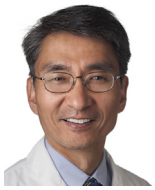
Gastroenterology 2018;154:319–332

EOSINOPHILIC ESOPHAGITIS

Epidemiology and Natural History of Eosinophilic Esophagitis



Evan S. Dellon[1] Ikuo Hirano[2]

[1]Center for Esophageal Diseases and Swallowing and Center for Gastrointestinal Biology and Disease, Division of Gastroenterology and Hepatology, University of North Carolina School of Medicine, Chapel Hill, North Carolina; and [2]Divsion of Gastroenterology and Hepatology, Northwestern University Feinberg School of Medicine, Chicago, Illinois

Eosinophilic esophagitis (EoE) has emerged over the past 2 decades as a major cause of upper gastrointestinal morbidity. Over this time, the epidemiology of EoE has also rapidly evolved. EoE has transformed from a rare case-reportable condition to disease that is commonly encountered in the gastroenterology clinic, hospital emergency room, and endoscopy suite. The incidence and prevalence are increasing at rates that outpace increased disease recognition. Current incidence estimates range from 5 to 10 cases per 100,000, and current prevalence estimates range from 0.5 to 1 case per 1000. We review the data and potential reasons behind this increase, examine risk factors, and identify important areas for research into disease etiology. The article also discusses the progression of EoE from an inflammatory to fibrostenotic phenotype. An accurate view of the natural history of EoE is central to discussions with patients regarding disease prognosis and decisions about long-term use of medical, endoscopic, and diet therapies. Progressive remodelling appears to be gradual, but not universal, and the duration of untreated disease is the best predictor of stricture risk. Ultimately, prospective, long-term outcome studies focusing on multiple aspects of disease activity are needed to fully understand the natural history of EoE.

Keywords: Incidence; Prevalence; Progression; Fibrosis.

Eosinophilic esophagitis (EoE) is an allergen/immune-mediated disease characterized by symptoms of esophageal dysfunction and eosinophilic infiltration of the esophageal mucosa in the absence of secondary causes of eosinophilia.[1,2] The first cases of EoE were reported in the late 1970s,[3,4] but the disease as it is recognized today was described in 3 case series in the early and mid-1990s.[5–7] Since then, EoE has transformed from a rare case-reportable condition to a disease that is commonly encountered in the clinic and endoscopy suite,[8] and a major cause of upper gastrointestinal morbidity and increasing health care costs.[9] Over this time, our understanding of the epidemiology of EoE has also rapidly evolved. The incidence and prevalence are increasing at rates that outpace increased recognition,[10–12] indicating the importance of environmental rather than genetic changes.[13,14] Descriptive epidemiology research in EoE has also matured, and there is now a focus on identifying etiologic factors. Although we know much about the pathogenesis of EoE,[15] we do not fully understand why EoE develops in an individual patient.[16] We review the incidence and prevalence of EoE, present potential reasons for the increase in EoE, examine possible risk factors, and discuss the natural history and possible progression of this chronic condition.

Epidemiology

Incidence of EoE and Time Trends

The incidence of EoE has been investigated in several population-based studies, conducted primarily in North America and Europe.[11,12,17–25] Using the most recent time point from these studies, incidence rates range from a low of 2.1/100,000/year in the Netherlands[22,26] to a high of 12.8/100,000/year in Ohio in the United States[17] (Supplementary Table 1). A meta-analysis calculated an overall pooled incident rate of 3.7/100,000/year (95% confidence interval [CI], 1.7–6.5), though there was substantial heterogeneity.[27] In this study, the incidence rate was higher in adults (7.0/100,000/year) than in children (5.1/100,000/year). When interpreting the published incidence data, it is important to recognize differences among studies performed at different centers and during different time periods. For example, proton pump inhibitor (PPI)-responsive esophageal eosinophilia may not have been excluded in some studies (there is controversy over

Abbreviations used in this paper: **CI, confidence interval; EoE, eosinophilic esophagitis; PPI, proton pump inhibitor.**

Most current article

0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2017.06.067

this topic)[28] and varying case-finding approaches might have been used.

All studies that have examined incidence rates of EoE over time have concluded that the incidence of EoE is increasing rapidly (Figure 1*A*; Supplementary Table 1). In the first report investigating this issue, incidence increased 40% over a 4-year period (2000–2003).[17] In similar analyses, incidence increased approximately 27-fold[20] and 5-fold at 2 other North American centers.[23] In European studies, rates of increase ranged from 6-fold to more than 100-fold.[11,12,18,19,22,24,25] Although it is tempting to attribute this rapid change to an associated increase in recognition of and knowledge about EoE, this is not the only explanation. Several studies have examined changes in rates of endoscopy with biopsy over the same time period as the change in rates of EoE, and have found that the increase in EoE incidence outpaces the relatively modest increase in rates of biopsy.[10–12,20,29] In addition, other studies have retrospectively reviewed archived esophageal biopsy blocks to determine if cases of EoE were previously present but missed.[30,31] Although cases of EoE were found, they were identified at rates that are far below what are currently observed. Therefore, it appears that the incidence of EoE is truly increasing, and is just not an artifact of increasing surveillance and detection. This information has major implications for understanding the etiology of EoE.

