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Book

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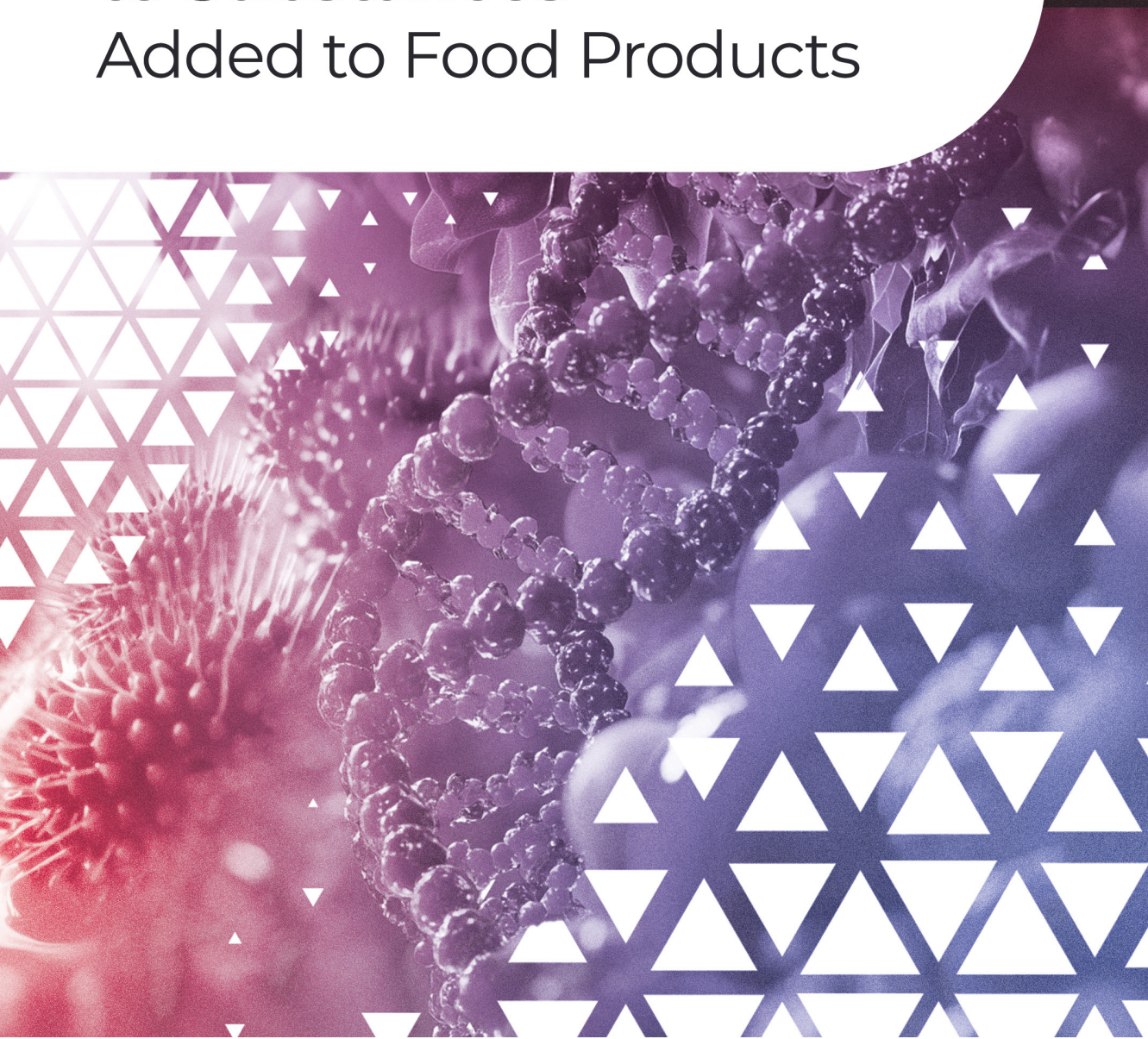

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ALLERGIES AND INTOLERANCE TO SUBSTANCES ADDED TO FOOD PRODUCTS

This monograph is devoted to an exhaustive analysis of the scientific and practical aspects of allergy and food additive intolerance, focusing on the mechanisms of their development, diagnosis, and treatment. The study reviews the essential differences between allergy and food additive intolerance, highlighting the different pathophysiologic mechanisms, symptoms, and treatment strategies. The influence of food processing technologies, including freezing, pasteurization, and canning, on food composition and their ability to alter allergenic properties is reviewed. The monograph integrates current scientific evidence from immunology, clinical allergology and food chemistry to elucidate the interactions between food additives and the human body. Key features include an examination of common allergens in foods and pragmatic suggestions for the diagnosis and treatment of allergic and intolerant reactions. This study is an important resource for scientists, allergists, nutritionists, and practitioners in the field of healthy eating, providing both theoretical foundations and practical direction for future research and clinical applications.

Maria Zofia Lisiecka is a PhD in Medicine and Assistant at the Department of Allergology, National Medical Institute of the Ministry of the Interior and Administration. Maria Zofia Lisiecka's scientific interests focus on clinical allergology, particularly the diagnosis, treatment, and prevention of respiratory and food allergies. She specialised in allergology and clinical immunology in Paris. Her research encompasses immunotherapy for pollen and food allergens, early detection of allergic diseases in children, and cross-reactivity mechanisms involving spice and plant proteins. She also investigates allergic contact dermatitis, especially related to skin sensitizers like nickel and rubber, and contributes to improving diagnostic methods through the use of specific IgE and patch testing. Her work is situated at the intersection of clinical practice and immunological research. Maria Zofia Lisiecka has authored over ten scientific publications indexed in international databases such as Scopus, PubMed, and Web of Science, primarily between 2020 and 2025. Her studies demonstrate a consistent integration of clinical observation with immunological diagnostics, contributing to the development of personalized allergy treatment strategies.

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Foreword

The investigation of allergies and intolerances to food additives has become a vital and swiftly advancing domain within biomedical and nutritional sciences, garnering heightened interest from academics, doctors, and public health experts globally. These disorders encompass intricate physiological and immunological processes that affect a considerable segment of the global population, posing great obstacles for precise diagnosis, efficient care, and thorough prevention methods. In the current landscape of global food production and consumption, coupled with the extensive use of various food additives to enhance taste, texture, appearance, and shelf life, it is essential to comprehend the nature and effects of allergic and intolerant reactions to protect public health and improve the quality of life for those affected.

Allergies and intolerances, however sometimes confused, signify distinct biological reactions that necessitate precise distinction. Allergies are defined by the immune system's responsiveness to particular proteins or chemical agents in meals, which can provoke acute and potentially fatal reactions, such as anaphylaxis. In contrast, intolerances mostly arise from non-immunological causes, such enzymatic deficits or metabolic dysfunctions, resulting in a range of symptoms that might be chronic and hinder everyday activities without direct involvement of the immune system. This complexity requires a multidisciplinary approach that combines immunology, gastrointestinal, toxicology, food chemistry, and clinical nutrition to clarify underlying causes, symptoms, and suitable treatment options.

The swift progression of food processing technologies – such as freezing, pasteurisation, canning, chemical preservation, and the incorporation of various synthetic and natural additives – has transformed food accessibility and safety while also introducing new factors affecting the allergenic potential and bioavailability of food constituents. The relationship between these technological interventions and human physiology is complex and not completely comprehended, highlighting the necessity for thorough scientific investigation into how processing modifies the immunogenicity and metabolic effects of food additives. This monograph offers a thorough and current synthesis of scientific understanding regarding the biological foundations of allergic and intolerant reactions to food additives, the diagnostic difficulties arising from overlapping clinical symptoms, and the developing therapeutic and management approaches. It also emphasises the significance of developing diagnostic technologies, such molecular allergy diagnostics and immunoglobulin profiling, which are expected to improve diagnostic accuracy and tailor patient management.

This monograph centrally focusses on the meticulous analysis of the differential pathophysiological causes of allergies and intolerances, highlighting the biochemical and immunological processes alongside the psychological ramifications for affected individuals. This study critically analyses the interactions among various food additives-preservatives, colourants, emulsifiers, thickeners, sweeteners, and flavour enhancers – and their effects on the human immune and metabolic systems, thereby enhancing the understanding of their role in adverse health outcomes. The monograph also examines regulatory frameworks, risk assessment protocols, and public health policies designed to reduce exposure and adverse reactions, emphasising deficiencies and opportunities for policy improvement.

This work is intended for a diverse readership, including medical practitioners, allergologists, nutritionists, food scientists, researchers, and public health policymakers dedicated to food safety and health promotion. It provides both fundamental theoretical frameworks and practical

guidance, fostering a comprehensive awareness of the issues associated with hypersensitivities due to food additives. Additionally, it seeks to promote multidisciplinary research and discourse to enhance diagnostic precision, patient care, and the formulation of preventive policies in this rapidly advancing domain.

In a progressively interconnected world characterised by varied dietary habits and an expanding food supply chain, the investigation of allergies and intolerances associated with food additives is crucial for enhancing human health and welfare. This monograph greatly advances the endeavour by clarifying the complex interactions among food ingredients, human biology, and clinical practice, thus establishing a strong basis for innovation in diagnosis, treatment, and policy. Ultimately, it aims to educate and motivate ongoing advancements in safer, more educated, and more inclusive strategies for nutrition and public health amid contemporary dietary problems.

Introduction

The modern food industry makes extensive use of various chemicals added to products to improve their taste, texture, appearance, and shelf life. These additives, which include preservatives, sweeteners, thickeners, emulsifiers and colours, are an integral part of most people's daily diets. However, along with improving the consumer properties of food, these substances can cause undesirable reactions, among which allergies and food intolerance are of particular concern [1]. Every year, the number of people suffering from allergic reactions and intolerance to certain food components is increasing worldwide. Incorrect identification of these disorders, as well as ignorance of their differences, can complicate diagnosis and treatment, and worsen the quality of life of patients [2]. Allergies and intolerance to food additives are complex phenomena that require detailed study, as the effect of different substances on the body varies depending on many factors, including individual characteristics of the immune system, metabolic processes and even food preparation methods.

This book seeks to explain the nature of allergic reactions and intolerance to food additives, their differences, diagnosis, and treatment. It also provides an overview of the most common substances added to food and their possible negative effects on the human body. An important aspect is the consideration of how technological processes, such as freezing, pasteurization, or processing of foods, affect their composition and structure, changing their nutritional value and possible health risks. The book will be a useful source of knowledge for doctors, scientists, and anyone interested in healthy eating and seeking to reduce the risks of allergic reactions or other health problems associated with food additives. The aim of this book is to provide a comprehensive overview of allergies and intolerances to substances added to food. It aims to explain to readers how these substances can affect the body, cause allergic reactions or metabolic disorders. The book is designed to help readers understand the differences between food allergies and intolerances, and to offer practical advice on diagnosing, preventing and treating these conditions. The book also explores the impact of various food processing, such as freezing, pasteurization or canning, and their possible health effects. It also analyses in detail the side effects of major food additives, such as colourings, preservatives, thickeners, and sweeteners.

The book is structured in such a way as to provide a consistent and logical immersion in the topic. The first chapter, which is an introduction, provides an overview of the current state of the food industry and the reasons for the rise in allergic reactions and intolerance to food additives. The second section is devoted to what food allergies and intolerances are. It defines these conditions and explains their differences. It also describes the symptoms and mechanisms of allergies and food intolerances. The third section discusses the various substances added to foods, including colours, preservatives, thickeners, gelling agents, sweeteners, antioxidants, emulsifiers, and flavour enhancers. This section also provides Stackham Tables, which provide a detailed list of the main food additives and their health effects.

The fourth section deals with side effects and symptoms of diseases that can be caused by food additives. It describes in detail the possible side effects for each group of food additives, as well as diseases that can occur due to allergic or toxic reactions to these substances. The fifth section deals with the topic of sugar intolerance, particularly lactose, which is a common problem in the modern world. It provides a detailed overview of symptoms, diagnosis and treatment, with a particular focus on lactose intolerance, as it is a common condition that is often encountered in everyday

life. The sixth chapter explores the relevant topic of the role of IgG in food allergy. This issue has become relevant in the context of food allergy diagnostics, and the position paper of the European Academy of Allergy and Clinical Immunology, which assesses the feasibility of using IgG testing for the detection of food allergy, is discussed in detail.

Food allergies and intolerances are serious problems that are increasingly common in modern society. Food allergies occur when the immune system mistakenly perceives certain food components as a threat, leading to a violent defensive reaction. The most common allergic reactions are associated with foods such as milk, eggs, nuts, fish, seafood, soy, and wheat [3]. Symptoms of food allergies can range from mild (rash, itching) to severe (anaphylaxis), and these reactions can be life-threatening. Even a minimal amount of an allergen can trigger an acute reaction. Food intolerances, on the other hand, are not the result of an immune reaction but are related to problems with digestion or metabolism of certain substances. Intolerance occurs when the body cannot properly process or absorb certain food components, which can lead to symptoms such as bloating, stomach pain, diarrhoea, or headaches. For example, people with lactose intolerance do not have enough of the enzyme lactase, which processes milk sugar, resulting in digestive problems after eating dairy products [4].

One of the key challenges is the difficulty of distinguishing between allergies and intolerances due to similar symptoms. Patients often self-diagnose with an allergy when they are actually experiencing a food intolerance. This can lead to inappropriate treatment and avoidance of foods that are not actually a threat. The increasing use of food additives such as colourings, preservatives, and flavour enhancers has also been an important factor in the rise of allergic reactions and intolerances [5]. Food additives may contain ingredients that are difficult for the body to recognize, causing reactions in sensitive individuals. For example, additives such as sulphites or tartrazine can cause reactions in people with hypersensitivity. In addition, the development of modern food processing technologies, such as freezing, pasteurization or canning, can change the chemical structure of foods and affect their perception by the body. Some processes can reduce the level of nutrients or change the composition of proteins, which increases the likelihood of an allergic reaction or intolerance [6].

Allergens used as food additives and food allergies are a complex topic that encompasses a wide range of substances and body reactions. Food additives such as preservatives, colourings, flavour enhancers, thickeners, emulsifiers, antioxidants, and sweeteners are among the most common allergens that can cause various reactions in people with hypersensitivities. Preservatives, such as sulphites, are often added to foods to increase their shelf life. They can cause symptoms ranging from mild skin irritation to serious respiratory problems, especially in people prone to asthma. Similarly, tartrazine, an artificial yellow colouring used in sweets, beverages and confectionery, is known for its potential to cause allergic reactions such as rashes or hives [7]. Flavour enhancers like monosodium glutamate (MSG) can also cause reactions known as “Chinese restaurant syndrome”, which include headaches, flushing, sweating, and nausea. This flavour enhancer is widely used in fast food and ready-to-eat meals, making it one of the most consumed allergens in the world. Sweeteners, such as aspartame, can also cause reactions in sensitive people, manifesting as headaches, dizziness, or skin rashes [8].

Food allergies are often associated with certain foods that contain proteins that can cause allergic reactions. The most common food allergens are milk, eggs, peanuts, tree nuts, soya, wheat,

fish, and seafood. For example, milk allergies usually occur in children and can cause various symptoms such as rashes, vomiting, diarrhoea, or even anaphylactic shock. Peanuts and tree nuts are also serious allergens that cause some of the most severe and dangerous allergic reactions. Even a small number of peanuts can cause severe anaphylaxis, a reaction that requires immediate medical attention [9]. Allergies to fish and seafood usually occur in adulthood and can manifest as skin rashes, swelling of the face and throat, and breathing problems. Seafood is one of the most common allergens in adults and often causes severe reactions. Soy allergy is more common among children and usually manifests itself at an early age, manifesting as skin reactions or digestive problems. It is important to note that some allergies can be temporary and disappear with age, as is often the case with milk or egg allergies in children. However, others, such as nut or fish allergies, usually last for life [10].

Food additives and allergens contained in foods cause allergic reactions in people of all ages. Allergies can be mild or lead to severe consequences, so it is important to be able to identify symptoms in time and diagnose allergies correctly. Thus, the problem of food allergies and intolerances is multifaceted and requires a comprehensive approach that includes diagnosis, management, and prevention. Accurate diagnosis and understanding of the differences between these conditions are key to ensuring the health of patients, as well as raising awareness of the impact of food additives and technological processes on our bodies.

Chapter 1.

What are food intolerances and food allergies?

Food intolerance and food allergy are two different types of reactions to food consumption that are often confused due to similar symptoms, but their mechanisms and consequences are significantly different. A food intolerance is caused by the body's inability to effectively digest or absorb certain food components, which is usually associated with enzyme deficiencies or other digestive system problems. Unlike food allergies, which are immune reactions, intolerances do not trigger an immune response and are not life-threatening, although their symptoms can be quite unpleasant. The most well-known examples are lactose intolerance, which occurs due to a lack of the enzyme lactase that digests milk sugar, and gluten intolerance (non-celiac sensitivity), which causes discomfort after eating gluten-containing foods. Symptoms of food intolerance may include nausea, abdominal pain, flatulence, diarrhoea, and headache. These manifestations depend on the amount of the substance consumed – larger amounts cause more severe symptoms, while small doses may not cause significant effects [11].

In contrast, a food allergy is an abnormal reaction of the immune system to certain proteins in food. The immune system mistakenly recognizes these proteins as threatening to the body and produces antibodies, which leads to the release of chemicals such as histamine that cause characteristic allergic reactions. Food allergies can be life-threatening, especially if anaphylaxis occurs – an acute allergic reaction that requires immediate medical intervention. The most common allergens are nuts, including peanuts, seafood, dairy products, eggs, and wheat. Symptoms of food allergies can range from mild skin rashes and itching to serious respiratory problems, swelling of the face and lips, and anaphylactic shock. Unlike intolerance, even small amounts of an allergen can cause a serious reaction.

1.1. Definition of food intolerance

Food intolerance is a problem faced by a significant proportion of the population. It is a pathological condition in which the body cannot properly digest or absorb certain food substances for a number of reasons, most often related to enzymatic defects, chemical imbalances or abnormalities in the digestive system. Unlike food allergies, food intolerance is not associated with an immune reaction. That is, it does not cause the activation of the immune system, which is typical for food allergies, but can lead to serious symptoms such as abdominal discomfort, diarrhoea, nausea, flatulence, and even headaches. One of the main causes of food intolerance is an enzyme deficiency, i.e. the lack or absence of specific enzymes that are necessary for the normal digestion of certain foods. For example, lactose intolerance is a common condition in which the body lacks the enzyme lactase, which is responsible for breaking down lactose, a sugar found in dairy products. Without lactase, lactose cannot be properly digested, which leads to fermentation of this substance in the intestines and, as a result, flatulence, diarrhoea and abdominal pain.

Another cause of food intolerance can be chemical imbalances or metabolic abnormalities. One such example is gluten intolerance, or non-celiac gluten sensitivity. Gluten is a protein found in cereals such as wheat, rye, and barley. People with gluten sensitivity may experience symptoms similar to celiac disease, but without an immune response or intestinal damage [12]. Symptoms include abdominal pain, fatigue, depression, and digestive disorders. Although this condition is

not yet fully understood, it differs from celiac disease in that it does not cause atrophy of the small intestinal villi and is not an autoimmune disease. Some food intolerances can also be caused by exposure to food additives such as sulphites, nitrates or monosodium glutamate (MSG). For instance, sulphites, used as preservatives in dried fruit, wines and many processed foods, can cause symptoms ranging from mild skin rashes to severe asthma attacks in people who are sensitive to them. Another example is a reaction to monosodium glutamate, a popular additive used to enhance flavour. In some people, it can cause headaches, nausea, and general malaise, although scientific evidence on this phenomenon is still controversial [13].

Food intolerance can be classified into several types, each characterized by different underlying mechanisms (Table 1). One of the most common forms is enzymatic intolerance, with lactose intolerance serving as a primary example. The World Health Organization (WHO) estimates that up to 70% of adults worldwide exhibit some degree of lactose intolerance. This condition arises from lactase deficiency, which may be congenital or acquired, and its prevalence varies significantly across ethnic groups. For instance, the prevalence among Europeans is relatively low, whereas it can reach as high as 90% in Asian and African populations [14]. Another type is chemical intolerance, which involves adverse reactions to certain food chemicals such as caffeine, tyramine (present in cheeses and chocolate), salicylates (found in some fruits and vegetables), nitrates, and various food additives.

Table 1. Main types of food intolerance

Type of intolerance	Reason	Symptoms	Example of products
Lactose intolerance	Lactase (enzyme) deficiency	Flatulence, diarrhoea, abdominal pain	Milk, cheeses, yoghurt
Gluten sensitivity	Gluten intolerance	Abdominal pain, fatigue, digestive disorders	Wheat, barley, rye
Sensitivity to sulphites	Reaction to preservatives	Asthma, rashes, headaches	Wine, dried fruit, canned food
Sensitivity to monosodium glutamate (MSG)	Reaction to the food supplement	Headache, nausea, fatigue	Fast food, Chinese dishes

Source: *compiled by the author*

Tyramine, in particular, is known to trigger migraines in sensitive individuals by affecting blood vessel function [15]. Functional intolerance arises from disorders within the digestive system. A notable example is irritable bowel syndrome (IBS), which is often associated with food intolerance; patients may experience difficulties digesting specific foods due to heightened intestinal sensitivity to stretching or irritation [16]. Lastly, psychosomatic intolerance is a form in which physiological symptoms occur as a consequence of psychological factors such as stress or anxiety related to food consumption. This is frequently observed in patients with eating disorders like anorexia or bulimia, where digestive discomfort may follow consumption of certain foods despite the absence of any clear digestive pathology [17].

Symptoms of food intolerance can be quite diverse and vary depending on the type of intolerance and the amount of the substance consumed. Among the most common symptoms of food intolerance, there are several main categories. Firstly, gastrointestinal symptoms, which include abdominal pain, diarrhoea, flatulence, and nausea. These symptoms often appear a few hours after eating and can last up to several days. Secondly, skin symptoms such as rashes, itching and hives,

which can occur as a result of chemical intolerance or a reaction to food additives. The third group of symptoms is neurological manifestations, including headaches, migraines, sleep disturbances and increased irritability. In addition, generalized weakness and fatigue are common symptoms that can result from impaired absorption of essential nutrients. Diagnosing a food intolerance is a complex process, as symptoms can be non-specific and appear several hours or days after eating. One of the most effective diagnostic methods is an elimination diet, where suspected foods are removed from the patient's diet and then gradually reintroduced to determine which one is causing the symptoms. Other diagnostic tests include a lactose intolerance test, which measures the level of hydrogen in the breath after consuming lactose, and food additive tests, which can help identify chemical sensitivities to substances such as sulphites or monosodium glutamate.

Scientific research on food intolerance is being actively conducted around the world. One of the key studies concerns lactose intolerance. A study conducted in Finland found that people in Northern Europe, where milk consumption has historically been high, have a better tolerance to lactose. Meanwhile, in South Asia and Africa, the majority of the population does not have the lactase enzyme, which is why lactose intolerance is very common there [18]. Another interesting study was conducted in the United States, where people's reactions to sulphites in wine were examined. The study showed that 1% to 5% of people are sensitive to this additive and may experience symptoms ranging from mild discomfort to severe asthmatic reactions [19].

Since food intolerance is not an immune disorder, its treatment usually involves eliminating or reducing the consumption of the problematic food (Table 2). For example, people with lactose intolerance are advised to avoid dairy products or consume them in small quantities together with enzyme preparations (lactase) to help digest lactose. In cases of gluten intolerance, wheat, rye, and barley products should be avoided, although some people with non-celiac gluten sensitivity may tolerate small amounts of this protein. An essential part of treatment is informing the patient about their condition and teaching them how to make the right food choices. For example, many food labels indicate the presence of potential allergens or additives, such as sulphites, that can cause reactions in sensitive individuals [20].

Table 2. Differences between food allergy and food intolerance

Characteristics	Food allergies	Food intolerance
Immune response	Yes, it involves the immune system	No, it does not include the immune system
Reaction type	Instant, can be severe or fatal	Usually delayed, less serious
Main symptoms	Anaphylaxis, rash, difficulty breathing	Diarrhoea, abdominal pain, nausea
Diagnostics	Skin tests, blood tests	Elimination diets, tests for enzyme intolerance
Common products	Nuts, fish, milk, eggs	Dairy products, gluten, chemical additives

Source: *compiled by the author*

Food intolerance is a complex and diverse phenomenon that requires a deep understanding of the specifics of digestion, metabolism, and the effects of food on the human body. It differs from food allergies in the absence of an immune response, but this does not make it any less serious for patients suffering from such disorders. Proper diagnosis and treatment can make patients' lives much easier and allow them to enjoy a wide range of foods without fear of unpleasant consequences.

1.2. Definition of a food allergy

Food allergy is a complex medical phenomenon that encompasses abnormal immune responses to certain foods. Whereas food intolerance usually results from enzyme deficiencies or other metabolic abnormalities, food allergy involves the immune system reacting to proteins in food as a threat, leading to the production of IgE antibodies. This section will review the mechanisms, causes, and symptoms of food allergy, current research, and clinical cases, and present tables and diagrams to help one better understand this phenomenon. Food allergies develop when the immune system mistakenly identifies certain proteins in food as harmful. When the immune system first encounters such an allergen, it reacts by producing specific IgE antibodies. Upon repeated exposure to the allergen, these antibodies activate mast cells and basophils, which leads to the release of mediators such as histamine, which cause allergic symptoms. The development of an allergy goes through several well-defined stages, each of which is characterized by a specific immune system response to the allergen.

The first stage is sensitization, when the immune system first encounters a food protein that is perceived as a threat. Accordingly, the body begins to produce specific antibodies of the IgE class, which are aimed at detecting and fighting this foreign protein (allergen). This process can take months or even years, and is often not accompanied by obvious symptoms. The second stage occurs when the allergen is repeatedly used. IgE antibodies, which are already present in the body after the first encounter with the allergen, attach to the surface of mast cells and basophils, cells that are part of the immune system and are responsible for protecting against infections. After repeated contact with the allergen, these cells are activated, which leads to the release of histamine and other chemical mediators of inflammation. This, in turn, triggers the development of an allergic reaction.

The third stage is the immediate allergic reaction, which occurs with each subsequent use of the product containing the allergen. Allergy symptoms can be varied and range from mild itching on the skin or in the mouth to serious manifestations such as hives, Quincke's oedema, or even anaphylaxis, a life-threatening condition that requires immediate medical intervention. Anaphylaxis can be accompanied by severe swelling of the throat, difficulty breathing, a sharp drop in blood pressure and loss of consciousness, making it the most dangerous manifestation of an allergic reaction. Thus, allergy is a complex and multi-stage process in which the immune system reacts to certain proteins as a threat, leading to the launch of a cascade of defence mechanisms that can have serious health consequences. Understanding the stages of this process is important for the effective diagnosis and treatment of allergic reactions, as well as for the development of measures to avoid allergens and prevent serious complications.

Symptoms of food allergies can manifest themselves as reactions from various body systems, including the skin, gastrointestinal tract, respiratory system and cardiovascular system. Such reactions occur in response to the consumption of certain foods containing proteins that the immune system mistakenly perceives as a threat. In response, the body triggers a series of immune reactions that lead to a variety of symptoms that can range from mild to life-threatening. One of the most common manifestations of food allergies is hives, a skin lesion that appears as itchy blisters or red spots. They can appear suddenly after eating an allergen and are often accompanied by severe itching, discomfort and redness of the skin. Hives can last from a few hours to several days, depending on the severity of the reaction and the duration of contact with the allergen.

Angioedema is another common symptom that involves swelling of the lips, tongue, throat or other parts of the body. This swelling may be painless, but it can cause difficulty breathing if it involves the airways, especially the throat. In severe cases, this swelling may interfere with breathing and require immediate intervention to avoid serious complications. Symptoms of the respiratory system often manifest themselves in the form of allergic rhinitis, which is accompanied by a runny nose, nasal congestion and itching. This is a typical reaction to inhalation or contact with food allergens that can penetrate the nasal mucosa. Allergic rhinitis can also be accompanied by coughing, difficulty breathing or even bronchospasm, especially in people with asthma. Gastrointestinal symptoms may include diarrhoea, abdominal pain, bloating, nausea, or vomiting. These symptoms are caused by the direct action of the allergen on the lining of the gastrointestinal tract, which can interfere with normal digestion and absorption of nutrients. In some cases, such symptoms can mimic food intolerance, which makes diagnosis difficult [21].

