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Eosinophils and allergic diseases of the gastrointestinal tract

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The association between increased tissue eosinophilia and allergic disease is particularly striking in the case of the gastrointestinal tract. About 80% of individuals with eosinophilic gastrointestinal disorders (EGIDs) are atopic, while half of the patients with gastrointestinal allergy show tissue eosinophilia. The function of eosinophils in gastrointestinal allergic disorders is unclear; however, a proinflammatory action is most likely. Cytokines (interleukins 5 and 3, granulocyte-monocyte colony-stimulating factor) and chemokines (eotaxin, RANTES, etc.) released by Th2 lymphocytes, mast cells and other tissue cells have been identified as major regulators of eosinophil chemotaxis and activation, but a convincing mechanism by which eosinophils are activated in an allergen-dependent manner is still lacking. The diagnostic approach comprises both histological and laboratory methods to assess eosinophilia and eosinophil activation, as well as tools to assess the allergic disease while excluding other gastrointestinal diseases such as food intolerances, infections and tumours. Treatment of allergic EGIDs includes elimination or elemental diets and drug therapy using classical anti-allergic agents such as topical corticosteroids and new approaches such as LTD4 receptor antagonists or antibodies against IL-5 or eotaxin.

Key words: eosinophils; eosinophilic oesophagitis; eosinophilic gastroenteritis; eotaxin; eosinophil-derived neurotoxin; interleukin-5; food allergy.

The gastrointestinal mucosa is predisposed to develop allergic reactions in individuals with a genetic risk for allergy because this site is particularly exposed to allergens (food, pollen, bacterial antigens, etc.) and is equipped with all prerequisites needed to develop allergic reactions (mast cells, eosinophils, lymphocytes, dendritic cells,

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nerves, etc.). Most allergic reactions of the gastrointestinal tract are triggered by food allergens, i.e. food proteins. The most relevant food proteins are listed in Table 1. In adults, cross-reactions between pollens – namely tree pollens (30–93%), mugwort (16–27%), and latex (17–42%) – and food allergens are of particular importance, since they account for most food-allergy manifestations in adults.[1]

In industrialised countries approximately 20–30% of the population suffers from adverse reactions to food (ARFs); however, only 1/4 cases (in children) and 1/10 cases (in adults) are caused by food allergy.[2,3] ARFs are defined as clinically abnormal reactions to ingested food or food additives. The reactions are divided into immune-mediated reactions (food allergies) and non-immune reactions (food intolerances). Food intolerances include carbohydrate intolerances (lactose, fructose, sorbitol, etc.), amine intolerances (histamine, serotonin, etc.) and other forms of intolerance.[4]

The present chapter focuses on food allergy – the immune-mediated hypersensitivity reaction against food – in which eosinophils are frequently involved.

PATHOPHYSIOLOGY OF FOOD ALLERGY IN THE GASTROINTESTINAL TRACT

Regulation of intestinal immune responses

The intestinal mucosa has to meet the challenge of protecting the host against possibly harmful nutrients, microbes and toxins on the one hand, while on the other hand ensuring the uptake of nutrients and antigens indispensable for life.[5] To do this, the gastrointestinal barrier is equipped with an innate immune system and other non-specific defence systems, including gastric acid, mucus and bicarbonate secretion, as well as an intact epithelial layer forming tight junctions, peristaltic movement, digestive enzymes, phagocytes, alternative complement pathways, and antimicrobial peptides such as defensins and cathelicidins.[6–8] Macrophages and neutrophils, but also mast cells and eosinophils, are important effector cells involved in such innate immune responses.[9,10] Conserved bacterial structures are recognised by these cells through 'pattern recognition receptors', including the Toll-like receptor family.[11] Upon recognition of 'danger signals', these effector cells trigger and/or support adaptive immune responses required for effective host defence and protection. On the other hand, the gastrointestinal immune system has the unique capacity to develop 'oral tolerance', a state of acceptance of foreign antigens such as food or particular bacterial antigens which is achieved by down-regulation of normal immune responses, and which is necessary for normal gut function.[12]

Table 1. Most relevant food allergens in children and adults.[1]

Children	Adults
Milk and milk products	Pollen-associated food allergens (e.g. apple, nuts, celery, carrots, rye, paprika, spices)
Egg	Nuts and seeds
Wheat	Peanuts, soy
Soy, peanuts	Fish and seafood
Nuts	Milk and milk products, egg
Fish	Latex-associated food allergens (e.g. banana, avocado, kiwi)