

## GLUTEN-FREE DIET - DOES IT MAKE SENSE IN GLUTEN-TOLERANT PEOPLE?

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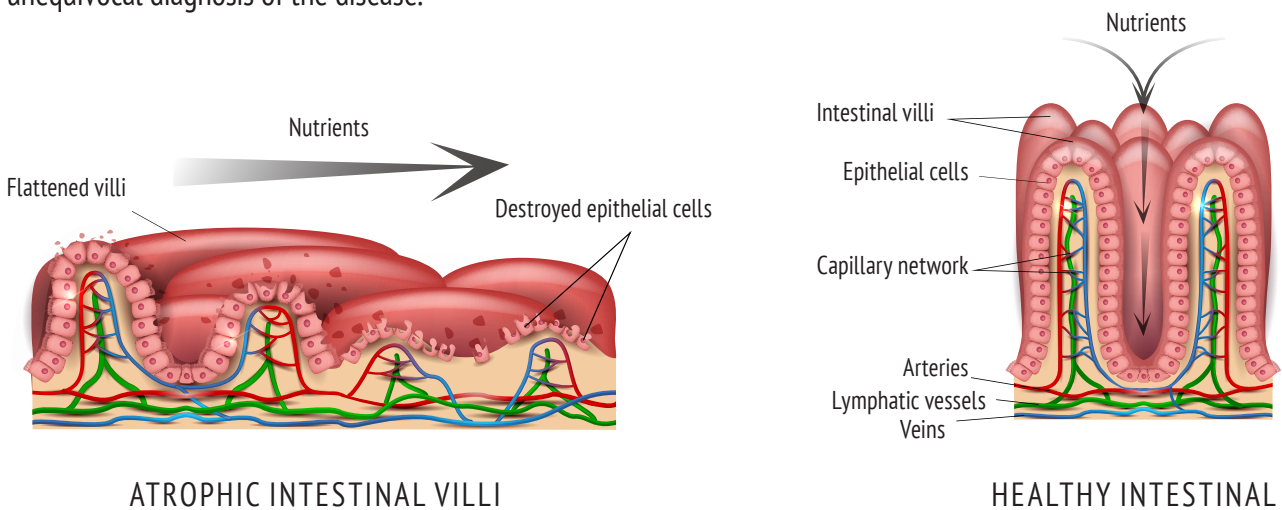
Gluten-free diet has been one of the most popular diets recently. Is it reasonable to use it in cases other than celiac disease? Can elimination of gluten in case of healthy individuals be reasonable? Are answers to those questions plain and simple?

### Know your enemy

Endosperm (storage area) of gluten-containing cereals contains much glutelin and prolamins. Depending on cereal species, the latter are divided into gliadin (wheat), secalin (rye), hordein (barley), and avenin (oat). Then dough made of flour and water is kneaded, those proteins form gluten – a viscous and elastic complex that makes bakery products elastic and firm [1]. Only recently, those structural properties of gluten had been used in bakery only, but at present gluten is added to many other products (meat, sausage, seasonings). Wheat itself may be also modified, for example, to increase the gluten protein content in endosperm, and better engineering properties. That makes it greatly different from normal wheat. It is possible that some part of human population failed to develop appropriate adaptive mechanisms, both associated with function of the gastrointestinal tract, and with response of the immune system to those modifications. However, unequivocal resolution of this issue requires further studies. Addition of gluten to products where it was normally absent, undoubtedly caused a great increase of its consumption. Can it be associated with the doubling of the number of diagnosed celiac disease cases noted during the last two decades? [2].

## Not only celiac disease

The best-known form of abnormal reaction to gluten is celiac disease – autoimmune visceral disease associated with enteropathy of intestinal villi [Fig. 1.]. In genetically pre-disposed individuals contact with the environmental factor (gluten) leads to production of antibodies that destroy cells of the small intestine. Atrophy of those cells impairs absorption of nutrients, which leads to malnutrition and development of numerous other symptoms, both associated with the gastrointestinal tract (chronic diarrhea, persistent digestive discomfort), and systemic (anemia, restricted growth, delayed development, osteoporosis, etc.). Celiac disease is the best-known gluten-dependent condition. A diagnostic protocol strictly defined by ESPGHAN (The European Society for Pediatric Gastroenterology Hepatology and Nutrition) and rapid improvement of condition following introduction of a gluten-free diet allow for correct and unequivocal diagnosis of the disease.



