

## Eosinophilic and Autoimmune Gastrointestinal Disease: New Insights and New Entities

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Nicholas J. Talley

#### Gut Eosinophilia in Food Allergy and Systemic and Autoimmune Diseases

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Nicholas J. Talley

Eosinophilic gastroenteritis is a rare disease characterized by striking tissue eosinophilia in any layer of the gut wall; however, many diseases can cause increased gut eosinophilia. Allergic reactions to food are an important cause of gut eosinophilia. Not all adverse reactions to food are IgE mediated, and most cases of IgE-mediated food allergy do not have eosinophilic gastroenteritis. Parasitic, bacterial, and viral pathogens as well as certain systemic diseases such as vasculitis can cause gut eosinophilia. These heterogeneous conditions are reviewed in this article.

#### Eosinophilic Gastroenteritis

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Seema Khan and Susan R. Orenstein

Eosinophilic gastroenteritis is an infrequently diagnosed condition that is characterized by prominent eosinophilic infiltration of the stomach or small intestine, generally localized to one level of the intestinal wall; the variable organ locus and wall depth produce heterogeneous clinical presentations. A strong association with atopy is present in most cases, supported by circumstantial evidence and the demonstration of Th-2 proinflammatory cytokine profiles in animal studies. A high degree of suspicion is required to establish the diagnosis, which must be based on intense gastrointestinal eosinophilia. Management is directed toward removal of offending allergens and use of anti-inflammatory agents. Novel and emerging treatments on the horizon are biologic therapies and selective anti-eosinophil agents.

#### Eosinophilic Esophagitis in Adults

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Ganapathy A. Prasad and Nicholas J. Talley

Eosinophilic esophagitis in adults is a disease characterized by eosinophilic infiltration of the esophageal mucosa and symptoms of

long-standing solid food dysphagia and food impactions. First described in 1978, this syndrome is being recognized increasingly in the developed world, with multiple case series reported from the United States, Europe, and Australia during the past decade. Diagnosis requires the presence of greater than or equal to 15 eosinophils/high-power field on esophageal biopsies. Successful treatment in adults has been reported with the use of systemic and topical swallowed steroids. Endoscopic treatment has been associated with increased an risk for tears and perforations.

### **Eosinophilic Esophagitis in Children: Clinical Manifestations**

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Philip E. Putnam

During the past decade, the increasing number of recognized cases of eosinophilic esophagitis in children and adults has resulted in a dramatic expansion of the medical literature surrounding it. Clinical and basic research has contributed to a better, but still incomplete, body of knowledge regarding its clinical and histologic manifestations, as well as its immunologic and genetic pathogenesis. This article provides a broad framework for recognizing the remarkable variety of clinical manifestations of eosinophilic esophagitis in children, which must be considered as part of the differential diagnosis in many different clinical situations.

### **Functional Gastrointestinal Disorders and the Potential Role of Eosinophils**

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Marjorie M. Walker and Nicholas J. Talley

The eosinophil–mast cell–neural pathway may be important in the pathophysiology of functional gastrointestinal disorders characterized by unexplained abdominal pain, disordered defecation, or meal-related discomfort. There is evidence that duodenal eosinophils are increased in functional dyspepsia, whereas mast cells are increased in the lower gut in irritable bowel syndrome, directly supporting a role for a hypersensitivity-type reaction in these disorders. The trigger may be a pathogen, food, or other allergen in the gut mucosa. This trigger may evoke eosinophils, mast cells, and other components to cascade to up-regulate serotonin release, with modulation of the enteric and central nervous systems, creating a vicious cycle. If correct, this theory suggests treatment should specifically target the eosinophil–mast cell pathway.

### **Enteric Autoantibodies and Gut Motility Disorders**

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Purna Kashyap and Gianrico Farrugia

Increasing evidence suggests that a subset of gastrointestinal motility disorders is associated with the presence of circulating antibodies. These antibodies are directed against various molecular targets, the best known being anti-neuronal nuclear antibody (ANNA-1 or anti-Hu) associated with paraneoplastic motility disorders. There is also evidence that the presence of distinct autoantibody profiles is associated with

non-paraneoplastic motility disorders. This review focuses on the types of antibodies associated with gastrointestinal motility disorders and the significance of these antibodies. Algorithms are suggested for the work-up and treatment of patients with circulating antibodies associated with gastrointestinal motility disorders.

## **Celiac Disease and Autoimmunity in the Gut and Elsewhere**

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Susan H. Barton and Joseph A. Murray

This review focuses on the autoimmune connective tissue diseases, endocrine, and dermatologic conditions associated with celiac disease, as well as the related gut inflammatory disorders of refractory celiac disease, autoimmune enteropathy, collagenous enteritis, and collagenous colitis.

## **(Auto)Antibodies in Inflammatory Bowel Diseases**

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Severine Vermeire, Nathalie Vermeulen, Gert Van Assche, Xavier Bossuyt, and Paul Rutgeerts

Patients who have inflammatory bowel diseases (IBD) express strong antibody responses to a variety of epitopes. A number of (auto)antibodies have been described in patients who have Crohn's disease or ulcerative colitis. These markers reflect a loss of tolerance toward bacterial and fungal flora and have been studied for their clinical value in IBD patients. However, currently, they have no place in the diagnostic work up. Their real promise may lie in their use as surrogate markers of complicated aggressive disease as shown in various retrospective studies, but prospective data are lacking.

## **Autoimmune Pancreatitis**

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Timothy B. Gardner and Suresh T. Chari

Autoimmune pancreatitis is the pancreatic manifestation of a systemic disorder that affects various organs, including the bile duct, retroperitoneum, kidney, and parotid and lacrimal glands. It represents a recently described subset of chronic pancreatitis that is immune mediated and has unique histologic, morphologic, and clinical characteristics. A hallmark of the disease is its rapid response to corticosteroid treatment. Although still a rare disease, autoimmune pancreatitis is increasingly becoming recognized clinically, leading to evolution in the understanding of its prognosis, clinical characteristics, and treatment.

## **Diagnosis and Treatment of Autoimmune Hepatitis**

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Bruce A. Luxon

Autoimmune hepatitis (AIH) is an idiopathic hepatitis characterized by inflammation of the liver, presence of autoantibodies, and evidence of increased gamma globulins in the serum. It represents an enigmatic

interaction between the immune system, autoantigens, and unknown triggering factors. This article provides a brief summary of the diagnosis of AIH, the natural history of AIH, an approach to the treatment and follow-up of AIH, and the role of liver transplantation in the treatment of AIH.

## **Antimitochondrial Antibody–Negative Primary Biliary Cirrhosis**

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Flavia Mendes and Keith D. Lindor

There is a subset of patients who have biochemical and histologic features consistent with primary biliary cirrhosis (PBC) who lack antimitochondrial antibodies (AMA). This entity is usually referred to as AMA-negative PBC or alternatively autoimmune cholangitis. Patients who have AMA-negative PBC are believed to have a similar clinical course, response to treatment, and prognosis as their AMA-positive counterparts. As more sensitive and specific serologic tests are developed to detect serum AMA, it is possible we may find that these patients initially believed to be AMA-negative are indeed AMA-positive, suggesting a single disease process.

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