Editorial

Intestinal complaints are frequent both in children and in adults. A direct link between food ingestion and subsequent gastrointestinal (GI) symptoms (such as pain, bloating, diarrhea, or constipation) is often suspected and easily categorized as adverse food reaction. And most often without asking for medical advice, patients experiment with food avoidance or specific restriction diets to relieve their symptoms. These restriction diets become more and more fashionable and are easily promoted as a healthy lifestyle. After lactose-free diet, cow's milk protein-free diet and, more recently, gluten-free diet became very trendy. It is suspected that in the USA, a strict gluten-free diet is followed by significantly more individuals in form of self-medication for presumably gluten-related symptoms without seeking medical advice than by patients with well-diagnosed celiac disease. A rising market for lactose-free and now gluten-free products parallels this trend – often promoted with the notion of healthier and better food. A recent analysis [1] showed that commercially available foods for children with a claim such as being gluten-free are not necessarily of high nutritional quality. In addition, the notion of a healthier life by using restriction diets is not necessarily true, especially for children, who are potentially exposed to nutritional deficiencies. Without any diagnostic analyses, often in self-evaluation, patients report on intolerance or “allergic” reactions to a specific food or food class. In the present series of 4 articles, we address this issue, raising the question of a link between food components and adverse reactions as true allergic reactions or mechanisms of food-induced intestinal complaints other than allergy, calling them “pseudo-allergic gastrointestinal disorders.” Over the last two decades, there was a marked increase of new allergic and

pseudo-allergic GI conditions, either due to a better recognition of these diseases or a true increase of their incidence, or a combination of both, which is the most likely explanation.

The terms food protein-induced enterocolitis syndrome (FPIES) and food protein-induced allergic proctitis (FPIAP) describe a well-defined but less well-known form of cow's milk allergy in infants and children. In contrast to classical cow's milk or other food allergies, FPIES/FPIAP is a non-IgE-mediated syndrome. In his update on FPIES, Professor Dupont [2] describes two main clinical presentations: a chronic form characterized by recurrent vomiting in patients repeatedly exposed to the offending food, and an acute form occurring after a single ingestion of the offending food within 1–4 h with massive vomiting, often followed by (bloody) diarrhea. In rare cases, FPIES can lead to severe dehydration, lethargy, and a hypovolemic shock responding to intravenous fluids but not to catecholamines. In contrast to other forms of cow's milk allergy, no skin or extraintestinal symptoms occur. In infants, FPIES is most frequently caused by cow's milk protein, followed by soy. In older children or adults, FPIES may occur to solid foods (grains like rice, oat, meats, fish, egg, and vegetables). Occasionally, FPIES occurs in the newborn or in exclusively breastfed infants, caused by the mother's consumption of offending foods. FPIAP is a common cause of rectal bleeding in the breastfed neonate.

A different and probably pseudo-allergic, but inflammatory, GI disorder also caused by cow's milk is in the form of an eosinophilic GI disorder (EGID). EGID can occur in patients with well-known allergy as well as in patients without any notion of atopy or allergy. The present

review of Doctor Koutri and Professor Papadopoulou [3] highlights that the clinical presentation depends on the involved GI sites as well as on the extent and the depth of eosinophilic inflammation of the intestinal mucosa, sub-mucosa, or muscularis. Eosinophilic esophagitis can occur at any age presenting as unspecific feeding disorder in infants and young children followed by vomiting and abdominal pain in older children, while adolescents and adults often experience dysphagia and food impaction. Patients with eosinophilic gastritis or gastroenteritis present with abdominal pain, nausea, vomiting, early satiety, sometimes associated with failure to thrive or weight loss. Patients with diffuse small intestinal involvement may develop malabsorption, anemia, and hypoalbuminemia. Involvement of the colon leads most often to abdominal pain and (bloody) diarrhea. As for FPIES or FPAP, cow's milk proteins are the most frequent triggers, but EGID caused by wheat, soy, or eggs were also reported.

Intolerance of the milk sugar lactose makes the clinical picture even more complex. Very often patients and parents confound cow's milk protein allergy and intolerance of lactose, considerably complicating the clinical care for these patients. Professors Berni-Canani and Di Costanzo [4] review the recent knowledge on lactose intolerance, a truly nonallergic but still cow's milk-mediated GI disorder. The clinical presentation is dominated by abdominal pain, meteorism, and watery diarrhea. Since primary lactase deficiency is genetically determined, and approximately 70% of the global adult population is lactase non-persistent (hypolactasia), the majority of individuals do not tolerate dairy containing high levels of lactose, while other milk products with lower lactose content or fermented milk products cause no symptoms.

The complexity of these intestinal symptoms and presumably allergic and nonallergic adverse food reactions is caused by the fact that different components of the same food can trigger different reactions. As shown for milk, the protein components elicit predominantly immune-mediated reactions, while carbohydrates provoke the vast

majority of nonimmune-mediated symptoms. In addition, different foods or nutrients can provoke similar or identical GI symptoms, as introduced by discussing the recently described non-celiac gluten sensitivity (NCGS) syndrome [5]. This entity can provoke clinical symptoms resembling celiac disease or wheat allergy but also FPIES or EGID, indicating the need for specific diagnostic tests. In contrast to lactose intolerance or IgE-mediated food allergies, in patients suffering from FPIES, EGID, or NCGS, no specific diagnostic biomarker exists. And as discussed in this series of 4 articles [2–5], the suspected diagnosis of a food-induced adverse event has to be proven by a provocation test in a blinded fashion. If positive, an exclusion diet of the responsible antigen or food component is the most efficient treatment option, in addition to anti-inflammatory drugs if a patient is suffering from an eosinophilic GI disorder. Since the long-term outcome is different according to the underlying disease, a clear diagnosis is important to avoid exposing patients/individuals to an unnecessary or prolonged restriction diet. On the other hand, it is easily conceivable that depending on a variety of environmental factors the intestinal mucosa can react to food components in many ways causing specific adverse reactions. The recognition of inflammatory GI disorders, such as eosinophil GI diseases or allergic disorders including FPIES/FPIAP, as well as complex functional disorders, such as NCGS, is steadily increasing, allowing better diagnosing and treating patients. In addition, the incidence of all these GI diseases is steadily increasing without any clear explication. Some data indicate that the quality of food is quite different in 2018 compared to the 1980s or 1950s. Another interesting field of research is to learn to what extent the intestinal fecal microbiome can cause/modulate these adverse food reactions. The global rise of allergic and pseudo-allergic GI disorders parallels a strong demand in the global population for healthier food and avoidance strategies of certain food compounds accused of causing GI and extraintestinal symptoms and complaints.

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References

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