[Fig.1] Comparison of the physiological presentation of intestinal villi and pathological changes characteristic for celiac disease

Unfortunately, celiac disease proves to be just a tip of an iceberg of gluten-associated conditions. There is also a classic food allergy to wheat (with symptoms developing soon after consumption) and a relatively recently described (and therefore often doubted) condition named Non-celiac Gluten Sensitivity (NCGS). The first of those conditions is relatively easy to diagnose – a rapid development of sudden and characteristic symptoms, and presence of specific IgE antibodies following a contact with the allergen enable a precise diagnosis. Unfortunately, the other condition – NCGS – does not manifest with celiac disease-characteristic deformation of intestinal villi, nor presence of specific antibodies, despite a probable activation of immune response [15]. Moreover, a study of 920 patients showing symptoms of irritable bowel syndrome (IBS) (often confused with NCGS) demonstrated hypersensitivity to gluten in as many as 30% of them [3]. Authors of numerous publications call for further diagnostics of this form of abnormal reaction to gluten.

Diseases associated with intolerance of the discussed protein complex are not limited to those causing gastrointestinal symptoms. There is also a set of conditions manifested by dermatological problems, such as Dühring's disease [13] and atopic dermatitis (AD). The article of French specialists in dermatology published in the European Journal of Dermatology [14] indicates an association between numerous chronic dermal diseases (including psoriasis and skin allergies) and gluten intolerance, and stresses a need for extended diagnostics for affected patients.



## Where does tolerance end?

Celiac disease, allergy to wheat, and NCGS are just some diseases that may be classified as forms of hypersensitivity to gluten. Does it mean that besides the above-mentioned conditions, the rest of the population is completely tolerant? Despite numerous opinions on the topic, the answer cannot be simply positive. There are numerous arguments questioning the ] neutral character of gluten for human organism, although the majority of people do not have clear and specific symptoms after eating it.

## Health starts in the gut

This slightly deceitful statement is largely true. Gut is not only a part of the gastrointestinal tract, but also constitutes an important organ of the immune system, having the biggest area of contact with the external environment (food, liquids, bacteria). To deal with continuous contact with toxins and allergens, the intestine – as an immune barrier – developed some complex immune mechanisms

## A tragic mistake

Structural similarity of gluten proteins and some proteins naturally occurring in human organism leads to development of a phenomenon of molecular mimicry, or a tragic mistake of the immune system, particularly in individuals with impaired immune system (as a result of chronic inflammation, predisposition for autoimmune diseases, etc.). Structural similarity of gluten proteins and auto-antigens in human organism may lead to increased production of antibodies and development of cross-reactions intensifying the immune attack on own tissues and organs. That phenomenon is characteristic for auto-aggressive conditions, including rheumatoid arthritis, sclerosis multiplex, Hashimoto disease, Graves' disease, celiac disease and type I diabetes. The longer the exposure to antigen (e.g. daily consumption of gluten), the higher the probability of a „mistake” of the constantly stimulated immune system. As a result, the organism may produce antibodies against its own tissues of the thyroid, pancreas, joints or intestinal mucosa, thus starting a chain reaction of auto-aggression. The reaction is hard to stop, particularly if the first cause (antigen) is not eliminated.



## Not so neutral, after all?

An interesting study [11] on healthy volunteers, whose diet was supplemented with 40 g of gluten a day (with typical daily gluten consumption of 15-20 g for adults in Europe [25]) challenged the opinion that gluten had no negative health consequences in people with no overt gastrointestinal symptoms. It turned out that several weeks of high-gluten diet resulted in unfavorable changes of the small intestinal mucosa, even in „healthy” participants. A discovery of the effect of gluten-free diet on composition of intestinal microflora was equally interesting. Conclusions of that study [12] indicate that elimination of gluten had a favorable effect on composition of intestinal microflora, significantly reducing the predominance of pathogenic *Clostridium* bacteria. Physiological balance of intestinal microbiota is a key aspect determining, among others, the condition of the intestinal mucosa, permeability of the intestinal barrier, and functioning of the immune system.

## Addicted to „white bread”

It turns out that preference to consume wheat-based bakery products may actually be not a preference or a habit for majority of people. Isolated (by enzymatic digestion of gluten proteins) peptides possessing properties characteristic for opioids, called exorphins, have a demonstrated ability to pass through the blood-brain barrier, and to combine with opioid receptors in brain and other internal organs. [19]. That may explain why are we so eager to eat gluten-rich products, and we find it so difficult to eliminate them from our diet. Existence of gliadomorphins and their addictive effect on the organism has been confirmed. Those compounds are commonly observed in autism-spectrum disorders (ASD). Deficiency of the DPP IV enzyme, characteristic for those disorders, impedes decomposition of gluten and accounts for formation of exorphins. Through leaking intestinal barrier (a common condition in ASD children) those compounds are transported to the intestinal-cerebral axis and lead to deterioration of behavioral disorders. The opioid effect is so strong, that elimination of those compounds from the diet may initially lead to deterioration of a child’s behavior (reaction similar to withdrawal syndrome). In time, however, condition of a child improves. Studies carried out by the Autism Research Institute demonstrated improved behavior in 81% of the study group of children with ASD as a result of introduction of gluten-free diet. [20] Those conclusions have been confirmed by many other studies, and the society of researchers seem to be generally concordant in this aspect. Similar effects were obtained in treatment of other disease, such as schizophrenia, where – as stated in conclusion of one of reviews – „there was a drastic reduction, or even complete remission, of schizophrenia symptoms achieved following introduction of gluten-free diet.” [21].

## Gluten-free diet – basic questions

Gluten-free diet is an elimination diet. It restricts the use of any gluten-containing products, including wheat and rye bakery products, and breaded meals. Particular attention should be paid to hidden sources of gluten, e.g. in sausage. Pursuant to the EU Directive, each manufacturer is obliged to indicate presence (or possible presence) of, among others, gluten-containing cereals and their processed products on a product label, regardless of their content. [23] The Regulation of the Commission (EC) No. 41/2009 of 20 January 2009 concerning the composition and labelling of foodstuffs suitable for people intolerant to gluten states that its presence had been scientifically confirmed in wheat (including durum, spelt and kamut), rye and barley. In accordance with the provisions laid down in this Regulation, „foodstuffs for specific food use which have been specially developed, processed or prepared to meet the nutritional needs of people intolerant to gluten and placed on the market as such should be designated as ‚very low gluten content’ (100 mg/kg of product) or ‚gluten-free product’ (20 mg/kg of product).” According to the Codex Alimentarius Commission FAO/WHO (2008), “Oat products are safe for most people with celiac disease, but their use in a gluten-free diet depends on national regulations.” Considering a high risk of polluting those cereals with gluten, particular attention should be paid to their correct certification and careful, individual incorporation to gluten-free diet.

## Gluten-free diet – myth busting

Popularity of gluten-free diet caused accumulation of both useful facts and half-truths and myths. The main plea put forward this type of elimination diet is associated with its deficient character, poor variability of foods, high level of processing, high energy consumption, low content of dietary fiber, vitamins, and microelements. However, weight of those pleas depends solely on composition of a gluten-free diet. The above-mentioned points will be hard to defeat, if elimination of gluten is the only priority, with no attention paid to alternative sources of nutrients. However, if the diet is based on naturally gluten-free, certified and unprocessed products, and supply of energy, essential nutrients and dietary fiber is carefully balanced, those pleas may be easily dismissed. This statement is supported by the study [24] indicating that gluten-free diet is deficient to the level similar to a conventional diet (mostly in respect to vitamin D deficiency in both diets), and moreover, it is able to improve the lipid profile (by increased consumption of monounsaturated fatty acids). Therefore, claiming that gluten-free diet is a diet of low nutritional value is not all that true. Besides elimination of gluten (possessing a negligible nutritional value) this diet should be based on similar recommendations as those for the rest of the population. The diet should contain an appropriate amount of gluten-free cereals, a complete set of exogenous amino acids, a correct ratio of fatty acids, and a correct supply of nutrients adapted to individual needs.

## Gluten-free diet – does it make sense in gluten-tolerant people?

Despite that many renowned experts claim that answer to this question is clear (positive or negative), it is worth to take an objective point of view and consider all pros and cons. The increase in the amount of consumed gluten, and its common presence in all kinds of food products, as well as long-term genetic modifications aimed at increased content of gluten proteins in cereals seems to be accompanied by increased incidence of auto-immune diseases and autism-spectrum disorders. It has to be considered, however, that the observed correlation does not necessarily indicate presence of a causal relation. This problem has to be verified in future scientific research. Fortunately, their number has been increasing recently. Much is also written and published about other forms of gluten intolerance (e.g. NCGS) that not always are manifested with gastrointestinal symptoms. The demonstrated effect of gluten on re-organization of zonulin (protein responsible for permeability of the intestinal barrier), a negative impact on composition of intestinal microflora, opioid character of gliadomorphin, the ability of antigenic molecular mimicry, and correlation with development and progress of auto-aggressive conditions surely vote against gluten. Negligible nutritional value of gluten and absence of any elements necessary for a normal functioning of the organism contained in the compound make it safe to be eliminated from diet, with no negative health consequences. That is provided the gluten-free diet is correctly balanced. Following the „gluten-free fashion” may be a mistake only in case the diet is introduced blindly and without consideration. Despite absence of any official recommendations regarding the use of gluten-free diet in gluten tolerant individuals, the diet may be reasonable, if it is correctly composed and advantages of elimination of gluten are known. Any possible inconvenience caused by gluten-free diet is surely counterbalanced by proven advantages of reasonable elimination of gluten in healthy people, providing the diet does not have a negative impact on their overall nutrition.

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