Anaphylaxis is the most serious and life-threatening systemic reaction to an allergen. It can develop within minutes of ingestion of an allergen and is accompanied by a sharp drop in blood pressure, severe breathing difficulties, heart rhythm disturbances and loss of consciousness. Anaphylaxis requires immediate medical attention and adrenaline injection to avoid a fatal outcome. Thus, food allergy is a multifaceted pathology that can manifest itself with various symptoms from several body systems. Understanding these symptoms and recognizing them in a timely manner is vital to prevent serious complications and ensure proper medical care. Table 3 presents common foods that are known to frequently trigger allergic reactions. These foods contain specific allergens – typically proteins – that can provoke immune responses of varying severity in susceptible individuals. Recognizing these allergens and understanding their typical sources is essential for effective diagnosis, management, and prevention of food allergy symptoms.

Table 3. Foods that are more likely to cause allergic reactions

Product	Allergens	Notes
Milk	Beta-lactoglobulin, casein	The main cause of allergies in children
Eggs	Ovalbumin	Found in many products, including baked goods
Peanuts	Arachin	High risk of anaphylaxis
Nuts	Albumin	Walnuts, almonds
Fish	Parvalbumin	Heat-resistant allergen
Shellfish	Tropomyosin	Oysters, shrimps, lobsters
Soybeans	Glycinins	Common in baby food
Wheat	Gliadin	Often confused with gluten intolerance

Source: *compiled by the author*

Scientific research into food allergies has shown that there is a significant genetic predisposition to this condition. Children whose parents suffer from allergic diseases (asthma, allergic rhinitis) are at a higher risk of developing food allergies. One of the most important studies conducted in the United States, led by the National Institute of Allergy and Infectious Diseases (NIAID), showed that the number of cases of peanut allergy has increased significantly over the past few decades [22]. This study focused on the population of children and found that early introduction of peanuts into the diet can reduce the risk of developing allergies. These findings provided the basis

for new recommendations for the prevention of food allergy through early introduction of allergens in low doses [23].

There are several approaches to treating food allergies, but the main method is to avoid allergens completely (Table 4). However, studies on oromucosal immunotherapy (OIT) show that by gradually introducing very small amounts of the allergen, tolerance can be increased in some patients. Anaphylaxis requires the immediate administration of epinephrine (epinephrine) in the form of an auto-injector such as the EpiPen [24]. This is a life-saving medication for patients at risk of severe food reactions.

Table 4. Approach to the treatment of food allergy

Approach to treatment	Methods	Notes
Avoiding allergens	Eliminating allergenic foods from the diet	The main method
Oral immunotherapy	Gradual introduction of allergens	Requires medical supervision
Antihistamines	H1 receptor blockers	Used to relieve symptoms
Adrenaline	Epinephrine injections	For emergency care in case of anaphylaxis

Source: *created by the author*

Children are the most vulnerable group to developing food allergies, especially to foods such as milk, eggs, peanuts, and fish (Table 5). Many children "outgrow" milk and egg allergies, but nut and fish allergies usually last a lifetime. One of the most common examples of childhood allergies is cow's milk allergy [25].

Table 5. The most common allergens in children

Product	Age at risk	Frequency of cases
Cow's milk	0-2 years	2-3%
Eggs	1-3 years	1-2%
Peanuts	2-5 years	1%
Wheat	1-4 years	0.5-1%
Fish	3-7 years	0.2-1%

Source: *created by the author*

Cow's milk contains several major proteins that can cause allergies. It is known that milk contains about 25 different protein components, but only a few of them are usually allergenic. The main allergens in milk can be divided into two groups: caseins and whey proteins. Caseins make up about 80% of milk protein and include αs1-casein, one of the most common allergens, αs2-casein, β-casein, and κ-casein. Whey proteins account for about 20% of milk protein and include β-lactoglobulin, the most allergenic whey protein, α-lactalbumin, serum albumin (a protein similar to blood proteins), and immunoglobulins. These proteins can cause an immune reaction in people who are sensitive to milk proteins. Most children with milk allergy react to several proteins at the same time. Adults can develop food allergies at any age, even after decades of eating foods without symptoms. The most common food allergens among adults are fish, shellfish, nuts, and fruits. Oral allergy syndrome is a phenomenon that occurs when people who are allergic to pollen also have reactions to fresh fruit and vegetables. Symptoms include itching or swelling of the lips, tongue, and throat after eating the product. This is due to cross-reactivity between plant proteins and pollen [26].

Genetic factors play a key role in predisposition to food allergies. Children who have parents with allergies are at a much higher risk of developing food allergies. In addition, environmental factors, such as the mother's diet during pregnancy, delivery and breastfeeding, also influence the development of allergies [27]. The world's medical science is conducting numerous studies aimed at investigating the causes and treatment of food allergies. For example, a study conducted in Australia examined the impact of probiotics on the development of allergies in children and showed a reduction in the frequency of allergic reactions in children who consumed probiotics in the early stages of life [28].

Prevention of food allergies. Preventive measures include the early introduction of allergens into children's diets (according to recommendations), control of food exposure, and regular medical examinations to identify possible allergic reactions. Milk intolerance and milk allergy are two different conditions, although they may have similar symptoms. The main difference between them is how the body reacts to dairy products. Milk intolerance is usually associated with lactase deficiency, which is a condition where the body cannot properly digest lactose, a natural sugar found in milk and dairy products. Lactose is made up of two sugars, glucose and galactose, and the body needs the enzyme lactase to break it down.

In people with lactase deficiency, insufficient amounts of this enzyme are produced, which means that lactose is not broken down in the small intestine and passes to the large intestine, where it is fermented by bacteria. Symptoms of milk intolerance include bloating, flatulence, cramps, diarrhoea, and nausea. These symptoms occur due to the accumulation of gases and acids that are formed during the fermentation of lactose in the large intestine. To diagnose lactose intolerance, a lactose breath test is used (measuring the level of hydrogen in the exhaled air after consuming lactose) and a blood glucose test, which measures the level of glucose in the blood after consuming lactose. Milk intolerance does not affect the immune system and usually does not pose a serious health risk.

A milk allergy is an immune response to one or more proteins found in milk, such as casein or whey proteins (β-lactoglobulin, α-lactalbumin, etc.). In allergies, the immune system mistakenly perceives these proteins as a threat and starts producing antibodies, in particular immunoglobulin E (IgE), which causes the release of histamine and other chemicals that cause allergy symptoms, such as skin rashes (hives), itching, swelling (including swelling of the lips, face, tongue), breathing problems (asthma), vomiting, diarrhoea, anaphylaxis (rare but life-threatening reaction). Milk allergy can occur even with small amounts of milk protein and affect several organs of the system – respiratory, digestive, and skin. This is a condition that can be life-threatening, so it requires careful monitoring and avoidance of dairy products. Diagnosis of milk allergy includes skin tests (an extract of milk proteins is applied to the skin to test for an allergic reaction), a blood test for IgE antibodies (the level of antibodies to milk proteins is measured), an elimination diet, in which dairy products are excluded from the diet and symptoms are monitored [29].

Table 6. Comparison of food intolerance and milk allergy

Characteristics	Milk intolerance	Milk allergy
Reason	Lack of the enzyme lactase	Immune response to milk proteins
Main symptoms	Bloating, diarrhoea, cramps	Rash, swelling, breathing problems, anaphylaxis

Table 6, Continued

Characteristics	Milk intolerance	Milk allergy
Systems involved	Digestive system	Skin, respiratory, digestive, sometimes cardiovascular
Time of occurrence	A few hours after consuming milk	Within minutes or hours after consumption
Danger to life	No	Can be dangerous (anaphylaxis)
Diagnostics	Lactose breath test, blood glucose test	Blood test for IgE, skin tests
Treatment	Avoiding lactose, taking lactase enzymes	Avoidance of milk, antihistamines, epinephrine injections

Source: *created by the author*

Treatment of lactose intolerance includes several main approaches. The first is dietary adjustments, which involve avoiding foods high in lactose, such as milk, ice cream, yoghurt, and other dairy products. Instead, lactose-free products are used, which retain the nutritional value of milk but do not contain lactose. The second approach is enzyme therapy, when patients are advised to take lactase enzymes before eating lactose-containing foods, which help break down this sugar in the digestive system, reducing intolerance symptoms. The third approach is the use of probiotics, which contain bacterial strains that can improve lactose digestion and improve the overall condition of the intestinal microflora.

Treatment for milk allergy is more serious, as allergic reactions can have severe consequences. The main method of treatment is to avoid dairy products. Patients are advised to strictly follow a diet that completely excludes milk and its derivatives, as even a small amount can trigger an allergic reaction. In the event of a serious allergic reaction, such as anaphylaxis, an immediate injection of epinephrine (epinephrine) is required to save lives, so patients are often advised to carry an epinephrine auto-injector. Another promising but experimental approach is allergen-specific immunotherapy (ASIT), in which small doses of an allergen are administered to a patient with a gradual increase in dose. This helps to reduce the body's sensitivity to milk proteins and can lead to less severe reactions over time [30].

As with milk, the difference between peanut intolerance and allergy to peanuts and bread (gluten) lies in the reactions that are triggered by the consumption of these products. Despite the similarity of symptoms, these conditions differ in their mechanisms, causes, and severity. For example, with peanut intolerance or gluten intolerance (a component of bread), a person experiences discomfort after eating these products due to digestive problems, but the immune system is not involved in this process. Peanut intolerance can include intestinal inflammation or other digestive problems due to the body's inability to break down certain components of this product. It is less common than a peanut allergy and is usually not a serious, life-threatening condition. Symptoms of peanut intolerance may include bloating, flatulence, diarrhoea, and nausea. Gluten intolerance, also known as non-celiac gluten sensitivity, is caused by the body's inability to properly digest gluten, a protein found in wheat, rye, and barley (the ingredients of bread). Symptoms include abdominal pain, bloating, diarrhoea or constipation, and fatigue.

Gluten intolerance does not cause an immune reaction or intestinal damage, as is the case with celiac disease, and is not life-threatening [31].

When one is allergic to peanuts or gluten (wheat), one's body produces IgE antibodies, which leads to the release of histamine, which causes symptoms of an allergic reaction. Peanut allergy is

one of the most common and potentially dangerous food allergies. Even small traces of peanuts can cause severe allergic reactions, including anaphylaxis. Symptoms of a peanut allergy include skin rashes (hives), swelling of the face, lips, tongue, breathing problems, vomiting, and anaphylaxis may also occur.

An allergy to wheat (including bread made from wheat) occurs when the immune system reacts to wheat proteins, including gluten. This can lead to respiratory and skin symptoms such as hives, asthma or swelling. Symptoms of a wheat allergy include swelling of the face, lips and tongue, vomiting, shortness of breath, asthma, and anaphylaxis. It is essential to understand that wheat allergy is not the same as celiac disease – they are different conditions. Celiac disease is an autoimmune disease caused by gluten and causes damage to the intestines, while wheat allergy is an immune reaction to one or more wheat proteins. Allergies are diagnosed through skin tests to identify allergens by applying an extract of the product to the skin, blood tests for IgE to detect antibodies to peanut or wheat proteins, and an elimination diet, as in intolerance, where foods are excluded from the diet to determine reactions.

Table 7. Differences between peanut and bread intolerance and allergy

Characteristics	Peanut/gluten intolerance	Peanut/gluten allergy
Reason	Digestive disorders due to enzyme deficiency	Immune reaction to peanut or gluten proteins
Systems involved	Only the digestive system	Skin, respiratory system, digestive system
Symptoms	Bloating, cramps, flatulence, diarrhoea	Rashes, swelling, breathing problems, anaphylaxis
Time of onset of symptoms	A few hours after consuming the product	Within minutes or hours after consumption
Risk to life	No	Can be life-threatening (anaphylaxis)
Diagnostics	Elimination diet	IgE test, skin tests
Treatment	Avoidance of the product causing the symptoms	Product avoidance, epinephrine in case of anaphylaxis

Source: *created by the author*

Treatment for peanut and gluten intolerance focuses on dietary adjustments and the use of alternative foods. The main approach is to avoid eating foods that cause intolerance, such as peanuts or foods containing gluten. At the same time, people with gluten intolerance can replace gluten-containing foods with alternatives, such as rice, corn, potatoes, and other gluten-free grains. Treatment of peanut allergy requires special attention due to the risk of severe reactions such as anaphylaxis. In the event of an anaphylactic reaction, immediate administration of adrenaline (epinephrine) is required, which is the only effective method of quickly eliminating dangerous symptoms. Furthermore, in some cases, a doctor may prescribe specific immunotherapy aimed at gradually reducing the body's sensitivity to peanuts. However, regardless of the possible treatment, strict adherence to a peanut-free diet remains the most critical measure to prevent allergic reactions.

Treatment for wheat allergy is similar to that for other food allergies. One treatment option is allergen-specific immunotherapy (ASIT), which aims to reduce sensitivity to wheat proteins. This method is not suitable for all patients, but can be effective in some cases. As with peanut, the treatment is based on strict avoidance of wheat-containing foods and careful dietary control. Intolerance and allergy to peanuts and gluten have different causes and different health effects. Intolerance usually only affects the digestive system and is less serious, while allergies can cause

life-threatening symptoms and require immediate medical attention. For example, lactose intolerance only affects the digestive system and is the result of an enzyme deficiency, while milk allergy is an immune reaction to milk proteins that can be life-threatening. Food allergies remain one of the main problems of modern medicine, given their prevalence and seriousness of consequences. It is important to understand the mechanisms of allergy development, identify trigger foods and implement modern methods of prevention and treatment to ensure safe nutrition for all age groups.

1.3. Differences between food intolerance and food allergy

The differences between food intolerance and food allergy are one of the most relevant topics in the field of clinical nutrition and immunology. Both conditions are associated with adverse reactions to food, but their mechanisms, manifestations, and treatments differ significantly. In this detailed scientific analysis, the key differences between food intolerance and food allergy, their symptoms, pathogenetic mechanisms, modern diagnostic methods and clinical examples will be considered. Diagrams and tables will also be provided to facilitate understanding of the topic. Food intolerance is a pathological response of the body to specific food components that does not involve the immune system. It generally arises from enzyme deficiencies, metabolic disorders, or the chemical properties of certain foods. Common examples include lactase deficiency, known as lactose intolerance, gluten intolerance seen in celiac disease, and reactions to sulphites. Lactose intolerance results from the absence or insufficient activity of the enzyme lactase, which normally breaks down lactose – the sugar in milk – into glucose and galactose. When lactose remains undigested, it passes into the large intestine where fermentation occurs, producing gas and leading to symptoms such as flatulence, diarrhea, and abdominal pain.

Celiac disease is an autoimmune disorder linked to intolerance to gluten, a protein present in cereals like wheat, rye, and barley. In individuals with celiac disease, gluten intake damages the villi of the small intestine, impairing nutrient absorption and causing systemic symptoms including weight loss, chronic diarrhea, and anemia. Additionally, some foods contain natural or artificial chemicals that provoke adverse reactions in sensitive individuals; for example, sulphites, commonly used as preservatives in wine, dried fruit, and confectionery, can trigger symptoms in susceptible people. The pathogenesis of food intolerance differs fundamentally from that of food allergies because it does not involve immune mechanisms. Instead, it stems from the body's inability to digest or metabolize specific food substances. This may be genetically determined, as in celiac disease, or related to enzymatic dysfunction, as observed in lactose intolerance. Symptoms of food intolerance are predominantly gastrointestinal and typically are not life-threatening. For instance, symptoms in lactose intolerance usually manifest within 30 minutes to two hours after consuming dairy products and may be dose-dependent, meaning the severity increases with the amount of lactose ingested.

Diagnosis of food intolerance involves several approaches depending on the type and suspected cause. One of the most common methods for detecting lactose intolerance is the hydrogen breath test, which measures the concentration of hydrogen in exhaled air after lactose consumption. Elevated hydrogen levels indicate incomplete digestion of lactose in the intestine, leading to bacterial fermentation and hydrogen release. Genetic tests are employed to identify congenital forms of food intolerance, such as lactose intolerance, by detecting mutations in genes responsible for encoding enzymes necessary for food digestion, like lactase. These tests help confirm or exclude

genetic factors as the cause of intolerance. Immunological tests for IgG-mediated food intolerance measure blood levels of food-specific IgG antibodies to identify foods that might trigger a delayed immune response; however, this approach remains controversial due to ongoing debate about its scientific validity. Another well-established and practical diagnostic tool is the elimination diet, where patients exclude suspected foods from their diet for a period and then gradually reintroduce them while monitoring symptoms. This method is especially useful for detecting intolerances that lack clear immunological mechanisms. For diagnosing gluten intolerance not related to celiac disease, tests measuring IgA and IgG antigliadin antibodies are utilized. The absence of antibodies typical of celiac disease, combined with clinical symptoms after gluten consumption, can suggest non-celiac gluten intolerance.

Food allergy is an abnormal immune system reaction to proteins in food that are typically harmless to the body. In individuals with food allergies, the immune system erroneously identifies these proteins as harmful pathogens and produces immunoglobulin E (IgE) antibodies, triggering a cascade of allergic responses. The most common food allergens include proteins found in milk, eggs, peanuts, nuts, fish, seafood, soy, and wheat. The pathogenesis of food allergy begins with the initial exposure to an allergen, during which the immune system generates IgE antibodies that bind to mast cells and basophils. Upon subsequent exposure, these sensitized cells release histamine and other inflammatory mediators, causing allergic symptoms that may affect multiple systems, including the skin, respiratory tract, gastrointestinal tract, and cardiovascular system [32]. Peanut allergy is particularly dangerous, as even minimal exposure can provoke anaphylaxis, a severe and potentially fatal systemic reaction. Research indicates that approximately 1 to 2% of the global population is affected by peanut allergy, and its prevalence is rising [30]. Milk allergy is common among children and may be transient or lifelong; unlike lactose intolerance, it involves an immune response to milk proteins such as casein and whey. Allergies to fish and seafood frequently develop in adults and can appear suddenly, even after years of consuming these foods without prior symptoms. It is critical to recognize that food allergies can be life-threatening, especially when anaphylactic shock occurs, as this severe systemic inflammation can lead to respiratory or cardiac arrest.

Diagnosis of food allergies involves several established methods aimed at identifying the specific allergens responsible for adverse immune reactions. One of the most commonly used techniques is the skin prick test, which entails injecting small amounts of suspected allergens into the patient's skin with a fine needle. The appearance of redness or swelling at the injection site, resembling a mosquito bite, indicates a positive allergic reaction, reflecting how the immune system responds to direct contact with the allergen. Another diagnostic approach is the specific blood test for IgE antibodies, which measures the concentration of immunoglobulin E produced in response to allergens. Elevated levels of these antibodies suggest an allergic reaction and this test is often used to corroborate skin test results or when skin testing is contraindicated due to the risk of anaphylaxis.

The allergen-specific IgE test, including methods such as RAST and ImmunoCAP, quantifies IgE antibodies targeting particular allergens in the blood. ImmunoCAP technology is especially valuable because it can assess sensitivity to multiple allergens simultaneously, facilitating the diagnosis of complex food allergy cases. Provocative food tests, considered the gold standard in food allergy diagnosis, involve the controlled and gradual reintroduction of a suspected allergen under strict medical supervision to observe the body's response. However, due to the potential risk of severe allergic reactions, these tests are performed exclusively in hospital settings. Additionally,

allergic component diagnostics (CRD) utilize a molecular approach to identify immune responses to specific proteins within food allergens. This precise method helps distinguish sensitivity to individual allergenic components within a single food, thereby aiding in preventing unnecessary dietary restrictions and providing a clearer assessment of the risk for severe allergic reactions.

Table 8. Differences in symptoms of food intolerance and food allergy

Symptoms	Food intolerance	Food allergies
Time of onset of symptoms	A few hours later	From a few minutes to hours
Systemic symptoms	Local (gastrointestinal)	Systemic (affecting the skin, respiratory system, heart)
Severity	Usually lightweight	Can be life-threatening
Anaphylaxis	No	Commonly encountered

Source: *created by the author*

Modern methods of diagnosing food allergy and intolerance include both classical clinical methods and the latest molecular approaches (Table 9). For an accurate diagnosis, it is critical to combine several methods, which allows not only identifying the specific allergen or product causing intolerance, but also assessing the severity of the reaction and the risks to the patient.

Table 9. Comparison of treatment of food intolerance and food allergy

Treatment	Food intolerance	Food allergies
Product exclusions	Required	Required
Pharmacological support	Enzymes, probiotics	Antihistamines, adrenaline
Emergency assistance	No need	Adrenaline (in case of anaphylaxis)

Source: *created by the author*

The main treatment for food intolerance is a diet that excludes the food that causes the symptoms. For example, in case of lactose intolerance, a patient is recommended to eat lactose-free foods or take enzyme preparations to digest lactose. Food allergies require complete avoidance of allergenic foods. Injectable forms of epinephrine (epinephrine) are used for emergency treatment of allergic reactions, especially anaphylaxis. Antihistamines can also be used to relieve the symptoms of mild allergic reactions. In many cases, food intolerance does not have serious consequences if the patient follows a diet. However, prolonged undiagnosed intolerance, as in the case of celiac disease, can lead to serious complications such as anaemia, osteoporosis and an increased risk of bowel cancer. Food allergies have a more serious prognosis because there is a risk of anaphylaxis. Some allergies, such as milk or eggs, may disappear with age, but peanut or fish allergies usually last a lifetime. The differences between food intolerance and food allergy lie in the different mechanisms of their occurrence, symptoms, and treatment. Food intolerance is associated with enzyme deficiencies or metabolic disorders, while food allergy is an immunological reaction to food proteins.

Chapter 2.

Sugar intolerance

Sugar intolerance, or sugar malabsorption, is a common disorder that encompasses a variety of conditions related to the bodily inability to break down and absorb sugars properly. Modern research shows that a significant proportion of the population faces this problem, and due to various causes, from genetic to environmental, research into sugar intolerance is constantly expanding and deepening. Problems can occur in a wide range of symptoms from mild gastrointestinal discomfort to serious health disorders [33]. Sugar intolerance is commonly divided into the following main types: lactose, fructose and sucrose intolerance. These three types of malabsorption have different causes and mechanisms of action. Lactose intolerance, for example, is caused by a deficiency of lactase, the enzyme responsible for breaking down lactose into simpler sugars. Fructose intolerance is associated with a reduced ability of the body to transport fructose across the intestinal cell membranes, which leads to its accumulation and fermentation in the large intestine.

Current data indicate that up to 68% of adults worldwide have some form of lactose intolerance, particularly among the populations of Asia, Africa and South America [34]. In the case of fructose and sucrose, the statistics are less clear, but numerous studies have shown an increase in these forms of malabsorption, which can be attributed to the increased consumption of fructose syrup in food and beverages, as well as changes in diet. Lactose intolerance is the most studied of all types of sugar malabsorption. International studies have shown significant differences in the incidence of lactose intolerance between different ethnic groups. In many European populations, particularly in Northern Europe, lactose intolerance is less common due to widespread persistence. In Asia, Africa, and South America, genetic mutations that enable lactose absorption in adulthood are less common, so the level of lactose intolerance is much higher [35]. According to research, about 90% of East Asians suffer from lactose intolerance. According to the World Health Organisation (WHO), recommendations for such individuals include dietary modification, the introduction of lactose-free or low-calorie foods, and enzyme replacement therapy [36].

Fructose intolerance is divided into hereditary and dietary. Hereditary fructose intolerance (HFI) is a rare genetic disorder associated with a deficiency of the enzyme aldolase B, which is involved in the metabolism of fructose. If fructose is consumed, patients with HFI can develop severe hypoglycaemia, liver failure, and other serious complications [37]. Dietary intolerance to fructose, or fructose malabsorption, is more common and is caused by a reduced ability of the body to absorb fructose in the intestine. Studies show that about 30% of the population in Europe and the US suffer from fructose intolerance, which leads to symptoms such as bloating, pain and diarrhoea after eating fructose. To treat dietary fructose intolerance, it is recommended to reduce the consumption of fruit products, especially fruit juices and sweetened beverages. In addition, research suggests that consuming fructose with glucose may alleviate symptoms, as glucose helps fructose to be absorbed more quickly [38]. Sugar intolerance (CSID) is the result of a deficiency in the enzyme sucrose isomaltase, which makes it difficult to break down sucrose (sugar). CSID is most common in people from Northern Europe. Although CSID is a rare disorder, its diagnosis has become easier in recent decades due to the development of genetic testing. The current approach to treating CSID includes a low-sugar diet and enzyme therapy. There is

also limited research suggesting the possible benefit of probiotics in improving symptoms in some patients [39].

There are several methods for diagnosing sugar intolerance. The most common method is the hydrogen breath test, which measures the level of hydrogen in the exhaled breath after eating a certain sugar. This method is effective for diagnosing lactose and fructose intolerance. Genetic tests are also used in medical practice to identify hereditary forms of fructose and sucrose intolerance. In international experience, the treatment of sugar intolerance is based on dietary changes and the use of enzyme replacement therapy. In Europe and North America, lactose-free and low-fructose products have become widespread, making life much easier for people with such diagnoses. Recent studies have highlighted the genetic aspects of sugar malabsorption, which may help to develop personalised treatment approaches. New biomarkers are also being studied to help better diagnose the condition and understand what factors influence its course. Interest in probiotics and prebiotics is also growing, as they are believed to improve the condition of patients with fructose and other sugar intolerances.

2.1. What is sugar intolerance?

Sugar intolerance, or sugar malabsorption, is a disorder in which the body cannot effectively absorb certain types of sugars due to a deficiency of specific enzymes or due to impaired transport mechanisms in the intestine. This disease encompasses several types of intolerance, each with different pathophysiological mechanisms and clinical manifestations. Sugar intolerance is quite common and is a significant health problem, as it can significantly impair the quality of life of patients and lead to nutritional deficiencies [40].

The main types of sugar intolerance include lactose intolerance, fructose malabsorption, and congenital sucrase-isomaltase deficiency (CSID). Lactose intolerance arises when the enzyme lactase, responsible for breaking down lactose – the primary carbohydrate in milk and dairy products – into glucose and galactose, is deficient. According to the World Health Organization, approximately 65 to 70% of adults' worldwide experience lactose intolerance, with higher prevalence rates observed in populations from Africa, Asia, and South America. In contrast, the prevalence is lower in Europe and North America due to genetic adaptations favoring milk consumption in adulthood [41]. When lactase activity is insufficient, lactose is not properly digested and passes into the large intestine where bacterial fermentation leads to symptoms such as gas, bloating, diarrhea, and abdominal discomfort.

Fructose malabsorption involves impaired absorption of fructose, a sugar naturally present in fruits, vegetables, honey, and processed foods. Normally, fructose is absorbed in the small intestine via the specific transporter GLUT5. Deficiency or malfunction of this transporter results in incomplete fructose absorption, which then undergoes fermentation by intestinal bacteria, causing symptoms similar to lactose intolerance. Studies conducted in Europe and the United States estimate that 30 to 40% of adults experience symptoms of fructose malabsorption. A related but distinct condition is hereditary fructose intolerance (HFI), a rare genetic disorder caused by a deficiency of the enzyme aldolase B, essential for fructose metabolism. Individuals with HFI can suffer severe adverse reactions, including hypoglycemia and damage to the liver and kidneys, even from small fructose amounts [42].

