

Images in Allergy and Immunology

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Immunopathology of food allergy

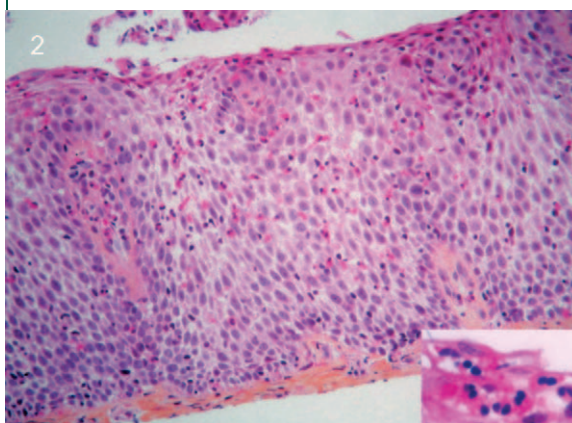
Editor's note: This feature, Images in allergy and immunology, is designed to highlight current concepts of the immunopathology of allergic diseases and other common immunologically mediated diseases. The presentation will appear as sets of images that involve cross-pathology, histopathology, and molecular pathology and will cover a range of topics of interest to allergists and immunologists.

Food allergy is an increasingly common problem. From a clinician's point of view, the manifestations of food allergy can take 2 distinct forms: allergy with systemic manifestations and food allergy with primary gastrointestinal manifestations. Systemic symptoms induced by food allergy are due to specific IgE directed against a wide variety of antigens. Ingestion of the offending food induces rapid cross-linking of IgE on

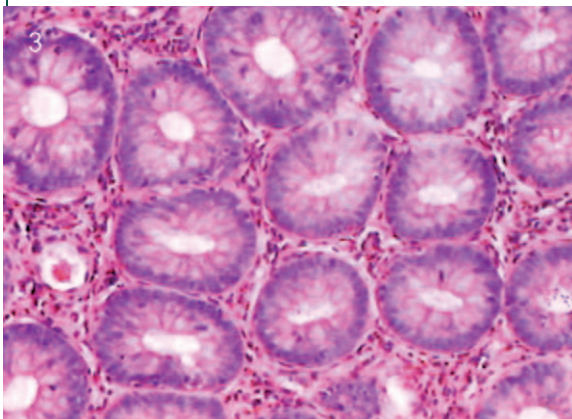
mast cells, leading to immediate hypersensitivity symptoms. These include bronchospasm; urticaria and angioedema (Fig 1 [courtesy of Dr Barry Zimmerman]); vomiting, diarrhea, or both; and, in severe cases, hemodynamic instability and shock.

Primary gastrointestinal food allergy is seen in both children and adults. There are 2 potential mechanisms for this syndrome: IgE mediated and non-IgE mediated. Symptoms of these disorders include gastroesophageal reflux, vomiting, diarrhea, abdominal pain, weight loss, and failure to thrive in children. The symptoms can be caused by localized pathology, such as esophagitis or a more widespread gastroenteritis. The most frequent pathologic hallmark of these disorders is eosinophilia. Eosinophilic esophagitis (Fig 2) is related to food ingestion in a significant number of cases, but the link to IgE-mediated food allergy is less clear.

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Eosinophilic gastroenteritis is also related to food allergies in about one third of patients (Figs 3 [courtesy of Drs Jean Perrault and Van-Hung Nguyen] and 4). However, cow's milk protein-induced enteropathy is a well-documented disorder in infants and young children. This disorder is associated with the



