Best Practice & Research Clinical Gastroenterology
Vol. 19, No. 2, pp. 177–198, 2005
doi:10.1016/j.bpg.2005.01.009
available online at http://www.sciencedirect.com

# 1

# Eosinophilic gastroenteritis

Seema Khan*,[1] MD

Assistant Professor of Pediatric Gastroenterology

*Division of Gastroenterology, University of Pittsburgh School of Medicine, Children's Hospital of Pittsburgh, 3705 Fifth Avenue, Pittsburgh, PA 15213, USA*

Eosinophilic gastroenteritis despite its uncommon occurrence is one of the most important primary eosinophilic gastrointestinal disorders, and most commonly presents with abdominal pain. The terminology is, however, misleading because all levels of the gastrointestinal tract from the esophagus to the rectum may be affected. A history of atopy and allergies is present in 25–75% cases. The heterogeneity in the clinical presentations of EG is determined by the site and depth of eosinophilic infiltration. Eosinophilic intestinal inflammation also occurs secondarily in the gastrointestinal tract in inflammatory bowel disease, autoimmune diseases, as reactions to medications, infections, hypereosinophilia syndrome, and after solid organ transplantation. Recent investigations providing an insight into the pathogenesis of eosinophilic gastroenteritis support a critical role for allergens, eosinophils, Th-2 type cytokines, and eotaxin in mediating eosinophilic inflammation. The diagnosis is confirmed by demonstrating prominent tissue eosinophilia on histopathology. Treatment recommendations based on data extrapolated from retrospective, uncontrolled studies, and expert opinion support the use of restricted diets, corticosteroids, leukotriene receptor antagonists, and mast cell stabilizers. Many unanswered questions remain with regard to the natural history, optimal duration of therapy, safer steroid-sparing long-term treatment agents, and the means of reliable and non-invasive follow-up.

**Key words:** eosinophilic gastroenteritis; abdominal pain; eosinophilia; food allergies; parasites.

Eosinophilic gastroenteritis (EG) is recognized as a rare albeit an important etiology for abdominal pain. Recent years have seen a growing familiarity with the wide range of gastrointestinal presentations attributed to usually discrete primary or secondary eosinophilic gastrointestinal disorders (EGID). The sites of inflammation determine the nomenclature for primary EGID. The most well characterized of these, eosinophilic esophagitis (EE) and eosinophilic gastroenteritis (EG), affect all ages; others, like food

* Tel.: +1 412 692 5180; Fax: +1 412 692 7355.
*E-mail address*: seema.khan@chp.edu.
[1] Address: Division of Pediatric Gastroenterology, Alfred I. duPont Hospital for Children, 1600 Rockland Road, P.O. Box 269, Wilmington, DE 19899, USA. Tel.: +1 302 651 4000; fax: +1 302 651 5838.

protein induced enterocolitis and eosinophilic proctitis, are uniquely pediatric diagnoses. All of these disorders exhibit prominent eosinophilic tissue infiltration and a strong association with allergies.[1] The collaborative efforts of gastroenterologists, allergists, and immunologists have made significant advances in understanding of the immunopathogenesis of EGID in recent years.

Eosinophilic intestinal inflammation also occurs secondarily in the gastrointestinal tract in inflammatory bowel disease (IBD), autoimmune diseases, reactions to medications,[2] infections, hypereosinophilia syndrome (HES), and after solid organ transplantation.[3,4] These disorders are not the subject of the current chapter, but one must consider them in the differential diagnosis of the primary eosinophilic diseases.

We will first review the molecular mechanisms and the key mediators in the inflammatory process in EGID, and then discuss the clinical characteristics of EG, and an approach to diagnostic evaluation and treatment. It should be recognized that the term EG is a misnomer as it includes a broad spectrum of clinical presentations due to eosinophilic infiltration involving anywhere from the esophagus to the rectum.

## PATHOGENESIS

### Eosinophil

The eosinophil, a bilobed granulocyte, containing cationically charged granular proteins with a high affinity for the acidic dye eosin, was first described by Paul Ehrlich in 1879. Eosinophils are synthesized in the bone marrow under the influence of transcription factors, GATA-1, GATA-2, and c/EBP,[5] and cytokines, interleukin (IL)-3, IL-5 and granulocyte macrophage colony stimulating factor (GM-CSF). Maturation of eosinophils is complete over 8 days following which they are released into the circulation with the help of cellular adhesion molecules, cytokines, and an eosinophil selective chemokine known as eotaxin. Eosinophils form 2–4% of the granulocyte pool and have a circulating half-life of 8–12 hours. They move along a concentration gradient of eosinophil selective chemoattractants and move to reside in tissues, mainly the gastrointestinal tract, thymus, hematopoietic organs, and mammary glands. In the gastrointestinal tract, eosinophils survive for about a week and finally undergo apoptosis.[6,7]

### Eosinophils and the gastrointestinal tract

The gastrointestinal tract is the main non-hematopoietic organ where eosinophils reside in the healthy state. Eosinophils are normally present in the lamina propria, but the number of eosinophils regarded as pathologic for various sites along the gastrointestinal tract is debated; the highest concentrations are found in the cecum and appendix. Within the gastrointestinal tract, the esophageal epithelium is unique in being devoid of eosinophils under non-inflammatory conditions.[7]

Eosinophils have a role in both host defense against parasitic infections, and believed to be critical in the pathogenesis of EGID. Recent investigations strongly support a role for eosinophils, Th-2 cytokines (IL-3, IL-5, IL-13) and eotaxin as the most critical factors in the pathogenesis of EGID, and their intimate connection with allergies and asthma.[8–10] In the case of eosinophilic gastrointestinal inflammation, an antigen exposure stimulates eosinophil synthesis, rolling, adhesion, diapedesis, and trafficking to the site of insult.