Congenital sucrase-isomaltase deficiency (CSID) is an inherited disorder characterized by insufficient activity of the enzyme sucrase-isomaltase, which is necessary for the digestion of

sucrose into glucose and fructose. CSID is considered rare but appears to be more prevalent among populations in Northern Europe, with increasing diagnosis rates attributed to improved testing methods. Patients with CSID typically experience bloating, diarrhea, and abdominal pain following consumption of sucrose- and maltose-containing foods [43]. Several factors contribute to sugar intolerance, primarily genetic predispositions, functional impairments, and intestinal microbiota composition. For example, genetic mutations in the LCT gene cause primary lactase deficiency, while fructose malabsorption and HFI are linked to dysfunctions in transport proteins and metabolic enzymes. The intestinal microbiota also plays a crucial role in carbohydrate metabolism; individuals with fewer bacteria capable of fermenting certain sugars may exhibit milder intolerance symptoms [44].

Clinical manifestations of sugar intolerance vary depending on the specific malabsorption type, enzyme deficiency severity, and sugar intake levels. Lactose intolerance commonly presents with bloating, abdominal pain, diarrhea, and nausea following dairy consumption, whereas fructose malabsorption elicits similar gastrointestinal symptoms after ingesting fruits, honey, and sweetened beverages. CSID symptoms typically arise after eating sucrose-rich foods, starch, or bakery products. Diagnostic approaches include the hydrogen breath test, which measures exhaled hydrogen levels after sugar ingestion to detect malabsorption, genetic testing for hereditary conditions such as HFI or CSID, and endoscopic examination with biopsy to rule out other gastrointestinal disorders that may mimic sugar malabsorption [45].In terms of treatment and recommendations, there are dietary restrictions: removal of foods containing the relevant sugar (dairy products for lactose intolerance, fruit and honey for fructose intolerance). Most often, enzyme replacement therapy is prescribed. Lactase enzymes can be used for people with lactose intolerance, allowing them to consume some dairy products. Studies have also shown that certain strains of probiotics can improve malabsorption symptoms by improving microbiota function.

Modern science addressed the study of intolerance to various types of sugars, due to their high prevalence in the world and significant impact on the quality of life. Lactose intolerance is one of the most common forms of sugar malabsorption in the world. According to a study published in Global Health Metrics in 2020, the prevalence of lactose intolerance varies significantly by region and ethnicity [46]. For example, among adults in East Asia, the proportion of people with lactose intolerance reaches approximately 90%. This is determined by the lack of genetic adaptation to dairy consumption after childhood. By comparison, the prevalence of lactose intolerance among adults in Northern Europe is only about 5-10%, as this region has retained the genetic mechanism for producing the lactase enzyme, which allows them to continue consuming dairy products without significant symptoms of malabsorption [47]. Lactose intolerance is an important indicator for dietitians and physicians, as symptoms such as bloating, gas and diarrhoea can be serious and affect patients' daily lives. Current research shows that individual lactose tolerance may depend not only on genetic factors but also on the composition of the gut microbiota, which may mitigate symptoms in some patients [48].

Fructose malabsorption, which is associated with a decrease in the function of the GLUT5 transporter responsible for fructose absorption in the small intestine, has also been the subject of numerous studies. It is common among the population of developed countries, especially the United States, where approximately 30% of adults report symptoms of fructose malabsorption. One of the main reasons for the high level of fructose malabsorption is the growing consumption of

fructose syrup, which is widely used in the food industry due to its high sweetness and relative cheapness. Fructose malabsorption can cause symptoms similar to lactose intolerance: bloating, pain, gas and diarrhoea. Poor fructose absorption can negatively affect the overall health of the intestinal tract and contribute to the development of irritable bowel syndrome (IBS). An understanding of the pathophysiology of fructose malabsorption is important for the development of individual dietary programmes and recommended intakes of fruit-containing foods [49].

Congenital sucrose isomaltase deficiency (CSID) is a rare genetic disorder in which the enzyme sucrose isomaltase is not produced or is produced in insufficient quantities. It interferes with the absorption of sucrose and maltose, leading to symptoms such as bloating, pain and diarrhoea. In Northern Europe, according to genetic studies, approximately 0.2% of the population has this trait. With the development of genetic technologies, CSID diagnostics have become more accessible, enabling early detection and appropriate treatment [50]. In modern medicine, the use of genetic tests is an important tool in determining susceptibility to CSID, as well as in creating individualised treatment and nutrition programmes. The disease is much more common in childhood, and symptoms can be severe, particularly when consuming common children's foods such as fruit and sweets. Early detection of CSID can ensure an appropriate diet, which includes limiting isomaltase-degradable sugars and reducing the risk of developing chronic intestinal disorders.

Thus, each type of sugar intolerance has its mechanisms of development, which are determined by both genetic and environmental factors. The development of the latest research methods, such as genetic testing and microbiome analysis, makes it possible to effectively identify these disorders at an early stage, which helps develop personalised approaches to dietary and other treatments. Sugar intolerance is a multifaceted problem that requires an individual approach to diagnosis and treatment. Despite the similar symptoms, each type of malabsorption has specific causes, mechanisms and methods of treatment. Current research suggests a significant role for genetic factors, as well as a link to environmental factors, including dietary habits and gut microbiota composition.

2.2. Symptoms, diagnosis and treatment of sugar intolerance

Sugar intolerance, or sugar malabsorption, is accompanied by several different symptoms that vary depending on the type of intolerance. The most common forms include lactose intolerance, fructose malabsorption and deficiency of the enzyme sucrose isomaltase (CSID). The current scientific literature provides important information about the diagnosis, symptoms and effective treatments for each type of malabsorption, which can improve the quality of life of patients. There are so-called common symptoms of sugar intolerance, which include bloating, flatulence, abdominal pain, diarrhoea, and nausea. These symptoms are caused by the fermentation of unassimilated sugars in the large intestine under the influence of the microbiota, which releases gases (hydrogen, methane) and other metabolites. In terms of lactose intolerance, the main symptoms will be bloating, flatulence, loose stools, abdominal pain and cramps after consuming dairy products.

According to one study, bloating (80%) and diarrhoea (60%) are the most common symptoms among lactose-intolerant patients [51]. A study conducted in China found that 90% of the adult population has varying degrees of lactose intolerance. In Northern Europe, this figure is much lower (about 5-10%), which is due to genetic adaptation to milk consumption [52]. Fructose malabsorption will be characterised by pain, bloating, diarrhoea and discomfort after eating fruit, honey, and foods high in fructose syrup. Several studies demonstrated that fructose malabsorption occurs

in 30% of adults in the United States, of whom about 40% complain of bloating after consuming even small amounts of fructose. Symptoms can be severe even with low fructose intake, especially if fructose is not combined with glucose, which facilitates its absorption. Sugar intolerance (CSID), on the other hand, will manifest itself not only with bloating, and diarrhoea but also with colic after eating sucrose and starch [53]. CSID is often diagnosed in childhood when parents report diarrhoea and severe discomfort in their children after eating sugar and starchy foods.

Modern diagnosis of sugar intolerance employs several advanced methods, each providing valuable information to identify malabsorption disorders accurately. The hydrogen breath test is a standard and highly sensitive technique widely used for diagnosing malabsorption of sugars such as lactose and fructose. This non-invasive test measures the concentration of hydrogen in the exhaled air after the patient consumes a sugar solution. An increase in exhaled hydrogen indicates improper absorption of the sugar in the small intestine, resulting in its fermentation by bacteria in the large intestine and subsequent hydrogen production. Patients typically undergo the test on an empty stomach, sometimes after following a specific diet to minimize interference from bacterial fermentation of other foods. The patient drinks a diagnostic dose of sugar solution, such as lactose or fructose, and breath samples are collected at intervals to measure hydrogen levels. Normal hydrogen values range from 0 to 20 parts per million (ppm), and a rise exceeding 20 ppm within 60 to 90 minutes after ingestion suggests sugar malabsorption, leading to a diagnosis of lactose intolerance or fructose malabsorption. The test also helps determine the severity of malabsorption, which informs personalized dietary recommendations. Although convenient and accurate, factors like recent antibiotic use or bacterial imbalances can affect test results. Numerous studies have validated the hydrogen breath test's effectiveness, reporting it detected lactose intolerance in 85% of patients experiencing gastrointestinal symptoms after dairy consumption [54]. Genetic testing represents a modern and precise method for diagnosing hereditary sugar malabsorption disorders, including congenital sucrase-isomaltase deficiency (CSID) and hereditary fructose intolerance (HFI). This approach analyzes specific mutations in genes responsible for synthesizing enzymes critical for sugar absorption.

Genetic testing has become increasingly useful in clinical practice, particularly for rare metabolic disorders. The procedure begins with collecting biological samples, usually blood or saliva, to extract DNA. Laboratory techniques such as polymerase chain reaction (PCR) and next-generation sequencing (NGS) are then used to detect mutations. PCR targets known gene mutations, while NGS provides a comprehensive analysis, identifying novel or rare variants. Detecting mutations in genes encoding enzymes like sucrase-isomaltase or aldolase B allows clinicians to confirm diagnoses of CSID and HFI, respectively. Early diagnosis is vital, especially for HFI patients, who can suffer severe metabolic complications upon fructose ingestion. Genetic testing facilitates timely and personalized treatment, including dietary adjustments to avoid offending sugars such as sucrose or fructose, and enables monitoring treatment efficacy. Additionally, it offers valuable information for assessing risks among family members and guiding preventive strategies. This diagnostic tool has redefined the prevalence of disorders like CSID, now identified in approximately 0.3% of the Northern European population, a figure higher than previously estimated [55].

The stool pH test is another relevant diagnostic method, particularly in pediatric practice, for detecting carbohydrate malabsorption, including lactose intolerance. Malabsorbed carbohydrates reach the large intestine where bacterial fermentation produces short-chain fatty acids (SCFAs)

such as acetic, propionic, and butyric acids. These acids lower the pH of feces, and a stool pH below 5.5 indicates increased SCFA levels, suggesting carbohydrate malabsorption. Although the stool pH test does not specify the type of sugar malabsorbed, it serves as a quick and child-friendly screening tool without requiring invasive procedures or prolonged medical interventions. A low fecal pH result typically prompts further diagnostic tests, including the hydrogen breath test or enzyme activity assays, to clarify the underlying cause. Combining stool pH measurement with other diagnostics provides valuable insights for managing symptoms like bloating, diarrhea, and abdominal pain in patients with suspected sugar malabsorption. Studies indicate that 75% of children under five diagnosed with lactose intolerance exhibit below-normal stool pH values [56].

Endoscopic examination and biopsy are essential diagnostic procedures in gastroenterology, enabling accurate detection and exclusion of various gastrointestinal diseases such as celiac disease, inflammatory bowel disease, and cancer. During endoscopy, a flexible tube equipped with a camera is inserted through the mouth or rectum to visualize the mucosal surface of the gastrointestinal tract. This examination can reveal pathological changes like inflammation, villous atrophy, or ulcers. Importantly, tissue samples obtained via biopsy allow microscopic evaluation of mucosal morphology, which is crucial when clinical symptoms and non-invasive test results are inconclusive. In suspected celiac disease, biopsy helps assess the integrity of intestinal villi, which often show atrophy and inflammatory alterations characteristic of the disease. Additionally, endoscopic biopsy assists in complex diagnostic scenarios where sugar intolerance symptoms overlap with other gastrointestinal conditions. Excluding alternative pathologies through biopsy can significantly influence treatment strategies. In advanced malabsorption cases, villous atrophy is detected in approximately 15% of patients via small intestinal mucosa biopsy, underscoring the need for comprehensive clinical management [57].

The main method of treating sugar intolerance is to avoid foods containing the sugar in question. For people with lactose intolerance, it is recommended to avoid dairy products or choose lactose-free alternatives. Studies have shown that 90% of patients with lactose intolerance were able to completely resolve their symptoms with a lactose-free diet. To help alleviate symptoms, enzymes containing lactase can be used to help digest lactose. These supplements allow many people with lactose intolerance to consume dairy products without discomfort [58]. Studies conducted among patients with moderate lactose intolerance have shown that 75% of participants were symptom-free after taking lactase supplements. Certain strains of probiotics (e.g. Bifidobacterium and Lactobacillus) may help improve symptoms of lactose and fructose intolerance due to their ability to improve gut microbiota and partially break down these sugars [59]. Studies have shown that 60% of patients with fructose malabsorption experienced a significant reduction in symptoms after taking probiotics daily for a month [60].

For patients with CSID, a low-sugar diet is recommended, as well as specialised enzyme supplements to help relieve symptoms. Many studies have shown that enzyme supplements with replacement therapy helped to alleviate symptoms in 85% of children with CSID. People with fructose malabsorption are advised to avoid foods high in fructose, especially in the form of fructose syrup. The combination of fructose with glucose can make it easier to absorb, so apples, cherries and pears are usually poorly tolerated. Most patients reported improvement after switching to a low fructose and sorbitol diet [61]. A detailed understanding of the types of sugar intolerance, their symptoms and diagnostic methods are used to identify problems in time and adjust our diet or use treatment

to alleviate symptoms. Modern scientific research is constantly providing new information on the prevalence, genetic characteristics and effective approaches to therapy, which significantly improves the quality of life of patients with sugar malabsorption.

2.3. Lactose intolerance: prevalence, symptoms and treatment

Lactose intolerance is a condition in which the human body has difficulty digesting lactose, a natural sugar found in milk and dairy products. This condition is caused by a deficiency or complete absence of the enzyme lactase, which is necessary to break down lactose into glucose and galactose, which are easily absorbed in the intestines. Lactose intolerance is one of the most common forms of food intolerance in the world and can have different frequencies depending on genetics and demographic factors [62]. Dairy intolerance and lactose intolerance are two different conditions that are often confused due to their similar symptoms. Despite some similarities in manifestations, both conditions have different causes, and mechanisms of development and require different treatment approaches.

Lactose intolerance is the inability of the body to break down lactose, a sugar found in milk and dairy products, due to the lack of activity or absence of the enzyme lactase. Lactose is composed of glucose and galactose. For its absorption, the enzyme lactase, produced in the mucous membrane of the small intestine, breaks down lactose into these two simple sugars. In the case of lactase deficiency, lactose is not broken down and enters the large intestine, where it is fermented by bacteria to produce gases (hydrogen, methane) and organic acids. There is primary lactose intolerance, a genetic condition that is common in adults and is associated with a decrease in lactase production after childhood, and secondary lactose intolerance, which occurs as a result of damage to the intestinal mucosa due to diseases (celiac disease, gastroenteritis, inflammatory bowel disease). Symptoms appear after eating lactose-containing foods and can vary depending on the level of lactase deficiency, usually bloating, pain, diarrhoea, flatulence, and nausea. Diagnosis is standard and includes a hydrogen breath test, lactose tolerance test, genetic tests, and stool analysis for hydrogen or pH. Treatment includes dietary restriction of lactose or the use of enzyme supplements (lactase). Some people can tolerate small amounts of lactose without symptoms, hence the number of dairy products consumed is determined on an individual basis.

Dairy intolerance can have several causes and is not limited to lactose intolerance alone. It covers a wide range of reactions to various components of milk, including proteins. The most common form is an immune response to milk proteins, particularly casein and whey proteins. When the immune system reacts to these proteins as foreign agents, an immune response develops, which causes several symptoms. In addition to an immune reaction, dairy intolerance can include intolerance to milk fat due to lipid metabolism or a reaction to other milk components. Intolerance to dairy products can be the result of a cow's milk protein allergy (CMA), in which the immune system produces IgE or IgG antibodies to milk proteins. It can also be associated with fat digestion disorders or a lack of enzymes necessary for their absorption. Symptoms can range from gastrointestinal (bloating, diarrhoea, abdominal pain) to systemic (rash, cough, swelling, anaphylaxis in severe cases of allergy). These symptoms may appear immediately or several hours after consuming dairy products [63]. One study reported that 30% of children with milk protein allergy have both gastrointestinal and skin symptoms, including urticaria and dermatitis [64].

Diagnosis usually involves skin tests and a blood test for specific IgE antibodies is used to confirm ABCA. For other forms of intolerance, various test diets are used that exclude dairy products to check for reactions. The main treatment is the complete exclusion of dairy products. In case of al-

lergy, it is important to avoid any traces of milk proteins, as even a small amount can cause a severe reaction. Lactose-free or vegetable alternatives (e.g. soya milk, almond milk) can be used instead of dairy products. Lactose intolerance and dairy intolerance are two different conditions that can have similar symptoms but differ in nature, and mechanism of development and require different approaches to diagnosis and treatment. Understanding these differences allows for more accurate diagnosis and effective treatment. Lactose intolerance varies across ethnic groups, countries and regions of the world. The World Health Organisation estimates that 65% of the world's population is lactose intolerant. This figure, however, may vary by country and ethnicity. The highest level of lactose intolerance is 90 to 100% among adults in East and Southeast Asia. Up to 80-90% of the population in some regions of Africa suffer from lactose intolerance, especially among the Southern and West African peoples. The incidence of lactose intolerance is much lower in Northern Europe, where approximately 5-10% of the population is lactose intolerant, while in Southern Europe this figure can reach 50-70%. Lactose intolerance among Native Americans and African Americans reaches 70-80%, while among European descendants this figure is much lower (10-20%) [65].

Lactose intolerance occurs as an acute reaction to the consumption of dairy products and is characterised by several gastrointestinal symptoms. These symptoms are caused by the fermentation of unassimilated lactose in the large intestine by microflora that produces gases, including hydrogen, methane and short-chain fatty acids. Bloating is the most common symptom that occurs due to the formation of gas in the large intestine. Studies have shown that 85% of lactose-intolerant patients experience bloating after consuming dairy products. Abdominal pain and cramps occur in 70% of patients and are caused by excessive intestinal peristalsis caused by the osmotic effect of lactose. Notably, cramps and discomfort are most common in patients with complete lactase deficiency. Lactase deficiency leads to the accumulation of osmotically active lactose in the intestine, which causes an increase in water flow and, as a result, loose stools. The products of lactose breakdown, such as methane and hydrogen, cause excessive gas production. In patients with lactose intolerance, exhaled hydrogen levels after drinking milk increased by an average of 80% compared to the control group [66].

Several methods are employed to diagnose lactose intolerance, each varying in accuracy and accessibility. The hydrogen breath test is widely regarded as the "gold standard" for this diagnosis. In this test, the patient consumes lactose, and the concentration of hydrogen in the exhaled air is measured. An elevated hydrogen level indicates lactose malabsorption due to bacterial fermentation of unabsorbed lactose in the colon. The US National Institutes of Health reports that when performed according to established protocols, the hydrogen breath test can detect lactose intolerance with an accuracy of 95% [67]. Another diagnostic approach involves measuring blood glucose levels after lactose ingestion. Since lactose is broken down into glucose and galactose, proper absorption should lead to a rise in blood glucose. However, if lactose is not absorbed, blood glucose levels remain unchanged. This test has been shown to be less accurate than the hydrogen breath test, particularly in individuals with mild lactase deficiency [68]. Genetic testing to detect mutations in the LCT gene, which regulates lactase production, offers a definitive diagnosis of primary lactose intolerance. This method is especially valuable for diagnosing lactose intolerance in children and predicting the likelihood of developing symptoms later in life. Studies indicate that 98% of individuals with genetically confirmed lactase deficiency exhibit clinical symptoms of lactose intolerance [69].

The main method of treating lactose intolerance is to avoid or partially limit lactose-containing foods. Treatment may include dietary adjustments, enzyme supplements and the use of probiotics. Avoiding dairy products and replacing them with lactose-free alternatives. For those with mild lactase deficiency, fermented foods such as yoghurt or kefir may be helpful. In one study conducted in Spain, 88% of patients with lactose intolerance were completely free of symptoms after switching to a lactose-free diet. Lactase supplements can break down lactose in the body and significantly reduce intolerance symptoms after consuming dairy products [70]. A study in the United States found that 75% of patients who took lactase supplements before eating dairy products did not experience symptoms such as bloating and abdominal pain. Probiotics can help improve the gut microbiota and partially break down lactose, making it easier to digest [71]. A study published in the Journal of Clinical Nutrition found that taking probiotics containing Lactobacillus acidophilus reduced symptoms of lactose intolerance in 60% of patients after 4 weeks of use [72].

Some people can tolerate small amounts of lactose without symptoms. Studies show that up to 12 g of lactose (approximately 240 ml of milk) can be tolerated by most patients with partial lactase deficiency. The European Organisation for the Study of Lactose Intolerance recommends cautiously introducing small portions of dairy products to determine the personal tolerance of each patient [73]. Based on numerous studies, international organizations such as the NIH and EUROLAC have established guidelines for managing lactose intolerance. One of the primary recommendations is lactose restriction, which advises patients to avoid consuming large amounts of lactose. It is equally important to replace traditional dairy products with lactose-free alternatives that are enriched with essential nutrients or to use appropriate supplements to ensure sufficient intake of calcium and vitamin D. Another strategy involves the use of enzyme supplements; taking lactase enzymes prior to consuming dairy products or opting for foods with low lactose content can help prevent the onset of symptoms. Additionally, certain probiotic strains have been recommended for long-term improvement of lactose intolerance symptoms, supporting digestive health and reducing discomfort [74].

Lactose intolerance is a common problem among the population, and its symptoms can have a significant impact on quality of life. Modern diagnostic methods and effective management through dietary correction, enzyme therapy and probiotics allow most patients to fully control this condition. Sugar intolerance is a complex and multifaceted phenomenon that has a significant impact on the health and quality of life of patients around the world. This disorder is characterised by the inability of the body to fully or partially absorb certain types of sugars, which leads to various symptoms and complications, depending on the type of intolerance and individual characteristics of the person. Thanks to active research in the fields of medicine, genetics and nutrition, the current understanding of sugar intolerance define the mechanisms of its development, diagnostic options and effective treatment methods in more detail. The most common types of sugar intolerance include lactose, fructose, and rarer forms such as sucrose-isomaltose intolerance (CSID). These disorders are caused by genetic or acquired factors that affect the production or activity of enzymes needed to break down certain sugars. For example, lactose intolerance, caused by a deficiency of the enzyme lactase, is the most common form and occurs in more than half of the world's adults, especially among Asians and Africans. Fructose intolerance, which includes malabsorption and hereditary fructose intolerance, is less common but can lead to serious complications if not properly diagnosed and treated.

Symptoms of sugar intolerance vary depending on the type of sugar that is not digested and the degree of enzymatic deficiency. Typical manifestations include bloating, diarrhoea, abdominal pain, flatulence, nausea and cramping. These symptoms are caused by the osmotic effect of undigested sugars, which attract water into the intestinal lumen, and their fermentation by microbes in the colon. Fructose malabsorption, for instance, can cause symptoms even in healthy people when large amounts of fructose are consumed, as its transport across the intestinal epithelium is limited compared to glucose. Modern diagnostic methods include the hydrogen breath test, genetic tests, and tests for tolerance to certain types of sugar. The breath test, which measures the hydrogen content of exhaled breath after consuming a specific sugar, is the standard for determining lactose and fructose malabsorption. Genetic tests can identify hereditary mutations that cause disorders such as hereditary fructose intolerance and CSID. The widespread use of molecular diagnostic methods ensures accuracy and speed in making a diagnosis, which is critical for selecting the appropriate therapy.

The main approach to treating sugar intolerance is to limit or eliminate sugars that the body is unable to absorb from the diet. For instance, patients with lactose intolerance are recommended to eat a lactose-free diet or use enzyme supplements to compensate for lactase deficiency. In the case of fructose malabsorption, patients are recommended a diet low in fructose and sorbitol. In cases of CSID, which is a genetic disorder, enzyme replacement therapy avoids greater dietary restrictions. In addition, probiotics and prebiotics can improve the gut microbiota, which has a positive effect on the symptoms of some types of intolerance. Recent research is aimed at finding new diagnostic methods, such as biomarkers, that could more accurately identify sugar intolerance, as well as developing innovative therapies. Genetic research is leading to a better understanding of hereditary forms of intolerance, which opens opportunities for early diagnosis and prevention. For example, a 2021 study found that adding certain strains of bacteria to the diet can reduce symptoms of lactose and fructose malabsorption. Further research is also looking at the potential for gene therapy to treat inherited enzyme deficiencies [75].

Due to the widespread prevalence of sugar intolerance, national and international organisations such as the World Health Organization (WHO) and the European Society of Gastroenterology recommend the introduction of educational programmes for healthcare professionals and patients. These focus on early recognition of symptoms, proper diagnosis and effective management of these conditions. Raising awareness about sugar intolerance and access to modern diagnostic and therapeutic methods contribute to a better quality of life for patients and prevent the development of complications associated with chronic irritation of the intestines and microflora [76]. Sugar intolerance is not only a food disorder, but also a relevant indicator of the need for an individualised approach to nutrition. Modern science effectively diagnoses different types of sugar intolerance and develops individual treatment regimens. Although there is no complete cure for genetic forms of sugar intolerance, proper management and a personalised diet can significantly reduce symptoms and improve patients' lives.

Prospects for the treatment and research of sugar intolerance are optimistic, as medical science is actively developing new methods of diagnosis, and therapy, and investigating individual aspects of the reaction to different types of sugars. Thanks to advances in genetic technology, diagnosis of hereditary sugar intolerance has become much more accessible. The use of genetic testing to identify mutations in the genes responsible for sugar-breaking enzymes ensures a more accurate determination of the type of intolerance and the prescription of appropriate therapy.

Enzyme replacement therapy has been widely used to treat lactose intolerance, but research is now underway to develop enzymes to facilitate the malabsorption of other sugars, such as fructose or sucrose. Modern enzyme preparations improve the quality of life of patients by enabling them to eat foods that were previously unavailable. Research into the impact of the gut microbiota on digestion continues to grow, and there is increasing evidence that certain strains of bacteria can reduce the symptoms of sugar intolerance.

Probiotics from Lactobacillus and Bifidobacterium can improve the breakdown of lactose and fructose in the gut, helping to maintain a balanced microbiota and reduce discomfort. Gene therapy is a promising area for the treatment of inherited enzyme deficiencies associated with sugar intolerance. Although the technology is still in its early stages, advances in gene editing, such as CRISPR/Cas9, offer the possibility of correcting genetic mutations that lead to enzyme deficiencies. This could be a breakthrough in the treatment of inherited disorders such as sucrose-isomaltose intolerance (CSID) and hereditary fructose intolerance. The use of mobile apps and new devices to track symptoms and monitor reactions to certain foods helps patients take a more informed approach to their diets. Apps that integrate food diaries track the impact of certain types of sugars and adjust your diet in real-time. The popularity of individualised diets is growing, and developing recommendations for people with sugar intolerance is an important part of this process. Researchers addressing possibilities of more accurate dietary advice for patients based on their characteristics and type of intolerance. Research into biomarkers in blood and faecal samples that may indicate intolerance to certain sugars holds the promise of improving early diagnosis. Thanks to accurate biomarkers, it is possible to detect disorders at an early stage and develop an appropriate diet. Thanks to advances in scientific technology and research, the future treatment of sugar intolerance may become much more effective and convenient for patients. Accurate diagnosis, personalised treatment and the integration of modern therapeutic approaches promise to significantly improve the quality of life of people with this condition.

Chapter 3.

Food Intolerance: Celiac Disease and Gluten Enteropathy

3.1. What is celiac disease?

Celiac disease is an autoimmune disorder that develops in people with a genetic predisposition as a result of eating foods containing gluten. Celiac disease, also known as gluten enteropathy, is a complex autoimmune disease that occurs in genetically predisposed individuals in response to the consumption of gluten, a protein complex found in wheat, rye and barley. The development of this disease is caused by multifactorial mechanisms, including the interaction of genetic, immunological and environmental factors, which together determine the peculiarities of its pathogenesis [77].

