, and IL-5 promote eosinophil trafficking to tissues through chemoattractants, contributing to esophageal remodeling, and IL-5 induces eosinophil differentiation in the bone marrow and extravasation into the bloodstream

How does chronic inflammation remodel the esophagus over time in EoE?

EoE is a progressive disease characterized by histologic and endoscopic changes to the esophagus due to chronic Type 2 inflammation.[1,3,11,13,23-25] Key Type 2 inflammatory mediators IL-4, IL-13, and IL-5 can propagate local inflammation, resulting in esophageal remodeling and fibrosis.[11,13] Endoscopic findings may include[23]:

SIGNS OF INFLAMMATION

- Furrows/ridges
- White exudates
- Pale, edematous mucosa, decreased vascularity
- Fragile mucosa: crêpe paper esophagus, with lacerations at the passage of the endoscope

SIGNS OF FIBROSTENOSIS

- Esophageal rings or diffuse esophageal stenosis, narrow-caliber esophagus
- Fixed esophageal rings (trachealization)
- Feline esophagus

Progressive remodeling and fibrosis may lead to esophageal strictures and worsen dysphagia. This may result in food impaction requiring dilation[1]

How is EoE currently managed?

Current EoE management approaches include[6,7,23-26]:

- Food elimination diets
- Cycles of swallowed TCS
- PPIs
- Esophageal dilation
- Upper endoscopy for the management of esophageal food impaction

Current standards of care may not fully address the underlying Type 2 inflammation in EoE.[2,6,25,26] There remains an unmet need to reduce esophageal dysfunction and the underlying Type 2 inflammation to improve endoscopic signs, clinical symptoms, and quality of life in patients with EoE.[25]

PPI, proton pump inhibitor; TCS, topical corticosteroid.

What is the goal of disease management in EoE?

The goal of EoE management is to achieve multiple measures of disease remission[27,28]:

- Clinical remission, characterized by lack or reduction of EoE-attributed symptoms
- Endoscopic remission, characterized by absence of inflammatory signs (eg, white exudates, furrows, edema), EREFS score ≤2
- Histological inflammatory remission, characterized by peak eosinophil count ≤6 EOS/HPF histology/HE stain

EOS, eosinophils; EREFS, endoscopic reference score; HE, hematoxylin and eosin; HPF, high-power field.

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