Intestinal Allergy: Food hypersensitivity in infancy and childhood
by Thomas Attard

Gastrointestinal symptoms are frequently attributed to food hypersensitivity by parents and increasingly by the medical community. Indeed, up to 38% of the general population in Western countries think they have "food allergy" although this is objectively confirmed in only 1-2% of the population. The incidence of food hypersensitivity appears to be on the rise, paralleled by the increase in atopic disorders over the last 30-40 years and concurrent with a decline in infectious disorders. This may be due to the emergence of the "hygiene hypothesis" which raised awareness of the role of microbes and their products in immune regulation; more recently, this has prompted important observations on the impact of beneficial bacteria (protective) in the prevention of allergic processes.

The mechanisms underlying food hypersensitivity are complex and only partially understood. The atopic individual appears susceptible to a variety of allergic processes. This is in part a result of disordered mucosal immune function including IgE deficiency, increased epithelial permeability, altered expression of major histocompatibility complex antigens, and the modulation of the immune system by extraneous factors including the intestinal flora (microbiome). The latter is balanced between beneficial bacteria and pathogenic organisms, with the predominance of the former being associated with a lower risk of atopic disorders. The gut-brain axis, although less common in exclusively breast-fed infants, also plays a role in the development of food hypersensitivity.

Clinical Scenarios of Food Hypersensitivity

Food hypersensitivity in infancy: Cows milk allergy (CMA); milk; soy protein intolerance; gluten enteropathy is a relatively common disorder in infancy; it appears to decrease in prevalence with age and affected infants are very likely to eventually outgrow it by the second year of life. Food allergies are not usually associated with anaphylaxis, although respiratory symptoms (rhinitis, asthma) are common in infants and young children with food hypersensitivity. In these patients, the initial presentation is often characterized by a "cradle cap" rash, irritability, and diarrhea, with a provocation test performed in the early years of life.

Food hypersensitivity in young adults: Food allergies in the older child include both IgE-mediated and IgE-independent mechanisms. In general, IgE-mediated reactions are more common in the younger age group, while IgE-independent reactions are more frequent in the older age group. The symptoms associated with food hypersensitivity in the older child may include a variety of conditions such as eczema, asthma, hay fever, and food intolerance. These symptoms may be localized to the skin, respiratory tract, or gastrointestinal tract and may vary in severity from mild to severe.

Milk Allergy or Lactose Intolerance?
Lactose intolerance is often confused with milk allergy, or more confusingly the two are hybridized as milk intolerance. Milk intolerance refers to a condition of relative or absolute inability to tolerate milk, which may be due to a variety of factors including inadequate production of lactase, gas and typically spasm abdominal cramps. Symptoms usually follow half an hour to several hours of ingestion of milk proteins. Treatment of milk intolerance is through avoidance of milk, dairy products, and milk-based beverages. In conclusion, allergic diseases are increasingly prevalent in our population including children. Specific food hypersensitivity disorders are age-dependent and overlap with functional disorders that may be difficult to diagnose. A clear and consistent understanding of the basic pathophysiology in order to effectively diagnose and treat these conditions is required.
Intestinal Allergy: Food hypersensitivity in infancy and childhood
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Gastrointestinal symptoms are frequently attributed to food hypersensitivity by patients and increasingly by the medical community. Indeed, up to 85% of the general population in Western countries think they have an allergy to food, although this is objectively confirmed in only 1-2% of the population. The incidence of food hypersensitivity appears to be on the rise, paralleled with the overall rise in atopic disorders over the last 50 years and concurrent with a decline in infectious disorders. This has led to the emergence of the ‘hygiene hypothesis’ which raised awareness of the role of microbes and their products in immune regulation; more recently, the hypothesis has prompted important observations on the impact of beneficial bacteria (probiotics) in the prevention of allergic processes.