Gluten is a complex protein found in wheat, rye, barley and products made from them. The main pathophysiological mechanism of celiac disease is an abnormal immune response to gliadin, a component of gluten that triggers autoimmune processes. The immune system in celiac disease begins to recognise gluten as a foreign threat. This results in the synthesis of autoantibodies that attack the body's tissues, particularly the mucous membrane of the small intestine. This damage leads to the destruction of the villi of the small intestine, which are responsible for absorbing nutrients. This process results in malabsorption, a condition where the body cannot absorb essential vitamins, minerals, fats and other nutrients. This pathological process causes not only intestinal disorders but also systemic complications, including anaemia, osteoporosis, growth retardation in children and even neurological symptoms. Gluten enteropathy may be accompanied by chronic diarrhoea, abdominal pain, bloating, and extraintestinal manifestations such as chronic fatigue, depression, dermatitis herpetiformis, and other disorders. Thus, celiac disease is a serious chronic condition that requires timely diagnosis and treatment. The main method of therapy is strict adherence to a gluten-free diet throughout life, which minimises symptoms, prevents complications and improves the patient's quality of life [78].

Genetic factors contribute to the development of celiac disease, as evidenced by the high level of association of the disease with specific alleles of the major histocompatibility complex (HLA) class II genes. In more than 95% of celiac disease cases, the presence of HLA-DQ2 or HLA-DQ8 alleles is detected, which encode proteins that can present gluten fragments, in particular gliadin, to T lymphocytes, initiating an immune response. HLA-DQ2 is present in approximately 90-95% of patients with celiac disease, while HLA-DQ8 is detected in 5-10% of cases [79]. The absence of these genes virtually eliminates the likelihood of developing the disease, although their presence alone is not a sufficient condition for the onset of pathology. In addition to HLA genes, other genetic factors have been identified that affect the risk of developing celiac disease. These are genes that regulate the intestinal barrier function, immune response and intercellular interaction. For instance, mutations in genes related to the production of interleukins or zonulin, a protein that regulates the permeability of intercellular junctions, can contribute to gluten sensitivity. Such genetic changes contribute to the disruption of the barrier function of the intestinal epithelium, facilitating the penetration of immunogenic gluten components and stimulating abnormal immune activation, which underlies the pathogenesis of celiac disease. Thus, genetic predisposition is a basic but not the only factor in the development of this complex autoimmune disease.

Gluten, the collective name for a group of proteins found in cereals such as wheat, rye and barley, is central to the development of celiac disease. The main protein components of gluten are gliadin and glutenin, but gliadin is recognised as the main antigen that can trigger an abnormal immune response in the small intestine of people with a genetic predisposition to the disease. Its interaction with the immune system involves complex mechanisms, including disruption of the intestinal barrier function, enzymatic modifications and activation of adaptive immunity. Gluten belongs to the class of prolamins, proteins rich in proline and glutamine [80]. Due to its high proline content, gluten fragments are resistant to complete breakdown by digestive enzymes such as pepsin and trypsin. This causes the formation of large peptides, in particular gliadin, which retain their immunogenic activity. This stability is a key prerequisite for their interaction with the epithelium and immune cells. Once gluten enters the gastrointestinal tract, its proteins are partially broken down by digestive enzymes. Gliadin, one of the gluten fragments, retains its structure due to its high proline content, which makes it difficult to completely break down by enzymes. Unfragmented gliadin fragments pass through the intestinal epithelial layer, where their pathological effect becomes crucial, triggering autoimmune processes (Table 10).

Table 10. Factors influencing the development of celiac disease

Factors	Description
Genetic (presence of HLA-DQ2/DQ8)	The presence of specific HLA alleles is a necessary but not sufficient condition for the development of the disease.
Abnormalities of the immune system	An overactive immune response, including activation of T cells and excessive production of cytokines, causes tissue damage.
Integrity of the intestinal barrier	Disruption of intestinal epithelial integrity facilitates the penetration of gliadin and activation of the immune system.
TG2 enzyme activity	The increased activity of TG2 promotes the deamination of gliadin, which enhances the immune response.
Environmental triggers (stress, infections)	Factors such as stress, early introduction of gluten and infections can trigger the disease.
Microbiota composition	An imbalance in the intestinal microbiota can increase inflammation and permeability of the intestinal wall.
Concomitant autoimmune diseases	Comorbidities, such as type 1 diabetes, Hashimoto's thyroiditis, and rheumatoid arthritis, contribute to autoimmune processes.

Source: *compiled by the author*

In healthy individuals, the intestinal mucosal barrier is a physiological barrier to the penetration of large protein molecules. However, in people with celiac disease, this function is impaired due to the increased permeability of the intestinal wall. Zonulin, a protein that regulates the permeability of intercellular junctions, is responsible for this process. An increase in zonulin levels causes the opening of intercellular gaps, through which gliadin can penetrate the subepithelial layer. In the subepithelial layer, gliadin is exposed to the enzyme tissue transglutaminase-2 (TG2), which converts it into a more immunogenic form. This enzyme deamidates glutamine residues in the gliadin structure, creating peptides with increased affinity for HLA-DQ2 and HLA-DQ8 molecules. This modification significantly enhances the immunogenicity of gliadin by promoting its binding to antigen-presenting cells. Deamidated gliadin peptides bound to HLA-DQ2/DQ8 are presented to T lymphocytes in the lymphoid tissue of the small intestine. This triggers an adaptive

immune response, accompanied by the production of proinflammatory cytokines such as interferon-gamma (IFN-γ) and tumour necrosis factor-alpha (TNF-α) [81]. B lymphocytes are also activated and begin to synthesise antibodies to gliadin, TG2 and some other antigens. These antibodies, in turn, exacerbate tissue damage.

The immune response to gliadin leads to chronic inflammation in the small intestine, accompanied by the activation of macrophages, eosinophils and cytotoxic T cells. The mucosal damage is reflected in villi atrophy, crypt hyperplasia and a decrease in the intestinal absorption surface, which significantly impairs nutrient absorption. In addition to the direct effect of gliadin, the intestinal microbiota plays a significant role in the development of celiac disease [82]. Dysbiosis – a change in the composition of the microflora, which is often observed in patients with celiac disease – can increase inflammation and contribute to increased epithelial permeability. For instance, an excessive growth of proteobacteria and a decrease in the number of lactobacilli and bifidobacteria are associated with disease progression.

Although gluten is a disease trigger, its impact depends on several environmental factors. These include:

- nutrition in early childhood, early introduction of gluten into the diet can increase the risk of developing celiac disease in children with a genetic predisposition;
- intestinal infections, some viral infections, such as rotavirus, can cause an increase in the permeability of the intestinal barrier;
- stress factors, chronic stress can modify the functioning of the immune system, which can contribute to the triggering of a pathological reaction to gluten [83].

Not all individuals with the HLA-DQ2 or HLA-DQ8 genes, or even those with increased intestinal barrier permeability, develop celiac disease. This suggests that the pathological process requires the interaction of additional factors that ensure a complex and multilevel pathogenesis of the disease. The immune system plays a central role in the development of celiac disease, and its characteristics can significantly affect the likelihood of developing the disease. Polymorphisms of genes responsible for the production of cytokines, such as interleukin-2 (IL-2), interleukin-15 (IL-15) and tumour necrosis factor-alpha (TNF-α), can increase inflammatory processes [84].

For instance, increased activity of IL-15 stimulates the proliferation of cytotoxic T-lymphocytes, which contributes to the destruction of the intestinal epithelium. A decrease in the activity of regulatory T cells (Treg), which are responsible for suppressing an excessive immune response, can contribute to an uncontrolled autoimmune reaction to gluten. In celiac disease, there is an abnormal activation of the innate immune system that precedes the launch of an adaptive immune response. For example, the activation of Toll-like receptors (TLRs) can increase inflammation and damage to the mucosa. TG2 is a key enzyme that modifies gliadin, converting it into a more immunogenic form. The level of expression of this enzyme may affect the risk of developing celiac disease. In individuals with increased expression of TG2 in the intestinal mucosa, the likelihood of forming immunogenic deamidated gliadin peptides increases significantly. This promotes more active binding of these peptides to HLA-DQ2/DQ8 molecules and activation of T lymphocytes.

Under normal conditions, TG2 has additional functions, including promoting tissue repair after injury. However, in the event of dysregulation, the enzyme can play a pathogenic role by enhancing the autoimmune response. Antibodies to TG2 are often detected in patients with celiac

disease, which are not only a diagnostic marker but also potentially contribute to tissue damage [85]. Celiac disease has a significant comorbidity with other autoimmune conditions, suggesting common mechanisms of pathogenesis. Thyroid dysfunction, in particular Hashimoto's disease, is often diagnosed in patients with celiac disease. The common features are genetic risk factors (HLA) and cross-activation of the immune system. Patients with type 1 diabetes often have coexisting celiac disease. Antibodies to antigens common to both conditions indicate a joint activation of the immune response. Rheumatoid arthritis and systemic lupus erythematosus are also associated with celiac disease, suggesting a possible role of chronic systemic inflammation in both pathologies [86].

Disruption of intercellular contacts in the mucous membrane can increase epithelial permeability, which creates prerequisites for the initiation of an autoimmune process. Dysbiosis can affect immune regulation and barrier function, contributing to the development of inflammation. Stress, infections, and a history of antibiotics can be important triggers that act synergistically with genetic factors. The presence of HLA-DQ2/DQ8 genes and increased intestinal permeability are important but not sufficient factors for the development of celiac disease. Individual characteristics of the immune system, TG2 expression level and comorbidity with autoimmune diseases determine the complex interaction of mechanisms that leads to the pathological condition. These additional factors are central to developing personalised approaches to the diagnosis and treatment of celiac disease [87]. Gluten, being the main trigger of celiac disease, initiates a complex cascade of immunological and inflammatory reactions that lead to serious damage to the small intestine. Its role in the development of the disease depends on the interaction of genetic, immunological and environmental factors, which together determine individual sensitivity to this protein. Determination of these mechanisms is essential for developing new therapeutic approaches and improving diagnostic methods.

Naturally, gluten-free foods are the mainstay of the diet of people with celiac disease or those following a gluten-free diet. These include: cereals and starchy products (white, brown, wild rice), corn, buckwheat, millet, amaranth, quinoa, teff, sorghum, tapioca, potatoes, pure corn starch; fruits and vegetables, meat, fish and eggs, dairy products, legumes, nuts and seeds, oils and fats, gluten-free flours and mixtures (rice flour, corn flour, potato flour, almond flour, coconut flour, tapioca flour); natural coffee and tea, fruit juices (100%), water, wine (natural), types of beer based on sorghum or other gluten-free grains. Foods that may contain gluten: processed foods, including sausages, sauces, condiments, canned foods, crisps, chocolate and other industrially produced foods. Gluten can be added as a thickener or stabiliser. When choosing foods, it is important to read labels carefully, searching the "gluten-free" designation, and avoid cross-contamination during cooking.

3.2. Symptoms of celiac disease in different age groups

Celiac disease can occur in a variety of symptoms, depending on age, the degree of intestinal damage and the presence of extraintestinal complications. The main manifestations differ between children and adults. Symptoms of celiac disease in children can include both gastrointestinal and extraintestinal manifestations. Among the gastrointestinal symptoms, chronic diarrhoea is often observed, manifested by watery or oily stools. Abdominal distention is a common symptom in young children. Abdominal pain can be either constant or intermittent, and vomiting is frequent in

infants. In some cases, constipation is common [88]. Extra-intestinal manifestations include stunted growth, which is associated with poor nutrient absorption, and weight loss, even with a normal appetite. Rickets or osteoporosis can occur due to calcium and vitamin D deficiency. Children often become irritable, and tearful, and may have a decrease in concentration. Delayed puberty is manifested by late onset of menstruation or other signs of puberty. Anaemia caused by iron or folic acid deficiency is another common manifestation. Rashes characteristic of dermatitis herpetiformis may appear on the skin, localised on the elbows, knees and buttocks. In infants, additional symptoms may include refusal to eat, delayed teething, and constant crying or discomfort.

Symptoms of celiac disease in adults can include gastrointestinal and extraintestinal manifestations. Among the gastrointestinal symptoms, the most common is chronic diarrhoea, which is characterised by oily, loose or frequent stools. Bloating and flatulence are accompanied by a feeling of heaviness after eating. Abdominal pain is often accompanied by cramps, and in some cases, constipation may be the main symptom [89]. Extraintestinal manifestations include weight loss, which occurs regardless of the amount of food consumed. Chronic fatigue is manifested by weakness and exhaustion. Anaemia is usually caused by a deficiency of iron, folic acid or vitamin B12. Bone density disorders, such as osteoporosis or osteopenia, increase the risk of fractures. Neurological symptoms may include peripheral neuropathy, headache, migraine, and ataxia. Depression and anxiety may be the only manifestations of the disease. Skin rashes, in particular dermatitis herpetiformis, are also common in adult patients. Reproductive dysfunction is another important aspect. In women, this can be manifested by infertility, miscarriages, or menstrual irregularities. In men, a possible problem is a decrease in testosterone levels.

Atypical manifestations of celiac disease can be difficult to diagnose, as children and adults often have the disease without obvious gastrointestinal symptoms. In such cases, extraintestinal manifestations that do not seem to be related to the digestive system dominate, which can be confusing for both patients and doctors. One of the most common atypical symptoms is anaemia, which is often caused by iron deficiency. Due to chronic damage to the mucous membrane of the small intestine, iron absorption is impaired, leading to anaemia, which can manifest itself as weakness, pale skin, shortness of breath and even tachycardia. Anaemia is often the first sign of the disease detected by laboratory tests. Another typical extraintestinal manifestation is chronic fatigue. Patients experience constant exhaustion and decreased performance, even if they follow a normal sleep and nutrition regime. This is related to both nutritional deficiencies and systemic inflammation that accompanies celiac disease.

Osteoporosis, or a decrease in bone density, can also be one of the first signals of atypical celiac disease. As a result of impaired absorption of calcium and vitamin D, bones become more fragile, which increases the risk of fractures. Such patients should present to the doctor with frequent injuries, and only a detailed examination reveals a celiac disease [90]. Slow wound healing is also a result of insufficient intake of nutrients such as proteins, zinc and vitamins. The body does not have sufficient resources to repair tissues, which leads to prolonged healing of even small injuries. Thus, the atypical manifestations of celiac disease cover a wide range of extraintestinal symptoms, which make the diagnosis of the disease very difficult. The absence of traditional signs, such as diarrhoea or abdominal pain, requires doctors to carefully analyse the clinical picture and conduct additional tests. Early diagnosis is key to preventing the progression of complications and improving the quality of life of patients (Table 11).

Table 11. The main differences between children and adults

Characteristic	Children	Adults
Main symptoms	Gastrointestinal (diarrhoea, abdominal pain)	Extraintestinal (anaemia, osteoporosis)
Frequent extraintestinal manifestations	Growth decrease, irritability	Fatigue, depression, reproductive problems
The risk of osteoporosis	Low (during early diagnosis)	High (due to chronic calcium deficiency)
Diagnostics	Often clinical manifestations	Often with the help of serological tests

Source: *compiled by the author*

Early detection of celiac disease in children and adults helps avoid serious complications and improves the quality of life of patients. Celiac disease is a complex disease with a variety of symptoms that often mimic other pathologies. The main manifestations include both intestinal and extraintestinal symptoms. The most common intestinal symptoms are diarrhoea, abdominal pain, bloating and weight loss. Extra-intestinal manifestations include anaemia caused by iron, folic acid or vitamin B12 deficiency, osteoporosis due to impaired absorption of calcium and vitamin D, chronic fatigue, dermatitis herpetiformis with characteristic pruritus, and neurological disorders such as depression and peripheral neuropathy. Modern research into the genetic aspects of celiac disease emphasises the importance of genetic predisposition as a major factor in the development of this autoimmune disease. One of the key discoveries is the identification of a link between the disease and specific alleles of the major histocompatibility complex (HLA) class II genes. According to a study published in 2021 in Nature Communications, approximately 40% of the genetic risk of celiac disease is associated with the presence of HLA-DQ2 and HLA-DQ8 alleles. These genes are responsible for the presentation of gluten fragments to immune cells, which triggers an autoimmune response [91; 92].

More than 95% of patients with celiac disease have HLA-DQ2, while the rest predominantly have HLA-DQ8. These alleles create a platform for the binding of gliadin, a component of gluten modified by the enzyme tissue transglutaminase-2 (TG2). The formation of immunogenic complexes with subsequent activation of T lymphocytes is a key point in the pathogenesis of the disease. However, the presence of HLA-DQ2/DQ8 is not sufficient for the development of celiac disease, which indicates the role of other genes and factors. Current research has identified more than 40 genetic loci that influence the risk of the disease, including genes that regulate the immune response, intestinal barrier function and intercellular interactions. For instance: genes related to the production of interleukins (IL-2, IL-21) – these cytokines play an important role in modulating the immune response, while genes for intercellular junctions, such as ZO-1 and CLDN, affect the permeability of the intestinal epithelial barrier.

An important advance in the practical application of this knowledge is the introduction of genetic tests. Testing for the HLA-DQ2/DQ8 alleles allows for the assessment of genetic predisposition to celiac disease, especially in patients with questionable serological results or in the absence of typical symptoms. These tests are particularly useful in risk groups, such as first-degree relatives of celiac patients or individuals with concomitant autoimmune diseases (type 1 diabetes mellitus, autoimmune thyroiditis). Genetic testing is also important for preventing complications of the disease. Early identification of a genetic predisposition allows timely preventive measures to be taken, such as regular medical monitoring, nutritional advice and avoidance of trigger factors.

This is especially relevant for patients whose disease may be atypical or asymptomatic. Thus, modern genetic research into celiac disease opens new opportunities for early diagnosis, personalised treatment and reduced risk of complications. Further study of the genetic immune mechanisms promises to make a significant contribution to the development of new therapeutic approaches, such as vaccines or gene-targeted treatments.

3.3. Diagnostic tests for celiac disease

Diagnosis of celiac disease in children is a complex, multi-stage process that relies on a combination of clinical evaluation, laboratory testing, genetic analysis, and histological examination of the small intestine. The initial step involves a thorough collection of anamnesis and assessment of symptoms, which can vary widely. Gastrointestinal manifestations commonly include chronic diarrhea, bloating, abdominal pain, and malabsorption leading to nutrient deficiencies. Extra-intestinal symptoms such as weight loss, chronic fatigue, anemia resistant to treatment, delayed growth or puberty, and the distinctive skin condition dermatitis herpetiformis also serve as important diagnostic clues. It is essential to note that celiac disease may present atypically or remain asymptomatic, especially in children. Therefore, family history of the disease and the presence of associated autoimmune disorders like type 1 diabetes must be carefully evaluated to guide the diagnostic approach [93].

Serological studies play a pivotal role in screening for celiac disease by detecting specific antibodies indicative of an autoimmune reaction to gluten. The most sensitive and widely used test measures IgA antibodies against tissue transglutaminase (anti-tTG IgA), which show high specificity for the disease and correlate strongly with intestinal mucosal damage. However, in about 2-3% of celiac patients who have selective IgA deficiency, anti-tTG IgA tests can yield false-negative results. In such cases, IgG-based tests, including antibodies against deamidated gliadin peptides (DGP IgG), are employed, especially in young children whose immune systems are still developing. Total IgA levels must be checked to identify IgA deficiency and to adjust the diagnostic strategy accordingly. Although serological tests are highly accurate, their results often require confirmation through biopsy, especially in cases with atypical clinical features or absent symptoms, to ensure diagnostic certainty and prompt treatment initiation [94].

Genetic testing is an important adjunctive diagnostic tool, primarily to detect the presence of HLA-DQ2 or HLA-DQ8 alleles, which are necessary but not sufficient for celiac disease development. These alleles encode major histocompatibility complex class II molecules involved in antigen presentation to T cells, a critical step in the immune response against gluten peptides modified by tissue transglutaminase-2 (TG2). Despite being present in 30-40% of the general population, only about 1% of carriers develop the disease, indicating additional factors influence pathogenesis. Genetic testing is particularly useful in patients with inconclusive serology, those on gluten-free diets, or for screening at-risk individuals such as first-degree relatives. The absence of HLA-DQ2/DQ8 effectively excludes celiac disease, reducing the need for invasive testing. However, a positive genetic test alone does not confirm the disease, underscoring the necessity of integrating clinical, serological, and histological data [95–97].

Biopsy of the small intestine remains the gold standard for definitive diagnosis by directly assessing mucosal morphology. Using endoscopy, multiple tissue samples are taken from the duodenum for histological examination. Key pathological features include villous atrophy,

characterized by partial or complete loss of intestinal villi leading to reduced absorptive surface; crypt hyperplasia, a compensatory enlargement of the crypts between villi; and increased intraepithelial lymphocytes, reflecting localized immune activation. Biopsy is essential in complex or uncertain cases, especially when serological results are ambiguous or the patient is already on a gluten-free diet, which can normalize antibody levels. To ensure accuracy, biopsies should be performed while the patient consumes gluten, with samples taken from several sites to account for patchy mucosal damage. Histological changes are classified according to the Marsh-Oberhuber system, which grades mucosal injury from normal appearance (Marsh 0) to varying degrees of villous atrophy (Marsh 3) [98–100]. Biopsies also serve to monitor mucosal recovery following dietary treatment, though the invasive nature of the procedure requires judicious use.

The gluten challenge, or provocative test, is a diagnostic procedure used primarily when patients have already initiated a gluten-free diet prior to diagnosis. Under medical supervision, gluten is reintroduced in controlled amounts, typically 3–10 grams daily for 6–8 weeks, followed by serological and possibly histological assessment [101]. This test helps confirm or exclude celiac disease, especially when initial testing was incomplete or ambiguous, and to differentiate it from non-celiac gluten sensitivity. Close clinical monitoring during the challenge is necessary due to potential symptom exacerbation, and the test should only be performed when other diagnostic methods are insufficient. A positive challenge involves recurrence of symptoms, elevated antibodies, or mucosal damage, whereas a negative test suggests alternative diagnoses [102].

Differential diagnosis is a crucial aspect of evaluating suspected celiac disease due to overlapping symptoms with other gastrointestinal conditions. Irritable bowel syndrome (IBS), wheat allergy, non-celiac gluten sensitivity (NCGS), and infectious intestinal diseases must be considered. IBS is characterized by functional bowel symptoms without serological markers or villous atrophy, and symptoms often relate to stress or diet rather than gluten specifically. Wheat allergy involves an IgE-mediated immune response leading to immediate hypersensitivity reactions, distinguishable by specific IgE antibodies and absence of mucosal atrophy. NCGS presents with symptoms similar to celiac disease but lacks autoimmune markers and histological damage; symptoms typically resolve on gluten withdrawal without systemic complications. Infectious diseases such as giardiasis can mimic celiac symptoms but are distinguished by pathogen identification and the absence of characteristic mucosal lesions. A comprehensive diagnostic approach integrating history, laboratory, genetic, and histological data ensures accurate diagnosis and appropriate management [103].

Additional examinations may include blood tests to evaluate nutritional deficiencies common in celiac disease, such as iron, folic acid, vitamin B12, calcium, and vitamin D levels, as well as bone density assessment to detect osteoporosis [104]. Early and accurate diagnosis in children is essential to prevent complications like growth retardation, anemia, neurological disorders, and bone disease. Treatment hinges on strict lifelong adherence to a gluten-free diet, which leads to symptom resolution and mucosal healing. Clinical manifestations in adults vary widely and depend on the degree of intestinal damage, malabsorption severity, and presence of associated complications (Table 12) [105].

Table 12. Comparison of diagnostics in children and adults

Diagnostic stage	In children	In adults
Symptoms	Mostly gastrointestinal	Extraintestinal or atypical
Serology	Often sufficient	Always used as a first step

Table 12, Continued

Diagnostic stage	In children	In adults
Genetic test	Used when in doubt	Used when in doubt
Biopsy	Can be skipped in definitive tests	Often required
A provocative test	Rarely used	More often needed

Source: *compiled by the author.*

The diagnosis of celiac disease in children and adults is based on serology, genetic testing and biopsy, but the approach to diagnosis depends on the age-related characteristics of the disease. Early diagnosis and timely treatment help avoid complications and improve quality of life.

3.4. Treatment and management of celiac disease

Celiac disease is a chronic autoimmune disorder that occurs in genetically predisposed individuals in response to the consumption of gluten, a protein complex found in wheat, barley and rye. Damage to the mucous membrane of the small intestine leads to malabsorption of nutrients and systemic complications. Treatment of celiac disease requires a strict lifelong gluten-free diet. However, due to the difficulty of maintaining such a diet and the possibility of complications, current research is aimed at improving therapeutic approaches for both children and adults.

The basic principles of celiac disease therapy revolve primarily around a strict gluten-free diet, which remains the "gold standard" for treatment. This diet necessitates the complete elimination of foods containing gluten, including wheat, barley, rye, and their derivatives. Modern research emphasizes that even trace amounts of gluten can cause damage to the intestinal mucosa, making avoidance of cross-contamination critical. The introduction of gluten-free labeling has significantly facilitated adherence to the diet. In children, dietary compliance requires special attention to ensure sufficient nutrient intake for normal growth and development. For example, iron, folic acid, and vitamin B12 supplements may be prescribed to treat anemia, while adults often require additional measures to prevent osteoporosis, such as calcium and vitamin D supplementation [105].

Drug therapy serves as an important adjunct in cases of refractory celiac disease or complications where a gluten-free diet alone is insufficient. Refractory celiac disease (RC) is characterized by the failure to achieve clinical or histological improvement after 6 to 12 months of strict dietary adherence. In such instances, pharmacological intervention aims to reduce inflammation and manage systemic manifestations. Glucocorticoids, including prednisone and budesonide, are typically the first-line agents due to their potent anti-inflammatory effects. However, their use is generally limited to short-term therapy to minimize adverse effects like osteoporosis, hypertension, and immunosuppression. Immunosuppressants such as azathioprine and 6-mercaptopurine are reserved for refractory type II celiac disease, which involves aberrant intraepithelial lymphocytes. These agents suppress the excessive immune response but require careful monitoring due to potential toxicities like myelosuppression and hepatotoxicity. Biological drugs, such as tumor necrosis factor-α (TNF-α) inhibitors like infliximab and adalimumab, have shown efficacy in reducing inflammation for patients unresponsive to glucocorticoids or immunosuppressants by targeting key inflammatory pathways [106].

Recent advances in therapy include immunotherapy approaches such as vaccines designed to modulate the immune response to gluten. For instance, the Nexvax2 vaccine, currently in clinical

trials, aims to "reprogram" the immune system to prevent it from recognizing gluten as an antigen. Preliminary results suggest a reduction in symptoms and intestinal damage following administration. Enzyme therapy is another promising field, involving enzymes that break down gluten into non-toxic fragments before reaching the small intestine. The enzyme proline endoprotease (AN-PEP) is available as an aid to mitigate the effects of accidental gluten exposure. Additionally, zonulin inhibitors like Larazotide Acetate are under investigation; these drugs target the intestinal epithelial barrier's permeability, which is abnormally increased in celiac disease, thereby potentially reducing symptom severity [107].

Internationally, standardized protocols guide diagnosis and treatment. In the US and Europe, guidelines from the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) are commonly used. These protocols include serological tests (anti-tTG, DGP) for primary screening, genetic testing (HLA-DQ2/DQ8) to exclude the disease, and endoscopy with biopsy to confirm diagnosis [108]. Countries like Italy have national programs promoting gluten-free products to facilitate dietary compliance, while Sweden has developed a comprehensive database for monitoring patients and assessing long-term therapy outcomes [109]. Therapy in children involves unique considerations due to ongoing growth and development. Adequate nutrition through vitamin and mineral supplementation is essential to prevent deficiencies. Regular monitoring of growth parameters helps detect developmental delays early, and psychological support is crucial to educate families and assist with social adaptation in environments such as schools and daycare. In 2020, ESPGHAN updated its recommendations to include non-invasive diagnostic methods in select pediatric cases, allowing diagnosis based on serology without biopsy under certain conditions [110].

