Opinion statement

Eosinophilic esophagitis (EE) is an important esophageal disorder with distinct clinicopathologic features, and the condition is associated with a high prevalence of food allergies and atopy. In the past decade, we have improved our ability to recognize the phenotype of EE, but our ability to treat EE effectively remains limited despite several reports of successful treatment using elemental or elimination diets, and systemic and topical corticosteroids. The limitations for developing effective treatment regimens are due to some still unresolved and ambiguous aspects of the pathogenesis of EE. Neither the predisposing factors for developing EE in a subset of patients with atopy, nor the variable responsiveness to control measures for allergens are fully understood. There also remain questions about the precise role of gastroesophageal reflux, and the natural history of the disorder, contingent on which is the optimal treatment of EE. In devising treatment for a patient with EE, all attempts should be made to identify and control food and other allergies. In patients who have no diagnosed allergies or who are unresponsive to allergy treatment, topical steroids are a safe and effective treatment option. Systemic steroids should be reserved for those patients who are refractory to topical steroids. Beyond the initial phase of induction treatment, it is crucial to develop effective and safe maintenance treatment regimens based on ongoing allergen control and mast cell inhibitors. There are limited but encouraging data to support further exploration of the role of leukotriene and interleukin-5 inhibitors as safe, effective, and steroid-sparing treatment options.

Introduction

DEFINITION
Eosinophilic esophagitis (EE) is being increasingly recognized as a clinicopathologic entity distinct from gastroesophageal reflux disease (GERD). It is characterized by the presence of a dense epithelial eosinophilic infiltrate, more than 15 eosinophils per high-power field (eos/hpf) in a macroscopically ringed or furrowed esophagus (Fig. 1), and commonly presents with vomiting, chest pain, dysphagia, and food impactions in predominantly young men with a background of atopy who have failed to respond to antireflux therapies [1••,2,3•,4].

EPIDEMIOLOGY
There are no epidemiologic studies to date that pertain to the precise incidence and prevalence of EE; however, a miniepidemic of EE has been noted by the pediatric gastroenterology community in recent years. The approximately 133 pediatric cases in the literature since the first published report by Picus in 1981 [5] have made a major contribution to characterization and management of EE [3•,5–7,8,9,10••,11]. Several reports of a similar esophageal disorder afflicting adults have also appeared and have been referred to as defiant esophagus, small-caliber esophagus, and corrugated...
ringed esophagus [12–15] in contrast with the more consistent pediatric usage of the term EE, probably representing the greater frequency of histologic sampling in grossly normal endoscopies in children. It is also speculated that a higher number of EE cases are diagnosed in children owing to the higher incidence of food allergies in the younger population.

PATHOGENESIS
Eosinophils have long been associated with allergies, but the link between allergens and EE has just begun to be elucidated. The hypothesis that food allergies produce EE is supported by observations assessing the symptomatic and histologic response to restricted and elemental diets in patients with EE. Moreover, some recent important observations have been made in animal models that support the role of aeroallergens in inducing eosinophilic inflammation in the esophagus by cytokine-mediated mechanisms shared with pulmonary inflammation [16••,17,18].

PRESENTATION
The clinical presentation of EE may be easily confused with GERD. Infants present with symptoms of vomiting, hematemesis, irritability, and failure to thrive, whereas older children and adolescents most commonly have obstructive esophageal presentations such as dysphagia, impactions, and strictures. Children of all ages with EE have been reported, although symptoms may peak in infancy and in 10- to 14-year-old individuals. The duration of symptoms before diagnosis may range from a few days to years depending on whether the presentation is acute with food impaction or chronic with GERD-like symptoms [1••,2•,3•,4••,9,19].

ASSOCIATIONS
There is a line of evidence for EE associated with food allergies, although these allergies are not always demonstrable by available laboratory tests. A fairly large number of patients with EE may have a personal (~60%) or family history (20% to 40%) of atopy, that is, allergic rhinitis, asthma, and dermatitis. Gastroesophageal reflux diagnosed by intraesophageal pH monitoring may be present in a smaller number of patients.

DIAGNOSTIC EVALUATION
The gold standard for diagnosis of EE is the presence of a dense eosinophilic infiltrate in the esophageal epithelium. According to most experts, an eosinophilic density of more than 15 eos/hpf in the esophageal squamous epithelium is strongly suggestive of EE and aids in differentiating it from GERD, which is usually associated with 5 eos/hpf or less [1••,3•,11]. The intermediate group of 5 to 15 eos/hpf remains an ambiguous entity and may represent allergies overlapping with GERD. Other notable pathologic findings in EE include superficial epithelial distribution of eosinophils, eosinophil aggregation, eosinophil abscess, and basal layer proliferation. In order to determine the cause of eosinophilic infiltration, further evaluation should be directed toward allergies (food and environmental), and other precipitants like parasitic infections, drug reactions, collagen vascular disease, and autoimmune disorders. Evaluation for food allergies rests on a complete history of foods suspected

Figure 1. Endoscopy photographs showing the characteristic macroscopic appearance of furrowed (A), and ringed (B) esophageal mucosa with exudates in a patient with eosinophilic esophagitis.