

# ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

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## Inflammatory Bowel Disease and Eosinophilic Esophagitis



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**G&H** Do patients with inflammatory bowel disease have a higher risk of eosinophilic esophagitis?

**EB** Several single-center studies have shown that patients with inflammatory bowel disease (IBD) have an increased risk of developing eosinophilic esophagitis (EoE) in their lifetime. A meta-analysis and systematic review published in 2025 showed that patients have an odds ratio of 3.9 for the increased risk of developing EoE in the setting of IBD. The opposite is also true; studies have demonstrated that having EoE also increases the risk for IBD in the patient's lifetime. Several years ago, a nationwide population study in Sweden showed that EoE patients have a 3.5-fold increased risk of developing IBD. The combination of EoE and IBD is more common in males and White patients, and these patients not only have an increased risk of EoE and IBD but also an increased risk of other immune-related diseases such as asthma or atopic dermatitis.

**G&H** Has anti-tumor necrosis factor therapy for IBD been shown to increase the risk for EoE?

**EB** This is a controversial issue. Some case reports and case series have shown that IBD patients who were started on an anti-tumor necrosis factor (anti-TNF) agent developed EoE after the start of the anti-TNF treatment. Anti-TNF agents such as infliximab might trigger a T-helper 2 (Th2) cytokine shift, leading to eosinophilic infiltration, but further research is needed to determine whether there is a real cause-and-effect relationship. On the other hand, other studies have shown that if a patient has IBD and is taking anti-TNF therapy, the risk of having EoE is actually lower.

**G&H** What are the similarities and differences between these conditions in terms of genetic factors?

**EB** The pathogenesis of IBD and EoE implicates several genetic polymorphisms, some of which overlap and some of which are distinct. However, it is well known that genetic predisposition by itself does not account for the development of both IBD and EoE, suggesting that disease onset and progression require a strong environmental component. Genetic variants at EoE-associated loci—including TSLP, CAPN14, LRRC32/EMSY,

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CLEC16A/DEX1, and STAT6—have been identified by genome-wide association studies and shown to impact the integrity of the epithelial barrier and the immune response involving Th2. As for IBD, more than 200 genes have been identified that can predispose patients to the risk of developing this disease, highlighting that it has an intricate and multifaceted nature. These genes are mainly involved in immune regulation, epithelial barrier function, and microbial interactions.

When looking at both IBD and EoE, mainly 3 genes have been identified that can potentially be involved in the overlap of the conditions in certain individuals. One

is the *STAT6* gene, which plays a crucial role in Th2 cell differentiation and signaling. It is thought that the pathophysiology of EoE mainly involves Th2 cell differentiation and signaling, like IBD. Polymorphisms of the interleukin (IL)-13 gene are also involved. IL-13 is a cytokine involved in regulating inflammatory responses and epithelial cell function. When there is overexpression of IL-13 in EoE patients, there is increased recruitment of eosinophils and esophageal tissue remodeling. Another genetic factor that has been identified is the *FLG* gene, which is crucial for epithelial barrier integrity. Disruption in the epithelial barrier facilitates allergens and antigens to trigger an inflammatory response in both EoE as well as IBD.

### G&H How are IBD and EoE similar and different in terms of environmental factors?

**EB** Environmental factors play an important role in the development as well as exacerbation of both EoE and IBD. It is known that early-life exposure to antibiotics and vitamin D deficiency, as well as cesarean section and lack of breastfeeding, have been associated with both conditions. However, in EoE, dietary allergens such as milk, eggs, wheat, and fish (including shellfish) are the predominant triggers. Aeroallergens as well as detergents are also known to play a role. As for IBD, a Western diet (high in fat and sugar intake), smoking, medications such as nonsteroidal anti-inflammatory drugs, stress, and growing up in an extremely clean environment can promote dysbiosis, leading to increased intestinal permeability and chronic inflammation in the gut.

### G&H Should every IBD patient be screened for EoE, or only if they present with symptoms?

**EB** General screening for EoE is not recommended for all IBD patients, according to the current guidelines. It is not supported by any of the societies. However, evaluation for EoE is warranted if IBD patients present with symptoms of esophageal dysfunction such as dysphagia or food impaction, refractory gastroesophageal reflux disease (GERD) in young adult patients, or food avoidance or lack of growth in children. It is also important to consider whether patients have other concomitant immune-mediated diseases such as asthma, eczema, or allergic rhinitis, as these conditions are often seen in patients with EoE and IBD.