Prevalence of EoE

The prevalence of EoE has been investigated worldwide, but most population-based studies have been conducted in North America and Europe,[11,12,17–24,32–40] with select studies in Australia and Asia.[41,42] In a study in Scandinavia and a study in China, researchers performed upper endoscopies using a population-based sampling frame of asymptomatic individuals in the community.[33,42] They found a rate of esophageal eosinophilia (defined as 15–20 eosinophils per high-power field) of approximately 400/100,000. These findings should be interpreted with caution because the studies included patients who would not meet diagnostic criteria for EoE. Other studies attempted to identify all known EoE cases within a specific population catchment area. If we use the most recent time point from these studies, prevalence values range from as low as 2.3/100,000 in Denmark[21] to as high as 90.7/100,000 in Ohio (Supplementary Table 2).[17] A meta-analysis estimated an

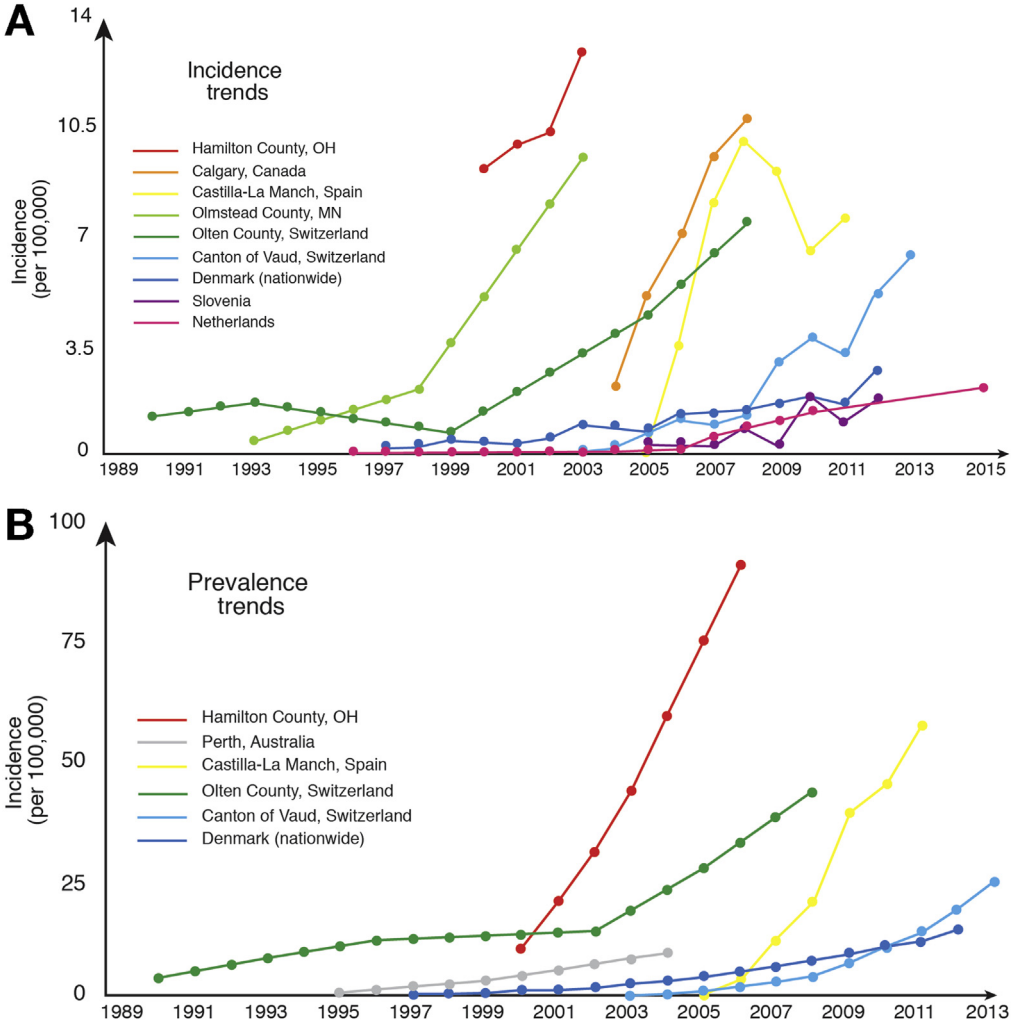


Figure 1. (*A*) Time trends in EoE incidence from estimates in population-based studies. (*B*) Time trends in EoE prevalence from estimates in population-based studies.