Systemic complications of untreated celiac disease require targeted management. Osteoporosis is treated with bisphosphonates alongside calcium and vitamin D supplementation, while anemia necessitates iron, folic acid, or vitamin B12 replacement. Dermatitis herpetiformis, a characteristic skin manifestation, responds to treatment with Dapsone in combination with a gluten-free diet. Neurological complications are managed through correction of vitamin deficiencies and symptomatic therapy [111]. The latest treatment protocols emphasize a multidisciplinary approach incorporating genetic testing for risk screening, personalized diets tailored to individual needs, and microbiome monitoring with probiotics and prebiotics to correct intestinal dysbiosis [112]. Overall, modern celiac disease therapy combines dietary management, pharmacologic treatment for complicated cases, and innovative therapies such as immunotherapy and enzyme supplementation. International experience underscores the importance of comprehensive care, including diagnosis, treatment, and prevention of complications. Continued research aims to develop novel interventions that could significantly improve the quality of life for patients living with celiac disease.

Untreated celiac disease in both children and adults leads to serious complications that adversely affect quality of life and may cause life-threatening conditions. These outcomes stem from chronic inflammation of the small intestinal mucosa, resulting in impaired nutrient absorption (malabsorption) and systemic autoimmune reactions. Complications of celiac disease in children are complex and affect both physical and psychosocial health. One of the most serious consequences of untreated celiac disease is stunted growth and development. This is due to malabsorption of essential nutrients, including proteins, fats, carbohydrates, vitamins and minerals. The lack of essential components for growth leads to a significant delay in physical development. Children may have short stature, underweight, and bone formation disorders. Of particular importance is

vitamin D and calcium deficiency, which causes rickets, weakened bone structure, delayed teething and increased bone fragility.

Anaemia is another common complication in children with celiac disease. It occurs due to a deficiency of iron, folic acid or vitamin B12, which is accompanied by impaired haemoglobin formation. The consequence is the development of iron deficiency or megaloblastic anaemia, which is manifested by chronic fatigue, weakness, decreased concentration and performance. Children with anaemia may also have pale skin, heart palpitations, and decreased physical endurance [113]. Hormonal disorders are a serious consequence of untreated celiac disease, especially in girls. Delayed onset of menstruation, irregularity of the cycle or even impaired puberty can be the result of chronic nutritional deficiencies that affect the function of the endocrine system. Hormonal imbalances, in particular insufficient production of sex hormones, affect the overall development of the body and can cause additional difficulties in adolescence.

The impaired barrier function of the intestinal mucosa, which is characteristic of celiac disease, increases the risk of infectious diseases of the gastrointestinal tract. The weakening of local immunity facilitates the penetration of pathogens into the body, causing infectious lesions that further worsen the child's condition. Psychosocial consequences also have a significant impact on children with celiac disease. Persistent physical symptoms, such as bloating, diarrhoea or chronic fatigue, can cause difficulties in adapting to the educational process and social environment. Children may feel isolated due to the need to follow a special diet, complicating their integration into the school environment. This can lead to low self-esteem, social isolation and emotional problems. As a result, untreated celiac disease in children poses a significant risk to their physical, intellectual and emotional development. Timely diagnosis and strict adherence to a gluten-free diet are key to preventing these complications and ensuring a healthy and fulfilling life.

Complications of celiac disease in adults cover a wide range of disorders that can affect almost all body systems. If left untreated, chronic inflammation of the small intestinal mucosa and impaired absorption of nutrients (malabsorption) can lead to serious physical and psycho-emotional consequences. One of the most common complications is osteoporosis and osteopenia. Due to impaired absorption of calcium and vitamin D in the intestines, bone density decreases. This significantly increases the risk of fractures even with minimal injuries. Decreased bone mass can be accompanied by bone pain, chronic fatigue, and reduced physical activity. In severe cases, osteoporosis can lead to vertebral compression fractures, which impair the patient's mobility and quality of life.

Anaemia is another common complication that occurs due to chronic deficiency of iron, folic acid or vitamin B12. This leads to a decrease in the level of haemoglobin in the blood, which causes persistent weakness, shortness of breath, headaches and reduced performance. Anaemia also affects the appearance of patients: pale skin, brittle nails and hair loss can be its manifestations. Chronic anaemia significantly worsens the quality of life and can complicate the course of other diseases. Neurological disorders are serious consequences of untreated celiac disease. Peripheral neuropathy, characterised by tingling, numbness or pain in the limbs, occurs due to a deficiency of B vitamins. Ataxia, manifested by impaired coordination of movements, and cognitive impairment, such as decreased concentration, brain fog, or memory problems, are also commonly observed in patients with untreated celiac disease [114].

Celiac disease is an autoimmune disease characterised by a chronic immune response to gluten. This pathological reaction is not limited to the gastrointestinal tract but also creates conditions

for the development of other autoimmune diseases, such as type 1 diabetes, autoimmune thyroiditis (Hashimoto's disease) and rheumatoid arthritis. The mechanism of this relationship is based on the common aspects of immune dysfunction that underlie celiac disease. Key elements of the mechanism. Genetic predisposition. Genetic predisposition plays a major role in the relationship between celiac disease and other autoimmune diseases. The HLA-DQ2 and HLA-DQ8 alleles, which are required for the development of celiac disease, are also associated with an increased risk of autoimmune diseases. These alleles encode major histocompatibility complex (MHC) class II molecules that present antigens to T lymphocytes, stimulating a pathological immune response [115].

Cross-activation of the immune system. In patients with celiac disease, T cells are activated that recognise gluten as an antigen. However, due to the similarity of the structures of some antigens (molecular mimicry), the immune system can attack its tissues, which leads to the development of other autoimmune diseases. For instance, in the case of autoimmune thyroiditis, the immune system begins to attack thyroid tissue, recognising it as an antigen. Chronic systemic inflammation. Celiac disease is accompanied by increased production of pro-inflammatory cytokines such as interferon-gamma (IFN-γ), tumour necrosis factor-alpha (TNF-α) and interleukin-15 (IL-15). Chronic inflammation creates an environment conducive to the development of other autoimmune diseases. IL-15 promotes the activation of cytotoxic T-lymphocytes that attack their cells. Impaired intestinal barrier function. In celiac disease, the permeability of the intestinal mucosa increases due to dysfunction of intercellular contacts, in particular, due to increased levels of zonulin. The breakdown of the barrier allows antigens and toxins to enter the bloodstream, activating the systemic immune response and contributing to the development of autoimmune conditions. Polyclonal activation of B lymphocytes. Celiac disease is accompanied by the activation of B lymphocytes that synthesise autoantibodies. For example, antibodies to tissue transglutaminase (anti-tTG) are a marker for celiac disease but can also affect other tissues. In patients with Hashimoto's disease, antibodies to thyroglobulin or thyroperoxidase are synthesised, and in rheumatoid arthritis, antibodies to rheumatoid factor.

Common triggers such as stress, infections, and other environmental factors not only precipitate celiac disease but can also initiate the development of other autoimmune disorders. Viral infections, including Epstein-Barr virus (EBV), have been implicated in the pathogenesis of both celiac disease and type 1 diabetes mellitus, suggesting overlapping etiological pathways [116; 117]. Patients with celiac disease are at a significantly elevated risk for type 1 diabetes, attributable to shared genetic predispositions, particularly the presence of HLA-DQ2 and HLA-DQ8 alleles, as well as chronic immune activation. Both diseases involve T-cell-mediated autoimmune destruction – of the small intestinal mucosa in celiac disease and pancreatic beta cells in type 1 diabetes. Similarly, autoimmune thyroiditis, or Hashimoto's disease, occurs more frequently in individuals with celiac disease, likely due to analogous immunopathogenic mechanisms and common environmental triggers. Rheumatoid arthritis is another autoimmune condition linked to celiac disease, wherein systemic inflammation and pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) play central roles in joint inflammation. The convergence of shared immunological mechanisms, genetic factors, and persistent systemic inflammation underpins the association between celiac disease and these autoimmune disorders. Early identification and management of celiac disease are essential to mitigate the risk of developing such comorbidities and to improve patient outcomes [118; 119].

Beyond autoimmune diseases, untreated celiac disease is associated with an increased risk of malignancies, particularly small intestinal lymphoma – especially T-cell lymphoma – and adenocarcinoma. This heightened cancer risk is attributed to ongoing chronic inflammation and sustained immune activation in the intestinal mucosa. Dermatitis herpetiformis is a distinctive dermatological manifestation of celiac disease characterized by intensely itchy rashes and erosions, which cause considerable discomfort and can severely impair quality of life if left unmanaged. Reproductive complications are also prevalent among patients with untreated celiac disease. Women may experience infertility, recurrent miscarriages, preterm deliveries, and infants with low birth weight, while men may suffer from reduced testosterone levels, adversely affecting fertility and sexual health.

Systemic complications stemming from malabsorption affect multiple organ systems. Nutritional deficiencies contribute to chronic fatigue, generalized weakness, impaired tissue repair, and delayed convalescence. These deficiencies compromise immune function, increasing susceptibility to infections. Moreover, cardiovascular risks are elevated in patients with vitamin deficiencies, notably folic acid deficiency. Elevated homocysteine levels – a known pro-atherogenic factor – can lead to coronary artery disease, stroke, and other cardiovascular pathologies [120]. Ultimately, untreated celiac disease profoundly diminishes quality of life through persistent physical symptoms, neuropsychiatric disturbances, and reproductive challenges. Chronic fatigue, depression, and anxiety frequently coexist, limiting social participation and deteriorating psychological well-being. Timely diagnosis and strict adherence to a gluten-free diet remain pivotal in preventing these serious complications and preserving both the physical and mental health of affected individuals. Untreated celiac disease in children and adults has serious consequences that affect all aspects of a patient's life, from physical health to psychosocial well-being. Early diagnosis, strict adherence to a gluten-free diet and regular medical monitoring are critical to preventing complications and ensuring a high quality of life.

The conclusion states that celiac disease is a complex autoimmune disease that develops in genetically predisposed individuals in response to the consumption of gluten, a protein complex found in wheat, rye and barley. The pathogenesis of celiac disease is based on the interaction of genetic, immunological and environmental factors, which together determine the nature and course of the disease. The main cause of celiac disease is a genetic predisposition associated with the presence of HLA-DQ2 and HLA-DQ8 alleles, which determine the ability of the immune system to react to gluten. The absence of these genetic markers virtually eliminates the possibility of developing the disease, but their presence does not guarantee the occurrence of celiac disease. Other genetic factors that regulate the immune response and intestinal barrier functions are also substantial. The disease can be triggered by infections, stressful situations or early introduction of gluten into the diet.

Symptoms of celiac disease range from mild intestinal disorders to severe systemic manifestations. In children, chronic diarrhoea, bloating, anaemia, growth retardation and puberty are most observed. In adults, the disease can manifest itself atypically, with a predominance of extraintestinal symptoms such as chronic fatigue, osteoporosis, neurological disorders, depression and anaemia. In many cases, celiac disease remains asymptomatic, which makes it difficult to diagnose promptly. The diagnosis of celiac disease is based on a comprehensive approach, including clinical assessment of symptoms, serological tests and small intestinal biopsy. Determination of antibodies to tissue transglutaminase (anti-tTG, IgA) is a standard screening method, supplemented by tests for antibodies to deamidated gliadin peptides (DGP) in the case of IgA deficiency. A small bowel

biopsy is a gold standard for diagnosis, allowing for the detection of villous atrophy, crypthyperplasia and lymphocytic infiltration. Genetic tests to determine HLA-DQ2/DQ8 are used to exclude the diagnosis in doubtful cases.

Currently, the only effective treatment for celiac disease is a strict gluten-free diet that excludes foods containing wheat, rye and barley. This helps to reduce inflammation, restore the intestinal mucosa and prevent the development of complications. Adherence to the diet requires careful meal planning, avoiding cross-contamination with gluten and controlling foods with hidden gluten content. In the case of refractory celiac disease, when the diet does not work, drug therapy is used, including glucocorticoids, immunosuppressants or biological products. In the future, innovative treatment approaches such as immunotherapy, enzyme therapy and zonulin blockers are being investigated. Celiac disease is a serious systemic condition that, if left untreated, can cause severe complications, including osteoporosis, anaemia, neurological disorders and an increased risk of cancer. Early diagnosis and strict adherence to a gluten-free diet are key to effective disease control, improving patients' quality of life and preventing complications. International experience confirms that a combination of modern diagnostic approaches and patient support helps to achieve the best results in the treatment of celiac disease.

Chapter 4.

List of Substances Added to Food

The use of substances added to food dates back to ancient times. For centuries, humanity has sought ways to preserve food, enhance its taste, and improve its appearance, which eventually led to the development of modern food additives. Even in antiquity, people discovered that salt could prevent meat and fish from spoiling, while honey and sugar could prolong the shelf life of fruit. In ancient Egypt and Babylon, natural dyes derived from berries, plants, and minerals were used to make food more visually appealing. The Romans extensively utilised saltpetre to preserve meat, as well as various spices and vinegar as natural preservatives [121]. During the Middle Ages, the increasing need to preserve food encouraged experimentation with methods such as fermentation, smoking, and pickling. For instance, sulphur dioxide began to be used to preserve wine, and brewers identified the stabilising properties of hops.

The rise of industrial food production in the 19th century marked the advent of artificial food additives. In the 1870s, saccharin, the first artificial sweetener, was synthesised, and this was followed by the development of synthetic dyes and preservatives. The food revolution of the 20th century saw the widespread adoption of emulsifiers, stabilisers, thickeners, and flavour enhancers [122]. The modern food industry utilises hundreds of food additives regulated by international standards, ensuring the quality, safety, and extended shelf life of products. However, growing attention to healthy eating is driving the search for more natural alternatives, bringing the food industry back to its roots – incorporating natural ingredients and traditional methods of food preservation. Modern industry employs various additives to enhance organoleptic properties, texture, appearance, shelf life, and the chemical stability of food products. While these substances play a crucial role in ensuring food safety and quality, they also raise concerns about potential impacts on human health. Food additives are subject to strict regulation, with their safety rigorously evaluated according to international standards [123].

Food additives can be classified into several categories, the most common of which include flavourings, preservatives, colourings, stabilisers, flavour enhancers, and texturisers. For instance, acetic anhydride and acetoin are used as flavourings to influence the taste properties of products. Particular attention in the classification of food additives is given to substances listed in the Statham Table (previously known as EAFUS), which provides a catalogue of food ingredients with potential applications in industrial production. Each food additive is assigned a unique E-number, which indicates its classification and approval for use in the food industry [124]. The widely accepted classification of food additives divides them into the following main categories:

- Dyes (E100–E199): Used to impart or restore colour to food products.
- Preservatives (E200–E299): Extend shelf life by preventing microbiological spoilage.
- Antioxidants (E300–E399): Prevent oxidation, thereby preserving the quality of fats and preventing rancidity.
- Stabilisers, thickeners, and emulsifiers (E400–E499): Ensure structural homogeneity and stability of emulsions.
- Flavour enhancers (E600–E699): Enhance or modify the flavour and aroma of products.
- Sweeteners (E900–E999): Provide a sweet taste without the use of sugar.

For more detailed information on the composition of food additives and their potential effects on the human body, it is advisable to consult official regulatory documents, such as the Codex Alimentarius, the European Food Safety Authority (EFSA) regulations, or resources on the chemical composition of food, such as Bill Statham's Chemical Maze [125]. Understanding the principles behind the use of food additives, their impact on food quality, and their potential effects on human health is an essential consideration for both consumers and food industry professionals. The use of food additives is strictly regulated by law, and all approved additives undergo rigorous safety testing. However, some individuals may experience intolerances or allergies to certain additives, making it crucial to carefully read ingredient labels on food products.

4.1. Dyes

Food dyes are an essential component of the modern food industry, as they enhance the appearance of products, increase their aesthetic appeal, and help maintain the natural look of food items. They are broadly classified into natural and synthetic dyes, with each group having distinct advantages and disadvantages that determine their suitability for different production purposes. Natural dyes are derived from natural sources such as plants, animals, or microorganisms. While they often contain biologically active substances with potential health benefits, they are less stable in terms of colour compared to synthetic dyes. One of the most widely used natural dyes is the group of carotenoids (E160a–E160f), which are powerful antioxidants found abundantly in carrots, tomatoes, pumpkins, and red peppers. Carotenoids provide yellow, orange, and red hues and are commonly used in the production of dairy products, margarine, confectionery, and beverages. Chlorophylls and their derivatives (E140, E141) are green pigments present in the chloroplasts of plants. These are used to colour foods requiring green shades, such as sauces, chewing gum, and liqueurs. Another prevalent natural dye is anthocyanins (E163), which produce red, purple, and blue hues. Anthocyanins are found in grapes, blueberries, cherries, and raspberries and are frequently used in juices, yoghurts, and desserts.

The yellow dye curcumin (E100), extracted from turmeric, serves not only as a colourant but also as an anti-inflammatory agent. It is widely used in mustard, sauces, and baked goods. Another natural red pigment, betaine (E162), is obtained from beets and is employed to colour meat products, ice cream, and confectionery. Natural dyes also include carmine (E120), which is derived from cochineal insects and is used in yoghurts, juices, and even cosmetic products. Caramel (E150a–E150d), produced by heating sugar, is widely employed in the manufacture of carbonated drinks, sauces, and baked goods. The yellow dye riboflavin (E101), a form of vitamin B2 obtained from bacterial cultures, is added to dairy products, cereal blends, and pharmaceuticals. Lutein, found in leafy vegetables such as spinach and cabbage, is used to colour butter, cheese, and food supplements.

In contrast to natural dyes, synthetic dyes are chemically produced, making them significantly more stable under varying conditions of temperature, light, and acidity. They offer more vibrant and intense colours that are often difficult to achieve with natural pigments. However, excessive consumption of certain synthetic dyes may lead to allergic reactions and other adverse effects. One of the most common synthetic dyes is tartrazine (E102), a bright yellow pigment added to sweets, carbonated drinks, and instant soups. It has been known to cause allergic reactions in some individuals, particularly those sensitive to sulphites [126]. Sunset Yellow FCF (E110) is an orange dye frequently used in baked goods, jams, and marmalades. Synthetic red dyes include azorubine (E122), which is used in candies, desserts, and fruit jellies, and Ponceau 4R (E124), a vibrant red dye

found in carbonated drinks and confectionery. Allura Red AC (E129) is another red dye commonly used in ice cream, desserts, and soft drinks.

Synthetic blue dyes include Patent Blue V (E131) and Brilliant Blue FCF (E133), both of which are used in desserts, carbonated drinks, and chewing gums. To produce green colouring, Green S (E142) is employed in beverages and confectionery. Lastly, Black PN (E151) is used to colour icings, baked goods, and dark confectionery. Despite the widespread use of synthetic dyes in the food industry, there are growing concerns about their potential health effects. Some studies have linked the consumption of specific synthetic dyes to an increased risk of allergic reactions, hyperactivity in children, and other adverse outcomes. As a result, ongoing research in many countries is investigating the potential restriction or prohibition of certain synthetic additives, particularly in products intended for children's food.

In general, the use of both natural and synthetic dyes is strictly regulated by food standards and legislation. Manufacturers are required to list all food additives, including their E-numbers, on product packaging. This enables consumers to make informed choices and avoid potentially undesirable substances. In today's world, an increasing number of people pay attention to product composition and prefer more natural alternatives, which drives the food industry to develop new, safe, and beneficial dyes. From a safety perspective, natural dyes are often considered more favourable, as they lack artificial compounds and may even possess antioxidant properties. However, their primary drawback lies in their low resistance to light, temperature variations, and acidity fluctuations, which can result in the fading or loss of product colour.

In contrast, synthetic dyes are significantly more stable, making them ideal for large-scale food production. Nonetheless, some synthetic dyes may have adverse effects on human health. Excessive consumption of synthetic dyes has been linked to allergic reactions, hyperactivity in children, and other undesirable outcomes. Consequently, their use is subject to regulation by legislative frameworks and guidelines, such as those established by the European Food Safety Authority (EFSA) and the US Food and Drug Administration (FDA). Thus, the choice between natural and synthetic dyes depends on achieving a balance between safety, technological efficiency, and the desired characteristics of the final product [127]. The food industry continues to innovate in the development of new dyes that combine the safety of natural pigments with the stability of synthetic compounds. This approach aims to achieve an optimal balance between product quality and its impact on human health.

4.2. Preservatives

Preservatives play a crucial role in maintaining the quality, safety, and shelf life of food products. They slow down or completely inhibit food spoilage caused by microorganisms, enzymatic processes, and oxidation. In the modern food industry, natural, synthetic, and microbiological preservatives are utilised, alongside antioxidants with preservative properties. Each type has its own characteristics, advantages, and potential health risks. All preservatives undergo rigorous safety evaluations before being approved for use in the food industry, with permissible concentrations strictly regulated by relevant authorities, such as the European Food Safety Authority (EFSA) and the World Health Organization (WHO).

The group of natural preservatives consists of substances of natural origin that have been used for centuries to preserve food. They are considered safe, as they often serve both preservative and

nutritional functions. One of the most commonly used natural preservatives is salt (sodium chloride), which is employed to preserve meat, fish, and vegetable products. Its preservative action is based on creating a hypertonic environment that inhibits the growth of bacteria and fungi, thereby preventing food spoilage [128]. A similar mechanism is utilised by sugar, which is widely used in the confectionery industry for making jams, jellies, and syrups. Due to its osmotic effect, sugar binds water, thus preventing the growth and reproduction of microorganisms.

Acetic acid (E260) is another natural preservative, commonly found in vinegar. It lowers the pH of food, creating conditions that are unfavourable for bacterial growth. As a result, vinegar is widely used in marinades, sauces, and for preserving vegetables. Citric acid (E330) is also known for its preservative properties and is added to drinks, confectionery, and various other products. It not only inhibits the growth of microorganisms but also functions as an antioxidant, protecting products from oxidation and preserving their colour. For liquid products such as fruit tinctures, liqueurs, and extracts, alcohol is used as a preservative by creating an environment unsuitable for the growth of bacteria and fungi. Additionally, certain essential oils, such as cinnamon oil, clove oil, and oregano oil, possess strong antimicrobial properties and can be used as natural preservatives.

Synthetic preservatives are chemically created to provide enhanced stability to food products. They often act more effectively than their natural counterparts and possess a broader spectrum of antimicrobial activity. However, their impact on human health can be uncertain with prolonged consumption in large quantities. Potassium sorbate (E202) is a highly effective agent against fungi and yeast, making it indispensable in the production of bakery products, cheeses, sauces, and carbonated drinks. Sodium benzoate (E211) is another commonly used preservative, found in soft drinks, jams, ketchups, and sauces. Its preservative action works by inhibiting the enzymatic processes of bacteria, thereby preventing their reproduction.

A separate group of synthetic preservatives includes nitrates and nitrites (E249, E250), which are commonly used in the meat industry to preserve sausages and hams. They effectively inhibit the growth of Clostridium botulinum bacteria, the causative agents of botulism, and help maintain the pink colour of meat. However, when heated, these compounds can form nitrosamines – potentially harmful substances that may have carcinogenic effects. To prevent the development of mould in bakery and dairy products, propionates (E280-E283) are used. Sulphur dioxide (E220) and related compounds are added to dried fruits, wine, and juices, where they act as both antioxidants and preservatives. However, these compounds can trigger allergic reactions in sensitive individuals. Preservatives of microbiological origin are derived from the metabolic activity of bacteria or fungi and are widely utilised in the production of dairy and meat products. Nisin (E234) is a natural antimicrobial peptide produced by the bacterium *Lactococcus lactis*. It is used in the production of cheeses, dairy products, and canned foods to inhibit the growth of spore-forming bacteria [129]. Lysozyme (E1105), an enzyme obtained from egg whites or bacterial cultures, works by breaking down bacterial cell walls, making it an essential additive in cheesemaking.

Some preservatives also function as antioxidants, preventing the oxidation of fats and preserving the colour, taste, and freshness of food products. Ascorbic acid (E300) is among the most widely used antioxidants, slowing oxidative processes and preventing the development of unpleasant odours and flavour degradation. Tocopherols (E306-E309), which are derivatives of vitamin E, are commonly added to vegetable oils, confectionery, nuts, and cereal products to prevent rancidity. Certain additives, though not traditionally classified as preservatives, also perform similar

functions. For example, monosodium glutamate (E621), widely known as a flavour enhancer, can exhibit a preservative effect by inhibiting oxidative processes. Formaldehyde (E240) was previously used in some canned foods but is now highly restricted due to its toxicity. Thiabendazole (E233) is applied to the skin of citrus fruits to protect against fungal infections.

Preservatives play a critical role in the modern food industry, enabling a significant increase in the shelf life of products while preserving their quality. Natural preservatives are generally considered safer but are less effective than their synthetic counterparts. Synthetic preservatives, while more efficient, may have potential adverse effects on the body if consumed in excessive quantities. For this reason, it is essential to pay attention to the composition of food products and prioritise more natural alternatives whenever possible. The use of preservatives in the food industry is strictly regulated by legislation, with permissible levels determined through toxicological studies. However, some preservatives can cause allergic reactions, gastrointestinal irritation, or impact metabolism, which is why their use is restricted by international standards such as the Codex Alimentarius and regulations set by the European Food Safety Authority (EFSA) and the US Food and Drug Administration (FDA) [130]. In conclusion, preservatives are vital components of food products, ensuring safety and extending shelf life. Nevertheless, it is important to monitor their consumption and, where possible, opt for natural preservatives.

4.3. Thickeners and Gelling Agents

Thickeners and gelling agents play a crucial role in the food industry by stabilising textures, improving product consistency, and enhancing organoleptic properties. They are widely used in the production of sauces, desserts, meat and fish products, and in the baking industry. Their origin can be either natural or synthetic, which determines their functional properties and potential effects on human health. Natural thickeners and gelling agents, derived from plants or animals, are generally considered safer for consumption. Agar-agar (E406), obtained from seaweed, is a key ingredient in jelly, marmalade, and certain types of ice cream due to its ability to form strong gel structures even at low concentrations. Gelatin, derived from animal sources, is widely used in jelly desserts, yoghurts, and the pharmaceutical industry, particularly for capsule production [131]. Guar gum (E412), extracted from guar tree seeds, is an effective thickener for sauces, syrups, and baked goods, providing products with a uniform and elastic structure.

Other natural thickeners, such as pectin (E440) and xanthan gum (E415), are equally important in food production. Pectin, found in fruits like citrus and apples, is extensively used in the production of jams and candies, where a thick consistency is essential. Xanthan gum, produced through the fermentation of glucose, delivers the desired viscosity to soups, sauces, and beverages, making it indispensable in the food industry. Carrageenan (E407), another natural thickener derived from red algae, is commonly used in dairy products such as yoghurts, desserts, and creams. Locust bean gum (E410), obtained from the seeds of the carob tree, is added to ice cream and curds to improve their consistency and prevent the formation of ice crystals [132]. However, alongside natural thickeners, synthetic or modified thickeners are extensively utilised in the food industry to provide longer-term product stability. Modified starches (E1404-E1452) are commonly used in soups, sauces, and ready-made meals, ensuring a homogeneous structure even under varying temperature conditions. Polyphosphates (E452) are added to meat and fish products, helping to retain moisture and preventing them from drying out or altering their consistency.

Carboxymethylcellulose (E466), used in beverages, creams, and sauces, functions as both a thickener and a stabiliser, improving texture and preventing separation. Methylcellulose (E461) and hydroxypropylmethylcellulose (E464) are widely employed in frozen desserts and baked goods, helping to maintain product shape during baking and reducing the risk of drying out. A distinct group of thickeners is the alginates (E400-E404), derived from brown algae, which form stable gels when combined with calcium ions. This property makes them highly effective in the production of ice cream, creams, and confectionery. Laminarin, a compound found in seaweed, is also used as a gelling agent, while guar gum is frequently added to pastries, beverages, and desserts to enhance their structure [133]. Inulin, a natural prebiotic, serves not only as a thickener but also as a promoter of healthy intestinal microflora, making it particularly beneficial in the production of yoghurts and cottage cheese products. Although thickeners and gelling agents are widely used in the food industry, it is important to carefully review product compositions, as excessive consumption of certain thickeners may cause allergic reactions or negatively affect the digestive system. Understanding their role in nutrition and selecting high-quality products with safe ingredients is essential for maintaining a balanced and healthy diet.

4.4. Sweeteners

Sweeteners play a significant role in the food industry by allowing manufacturers to adjust the sweetness of products, reduce calorie content, and improve organoleptic properties. They are used as substitutes for traditional sugar, helping to lower the glycaemic load and expanding the range of products suitable for people with diabetes or those following low-carbohydrate diets. Sweeteners are categorised into natural and artificial types, each with its own characteristics, benefits, and potential risks.

Natural sweeteners are derived from natural sources such as fruits, plants, and other organic materials. One of the most common natural sweeteners is sucrose (regular sugar), which is extracted from sugar cane and sugar beets. Sucrose is widely used in baking, beverages, and confectionery, but it has a high glycaemic index, leading to rapid spikes in blood glucose levels. Fructose, naturally present in fruits and honey, is about 1.5 times sweeter than sucrose. It is often included in diabetic-friendly products due to its lower glycaemic index, but excessive consumption may contribute to metabolic disorders10 Glucose, or grape sugar, is the body's primary energy source and is quickly absorbed. It is frequently added to energy drinks and desserts [134]. Honey, one of the oldest natural sweeteners, contains not only sugars but also enzymes, vitamins, and minerals that support immune function.

Maple syrup, produced by evaporating the sap of maple trees, has a distinct caramel flavour and is often used as a sugar alternative in baking and desserts. Molasses, or blackstrap molasses, is a by-product of sugar production and is rich in minerals such as iron and calcium, making it a nutritious addition to the diet. Coconut sugar, derived from the nectar of coconut flowers, has a lower glycaemic index than sucrose and is used in baking and confectionery. Agave syrup, another popular natural sweetener, contains high levels of fructose, making it very sweet. However, excessive consumption may place stress on the liver [135]. Among sugar alcohols, which are also considered natural sweeteners, the most common are sorbitol, xylitol, and erythritol. Sorbitol, found in fruits like apples and pears, is used in chewing gum and diabetic products due to its low glycaemic index, though excessive intake may have a laxative effect. Xylitol, derived from birch or corn, is known for

reducing the risk of cavities and is commonly added to toothpastes and chewing gum. Erythritol, produced through the fermentation of corn starch, has about 70% of the sweetness of sucrose, does not affect blood sugar levels, and contains no calories, making it popular among health-conscious consumers. Stevia, extracted from the leaves of the Stevia rebaudiana plant, is 200-300 times sweeter than sugar and contains no calories, making it one of the healthiest alternative sweeteners.

Unlike natural sweeteners, artificial sweeteners are the result of chemical synthesis and are significantly sweeter than sugar while having considerably lower calorie content. They are widely used in diet products, beverages, and chewing gum. One of the most popular artificial sweeteners is aspartame (E951), which is approximately 200 times sweeter than sugar. Aspartame is commonly used in soft drinks; however, it decomposes at high temperatures, making it unsuitable for baking. People with phenylketonuria, a metabolic disorder, cannot process one of its components – phenylalanine – and are therefore prohibited from consuming products containing aspartame. Saccharin (E954), discovered in the 19th century, is 300-500 times sweeter than sucrose but has a bitter aftertaste, which limits its applications. Sodium cyclamate (E952) is 30-50 times sweeter than sugar and is heat-stable, making it suitable for baked goods and hot beverages.

Acesulfame potassium (E950) is another artificial sweetener, with sweetness approximately 200 times that of sugar. It is commonly found in soft drinks and desserts. Sucralose (E955) is 600 times sweeter than sucrose and is one of the few artificial sweeteners that remains stable when heated, making it ideal for baking. Neotame (E961) is an extremely potent sweetener, 7,000-13,000 times sweeter than sucrose, while advantame (E969) is even more intense, with a sweetness 20,000 times that of sugar. Both are used in soft drinks, chewing gum, and long-shelf-life products. Thaumatin (E957) is unique among sweeteners, as it is a natural substance derived from the seeds of African plants. It is approximately 2,000 times sweeter than sucrose and is often used to enhance flavours in certain products. In addition to primary sweeteners, there are substances used in the food industry as flavour enhancers and carbohydrate substitutes. Maltodextrin, a rapidly digestible carbohydrate, is commonly added to sports nutrition products as a quick energy source. Isomalt (E953) and lactitol (E966) have a minimal impact on blood glucose levels, making them suitable for baked goods and diabetic-friendly products [136].

Sweeteners play a vital role in determining the taste and calorie content of food products, offering a practical alternative to traditional sugar. The choice of a sweetener depends on factors such as its metabolic effects, stability under heat, and potential side effects. Despite advancements in the development of safe sugar substitutes, it remains important to consume them in moderation, keeping in mind possible health implications.

4.5. Antioxidants and Food Stabilizers

Antioxidants and food stabilisers play a crucial role in the modern food industry, ensuring the preservation, stability, and safety of products for consumption. These substances extend the shelf life of food products, prevent undesirable changes in colour, consistency, taste, and texture, and are therefore indispensable in the production of a wide range of food items. Their use is regulated by food standards across different countries, and they must be safe for health when consumed within acceptable limits.

Antioxidants are substances that protect food products from oxidation. During oxidation, fats and oils become rancid, leading to deterioration in taste and smell, while vitamins and other biologically active compounds degrade due to exposure to oxygen [137]. Antioxidants work by

neutralizing free radicals, which are the primary agents responsible for chemical degradation in food products. One of the most well-known natural antioxidants is ascorbic acid (vitamin C, E300), widely used in juices, meat products, and confectionery to prevent oxidation and preserve colour. Tocopherols (vitamin E, E306-E309) are employed in vegetable oils, margarines, and fatty foods to stabilize fats and prevent spoilage. Citric acid (E330) is another commonly used antioxidant, added to fruits, vegetables, and beverages to prevent browning and enhance flavour. Among synthetic antioxidants, butylated hydroxyanisole (BHA, E320) and butylated hydroxytoluene (BHT, E321) are widely utilized to preserve high-fat foods such as crisps, snacks, breakfast cereals, and confectionery. Propyl gallate (E310) is another effective synthetic antioxidant applied in margarines, sauces, and fatty products [138]. These antioxidants inhibit the deterioration of fats, extend the shelf life of food products, and help maintain their quality.

Stabilizers are substances that help maintain the uniformity of food products by preventing component separation and retaining moisture. They provide the desired consistency, increase viscosity, and enhance storage stability. Among natural stabilizers, gelatine is extensively used in the production of desserts, marmalade, and marshmallows [138]. Agar-agar (E406), derived from seaweed, imparts a gel-like structure and is commonly utilized in the confectionery industry. Pectin (E440), a natural polysaccharide found in fruits, is widely employed in jams, preserves, and yogurts to provide thickness. Among synthetic stabilizers, guar gum (E412) and xanthan gum (E415) are particularly popular, added to ice cream, sauces, baked goods, and beverages to improve thickness and stability. Carboxymethylcellulose (E466) is another frequently used stabilizer, which gives sauces, creams, and desserts a creamy consistency. Sorbitol (E420), serving both as a stabilizer and sweetener, is commonly found in chewing gum and diet products.

Natural antioxidants such as vitamins C (E300) and E (E306-E309) are not only safe but also beneficial for health, as they protect the body's cells from oxidative stress. However, the safety of certain synthetic antioxidants, including BHA (E320) and BHT (E321), has been subject to debate. Evidence suggests that at high doses these compounds may have potential carcinogenic effects, raising concerns about their long-term consumption.Stabilisers are generally considered safe when consumed within acceptable concentrations [139]. However, excessive intake of certain thickeners, such as sorbitol or gums, may cause gastrointestinal discomfort, including bloating or diarrhoea [140]. In conclusion, antioxidants and stabilisers are indispensable components of the modern food industry. They help to extend the shelf life of products, maintain their quality and stability, and ensure consumer safety when used in accordance with established standards. Advances in food technology continue to drive the development of new, more natural, and safer alternatives, reducing the reliance on synthetic additives in food production.

4.6. Emulsifiers and Flavour Enhancers

Emulsifiers and flavour enhancers play a vital role in the modern food industry, improving the texture, uniformity, aroma, and taste of products. These additives enhance the appeal of food to consumers, extend shelf life, and improve organoleptic properties. However, it is important to understand their effects on food structure, their main characteristics, and the potential health risks associated with their consumption. Emulsifiers are surface-active substances that facilitate the mixing of components that do not typically combine, such as water and fat. They stabilise emulsions, prevent separation, and ensure a uniform consistency in food products. The most common

natural emulsifier is lecithin (E322), which is derived from egg yolk or soybeans. Lecithin is used in chocolate, baked goods, sauces, and margarines, where it helps to evenly distribute fat particles and improve the texture of products. In addition to its functional benefits in food production, lecithin has health advantages, as it contains phospholipids, which are essential for the proper functioning of cell membranes.

Mono- and diglycerides of fatty acids (E471) can be of either natural or synthetic origin. They are commonly added to bakery products, ice cream, and margarine to improve consistency and increase product volume. These substances help to prevent bread from becoming stale and enhance the structure of fats in baked goods [141]. Carboxymethylcellulose (E466), a synthetic thickener and emulsifier, is widely used in sauces, desserts, and dairy products to provide a smooth and uniform texture. Polysorbates (E432-E436) represent another group of synthetic emulsifiers, frequently added to glazes, creams, ice cream, and confectionery. These substances stabilise product structures and improve texture. For example, polysorbate-80 is often used in ice cream to prevent the formation of large ice crystals, resulting in a smoother, more homogeneous product. Another widely used emulsifier is sodium stearoyl-2-lactylate (E481), which is added to baked goods and frozen foods to enhance structure and stabilise fat components.

In addition to emulsifiers, flavour enhancers are widely used in the food industry to amplify or restore the taste of products, making them more pronounced [142]. One of the most well-known enhancers is monosodium glutamate (E621), commonly added to crisps, instant soups, sauces, and convenience foods. This substance provides the characteristic “umami” taste, which enhances the natural flavours of protein-rich foods. Monosodium glutamate is naturally present in many foods, such as meat, cheese, and tomatoes. However, in large doses, it may cause side effects such as headaches and heightened taste sensitivity in some individuals. Another frequently used flavour enhancer is monosodium inosinate (E631), which is often combined with monosodium glutamate to intensify the taste of meat products, snacks, and fast food. Similarly, monosodium guanylate (E627) is a popular enhancer added to soups, sauces, and snacks, contributing to a rich and savoury aroma. These substances are commonly used together, as their combined effects create a more robust and complex flavour profile.

Among artificial flavour enhancers, aspartame (E951) holds a significant place, functioning not only as a sweetener but also as a flavour enhancer. It is widely used in the production of carbonated drinks, chewing gum, and diet products. However, aspartame is unsuitable for individuals with phenylketonuria – a rare genetic condition in which the body cannot metabolise phenylalanine, one of its components. Maltodextrin, a semi-synthetic substance, is commonly used in instant soups, sports nutrition products, and energy drinks. It serves as a quick source of energy and helps improve product texture. Yeast extract, a natural flavour enhancer, is frequently added to bouillon cubes, snacks, and sauces to deliver a rich taste without the need for synthetic additives [143]. While emulsifiers and flavour enhancers offer numerous benefits, it is important to be aware of the potential risks associated with their excessive consumption. Some synthetic additives may cause allergic reactions, individual intolerance, or side effects when consumed in large quantities. For instance, overconsumption of monosodium glutamate (E621) can lead to “Chinese restaurant syndrome”, characterised by symptoms such as headaches, skin flushing, and an increased heart rate. Additionally, certain emulsifiers, such as polysorbates, may impact the intestinal microflora and cause gastrointestinal discomfort.

The use of emulsifiers and flavour enhancers is strictly regulated by food standards and legislation. Each food additive has defined acceptable levels of consumption, established by relevant regulatory authorities such as the European Food Safety Authority (EFSA) and the US Food and Drug Administration (FDA). To minimise potential adverse effects, it is essential to carefully read product labels and prioritise those containing natural or minimally processed ingredients. Thus, emulsifiers and flavour enhancers are vital components of the modern food industry, enhancing the texture, taste, and shelf life of products. They are widely used in the production of confectionery, beverages, sauces, baked goods, and numerous other food items. However, despite their benefits, it is important to maintain a balanced diet, opt for natural alternatives where possible, and control the intake of artificial additives to safeguard health and minimise potential risks. Food additives are an indispensable part of the modern food industry, as they enhance the taste, structural, and organoleptic properties of products, as well as extend their shelf life. They are categorised into different groups based on their functional purpose, including preservatives, emulsifiers, thickeners, colourings, sweeteners, and flavour enhancers. Research indicates that each class of additives has specific effects on the human body, underscoring the need for careful use and regulation of their levels in food products.

Natural food additives, such as lecithin, agar-agar, pectin, and citric acid, often provide additional health benefits. In addition to improving texture and stabilising products, they may exhibit antioxidant, anti-inflammatory, or prebiotic properties. In contrast, synthetic additives, such as nitrates, benzoates, polysorbates, and aspartame, tend to be more effective in achieving their functional purposes but can pose risks when consumed excessively. Potential adverse effects include allergic reactions, digestive disturbances, or metabolic disorders. The legislative regulation of food additives is critical to ensuring food safety. International organisations, such as the European Food Safety Authority (EFSA) and the US Food and Drug Administration (FDA), establish acceptable levels of consumption and continuously monitor the safety of additives [144]. In conclusion, food additives are an essential element of modern nutrition, but their use requires a balanced approach. The rational consumption of natural additives and the careful regulation of synthetic substances can help maintain a balance between product quality and consumer health.

Chapter 5.

Side effects of food additives and their impact on health

Food additives have become an integral part of the modern diet, used in most consumer foods. They are central to improving the taste, extending the shelf life and preserving the structure of food products. However, at the same time, many questions about their impact on human health, especially in terms of potential side effects, are present. Although regulatory authorities in many countries around the world set certain standards for the use of food additives, there are strong scientific reasons to believe that their long-term use can have undesirable effects on the body. From a historical perspective, food additives have been used by mankind for thousands of years. Long before the advent of the industrial food industry, people used salt, honey, vinegar and spices as natural preservatives. However, with the development of science and technology in the XX century, the production of food additives became massive. There are now thousands of different compounds on the market to improve the quality of products, including colourants, preservatives, antioxidants, sweeteners, flavour enhancers and emulsifiers. At the same time, the prevalence of these substances has sparked significant scientific debate about their impact on human health [145].

The main problem with food additives is the difficulty of predicting their long-term effects on the body. Some of them can cause allergic reactions, others – affect the hormonal system, and metabolism or even have carcinogenic potential. For example, preservatives such as benzoates (E210-E213) can cause hyperactivity in children, and some artificial colours have been linked to behavioural risks. Sweeteners, in particular aspartame (E951), are often the subject of scientific controversy due to possible neurotoxic effects [146]. In addition, certain groups of emulsifiers and stabilisers, which are widely used in the food industry, can alter the gut microbiome and contribute to the development of inflammatory processes in the gastrointestinal tract. An equally important aspect is the cumulative effect of food additives, i.e. their accumulation in the body over time. Studies point to the possible negative impact of excessive consumption of additives on the liver, kidneys and cardiovascular system. For example, nitrites and nitrates (E249-E252), which are widely used in the production of meat products, can form nitrosamines – compounds with carcinogenic activity. In addition, prolonged exposure to certain antioxidants, such as butyl hydroxytoluene (BHT, E321), can contribute to oxidative stress in cells, which in turn is associated with an increased risk of neurodegenerative diseases [147].

Modern science is actively studying the mechanisms of interaction between food additives and the human body, but even the most thorough research cannot always account for all possible risks. The main factor that complicates the safety assessment of additives is their interaction with each other and with other food components. In real life, a person rarely consumes one supplement in its pure form but may have dozens of such substances in their diet at the same time. This creates additional challenges for scientists, as the combined effect of many chemical compounds on the body can be significantly different from the effect of individual components. Particular attention should be devoted to populations that are more sensitive to food additives, such as children, pregnant women, people with chronic illnesses and the elderly. For instance, children's liver and kidneys are not yet fully developed, so they may have reduced capacity to detoxify harmful substances. In pregnant women, food additives can affect the development of the foetus, and in the elderly, their use

can increase inflammatory processes in the body. This underscores the need for careful regulation of the use of food additives and informing the public about potential risks [148].

Notably, many food additives are considered safe as long as they are consumed within acceptable levels. For example, international organisations such as the European Food Safety Authority (EFSA) and the US Food and Drug Administration (FDA) set maximum allowable doses for each substance [149]. However, the problem is that the actual consumption of many additives in everyday life can exceed these limits, especially if a person regularly consumes foods with a high content of artificial ingredients [150]. Thus, the issue of food additive safety is complex and multifaceted. While some of them may be safe when used in the correct dosage, others raise serious concerns about their potential health effects. The need for further research in this area is clear, especially given the increasing use of synthetic additives in modern nutrition. Educational activities are also important to help consumers make informed food choices and minimise the risks associated with food additives. A responsible attitude to nutrition and awareness of the composition of products can be key factors in maintaining health for many years.

5.1. Side effects of food supplements

Food additives are an essential part of modern food production. They are used to enhance flavour, preserve structure, extend shelf life and improve the overall appearance of products. However, along with their beneficial properties, many of them have side effects that can affect human health in both the short and long term. The modern food industry makes extensive use of additives to improve the taste, texture, colour and shelf life of products. However, their effects on the body are controversial among scientists and medical experts. Some food additives can have negative health effects, including affecting metabolism, the gut microbiome, the nervous system, and even increasing the risk of cancer. One of the most common groups of food additives is preservatives, which prevent food spoilage by inhibiting the development of microorganisms. For example, nitrates and nitrites (E249-E252), often used in meat products, can be converted in the body into nitrosamines – compounds with carcinogenic potential. Sorbic acid (E200) and sodium benzoate (E211), which are used to maintain product safety, can cause allergic reactions and irritation of the digestive system. Sulphur dioxide (E220) triggers asthma attacks in sensitive individuals and affects the functioning of the gastrointestinal tract [150].

Another important group of additives is – flavour enhancers, which make food more appealing to the consumer, but can cause negative reactions. Monosodium glutamate (E621) is one of the most well-known flavour enhancers, and excessive consumption of this additive is associated with "Chinese restaurant syndrome", which includes headaches, nausea, weakness and heart palpitations. Inosinates (E631) and guanylates (E627) can also cause high blood pressure and adversely affect people with gout [151]. No less controversial is the group of food colours, as some synthetic dyes can adversely affect the nervous system and metabolism. For instance, tartrazine (E102) is often associated with hyperactivity in children and allergic reactions, while azo dyes (E110, E122, E124) have potential carcinogenic properties and can affect the hormonal system. Stabilisers, thickeners and emulsifiers are used to create the desired consistency of products, but some of them can have a negative impact on health. For example, carboxymethyl cellulose (E466) can alter the balance of intestinal microflora, causing inflammation, and polysorbates (E432–E436) can disrupt the intestinal barrier function, which is associated with the development of irritable bowel syndrome [152].

One of the main aspects of the impact of food additives is their effect on the gut microbiome. Certain preservatives and emulsifiers can alter the composition of the intestinal microflora, leading to dysbiosis, inflammation and an increased risk of autoimmune diseases. Another danger is the carcinogenic potential of some food additives. For example, nitrosamines, which are formed from nitrates and nitrites, can contribute to the development of cancer. Titanium dioxide (E171), which is used as a bleaching agent in food, is a concern among scientists because it can damage DNA and promote the development of malignant cells. Food additives can also affect metabolic processes. Sweeteners such as aspartame (E951) and saccharin (E954), although considered safe in small amounts, can cause changes in insulin levels and increase the risk of developing metabolic syndrome and diabetes. Studies show that some sweeteners can even alter the body's response to glucose, which can have a negative impact on metabolic health in the long run [153].

In addition, certain colours and flavour enhancers can affect the nervous system, causing hyperactivity among children, increased anxiety levels and difficulty with concentration. Compounds such as monosodium glutamate and tartrazine can affect neurotransmitter levels in the brain, which can affect behaviour and cognitive function [154]. The human body has developed detoxification mechanisms to help neutralise potentially harmful substances. The liver is the main organ responsible for neutralising toxins by breaking them down into safe compounds that are then excreted by the kidneys or through the bile. The kidneys filter blood and eliminate toxic substances in the urine. The intestinal microflora is also substantial in this process, helping to break down food components and may help to neutralise some harmful compounds. To support these mechanisms, it is recommended to consume more fibre, which helps to eliminate harmful substances and maintains the balance of the intestinal microflora. Fibre sources include vegetables, fruits, whole grains and legumes. Drink enough water to help eliminate toxins through the kidneys. Limit the consumption of ultra-processed foods that contain many additives. Give preference to natural foods, avoiding excessive consumption of foods with a high content of synthetic additives.

Thus, although food additives are a substantial part of modern nutrition, their impact on the body can have both positive and negative consequences. Making informed food choices, eating a balanced diet and supporting the body's natural detoxification mechanisms are important components of a healthy lifestyle. Food supplements have both positive and negative aspects. Excessive consumption of certain substances can cause allergies, metabolic disorders, neurological and even cancer. It is important to read the ingredients of foods carefully, control the number of artificial additives in your diet, and support the body's natural cleansing mechanisms.

5.2. Symptoms of diseases caused by food additives

Food additives are an integral part of the modern food industry, helping to extend the shelf life of products and improve their taste and texture. However, some of these substances can cause negative reactions in the body, including allergies, metabolic disorders, and neurological and gastroenterological disorders. Below, the main diseases and symptoms that may be associated with the consumption of food additives will be discussed. Allergic reactions to food additives are a significant problem, as they can cause a variety of clinical manifestations, ranging from mild skin symptoms to life-threatening conditions. The most common allergens in food additives include colours, preservatives and flavour enhancers. Dyes such as tartrazine (E102), sunset yellow (E110) and red magic AC (E129) often cause rashes, itching and even exacerbation of asthma. Studies indicate that these

synthetic dyes can interact with the immune system and cause increased production of histamine, which triggers an allergic reaction.

Another group of hazardous substances are preservatives, in particular sulphites (E220-E228), which are used to preserve the freshness of foods such as dried fruit, wine and canned vegetables. In sensitive individuals, sulphites can cause asthma attacks, laryngeal oedema, and even anaphylactic shock. The effect of sulphites is due to their ability to stimulate the contraction of bronchial smooth muscle, which leads to bronchospasm. In addition, certain flavour enhancers, such as monosodium glutamate (E621), can cause the so-called "Chinese restaurant syndrome", characterised by redness of the skin, a feeling of heat, headache, tachycardia and general weakness. In some people, this syndrome may be associated with an excessive release of neurotransmitters in the central nervous system, which provokes the above symptoms. Thus, allergic reactions to food additives are a serious medical problem that requires careful diagnosis and dietary correction, especially for people prone to allergic diseases or chronic respiratory pathologies [155].

Metabolic disorders are one of the most substantial problems associated with food additives in the human body. Some of them can significantly alter hormonal and enzymatic activity, which in turn affects metabolism. For instance, aspartame (E951) is an artificial sweetener widely used in the production of soft drinks and dietary products. Its metabolism leads to the formation of methanol, phenylalanine and aspartic acid, which can cause blood glucose levels to be affected. In people with diabetes mellitus or carbohydrate metabolism disorders, aspartame can cause fluctuations in sugar levels, provoking hyperglycaemic or hypoglycaemic states. Another group of additives that affect metabolism are phosphates (E338-E341, E450-E452). They are used as acidity regulators, emulsifiers and stabilisers, but if consumed in excess, they can disrupt the balance of minerals in the body. Phosphates bind calcium, contributing to its leaching from bone tissue, which increases the risk of osteoporosis, especially in the elderly and those with calcium or vitamin D deficiency. Thus, the impact of dietary supplements on metabolism is a serious factor to consider when choosing a diet, especially for risk groups such as people with endocrine disorders, osteopenia, or other metabolic disorders [156].

Food additives can have a significant impact on the functioning of the central nervous system, causing a variety of neurological disorders such as headaches, irritability, sleep problems and even depression. One of the most well-known substances that can cause such effects is monosodium glutamate (E621), a widely used flavour enhancer. Studies show that in sensitive individuals, it can cause the so-called "Chinese restaurant syndrome", which is accompanied by headaches, chest tightness, weakness and even short-term mood changes. Its effect is associated with excessive stimulation of glutamate receptors in the brain, which can lead to neurotoxicity at high doses [157]. Another potentially dangerous additive is aspartame (E951), an artificial sweetener found in many products, including diet drinks, chewing gums and medicines. Aspartame is composed of phenylalanine, aspartic acid and methanol, and its metabolism can produce toxic breakdown products that affect neurotransmitter balance. Some studies suggest that it can cause cognitive impairment, depression, anxiety, headaches and even seizures in susceptible individuals. Its effects can be particularly dangerous for people with phenylketonuria, as they cannot effectively metabolise phenylalanine, which is part of aspartame [158].

In general, neurological disorders caused by food additives can range from mild, such as occasional headaches and fatigue, to serious neurological conditions, including cognitive impairment

and chronic depression. While most people's exposure to these substances remains within physiologically acceptable limits, hypersensitivity to them can cause significant health effects. Gastroenterological diseases can develop under the influence of various food additives, which, when ingested, interact with the mucous membrane of the gastrointestinal tract, causing negative reactions. One of the most common disorders is dyspepsia, which is manifested by bloating, stomach pain and nausea. For example, carrageenan (E407), which is used as a thickener and stabiliser in many products, can cause digestive irritation and gastric motility disorders. Another common consequence of consuming certain food additives is dysbiosis, which occurs due to changes in the composition of the intestinal microflora. Sweeteners, such as sorbitol (E420) and mannitol (E421), have an osmotic effect, which can lead to water retention in the intestines and diarrhoea. This is especially true in case of excessive consumption of products containing these additives. In addition, some preservatives, in particular benzoates (E210-E213), can irritate the gastric mucosa, which increases the risk of gastritis and even peptic ulcers [159]. They are used in the food industry to increase the shelf life of products, but their prolonged or excessive exposure can cause chronic inflammation of the mucous membrane, increased acidity of gastric juice and the formation of erosions or ulcers. Thus, the use of food additives should be controlled, especially among individuals with digestive system sensitivities or pre-existing gastroenterological diseases.

Certain food additives can significantly increase cardiovascular risks, contributing to the development of diseases such as atherosclerosis, hypertension and general disorders of the vascular system. Trans fats contained in stabilisers and emulsifiers, such as fatty acid mono- and diglycerides (E471), can alter the lipid profile of the blood, increasing the level of "bad" cholesterol (LDL) and decreasing the level of "good" cholesterol (HDL). This contributes to the accumulation of cholesterol plaques in blood vessels, which gradually narrows their lumen, restricts blood flow and increases the risk of heart attacks and strokes. In addition, nitrites (E249, E250) and nitrates (E251, E252), which are widely used for preserving meat products, can have a negative impact on the cardiovascular system [160]. Once in the body, they can be converted into nitrosamines – compounds that have potentially toxic and carcinogenic effects. In addition, they can cause an increase in blood pressure, oxidative stress, and vascular endothelial dysfunction, which together put an additional burden on the heart and contribute to the development of hypertension. Thus, excessive consumption of foods containing these food additives can have a significant negative impact on the cardiovascular system and increase the risk of developing serious diseases.

The cancer risks associated with the use of food additives remain a hot topic of scientific research. Some of these substances have a potential carcinogenic effect, especially if consumed in high doses over a long period. For example, nitrosamines, which are formed from nitrites (E249, E250), are associated with an increased risk of stomach cancer. Nitrites are used as preservatives in meat products because they inhibit the growth of bacteria, including Clostridium botulinum, but they can form carcinogenic nitrosamines when cooked or interact with amines in the stomach. Research suggests that frequent consumption of nitrite-rich foods may increase the probability of developing malignant tumours [161].

Another potentially dangerous additive is aspartame (E951), which is used as a sweetener in beverages, chewing gum and dietary products. In high doses, aspartame is associated with an increased risk of developing brain tumours. Some studies on laboratory animals have shown that its metabolites, in particular methanol, can have toxic effects on the body and affect cellular processes

involved in carcinogenesis. Although regulatory authorities such as the European Food Safety Authority (EFSA) and the US Food and Drug Administration (FDA) consider aspartame safe in acceptable doses, its long-term health effects remain a matter of debate. Thus, although food additives are substantial in the food industry, their excessive consumption can pose health risks. Therefore, it is recommended to closely monitor the composition of products, limit the consumption of highly preserved meat products and products with synthetic sweeteners, and maintain a balanced diet that helps reduce the probability of cancer [162].

Some food additives can have a negative impact on kidney and liver function, putting additional strain on these organs responsible for filtering and detoxifying the body. One of these additives is cyclamate (E952), an artificial sweetener often used in soft drinks, confectionery and reduced sugar products. Studies show that excessive consumption of cyclamate can cause nephrotoxic effects, i.e. kidney damage, as metabolites of this substance can accumulate in tissues and disrupt normal filtration processes. Some animal studies suggest a risk of inflammatory processes and degenerative changes in the kidneys under the influence of cyclamate, although the effect on humans requires further study [163].

Another group of potentially hazardous additives is benzoates (E210-E213), which are used as preservatives to prevent the growth of bacteria and fungi in food, beverages, and cosmetics. Benzoates can affect the activity of liver enzymes involved in the metabolism and neutralisation of toxins. After ingestion, benzoates are converted to benzoic acid, which is conjugated with glycine in the liver to form hypuric acid, which is excreted in the urine. With excessive consumption of benzoates, this process can be overloaded, leading to a decrease in detoxification efficiency and accumulation of toxic metabolites. This, in turn, can cause hepatotoxic effects, such as damage to liver cells, impaired liver function, and the development of inflammatory processes. People with impaired liver function or genetic defects in enzyme systems are particularly susceptible to the effects of benzoates [164].

Thus, the systematic and uncontrolled use of food additives such as cyclamate and benzoates can put a significant strain on the kidneys and liver, increasing the risk of toxic damage, inflammation and dysfunction of these vital organs. This is especially dangerous for people with chronic kidney and liver disease, as well as children, the elderly and people with hypersensitivity to food additives. Food additives can be safe in moderate doses, but their excessive or regular use can lead to the development of serious diseases. Reducing the consumption of foods with synthetic additives, choosing natural products and carefully reading the ingredients of products are effective prevention measures. In case of suspicious symptoms, a doctor should be consulted to identify the possible dependence of health on food additives.

The issue of the impact of food additives on human health is extremely relevant in the modern world, as the food industry is constantly expanding the range of synthetic substances to improve the quality, shelf life and organoleptic properties of products. The results of numerous studies demonstrate both positive and negative aspects of the use of food additives, which makes the scientific community and regulatory authorities review standards and regulations regarding their safety. The impact of food additives on human health depends on many factors, such as chemical composition, dose of consumption, duration of exposure, and individual sensitivity [165]. One of the biggest concerns about the use of food additives is their potential toxic effects on the body, especially when consumed in excess or over a long period of time. Certain synthetic preservatives,

colourings, flavour enhancers and stabilisers can cause allergic reactions, and metabolic disorders and adversely affect the function of internal organs. For instance, benzoates and nitrates, which are widely used as preservatives, can have carcinogenic effects, causing cell mutations and increasing the risk of developing cancer. Nitrates, which are converted into nitrosamines in the body, can interact with protein structures, disrupting their functionality [166].

Another important issue is the impact of food additives on the nervous system, in particular their connection with the development of neurological disorders and behavioural disorders. Studies show that some synthetic dyes, such as tartrazine (E102) and azorubin (E122), can cause hyperactivity in children, which is particularly relevant for people with attention deficit hyperactivity disorder (ADHD). In addition, monosodium glutamate (E621), widely used as a flavour enhancer, can cause the so-called "Chinese restaurant syndrome", characterised by headaches, dizziness and heart rhythm disturbances. Long-term exposure to glutamate can also affect cognitive function and memory processes [167]. The cardiovascular system can also be adversely affected by certain food additives. For instance, trans fats, which are included in some foods as emulsifiers and stabilisers, contribute to high cholesterol levels, which increases the risk of atherosclerosis, coronary heart disease and stroke. Some studies have also suggested a possible link between excessive consumption of artificial sweeteners such as aspartame (E951) and an increased risk of developing metabolic syndrome and type 2 diabetes due to their effect on insulin resistance [168].

Another issue is endocrine disruption caused by food additives, especially those containing oestrogen-including substances. Certain preservatives and antioxidants can act as endocrine disruptors, upsetting the balance of the hormonal system. For example, parabens used as preservatives in the food industry can mimic the effects of oestrogen, potentially increasing the risk of developing hormone-dependent tumours, including breast cancer [169]. It is also worth noting that the body's reaction to food additives is individual. In some people, the consumption of certain supplements may not cause any negative effects, while in others, especially those with hypersensitivity or chronic diseases, they can lead to significant complications. For this reason, a personalised approach to nutrition should be considered and foods with a minimum content of synthetic additives should be chosen.

In addition to their direct effects on the human body, food additives can also have indirect effects, through their impact on the gut microbiome. Scientific research shows that some emulsifiers and preservatives can disrupt the balance of intestinal microflora, causing dysbiosis and inflammation in the gastrointestinal tract. This, in turn, can lead to immune disorders and an increased risk of developing autoimmune diseases [170]. Thus, the issue of the use of food additives and their impact on human health remains relevant and requires further research. Despite the existence of regulations and requirements for the safe use of supplements, there is a need for stricter control and updating the regulatory framework in line with new scientific data. Consumers should be more conscious when choosing products, avoiding excessive consumption of food additives and preferring natural and minimally processed foods. The scientific community, in turn, should continue researching the long-term effects of food additives to develop more effective and safe alternatives for the food industry. Only a comprehensive approach that combines scientific research, regulatory measures and conscious consumer choice will reduce the risks associated with the use of food additives and contribute to the improvement of public health in general.

Chapter 6.

Impact of freezing and other factory operations on food structure and disease symptoms

The modern food industry relies on a wide range of technological processes that affect the structure of food and, consequently, its nutritional value and biological activity. Among the most common methods of food processing, freezing occupies a special place, being considered one of the most effective ways to preserve nutrients and microbiological safety of food products. However, the impact of low temperatures on the macro- and microstructure of food, as well as on the interaction of its components with the human body, remains the subject of active scientific research. In addition to freezing, other factory operations, such as pasteurization, sterilization, freeze-drying, fermentation, homogenization and extrusion, play a significant role in modifying the structure of food products. These methods are used to extend shelf life, improve organoleptic properties and enhance product safety. However, such processes often change the molecular composition of food, which can affect both its digestibility and the potential development of certain diseases [171].

Recent research in the field of nutrition and molecular gastronomy suggests a possible link between food processing and changes in human metabolism. For example, thermal denaturation of proteins, lipid oxidation, changes in fibre structure and the destruction of trace elements can affect the development of conditions such as dysbiosis, insulin resistance, food allergies and chronic inflammation. In addition, certain technological processes can contribute to the formation of undesirable compounds, such as acrylamide, trans fats and glycation end products, which are associated with an increased risk of cardiovascular disease and neurodegenerative disorders [172].

This section provides a detailed analysis of the impact of various food technologies, including freezing and other factory operations, on the structure of food, its nutritional value and potential link to the development of pathological conditions in the human body. Particular attention is paid to the molecular mechanisms of changes that occur under the influence of low temperatures, high pressure and heat treatment, as well as their significance for human health in the context of current challenges in nutrition and preventive medicine.

6.1. Effect of freezing on food structure

Freezing is one of the most effective ways to preserve food. The process involves cooling to a temperature below 0°C, which results in the formation of ice crystals within the cells of the product. Freezing has numerous benefits, including preserving nutrients, inhibiting microbial growth and extending shelf life. However, it also causes a number of changes in the structure of foods, which affects their texture, flavour, physicochemical properties and potential impact on human health [173].

Food freezing is a complex physicochemical process that involves three main stages, each of which is essential for preserving the quality, texture and nutritional value of food. The first stage – cooling – involves gradually lowering the temperature of the product to the freezing point of water, which depends on its chemical composition and solids content. At this stage, the temperature drops, but the water remains in a liquid state, as only heat is removed without forming ice. The next

stage, the phase transition, is the critical moment when the water contained in the product crystallizes. During the crystallization process, the structure of the tissues changes, and the speed of freezing is an important factor: slow freezing produces large ice crystals that can damage cell membranes, causing loss of juice and changes in consistency after thawing; fast freezing promotes the formation of small crystals that minimize tissue damage. The final stage – final cooling – involves further lowering the product temperature to a level at which all physiological and microbiological processes slow down completely, and the product enters a state of stable storage. The right choice of temperature and freezing speed plays a key role in ensuring food quality, as it affects the texture, taste, and preservation of vitamins and other beneficial components [174].

Freezing speed is one of the key factors that determine the quality of the final product. High-speed freezing promotes the formation of small ice crystals, while slow freezing leads to the formation of large crystals that destroy cell walls. During freezing, the water contained in the cells turns into a solid phase, forming ice crystals. This process is determined by a number of physical factors, including the speed of freezing, the temperature of the environment, and the chemical composition of the liquid. One of the most important aspects is the size of the formed ice crystals: when cooling slowly, water molecules have enough time to form large crystal structures that can mechanically damage cell membranes, causing tissue destruction. This leads to loss of texture, changes in flavour and a reduction in the quality of frozen food. Instead, rapid freezing promotes the formation of numerous small crystals that have minimal impact on the cellular structure, keeping it intact [175].

Another important aspect is sublimation, which occurs under conditions of insufficiently hermetic storage. When a product is exposed to low humidity or temperature fluctuations for a long time, ice can evaporate from the surface layers, causing the formation of a so-called 'frostbite'. This process is accompanied by tissue dehydration, which changes the texture, causes discolouration and degrades the overall quality of the product. The dynamics of crystal formation also depend on substances dissolved in water, such as mineral salts, proteins, and carbohydrates. They affect the freezing point by changing the nature of the water's phase transition. For example, the presence of salts lowers the freezing point of the solution, slowing down the process of crystal formation and affecting the final structure of the frozen product [176].

The type of environment in which the freezing takes place is also important. Different methods of rapid cooling are used in industrial environments: contact freezing, cryogenic freezing (using liquid nitrogen or carbon dioxide) and freezing in cold air streams. Each of these methods affects the morphology of the ice crystals and the preservation of the cell structure. Thus, the physical aspects of freezing are a complex process involving phase transformations of water, mechanical effects on cells, the possibility of sublimation, and interaction with dissolved substances. Optimizing this process is key to maintaining the quality of frozen food [177].

Proteins are high molecular weight biopolymers whose structure determines their functional properties, including the ability to hydrate, stability and the formation of specific textures in food. At low temperatures, proteins undergo significant structural changes, which can affect the physical and chemical properties of products such as meat and fish. One of the key processes is the denaturation of proteins, which can occur even without significant heating, due to water crystallization, reduced hydration and changes in intramolecular interactions. The loss of the native structure of proteins during freezing causes them to aggregate, which changes the mechanical properties of

meat and fish, making their texture tougher and less uniform. In addition, a decrease in the ability of proteins to bind water occurs due to the destruction of hydrogen bonds and the dissociation of hydrophilic groups, which leads to a significant loss of moisture during thawing, which in turn causes dryness and reduced juiciness of the final product [178].

Fats, being an important part of many food products, can undergo changes in their phase structure, which directly affects the texture, taste, and even safety of the product. One of the key processes is the crystallization of fats, which occurs when the temperature drops, especially during storage in the freezer. As a result, fats change into harder forms, which can lead to changes in consistency and make the product less homogeneous. Different fat fractions have different melting points, so uneven distribution of fat crystals can occur in frozen products, which affects the structure and organoleptic characteristics. Another important process is the oxidation of fats, which is possible even at low temperatures. Oxidative reactions occur as a result of the interaction of unsaturated fatty acids with oxygen, which leads to the formation of peroxide compounds, aldehydes, and ketones [179]. This not only changes the taste and smell of the product, giving it a rancid flavour, but can also have a negative impact on health due to the formation of potentially toxic compounds. Oxidation is especially pronounced in foods rich in unsaturated fatty acids, such as vegetable oils or fish, where this process can develop even under vacuum packaging conditions if traces of oxygen or reaction catalysts such as metals (iron, copper) are present. Thus, changes in the fat phase are an important factor affecting the quality and safety of food during storage [180].

When food is frozen, a number of chemical changes occur that affect its structure, composition, and quality. These processes can be caused by the effect of low temperatures on macromolecules, oxidation, and degradation reactions of certain compounds. One of the key processes is the denaturation of proteins. During freezing, water crystallizes, which changes the structure of proteins, especially in meat and fish products. This results in the loss of their tertiary and quaternary structure, which causes proteins to lose their ability to bind water. As a result, after defrosting, the product becomes less juicy, and its texture may change. Another chemical process is the hydrolysis of carbohydrates, which occurs through enzymatic activity that continues even at low temperatures [181]. For example, starch can be partially broken down into simple sugars, which changes the taste and texture of the product. This is especially noticeable in potatoes, which can become sweet after freezing due to the accumulation of glucose and maltose. Oxidation of fats is another important process that affects the quality of food during freezing. Unsaturated fatty acids can undergo auto-oxidation, even at low temperatures, especially in the presence of oxygen. This leads to the formation of compounds such as aldehydes and ketones, which alter the taste and aroma and can be harmful to health due to the generation of free radicals. Oxidation is particularly noticeable in fatty foods such as fish, nuts, and butter [182].

Freezing also causes changes in the vitamin composition of foods. Vitamin C and B vitamins are the most sensitive to low temperatures. Their loss depends on the duration of storage, temperature, and packaging conditions. For example, the presence of oxygen accelerates the degradation of ascorbic acid (vitamin C), which reduces the nutritional value of vegetables and fruits after prolonged storage in a frozen state. Thus, while freezing allows for the preservation of food for a long time, it also causes several chemical changes that can affect its quality, texture, taste, and nutritional value [183]. The impact on human health directly depends on the quality of food products, their processing, and storage methods. Oxidation processes, microbiological risks and

changes in nutritional value play an important role, which can have a significant impact on the human body. The oxidation of fats and proteins is a natural process that occurs under the influence of oxygen, heat, and light. Oxidation products, such as peroxides and aldehydes, can be toxic if they accumulate in the body. They cause chronic inflammation, oxidative stress and cellular damage, which increases the risk of cardiovascular disease, as well as neurodegenerative conditions such as Alzheimer's disease. For example, fried foods, especially when oil is reused, contain a significant number of oxidized compounds that have a negative impact on health [184].

Microbiological risks are another critical factor. Freezing foods only inhibits the development of microorganisms, but does not completely destroy them. After defrosting, pathogenic bacteria such as Salmonella, Listeria monocytogenes and Escherichia coli can multiply rapidly if the food is not stored at the correct temperature or is not properly heat treated. For example, failure to defrost meat or seafood properly can lead to food poisoning, which is accompanied by vomiting, diarrhoea, and dehydration [185]. In terms of changes in nutritional value, frozen foods may contain fewer vitamins and minerals than fresh foods, especially when stored for a long time. Vitamins C and B9 (folic acid) are the most unstable and are rapidly destroyed when exposed to oxygen and light. For example, after six months of freezing, the vitamin C content of spinach can decrease by 30-50%. However, it is worth noting that some freezing methods (e.g., shock freezing) help to preserve more nutrients than prolonged transportation and storage of fresh produce in inappropriate conditions. Thus, food quality and processing methods play an important role in maintaining human health. Oxidation, bacterial contamination, and loss of nutrients can have serious consequences for the body, so it is important to follow the rules of storage, heat treatment, and consumption of food [186].

Freezing is one of the most effective methods of preserving food, but it can have a negative impact on its physicochemical properties, texture and nutritional value. The main problems encountered during the freezing process include the formation of large ice crystals, oxidation of fats, protein degradation and moisture loss. Various methods are employed to minimize the negative effects associated with freezing and storage of food products. One effective approach is fast freezing, which involves the use of low temperatures and high freezing speeds to promote the formation of small ice crystals that cause less damage to cellular structures. For instance, shock freezing at temperatures below -30 °C preserves the texture and significantly reduces tissue degradation in meat and vegetables [187]. Another important strategy is the use of antioxidants to combat the oxidation of fats during frozen storage, which otherwise leads to the formation of harmful compounds and deterioration of taste characteristics. Antioxidants such as ascorbic acid (vitamin C) and tocopherols (vitamin E) neutralize free radicals and slow down the oxidation process. For example, adding ascorbic acid to fruit prior to freezing helps maintain its natural colour and flavour [188].

Airtight packaging also plays a critical role in preserving food quality by preventing exposure to oxygen, which can cause oxidation and moisture loss. Vacuum packaging or airtight containers reduce these adverse effects effectively. For example, frozen seafood packaged in vacuum bags retains its flavour and texture better than products stored in open containers [189]. Proper defrosting methods are essential as well, since a rapid temperature increase can stimulate bacterial growth, whereas slow defrosting allows the product to restore its structure more evenly. The recommended approach is to defrost food in the refrigerator over several hours or overnight. For instance, frozen meat thawed in the refrigerator loses less juice compared to thawing at room temperature or under hot water [190]. The combined use of these methods contributes to preserving product quality,

minimizing nutrient loss, and extending shelf life. Although freezing is an effective food preservation technique, it inevitably involves numerous physical and chemical changes that can impact both product quality and human health. Therefore, optimizing freezing and storage processes is essential to reduce these negative effects and maximize the benefits of frozen foods.

6.2. How factory operations affect foodborne illness symptoms

Factory operations used in food processing can have a significant impact on the symptoms of various foodborne illnesses. These operations include mechanical, thermal, chemical and biological treatments that not only improve the appearance and shelf life of a product, but can also lead to changes in its nutritional value or even harmful health effects. One of the main factors affecting food after processing is the additives and chemicals used to improve the appearance, texture, and taste of the product, as well as to extend its shelf life. For example, stabilizers, antioxidants, and emulsifiers are added to foods when they are frozen to help the product retain its shape and texture after defrosting [191]. In the case of frozen desserts such as pies, cakes and ice cream, special additives are used to prevent the formation of large ice crystals. For example, stabilizers such as glycerin or potassium sorbate may be used in the production of cakes and other desserts to ensure moisture retention and prevent mould growth. This allows the products to retain their attractive appearance and texture after prolonged storage, but it can also contribute to the accumulation of harmful chemical compounds in the body, which can lead to metabolic disorders over time. Antioxidants such as ascorbic acid (vitamin C) and tocopherols (vitamin E) are often used in frozen foods. These substances help to preserve colours and prevent oxidation of the fatty components of the product. However, high consumption of such antioxidants can disrupt the normal functioning of the digestive system and gastrointestinal tract, which can lead to gas, abdominal pain, or other symptoms [192].

Another example is chemicals added during the manufacturing process of canned foods and other products with a long shelf life, such as sodium salts and preservatives (e.g. sodium benzoate or sulfites). They help to extend the shelf life of foods and reduce the risk of harmful microorganisms, but they can cause allergic reactions in some people, especially those with asthma or other respiratory conditions. Such additives can contribute to inflammation of the mucous membranes and exacerbate asthma symptoms [193]. In addition, large amounts of salt and sugar are often added to various marinades or sauces. Excessive sodium intake can lead to high blood pressure, and high sugar content contributes to the development of obesity, diabetes, and other metabolic disorders. Another example is the chemical additives used in the production of crisps, crackers and other snack foods. Monosodium glutamate (MSG) is often added to them to improve their taste and flavour, which can lead to the so-called 'Chinese restaurant syndrome', characterized by headaches, sweating, chest pain and high blood pressure. Therefore, some studies show that regular consumption of foods high in glutamate can have a negative impact on health, especially if one has a predisposition to allergies or problems with the nervous system [194].

Fat, sugar, and stabilizer substitutes are used for a variety of purposes in the food industry, especially when it comes to products that are to be frozen. Freezing changes the texture, flavour, and stability of the product, so it is important to choose the right ingredients to maintain the desired product quality after the freezing process and subsequent thawing. In this article, we'll look at how fats, sugars, and gelling agents are replaced depending on the type of product to be frozen. Fats

are one of the key ingredients in many food products, such as ice cream, desserts, yoghurts, sauces, etc. Fats add flavour and texture to foods and help maintain their stability. However, when frozen, common dairy fats (such as butter, cream, milk) can form large ice crystals, which makes the texture of the product less pleasant. To avoid this, various fat substitutes are used. Dairy fats such as butter or cream can be replaced with vegetable oils or mixtures of both. This is especially important for frozen foods, as vegetable oils can have a high melting point, which allows them to maintain their consistency even at low temperatures. For example, coconut oil or palm oil is often used to make ice cream, which gives the product the necessary creamy texture without freezing it too hard.

For frozen desserts, emulsifiers such as lecithin can also be used to help create a stable structure without crystallizing the ice. Emulsifiers allow the fat to be evenly distributed in the product, which improves its texture and helps to retain moisture, preventing the formation of large ice crystals that can spoil the taste and texture of the product. There are also dry fat substitutes that are used to reduce the calorie content of a product. These can be various types of modified starches or cellulose that retain moisture and provide the desired texture without adding extra calories. This approach is often used in dietary or reduced-calorie desserts that are also intended to be frozen [195]. Sugar not only adds sweetness to foods, but also plays an important role in the consistency and stability of frozen foods. It helps to maintain texture and prevents the formation of large ice crystals. However, due to its high calorie content and other health concerns, sugar is often substituted for other ingredients, especially in products that are to be frozen. One popular sugar substitute is xylitol, a natural substitute that has a lower glycaemic index and fewer calories.

Xylitol also does not crystallize at low temperatures, so it is often used in frozen desserts such as ice cream or jelly. Instead of regular sugar, erythritol, and stevia can also be used – natural sweeteners that not only reduce calories but also prevent the formation of large ice crystals. However, when using stevia, it is important to adjust the dosage so as not to compromise the taste of the product. For products that need to be frozen, glucose and fructose are effective sugar substitutes because they have a lower crystallization rate at low temperatures. Glucose, in particular, is widely used in ice cream as it helps to keep the texture of the product at a level that prevents ice crystals from becoming too large. This makes the ice cream smoother and softer. Honey and syrups, such as maple syrup or agave syrup, are less common sugar substitutes in frozen foods, but they add a specific flavour and can give a product unique taste properties. However, they are less stable when frozen, so they are often combined with other sweeteners to achieve the desired effect [196].

Stabilizers and gelling agents play an important role in frozen foods, as they help to maintain a stable texture and consistency even after the freezing process. Without stabilizers, frozen foods can become hard, crumbly or have an unpleasant texture after thawing. Gelling agents are used to create a certain consistency in frozen foods. One of the most popular stabilizers is agar-agar, a vegetable product derived from algae that has excellent gelling properties. Agar-agar does not crystallize when frozen, making it ideal for use in jellies, jams, or some types of frozen desserts. Pectin, a natural gelling agent, is often used in frozen jams or fruit desserts. It helps maintain a stable structure, preventing water from separating from the bulk of the product during freezing. Pectin is commonly used in products containing large amounts of fruit, such as fruit yoghurts or fruit drinks. Other gelling agents that can be used for frozen foods are carrageenan and guar gum. Carrageenan, derived from red algae, is an effective stabilizer in milk or coconut milk products. It helps to maintain a creamy texture even after freezing, preventing ice from splitting or forming

crystals. Guar gum is also used to increase the viscosity and stability of products such as frozen ice cream or yoghurts [197].

Modified starches are often added to frozen foods to improve texture and prevent the formation of large amounts of ice crystals. They retain moisture and ensure even freezing, which prevents the formation of hard pieces in the product. Freezing can change the physical properties of a product, so choosing the right fat, sugar, and stabilizer substitutes is important to maintain the texture, flavour, and stability of the product. The use of vegetable oils, sweeteners such as xylitol and stevia, and stabilizers such as agar-agar and pectin help to keep the product in perfect condition even after freezing and thawing. The choice of substitutes depends on the type of product and the desired result, which allows for the creation of high-quality frozen products without losing their taste and texture properties [198].

Thus, many chemical additives used during factory food processing operations can affect human health, causing both temporary symptoms and long-term effects, including diseases. Therefore, it is important to pay attention to the composition of foods, especially the presence of preservatives, stabilizers, sweeteners, and other chemical additives that can contribute to the development of foodborne illness and poor overall health. Freezing and other factory operations, such as pasteurization, sterilization and vacuuming, have a significant impact on the structure of food, changing its physical and chemical properties, texture, flavour and nutritional value. Freezing, in particular, can lead to the formation of ice crystals, which affects the cell structure, thereby changing the consistency and properties of the product after thawing. This process can also reduce the content of vitamins and minerals, in particular vitamin C and some antioxidants, which are sensitive to low temperatures.

In terms of disease symptoms, changes in the structure of food due to factory operations can also affect the body's susceptibility to certain diseases. For example, improper freezing or storage of food can lead to the development of harmful bacteria or mould, which increases the risk of food poisoning or infection. In addition, certain food processing methods can lead to the formation of trans fats or other harmful compounds that can have a negative impact on the cardiovascular system or metabolism. In general, the impact of freezing and other factory operations on the structure of food has both positive and negative aspects. This requires careful control of technological processes and the application of the latest methods to preserve the nutritional value of products and minimize potential risks to consumer health.

Chapter 7.

Assessment of IgG titres in food allergy: Position paper of the European academy of allergy and immunology

Food allergies are one of the most common allergic reactions experienced by people of all ages around the world. It is characterised by an excessive immune response to certain food components perceived by the immune system as harmful or dangerous. The main pathophysiological mechanisms of food allergy are the activation of immune cells, in particular, IgE-mediated reactions, which lead to clinical manifestations such as urticaria, angioedema, bronchospasm, and even anaphylaxis. At the same time, there are other mechanisms, such as IgG-mediated reactions, that can also contribute to the development of food intolerance or allergy symptoms.

In the context of food allergy, special attention should be paid to the assessment of IgG titres as one of the markers of the body's immune response to certain foods. IgG antibodies are a class of immunoglobulins that play an important role in the body's secondary immune responses, in particular in chronic inflammatory processes, allergic reactions, and in the context of food intolerance. The ambiguity in the assessment of the role of IgG antibodies in the pathogenesis of food allergy is due to the fact that there is a lot of controversy among researchers and clinicians regarding the significance of elevated IgG titres in food allergy. On the one hand, a high concentration of IgG antibodies to certain foods may be an indication of immune sensitisation, but on the other hand, the presence of these antibodies is not always accompanied by clinical symptoms of allergy or intolerance. This gives rise to much debate whether IgG titres are clinically relevant and should be used as a diagnostic criterion for food allergy.

The European Academy of Allergy and Clinical Immunology (EAACI) has been working for several years to investigate various aspects of the role of IgG antibodies in food allergies and intolerances. In this regard, a position paper has been developed to bring together all available scientific information and the experience of experts in this field to create a consensus on the use of IgG titres in the diagnosis of food allergy. This document aims to clarify for the medical community, clinicians, and patients which diagnostic methods are the most reliable and correct in the context of food allergy, and to provide recommendations for the use [199]. Given the importance of this problem for modern allergology and immunology, it is necessary to pay attention to both the mechanisms of IgG antibody formation and the specifics of the effect on the body in food allergy. The assessment of IgG titres is an important part of the development of new methods for the diagnosis and treatment of food allergies. However, despite numerous studies, the question of the clinical relevance and practical application remains open, and existing recommendations and standards need to be updated and supplemented with new data [200].