The mechanisms underlying food hypersensitivity are complex and only partially understood: the atopic individual appears susceptible to a variety of allergic processes. This is in part a result of disordered mucosal immune function including IgE deficiency, increased epithelial permeability, loss of regulatory T lymphocytes, and alterations in the microflora present in the gut. These factors contribute to the development and exacerbation of allergic symptoms and diseases. The role of the gut microbiota in the regulation of the immune system is increasingly recognized. The gut is the largest organ in the body, containing trillions of microorganisms that play a crucial role in maintaining health and preventing disease. The gut microbiota is a complex ecosystem that is shaped by factors such as diet, health, and genetic factors. The gut microbiota has been shown to play a key role in the development of immune responses and the regulation of allergic diseases. Gut dysbiosis, which is an imbalance in the gut microbiota, has been associated with an increased risk of allergic diseases.

Food hypersensitivity in infancy: Cows milk allergy (CMA): milk induced gastrointestinal intolerance (MIGI) is a relatively common disorder in infancy. It appears to decrease in prevalence with age and affected infants are very likely to eventually outgrow it by the second year of life. It is not necessarily associated with an increased risk of other atopic disorders including asthma, hay fever, or eczema (‘atopic march’) later in life. Affected infants typically present with gastrointestinal or skin manifestations. In the first weeks of life, gastrointestinal symptoms such as colic, vomiting, or diarrhea may be the presenting features. The symptoms are usually associated with the ingestion of milk or dairy products. The diagnosis of milk allergy is based on clinical symptoms and the exclusion of other causes of gastrointestinal symptoms. The treatment of milk allergy involves the exclusion of milk from the diet and the use of alternative formulas. In severe cases, immunotherapy may be considered.

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Food hypersensitivity in childhood: Food allergy in children is a heterogenous condition with different clinical presentations and severity. The diagnosis of food allergy in children can be challenging, as the symptoms can be mild to severe and the triggers can be difficult to identify. In some cases, the symptoms may overlap with other medical conditions, making the diagnosis even more difficult. It is important to consider the possibility of food allergy in children presenting with symptoms such as hives, anaphylaxis, respiratory symptoms, or gastrointestinal symptoms. The diagnosis of food allergy in children is typically made through a combination of clinical history, physical examination, and laboratory tests. The treatment of food allergy in children involves dietary elimination and sometimes immunotherapy.

Esophageal Esophagitis (EE)

A more recently recognized pattern of allergic enteropathy is esophageal esophagitis. Although initially described in children, it is also now recognized as an adult disease. Patients with EE typically present with upper gastrointestinal symptoms such as dysphagia, heartburn, and regurgitation. The esophageal mucosa is typically inflamed and may have ulcerations.

Milk Allergy or Lactose Intolerance?

Lactose intolerance is often confused with milk allergy, or more confusingly the two are hybridized as milk intolerance (Figure 2). Lactose intolerance refers to a condition of relative or absolute lactase deficiency, which brings about malabsorption of foods containing lactose, notably dairy. Undigested lactose is fermentatively active and is metabolized in the colon with the liberation of gases (flatulence, belching, and diarrhea), and gas and typically spasmotic abdominal cramps. Symptoms usually follow a half or several hours of ingestion. The diagnosis is confirmed through breath hydrogen testing or a clinical test to detect for lactose malabsorption.

Celiac Disease

Although not following the classic paradigm for a food hypersensitivity disorder, celiac disease is an environmentally triggered autoimmune disorder which shares several features with intestinal allergies. An in-depth discussion of celiac disease is beyond the scope of this review, but it is worth reiterating that several reviews have highlighted the significant co-occurrence of undiagnosed celiac disease in our society. A recent review of the literature suggests that in several Mediterranean countries, amongst the low-risk and general population the prevalence of celiac disease is comparable to the seropositivity screening rates ranging from 0.1-1.2%. The increasing incidence of celiac disease appears to parallel the presentation of more atypical clinical presentations. It is also considered to be a consequence of environmentally triggered autoimmune disorders. A more recent study suggests that celiac disease may be associated with other autoimmune disorders, including diabetes, thyroid disease, and inflammatory bowel disease. The diagnosis of celiac disease is typically made through a combination of clinical history, physical examination, and laboratory tests. The treatment of celiac disease involves dietary elimination, with the avoidance of gluten-containing foods.