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)
- 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

**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:

**B-CR**

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. Key Type 2 inflammatory mediators IL-4, IL-13, and IL-5 can propagate local inflammation, resulting in esophageal remodeling and fibrosis.

Endoscopic findings may include:

**SIGNS OF INFLAMMATION**

- Furrows/ridges
- White exudates
- Pale, edematous mucosa, decreased vascularity

**SIGNS OF FIBROSTENOSIS**

- Fragile mucosa: crêpe paper esophagus, with lacerations at the passage of the endoscope
- 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.
How is EoE currently managed?

Current EoE management approaches include:

- 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. 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.

What is the goal of disease management in EoE?

The goal of EoE management is to achieve multiple measures of disease remission:

- 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

References: