

Food-Induced Immune Responses as Origin of Bowel Disease?

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I. The Immune System of the Gastrointestinal Tract

- The gastrointestinal tract assures the absorption of essential nutrients and discriminates between harmless food antigens and infectious agents.
- Several barriers (mucosal barrier, established by epithelial lining) and specific mechanisms contribute to the prevention of infections and ensure that most of the antigens are not presented to the immune system.

I. The Immune System of the Gastrointestinal Tract

- **Gastrointestinal flora** is of major importance for the intestinal immune system:
at least 17 families of bacteria; bacteria interact with food by promoting polysaccharide digestion and metabolic products of bacteria may be of importance for epithelial cells. Glycoproteins and Glycolipids are key components involved in receptor signalling and coordination of the immune response.
 - **Innate** and **adaptive immune system** protect the host in specific ways
- > If these mechanisms fail an immune response can be observed





I. The Immune System of the Gastrointestinal Tract

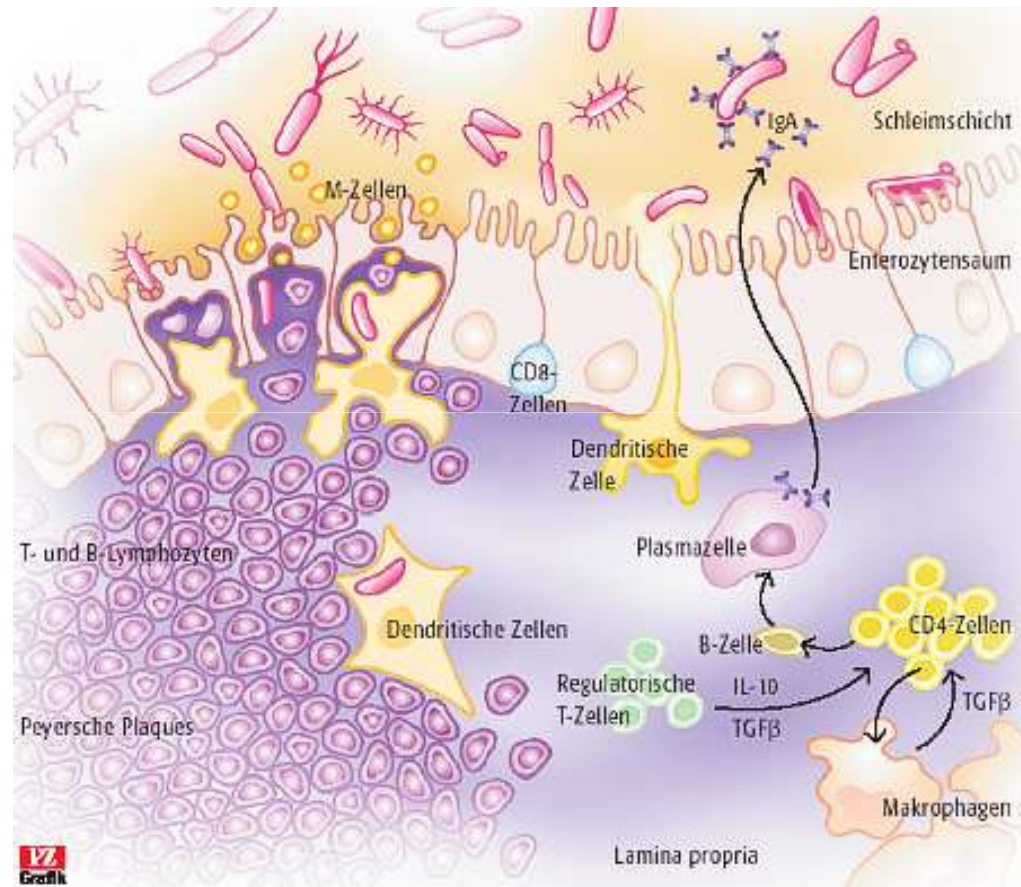
- **Innate immune system:** composed of physical and chemical barriers, blood proteins and members of the complement system; phagocytes (macrophages, neutrophils, natural killer cells)
-> low diversity and specificity for microbes
- **Adaptive immune system:** consisting of B and T lymphocytes responds to foreign antigens with the help of antigen presenting cells. Number of cells and the phenotypes of the T cells are dependent on the anatomical site (e.g. CD8+ cells more in small intestine, CD4+ predominate in colon)

Oriented towards tolerance -> most food and microbial antigens (own gut flora) don't elicit an adaptive immune response

II. The Immune System of the Gastrointestinal Tract

small intestine:

- APC: M cells (membraneous cells) and dendritic cells (extend pseudopods across epithelial lining)
- CD8 cells in the epithelial layer
- CD4 cells in the lamina propria
- regulatory T cells and immunosuppressive cytokines inhibit here harmful immune response
- B cells, Plasmacells secrete IgA (it can bind antigene, neutralize or prevent it's uptake)



II. Food Allergy

- more commonly seen in children (6-8%)
- Symptoms: nausea, vomiting, abdominal pain, diarrhea
- reactions in the skin, cardiovascular or respiratory organ systems are also possible
- foods responsible for the majority of allergic reactions: milk, eggs, peanuts, tree nuts, soy, seafood
- increasing frequency of wheat allergies



II. Food Allergy

- most of reactions are caused by type I hypersensitivity reaction (immediate or anaphylactic hypersensitivity):

Production of immunoglobuline E antibodies in response to certain allergens -> Pre-sensitized IgE on the surface of mast cells bind to food allergens resulting in mast cell degranulation releasing pro-inflammatory factors such as histamine and proteases.