### G&H Do eosinophils in colonic biopsies warrant evaluation for EoE?

**EB** Not always. Eosinophils are very common in colonic biopsies of patients with IBD, and not all patients with

eosinophils in the colon will have EoE. Doctors should always look at the bigger picture, and if these patients have symptoms of esophageal dysfunction such as dysphagia, food impaction, or refractory GERD, they should be evaluated for EoE. Just seeing eosinophils in colonic biopsies should not mean that a patient needs an upper endoscopy.

### G&H What are the main overlaps in the diagnostic approach of each condition?

**EB** There are a number of overlaps between the diagnostic approaches for IBD and EoE. Both conditions need endoscopic evaluation and tissue sampling for histologic evaluation to make the diagnosis. The current diagnostic criteria for EoE were established by international consensus at the AGREE conference and are endorsed by the most recent guidelines from the American College of Gastroenterology, which were published last year. These criteria include, first and foremost, symptoms such as esophageal dysfunction, as well as biopsies showing at least 15 eosinophils per high-power field. It is recommended to take at least 6 biopsies in different parts of the esophagus (typically the proximal and distal parts of the esophagus). Patients also need to be evaluated for non-EoE disorders that could increase the number of eosinophils in the biopsies such as GERD.

A patient's symptoms and presentation should also be taken into consideration when diagnosing IBD. Endoscopic evaluation with a colonoscopy and/or upper endoscopy is recommended to establish the diagnosis. Segmental biopsies should be taken throughout the colon, with guidelines recommending that providers obtain at least 2 biopsies per segment, including the terminal ileum. Histology is an important component for IBD diagnosis, as signs of chronicity such as crypt architectural distortion should be noted in the tissue. Imaging studies also play an important role, especially in patients with small bowel disease. Magnetic resonance enterography or computed tomography enterography can help to stage disease activity and evaluate for complications such as strictures and fistulas in patients with Crohn's disease. Intestinal ultrasound has also been widely used for disease monitoring in clinical practice.

### G&H What are the treatment goals for IBD and EoE?

**EB** For EoE, the aim, first and foremost, is symptom relief. Patients should be able to eat well and swallow their food without any discomfort. Endoscopic and histologic remission, which is defined as an eosinophil count below 15 per high-power field, is recommended. Additionally,

providers want to prevent complications. If EoE is left untreated, similar to Crohn's disease, it will lead to structural damage such as strictures.

The goals for IBD are similar. Providers should aim first for symptomatic improvement and symptomatic remission. Mediations should be adjusted using a treat-to-target approach following the STRIDE II guidelines to

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aim for normalization of biomarkers such as calprotectin and C-reactive protein as well as endoscopic remission. Overall goals are improvement in quality of life, prevention of complications, and reduction in the need for surgery and hospitalization.

#### G&H Does treatment for EoE impact IBD?

**EB** Usually not. EoE treatment can be given in parallel with IBD therapy. Dupilumab (Dupixent, Sanofi and Regeneron), the only US Food and Drug Administration–approved monoclonal antibody to treat EoE, blocks IL-4 and IL-13, and a few case reports have suggested that dupilumab can trigger colitis mimicking ulcerative colitis. However, there are small studies demonstrating the safety of dupilumab in atopic or psoriasiform dermatitis patients with IBD. Dupilumab is also being studied as a primary treatment for patients with ulcerative colitis with an eosinophilic phenotype. If a patient needs dupilumab, I would not let them go without therapy just because they have IBD.

#### G&H Are there any other similarities or differences between IBD and EoE worth discussing?

**EB** Treatment is different. Treatment for EoE usually starts with a course of acid-suppressive medications such as proton pump inhibitors (PPIs). Dietary interventions

such as an elimination diet are also very effective to treat EoE and are frequently offered to patients who fail a PPI trial. Topical corticosteroids such as budesonide or fluticasone are also frequently used to promote healing. Dupilumab is reserved for corticosteroid-refractory disease or patients with a severe fibrostenotic phenotype. On the other hand, IBD treatment involves broader immunosuppressive agents such as systemic corticosteroids, immunomodulators, biologics, and small molecules such as Janus kinase inhibitors. Dietary interventions have been associated with improvement of symptoms, but not with biomarker remission or endoscopic healing in IBD.

#### G&H What are the priorities of research in this area?

**EB** Key research priorities are to identify predictors of treatment response and biomarkers for noninvasive disease monitoring to guide and personalize therapy. It is also important to better understand the pathogenic mechanism and molecular pathways of both IBD and EoE, which would help the development of new therapeutic targets as well as the development of a drug that could possibly treat these two conditions at the same time in the future.

#### Disclosures

*Dr Bellaguarda has served as a speaker and consultant for AbbVie, Janssen, Pfizer, Lilly, Celltrion, and Medscape.*

#### Suggested Reading

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