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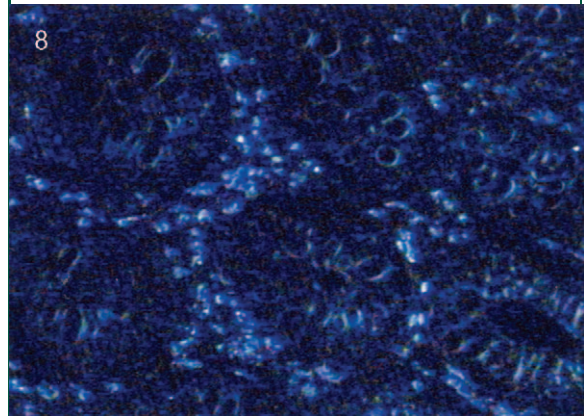
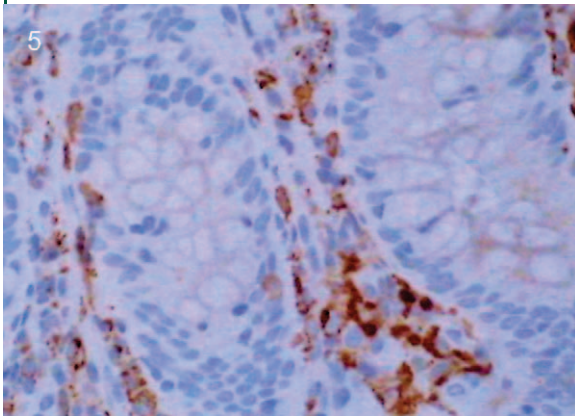
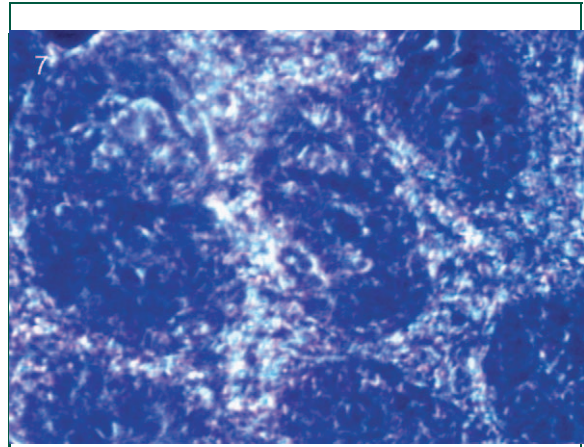
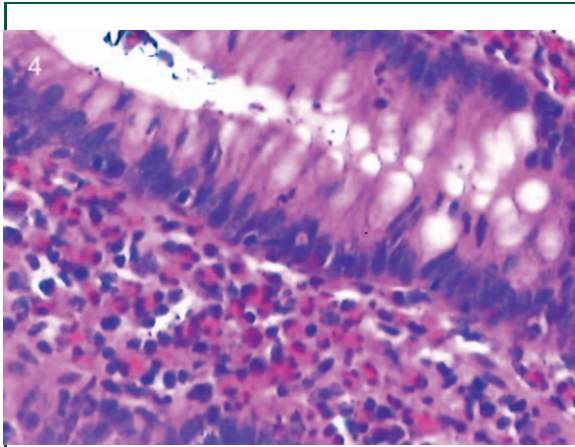
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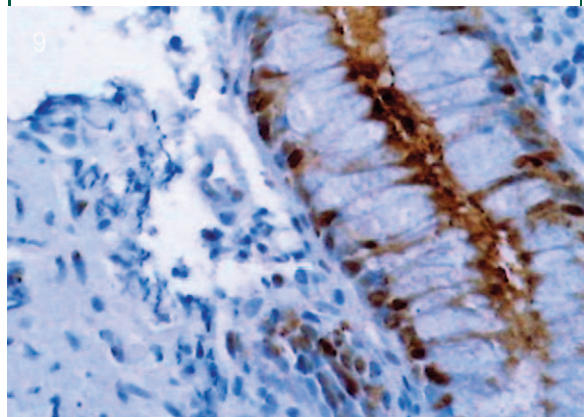
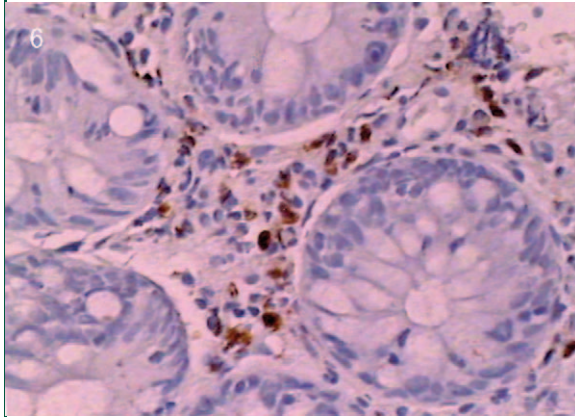
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production of IgE in a minority of cases. The best potential mechanism is through infiltration of the gut by antigen-specific T cells (Fig 5 [immunocytochemistry]). This is associated with the production of cytokines, including IL-5, which will support eosinophil survival in the inflamed gut (Fig 6 [immunocytochemistry]). Other cytokines associated with these disorders include TNF- α and IL-13 (Figs 7 and 8 [in situ hybridization]).



IgE plays a role in these disorders. Inflamed gut tissue will allow for more antigen transfer, causing immune recognition and often production of antigen-specific IgE. Locally produced IgE can sensitize mast cells and contribute to the immediate hypersensitivity reactions that occur after ingestion of an offending antigen. IgE might also be taken up on CD23, the low-affinity Fc ϵ receptor. It has been proposed that the

enterocytes can express CD23 (Fig 9 [immunocytochemistry]); in sensitive individuals this can lead to more rapid antigen uptake and antigen presentation.

Infiltration of the gut mucosa with inflammatory cells and T_H2 cytokine-producing cells could also be

a manifestation of allergic disease affecting other organs, such as atopic dermatitis. Similarly, a significant percentage of children with food allergy have evidence of other allergic diseases, including asthma, rhinitis, conjunctivitis, and dermatitis.