- cross-reactivity between allergens (e.g. allergen epitopes found in birch polls, food allergens in soybean, celery and fruits)
- allergy to food antigens is relativley frequent and can be dangerous because of anaphylactic reactions
- **therapy**: avoid the foods that cause reactions and treat the symptoms caused by allergic reactions.



II. Food Allergy

Food Intolerance: symptoms provoked by certain foods without specific immunological findings;
Those reactions maybe due to direct toxic effect -> vasoactive amines or alkaloids



III. Celiac Disease

- identified in 1888, importance of wheat flour in this condition demonstrated in early 1950s
- prevalence between 1:300 and 1:500 in most countries, relatively frequent in Western hemisphere
- **characteristics**: villous atrophy, symptoms of malabsorption with diarrhea, steatorrhea, weight loss and vitamin deficiency
- caused by **gluten** (main protein groups are gliadins and glutenins); a gluten free diet reverses the findings in celiac disease and clinical symptoms and villous atrophy
- Initial event in pathogenesis unclear



III. Celiac Disease

- classified among the autoimmune diseases: abnormal immune response is directed against the specific antigen tissue transglutaminase (modifies gliadin, converts glutamine residues with gluten to glutamic acid)
- several gliadin epitopes have been predicted immunogenic, so far 5 epitopes of gliadin recognized by T cells have been identified
- Gliadin is recognized by the adaptive immune system and leads to activation of B and T cells ; B cells secrete antibodies to gliadin and tTGase ; Th1 reaction leads to inflammation -> causes flattening of the lining of the small intestine -> interferes with the absorption of nutrients
- **therapy:** at present the only effective treatment is a life-long gluten-free diet



IV. Inflammatory Bowel Diseases

- **Crohn's disease** can occur anywhere in the gastrointestinal tract
characteristics: transmural inflammation
- **Ulcerative colitis** is restricted to the colon
characteristics: mucosal inflammation
- symptoms: abdominal pain, diarrhea with and without gross bleeding, fatigue, weight loss, fever and various extraintestinal manifestations
- pathogenesis of these diseases has not yet been solved;
Pathogenesis includes genetic, immunological and environmental factors (including enteric microflora and nutritional environment)



V. Inflammatory Bowel Diseases

- Role of enteric bacteria in regulating barrier function may be of importance -> modulation of intestinal flora -> may alter the immune response -> contribution to perpetuation of a mucosal chronic inflammation
- Food may modulate these bacteria and could therefore be able to modulate intestinal disease -> unclear
- **Breast feeding:**
Studies showed protective effect of breast feeding which may be due to growth factors in human milk, that protect infants from gastrointestinal infections or prevent the confrontation of food antigens other than human milk to the mucosal surface



V. Inflammatory Bowel Diseases

⇒ **Environmental factors:** important in pathogenesis of IBD -> an early antigen presentation may lead to an induction of immune tolerance, and increased hygiene (lack of parasitic infections) may contribute to the increased incidences of IBD

⇒ little evidence that food plays a causative role in IBD. Nutritional factors may either alter mucosal immune response or the intestinal flora which leads to modification of disease activity



V. Inflammatory Bowel Diseases

Food as therapeutic option in IBD

- there are several compounds in food capable of modulating disease activity by interaction with inflammatory cascade
- Eicosapentenoic acid, a component of fish oil is able to reduce the formation of leukotriene B, an important component in the inflammatory process in IBD.
- Western diet contains polyunsaturated fatty acids, which are precursors for inflammatory mediators.
- Studies suggest that nutritional therapy with glutamine, bioactive lipids and omega-3 fatty acids influences the disease activity in IBD



IV. Inflammatory Bowel Diseases

Food as therapeutic option in IBD

Food influences bacterial flora -> use of Prebiotics (e.g. Oligosaccharides metabolized by colonic bacteria) -> hope that influence microflora to grow probiotic bacteria, which are able to modulate mucosal immune response



V. Conclusion

An intact mucosal barrier, a functioning innate immune system, a tolerant adaptive immune system, in cooperation with the bacterial intestine flora prevent food-induced immune responses.

If these mechanisms fail, food components play a direct causative role in some diseases such as **food allergy** and **celiac disease**. In other diseases such as **inflammatory bowel diseases**, food antigens may contribute in the perpetuation of a mucosal chronic inflammatory process.

- > Initial events leading to these immune disturbances remain unclear.
- > research to improve understanding of the composition and physiological function of the commensal flora

