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# Idiopathic eosinophilic gastrointestinal diseases in adults

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This review focuses on the latest cognitions, diagnosis and treatment strategies of the three main representatives of the eosinophilic gastrointestinal disorders (EGID): idiopathic *eosinophilic oesophagitis* (EE), idiopathic *eosinophilic gastroenteritis* (EGE) and idiopathic *hypereosinophilic syndromes* (HES) with gastrointestinal involvement. These disorders share important similarities: their origin is unknown and their pathogenesis is due to a histological inflammatory response characterised by eosinophilic tissue infiltration.

In spite of these parallels, the courses and prognoses of the diseases differ radically: EE is restricted to the oesophagus, and though it may significantly decrease the patient's quality of life, it has a favourable long-term prognosis. In EGE, the inflammatory process involves several segments of the gastrointestinal tract but this chronic inflammation may also be considered a benign disorder. In contrast, HES is primarily a multisystem disorder that may involve several organs, including the digestive tract, and often has a fatal outcome.

**Key words:** eosinophilic gastrointestinal disorders; eosinophilic oesophagitis; eosinophilic gastroenteritis; hypereosinophilic syndrome.

## INTRODUCTION

The adjective, 'idiopathic' , stems from two Greek roots, *idio* (reflexive or pertaining to itself) and *pathy* (suffering or disease), and is used to classify diseases in which the mechanisms or origin of a condition is obscure or unknown. The idiopathic disease may comprise several different entities. The term, 'eosinophilic' , denotes that the

*Abbreviations:* ECP, eosinophil cationic protein; EDN, eosinophil-derived neurotoxin; EE, eosinophilic oesophagitis; EGE, eosinophilic gastroenteritis; EGID, eosinophilic gastrointestinal disorder; GERD, gastro-oesophageal reflux disease; HES, hypereosinophilic syndromes; HPF, high power field.

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histological inflammatory response is predominantly characterised by an eosinophilic tissue infiltration. Moreover, it is likely that eosinophils play a pivotal role in the pathogenesis of these disorders. Recent practice classifies those idiopathic eosinophilic infiltrations that occur primarily in the gastrointestinal tract under the umbrella acronym of eosinophilic gastrointestinal disorder(s) (EGID).[1]

In this review, we focus on the three main representatives of the EGID, in particular, on idiopathic *eosinophilic oesophagitis* (EE), idiopathic *eosinophilic gastroenteritis* (EGE) and idiopathic *hypereosinophilic syndromes* (HES) with gastrointestinal involvement. Because each of these conditions has different properties and likely its own pathogenesis, to subsume them into one single category is quite arbitrary and based exclusively on descriptional features. EE is definitely an oesophageal-restricted disease with a favourable long-term prognosis.[2] In patients with EGE, the inflammatory process involves several segments of the gastrointestinal tract but, nevertheless, this chronic inflammation can also be considered a benign disorder. In contrast, HES is primarily a multisystem disorder that may involve several organs, including the digestive tract, and often has a fatal outcome.[3,4] Despite these fundamental differences, all three conditions share the same features of being 'idiopathic' and 'eosinophilic' , and, as long as our understanding of the underlying mechanisms remains so fragmentary, we may take the liberty of classifying them into one single category.

## EOSINOPHILIC OESOPHAGITIS

Eosinophilic oesophagitis (EE) is by far the most common EGID. Because of its clinical relevance, EE is discussed here in more depth than are the other EGIDs.

### Definition

Considering that the first comprehensive descriptions of this inflammatory oesophageal disease were published in the early 1990s, not quite 15 years ago, EE can be viewed as a relatively young disorder.[5–7] Nevertheless, in this short time, EE has become an acknowledged and well-recognised disease. However, as the presenting symptoms may mimic those of gastro-oesophageal reflux disease (GERD), defining EE is not always straightforward. Moreover, oesophageal eosinophilia is not found uniquely in EE and the endoscopic features of EE are often uncharacteristic or confusing. The following paraphrase, based on clinical and pathological features, has proven feasible for clinical as well as for research purposes: EE is characterised by oesophagus-related symptoms in combination with a dense oesophageal eosinophilia, both of which persist despite prolonged treatment with proton pump inhibitors.[8]

### Epidemiology

During the last few years, gastroenterologists in industrialised countries all over the world have experienced a dramatic increase in the number of diagnosed EE cases.[9–13] Interestingly, so far no patients have been reported from developing countries or from tropical areas. EE seems to be a typical disease of civilisation. There is a huge body of evidence suggesting that EE's prevalence is increasing at a startling rate, but there is still an on-going debate about how common this disorder actually is. Recent data from a population-based longitudinal study showed that throughout the observation period lasting more than a decade and a half, EE has an average annual incidence of