From this point of view, the EAACI position paper is an important step in the development of this field of science, which allows accumulating available data, systematising these data and answering the main questions regarding the role of IgG antibodies in food allergy. This document is supported by the latest scientific research and is of relevance not only to clinicians but also to researchers and diagnostic test manufacturers working in the field of food allergy. IgG antibodies are the main components of the immune system that provide a specific immune response to antigens that enter the body. The antibodies are formed after contact with foreign substances,

in particular with food proteins. In the case of food allergies, IgG antibodies can be formed after repeated exposure to certain foods that cause sensitisation. However, in contrast to IgE, which is directly involved in allergic reactions such as anaphylaxis, IgG antibodies are not usually associated with immediate clinical symptoms. Instead, IgG antibodies can be a marker of chronic, less severe reactions, such as inflammation of the gastrointestinal mucosa or dermatological manifestations [201]. However, it is worth noting that not all elevated levels of IgG antibodies lead to clinical manifestations of allergy. This raises the question whether the assessment is useful for making a diagnosis or choosing treatment methods.

In the previous years, several important scientific studies have emerged regarding the role of IgG in food allergy. Most of the studies show that the presence of elevated titres of IgG antibodies may indicate sensitisation to certain foods. However, this does not always correlate with clinical manifestations of food allergy, which makes it difficult to use IgG antibodies as the main indicator in diagnosis. On the other hand, some studies confirm that certain types of IgG antibodies may have a protective role in helping the body cope with food allergens, reducing the severity of allergic reactions. This suggests that there is a need for a better understanding of how IgG antibodies interact with other components of the immune system and how these antibodies may contribute to the development or prevention of food allergies [202]. The position paper of the European Academy of Allergy and Immunology aims to summarise the available data to create standards for the assessment of IgG titres in food allergy. This includes an analysis of different diagnostic methods, consideration of the aetiology of food allergies and the pathophysiological mechanisms. This document also highlights the need for further research to elucidate the precise mechanisms by which IgG antibodies may influence the development or counteraction of food allergies [203].

In the future, more clinical trials are needed to determine how IgG antibodies can be used to predict the development of food allergies, as well as to improve treatment and prevention methods. As the role of IgG antibodies in food allergies is not yet fully understood, future research should include new approaches to analyse the significance in the context of different types of food allergies. Overall, the EAACI position paper will be an important step in the development of accurate and reliable diagnostic and therapeutic standards for food allergies, given the importance of IgG antibodies in this process.

7.1. Assessment of IgG titres in food allergy

An important component in the diagnosis of food allergies is the determination of the levels of various classes of immunoglobulins, in particular IgG. These antibodies are important as markers for the diagnosis of allergies, but the role in clinical practice is often controversial due to the ambiguity of the results. Assessment of IgG titres can help to determine the sensitisation of the body to certain foods, but the clinical relevance of these titres remains open. IgG immunoglobulins are antibodies that are produced in response to infections, allergens, or other foreign proteins. These antibodies usually have high affinity for antigens and play an important role in secondary immune responses. There are different isotypes of IgG (IgG1, IgG2, IgG3, IgG4), which can be involved in various pathological processes. These isotypes are formed after the initial contact with an antigen and provide immune defence by neutralising or phagocytising foreign particles.

In the case of food allergies, unlike IgE, which is key to the development of immediate allergic reactions, IgG antibodies can be associated with chronic or delayed reactions, such as abdominal pain, bloating, indigestion, skin rashes and other symptoms that appear several hours or days after eating the product. This opens up new possibilities for the use of IgG titres as potential indicators for identifying specific allergens that cause these reactions [204]. The diagnosis of food allergy by measuring IgG antibody levels has been the subject of numerous scientific studies, but there is still controversy whether these antibodies are a marker of a clinically significant allergic reaction. Some studies have shown that elevated IgG levels may indicate chronic inflammation or sensitisation to certain foods, while other studies have found no clear correlation between IgG levels and the development of allergic reactions.

Thanks to technological advances in the fields of immunology and molecular biology, modern diagnostic methods enable accurate and detailed assessment of IgG antibody levels to specific food allergens. Among the primary technologies used to measure IgG titres, enzyme-linked immunosorbent assay (ELISA) is one of the most popular and widely applied methods for quantitative determination of specific antibodies in biological fluids such as blood serum. ELISA is a fundamental tool in diagnosing various diseases, including infectious diseases, autoimmune disorders, allergies, and other clinical conditions [205]. Its main application in the context of food allergies is measuring titres of immunoglobulins, particularly IgG antibodies produced in response to diverse antigens, including food allergens. Detecting IgG levels is crucial for assessing the body's sensitization to certain foods, which holds significance in food allergy diagnosis.

The ELISA technique relies on enzyme-bound antibodies to detect IgG antibodies in samples and quantify their concentration through a colorimetric reaction. Despite its advantages, ELISA's use in diagnosing food allergies remains controversial because IgG antibody titres do not always correlate with clinical allergy symptoms. This article reviews ELISA's mechanism, its application in detecting IgG antibodies, and the scientific debate surrounding its use in food allergy diagnostics. ELISA is an extremely sensitive method that allows quantitative detection of specific molecules in a sample. Its principle is based on the antigen-antibody interaction, fundamental to the immune response. The method involves several key steps [206]. First, antigens are adhered to the surface of plates coated with polystyrene or other materials, commonly associated with food allergens, binding through physical and chemical interactions. Subsequently, nonspecific binding sites are blocked to prevent interactions that could skew results.

Then, the patient's serum containing specific antibodies, such as IgG to food allergens, is added; if present, these antibodies bind to the antigens forming antigen-antibody complexes. Next, enzyme-linked antibodies (often conjugated to horseradish peroxidase) with high affinity for bound IgG are introduced. Finally, a substrate reacts with the enzyme, producing a clear color change proportional to the IgG concentration. The results are read using a spectrophotometer measuring optical density (OD), converting it into numerical values indicating antibody concentration [207]. ELISA offers several advantages that make it widely used for measuring IgG antibodies in clinical contexts. Its ability to detect very low antibody concentrations enables diagnosis even at early disease stages. The method's sensitivity allows precise quantification of IgG antibodies to food allergens, even at low blood concentrations. Additionally, ELISA facilitates simultaneous processing of numerous samples, which is valuable for large-scale clinical trials and screening. Due to its reliance on clear chemical reactions, ELISA provides reproducible and reliable quantitative results.

Moreover, it can be adapted for diverse immunodiagnostic purposes, such as detecting infections, autoimmune diseases, and allergies, demonstrating considerable laboratory versatility.

Nevertheless, ELISA has limitations in assessing IgG antibody levels related to food allergies. Several studies indicate that elevated IgG levels do not always coincide with clinical allergy symptoms. Some patients may show increased IgG titres without manifesting allergic reactions, complicating the interpretation of ELISA results in food allergy contexts. This discrepancy may lead to false-positive findings, resulting in misdiagnosis and unwarranted dietary restrictions. Additionally, no universally accepted standard exists for measuring IgG to food allergens, contributing to variability in results across laboratories and test kits. Many studies suggest that IgG antibodies may not solely indicate sensitization but could reflect previous allergen exposure. Thus, further clinical research is essential to clarify the clinical significance of IgG in food allergies. The use of ELISA to determine IgG titres remains a vital tool for investigating food allergies in scientific and clinical research. For example, a study in Germany applied ELISA to measure IgG levels to various food allergens in patients reporting symptoms of food intolerance. The study found elevated IgG levels to certain foods such as milk, eggs, and wheat in many patients, though only a subset exhibited clinical allergy symptoms. Similarly, research in the United States compared ELISA with skin prick tests for food allergens, revealing that patients with elevated IgG often did not have positive skin test results, underscoring the complexity of interpreting ELISA findings in allergy diagnosis.

Enzyme-linked immunosorbent assay is a highly sensitive and specific method for measuring IgG antibody levels, allowing effective detection of sensitization to food allergens. However, its diagnostic use in food allergy remains controversial due to the lack of clear correlation between IgG titres and clinical allergy manifestations. Therefore, ELISA results should be interpreted alongside other diagnostic methods and thorough clinical assessments to accurately identify causative allergens [208]. Fluorescence immunoassay (FIA) is another diagnostic method based on fluorochromes – molecules emitting light upon excitation by specific wavelengths. In FIA, antibodies or antigens are labelled with fluorescent tags such as fluorescein, rhodamine, or Alexa Fluor. Following antigen-antibody complex formation, excitation by ultraviolet or laser light induces fluorescence detected by sensitive instruments. FIA offers high sensitivity (down to 10^{-15} mol/l), the capability for multiplex analysis detecting several IgG antibodies to different allergens simultaneously, and compatibility with automated platforms.

Chemiluminescence immunoassay (CLIA) relies on chemical reactions wherein labelled substances emit light upon interacting with substrates. Labels based on acridinium esters, luciferase, or horseradish peroxidase are commonly used. The luminescence intensity directly correlates with the amount of specific antibody (e.g., IgG) bound to the antigen. CLIA is regarded as the most sensitive among non-radioactive immunoassays and is widely employed in reference laboratories for precise allergy diagnostics. Its advantages include extreme sensitivity (up to 10^{-16} mol/L), the ability to detect minimal antibody amounts such as IgG4, rapid analysis times (30-60 minutes), and full automation [209]. Food allergy encompasses IgE-dependent reactions as well as IgG-mediated or mixed immune responses. Assessing specific IgG, particularly the IgG4 subclass, is especially relevant in chronic gastrointestinal symptoms such as dispersion, bloating, and pain; delayed skin reactions including eczema and psoriasis-like manifestations; neurological symptoms like headaches and mood changes; and respiratory complaints absent classic IgE allergy signs.For example, a study conducted at the University of Cambridge (2021) showed that in patients with irritable

bowel syndrome (IBS), 78% of cases had an elevated IgG4 titre to casein and β-lactoglobulin, which was successfully determined by chemiluminescence analysis. As a result of eliminating these foods from the diet, 64% of participants experienced a 50% or more reduction in symptoms within 4 weeks [210].

The most famous automated systems for chemiluminescent and fluorescent analysis are:

1. IMMULITE® (Siemens) is one of the most widely used platforms that uses CLIA to quantify specific IgG to more than 200 food allergens. It can be adapted to the needs of a large laboratory.

2. Cobas e 411/601 (Roche) – uses the electrochemiluminescent principle, provides a wide dynamic range and high accuracy at low antibody titres.

3. Luminex xMAP is a multiplex fluorescent system that allows the simultaneous detection of up to 100 allergens in a blood sample using beads labelled with fluorescent barcodes. It is extremely effective for individual allergy profiling.

4. Phadia™ ImmunoCAP ISAC is a fluorescence-based microchip used for semi-quantitative IgE and IgG4 determination of up to 112 allergens.

It is used in studies of tolerance and allergen-specific immunotherapy. In 2023, a multicentre study was published (Harvard Medical School in collaboration with Karolinska Institutet) involving 320 patients with suspected food allergy but negative results of classical IgE tests. Elevated levels of IgG4 to wheat, egg and dairy proteins were detected in 72% of the patients by CLIA. After an 8-week elimination diet, 68% of patients experienced a reduction in symptoms, including improvements in overall skin condition, mood, and sleep [211]. Not long ago, a new approach has emerged – digital chemiluminescence (Digital CLIA), which allows not only detecting the amount of antibodies but also analysing the kinetics and affinity of IgG interaction with allergens. This technology makes it possible to differentiate between 'useful' IgG (for example, as a result of tolerance or immunotherapy) from potentially pathogenic ones.

The use of machine learning algorithms to process CLIA and FIA results allows for the development of personalised diets. Based on the processing of more than 500,000 patient samples (data from Everlywell, USA), typical IgG profiles were identified that are associated with specific clinical phenotypes (chronic urticaria, migraine, dyspepsia) [212]. Despite its wide potential, the use of IgG testing is not universally accepted. The European Academy of Allergy and Clinical Immunology (EAACI) in its documents emphasises: IgG is a marker of exposure, not hypersensitivity. That is, elevated titres can only mean frequent consumption of a product, not an allergic reaction. Therefore, fluorescent or chemiluminescent IgG testing should be used in conjunction with a medical history, dietary diary, and provocation tests, and not as a stand-alone diagnostic method.

Fluorescent and chemiluminescent immunochemistry are opening up new horizons in the diagnosis of food allergy, in particular through the assessment of specific IgG and IgG4. Due to the high sensitivity, speed and accuracy, these methods allow for early detection of sensitisation, providing the basis for an individual approach to each patient. At the same time, the results of such tests should be interpreted in the context of the clinical picture and with the participation of a specialist. With the development of technologies such as digital chemiluminescence and machine learning, the future of such methods looks promising – not only as a diagnostic tool, but also as a platform for a deeper understanding of the mechanisms of food tolerance and allergy.

Mass spectrometry (MS) is one of the most powerful analytical methods in modern science, which is actively used in immunology, biochemistry, proteomics, toxicology, pharmacology, and food

safety. This method is based on the measurement of the mass and charge of ionised molecules, including proteins and peptides, with extremely high accuracy. Due to the possibility of detailed analysis of even small amounts of substances, mass spectrometry has opened up new horizons in the study of immunological reactions, in particular, the interaction of IgG antibodies with food allergens. This approach not only allows detecting IgG as a marker of the previous or active immune contact with an allergen, but also allows studying in detail the structure of allergenic proteins, the epitopes (antigenic regions), and the ways in which immunocomplexes are formed. In the context of food allergy, such precision and analytical power are of great clinical importance – from diagnosing and predicting reactions to individualised nutritional therapy. Mass spectrometry involves several key steps:

1. Ionisation of the sample – molecules (e.g. proteins or antibodies) are converted into charged particles (ions) using one of the technologies: MALDI (matrix-assisted laser desorption/ionisation), ESI (electrospray ionisation), DESI (desorption-ionisation in an open environment), etc.

2. Mass and charge analysis of ions – using an analyser (e.g. quadrupole, ion trap, TOF – time-of-flight), the mass and charge of each molecule are determined.

3. Interpretation of spectra – a mass spectrum is created that shows the intensity of ions depending on the mass. This allows for the recognition of amino acid sequences, protein modifications, and features of the spatial structure [213].

Immunoglobulins of class G (IgG) are glycoproteins consisting of four polypeptide chains: two heavy and two light chains. Mass spectrometry can be used to identify IgG isotypes (IgG1, IgG2, IgG3, IgG4), each of which has unique functions in the immune response. For example, IgG4 is more commonly associated with tolerance than with allergy; glycosylation, a post-translational modification that significantly affects the functionality of an antibody, can be analysed. Glycosylation of an Fc fragment changes its interaction with immune cells (e.g., via Fcγ receptors) and identifies allergen specificity – for example, to determine whether IgG binds to β-lactoglobulin (milk protein) or the peanut protein Arah1 (peanut) [214]. Fragmentation methods (CID, HCD) allow the antibody molecule to be 'broken down' into smaller fragments to study its structure, which is especially useful in deciphering unknown antibody variants in patients with unusual immune reactions.

One of the most important tasks is to identify proteins that cause allergies. Mass spectrometry allowed identifying Ara h 1, 2, 3, 6, the main allergenic proteins in peanuts that cause severe reactions. Ara h 2 was found to have the highest immunogenicity. Also, Bos d 5 (β-lactoglobulin) in cow's milk was identified as a key allergen in children and wheat proteins (Tri a 19) were identified as markers of gluten sensitisation [215]. Some food companies use enzymatic processing or thermal denaturation technologies to reduce the allergenicity of products. Mass spectrometry helps to verify whether epitopes that can trigger an IgG or IgE response are retained. For example, a study of a modified egg protein (ovomucoid) showed that heat treatment reduces IgE affinity but does not completely eliminate the ability to bind IgG. This means that delayed-type reactions may remain when such products are consumed.

Using LC-MS/MS (liquid chromatography combined with mass spectrometry), it is possible to create an 'immune portrait' of the patient – to determine which allergens the patients are reactive to, what types of antibodies are present, and which glycosylated variants of IgG dominate. A 2023 study at Boston Children's Hospital found that children with multiallergenic sensitisation have a distinctive profile of glycosylated IgG4 compared to children who react to only one protein (e.g. soya or egg). The latest advances have made it possible to combine mass spectrometry with microfluidics

to analyse individual cells of the immune system [216]. This has made it possible to determine which B cells produce antibodies to a particular allergen, to study the development of tolerance (for example, during oral immunotherapy) – how IgG4 production changes at the cellular level [217].

The advantages of the method include incredible accuracy (identification of even 1 pg of protein), a wide dynamic range (detection of both low- and high-concentration samples), the ability to analyse complex matrices (plasma, serum, food), and high sensitivity to modifications, namely, detection of changes after heat or enzymatic treatment. Limitations include the high cost of equipment and maintenance, the need for highly qualified personnel, complex data interpretation (requires bioinformatics tools), and limited availability in routine clinics (mainly research or private laboratories) [218]. Mass spectrometry will become even more accessible in the near future, especially thanks to automated platforms that combine sample, ionisation and analysis at the touch of a button, artificial intelligence in spectrum interpretation, which will reduce human error, and nanospectrometry, which will allow for the analysis of minimal samples, such as tears, saliva or microdrops of blood. Mass spectrometry is an indispensable tool in modern allergology for the analysis of IgG antibodies and food allergens. Its unique ability to identify protein structures, evaluate post-translational modifications, analyse immune complexes and even determine the functional activity of antibodies makes it one of the world's top diagnostic and personalised medicine technologies. The application of mass spectrometry in food allergy not only allows better understanding the nature of immune reactions, but also opens the door to the creation of accurate, scientifically based dietary recommendations for millions of patients worldwide.

In modern medical diagnostics of food allergy, the use of highly accurate, sensitive and multipurpose platforms that allow for rapid and comprehensive analysis of biomarkers has become an important area [219]. One of these innovative methods is testing using microarrays and biosensors, which are increasingly being implemented in clinical practice. These technologies open up new possibilities for diagnosing, monitoring and even predicting food sensitisation, in particular by the level of immunoglobulins of class G (IgG), which can be markers of food intolerance or delayed immune responses. A biosensor is an analytical device that integrates a biological component – such as an antigen, antibody, or enzyme –with a physicochemical sensor capable of converting biochemical interactions into measurable signals. In the context of IgG-sensitive testing for food allergies, the biological receptor is most commonly represented by antigens (proteins derived from food) immobilized on the surface of a microarray or sensor. When a patient's blood sample containing specific IgG antibodies to these antigens comes into contact with the sensor, binding occurs and is detected by the sensor system [220].

One common type of biosensor used for IgG detection is the optical biosensor, which detects antigen-antibody interactions by monitoring changes in optical properties such as absorption, fluorescence, or surface plasmon resonance (SPR). SPR technology, in particular, is widely applied in devices like Biacore (Cytiva, Sweden) for quantitative analysis of IgG antibodies. An example is the AllergyScreen system (Germany), which employs chips coated with multiple allergens; upon fluorescent excitation, this system can simultaneously detect IgG antibodies against more than 50 food allergens. Electrochemical biosensors represent another category, operating based on changes in electrical current or potential when IgG antibodies bind to antigens. These sensors are characterized by high sensitivity, do not require optical detection methods, and can be miniaturized into portable devices. For instance, researchers at the University of Toronto developed a portable

electrochemical biosensor capable of simultaneously detecting IgG, IgA, and IgM antibodies to over ten food proteins. This device was successfully validated in a clinical study involving 120 patients with suspected food intolerance.

Mechanical biosensors, also known as membrane biosensors, function by detecting changes in mass on the sensor surface due to antibody binding, which alters the oscillation frequency of a micromechanical device. This principle is applied in quartz crystal microbalances and nanocantilevers, technologies derived from nanotechnology, that provide extremely accurate measurements. However, these sensors tend to be expensive due to their complexity and precision. Microarrays are high-tech devices with microscopic amounts of food proteins (antigens) deposited on the surface. The microarrays allow for multiplex analysis, i.e. simultaneously studying the immune system's response to tens or hundreds of allergens. The advantages of microarrays include the analysis of numerous IgG antibodies in a small volume of blood (10-20 µl); the ability to determine an individual sensitivity profile to foods; minimal analysis time (up to 2 hours) and automated analysis of results with software. For example: the ImmunoCAP ISAC system (Thermo Fisher Scientific) is the gold standard in allergy for IgE determination, but since 2020, an experimental module for IgG4 analysis has been added, which is used in chronic allergy studies.

The NutriSMART programme (Switzerland) is a system for the rapid analysis of IgG antibodies to 57 common food proteins using a biosensor test based on thin chromatography. This programme has been approved for use in the European Union and is actively used in functional medicine clinics to correct patients' eating habits. It allows for the rapid detection of immune reactions to specific foods, which helps to personalise nutritional recommendations and optimise patients' diets. The iFOOD project in Japan is being implemented by the Tokyo Institute of Technology, where a graphene-based biosensor has been developed. This sensor can identify even traces of IgG antibodies to 12 food allergens in just 15 minutes. A special feature of the technology is the ability to integrate this sensor into smartwatches or bracelets, which demonstrates the transition to personalised and mobile diagnostics. This approach allows for real-time monitoring of food allergens, which can greatly facilitate the lives of people with food allergies or intolerances [221]. Harvard Medical School (USA) conducted a study that resulted in the development of a biosensor chip that allows detecting the dynamics of changes in IgG titres in patients with irritable bowel syndrome (IBS). IBS is often accompanied by food intolerance, and the use of this chip in clinical practice has allowed for more accurate adjustment of patients' diets. In more than 70% of cases, the chip led to a significant reduction in IBS symptoms, which increases the effectiveness of treatment and improves the quality of life of patients [222].

These innovative technologies and research provide new opportunities for accurate diagnosis and effective treatment of food allergies and intolerances, which contributes to the development of personalised medicine and improved management of these conditions. The presence of elevated IgG titres to certain foods does not always indicate a classic allergy. It is often a marker of chronic exposure to a food antigen that can cause: chronic intestinal inflammation; pseudoallergic reactions; metabolic instability and autoimmune reactions. The biosensor analysis data helps to create individual elimination diets that reduce IgG levels and, consequently, clinical symptoms. A case study: a patient with chronic dermatitis who did not respond to conventional treatment was found to be hypersensitive to dairy products, wheat, eggs, and nuts after testing for IgG to 96 allergens. Removing these foods from the diet gave a positive result within 3 weeks.

The development of nanotechnology makes it possible to create nanochips that can work with tiny concentrations of IgG and integrate into eHealth systems. Such sensors will be built into household appliances (smart refrigerators, kitchen scales), warn patients about potentially dangerous ingredients, and provide real-time nutritional advice. Microarrays and biosensors are not just a technological innovation, but a real breakthrough in the diagnosis of food allergies and immunological intolerance. The high sensitivity, multiplexity, speed and convenience make microarrays and biosensors an indispensable tool for doctors, nutritionists and functional therapists. When used correctly, these devices can significantly improve the quality of life of patients, reduce diagnostic time, and provide accurate, scientifically based individual nutrition planning [223].

Studies conducted in different countries indicate progress in understanding the role of IgG antibodies in food allergies and new approaches to the assessment and treatment. In the United States, large-scale studies, including clinical trials, are being conducted to evaluate the role of IgG antibodies in the diagnosis and treatment of food allergies. One such study is the work of Johns Hopkins University, which examined the relationship between the levels of IgG to various foods and the development of allergic reactions in children. The results of the study showed that in some cases, elevated IgG levels can be associated with chronic problems, such as bloating or stomach pain, but do not always indicate a classic allergic reaction. In the European Union, particularly in Germany and France, IgG testing is widely used as part of individualised diets and therapeutic plans for patients with food allergies. This helps to determine which foods should be restricted in patients' diets to reduce the symptoms of food intolerance or allergy. Such tests are carried out in specialised clinics and include innovative technologies such as chemiluminescent diagnostic methods. Australia is actively researching the impact of food additives and the interaction with IgG antibodies. Researchers from the University of Melbourne have studied how various additives can change the level of IgG and influence the development of allergic reactions. This research has led to the development of new recommendations for the use of food supplements for people with hypersensitivity to certain foods.

The assessment of IgG titres in food allergies is one of the most important areas of modern allergology and immunology. Modern diagnostic methods provide accurate results on the level of IgG antibodies to specific food allergens, which makes it possible to more accurately identify allergens and correct patients' diets. However, given the ambiguity of the results, further research is needed to clarify the role of IgG in the development of food allergies and its impact on clinical symptoms. International experience in this area shows a gradual improvement in diagnostic and therapeutic methods, which gives hope for improving the quality of life of patients with food allergies in the future.

7.2. Position paper of the European Academy of allergy and immunology

The European Academy of Allergy and Clinical Immunology (EAACI) is the leading European organisation for research, education, and guidelines development in the field of allergy and immunology. In its position papers and guidelines, EAACI provides detailed recommendations for the diagnosis and management of various allergic conditions, including food allergy. Diagnosis of food allergy is a complex and multifaceted process that requires the use of a variety of methods to establish an accurate diagnosis. The European Academy of Allergy and Clinical Immunology (EAACI) emphasizes the importance of a comprehensive approach that integrates clinical assessment,

laboratory testing, and other specific diagnostic methods to identify food allergy. The initial and most critical step in this process is anamnesis and clinical assessment.

A thorough medical history is essential, during which the physician collects detailed information about the patient's symptoms, including their onset, duration, and temporal relation to the consumption of particular foods. It is also important to determine whether there is a family history of allergic reactions, as food allergies have a genetic component and can be inherited. Understanding environmental exposures, comorbid conditions, stress factors, and dietary changes further contributes to evaluating the risk of allergy development. Clinical symptoms such as skin rashes, itching, swelling of the lips, tongue or throat, difficulty breathing, abdominal pain, diarrhea, and even anaphylactic reactions are carefully assessed. Recognizing which foods provoke these symptoms and the timing of their onset provides crucial data for identifying potential allergens and guiding further diagnostic testing.

Skin prick tests and the determination of specific IgE antibodies constitute the second stage of diagnosis. Skin prick testing is among the most effective and rapid methods for detecting sensitization to specific allergens. In this test, small amounts of allergens are introduced into or onto the skin, and the appearance of a localized reaction – redness or swelling – indicates the presence of specific IgE antibodies to those allergens. This method enables quick identification of the foods or components to which the patient is allergic [224]. However, skin prick tests have limitations; they may be less informative in patients with chronic skin conditions such as eczema or those taking medications that can alter test responses. In such cases, additional diagnostic modalities are necessary.

The oral provocation test (OPT) is regarded as the "gold standard" in food allergy diagnosis. This procedure involves administering suspected allergenic foods to the patient under strict medical supervision, gradually increasing the dose while monitoring for adverse reactions over several hours. Due to the potential risk of severe allergic reactions, including anaphylaxis, OPT is conducted exclusively in hospital or clinical settings equipped to provide immediate emergency care. This test enables definitive confirmation of food allergy by directly observing clinical reactions to the ingestion of suspected allergens.

A stepwise, comprehensive diagnostic approach – comprising anamnesis, skin prick testing, and oral provocation – is essential to obtain a complete understanding of the patient's allergic responses and to establish an accurate diagnosis. Utilizing multiple methods helps avoid misdiagnosis, as each diagnostic tool has inherent strengths and limitations. For instance, a positive skin test does not always correspond to clinically relevant allergy, whereas oral provocation provides the most definitive evidence of clinical reactivity. Timely consultation with healthcare professionals is crucial because food allergies can range from mild to severe manifestations. Only after comprehensive diagnosis can effective treatment begin, often involving allergen avoidance, antihistamines, and, when appropriate, immunotherapy [225].

Tests measuring IgG or IgG4 antibodies to foods are frequently discussed in the context of food allergy diagnosis, but the EAACI does not recommend their use for this purpose. The presence of specific IgG antibodies reflects previous exposure to foods rather than allergic sensitization. IgG antibodies are part of the normal immune response and do not indicate pathological allergic reactions. Consequently, such tests lack specificity for diagnosing food allergies and may lead to unnecessary dietary restrictions, which can compromise nutritional diversity and health. The EAACI advocates for the use of more accurate diagnostic methods, such as skin prick tests and oral

provocation, which directly assess sensitization and clinical response to allergens. While skin prick tests are widely used due to their speed, cost-effectiveness, and valuable information, they too may not fully capture the clinical picture. Oral provocation remains the definitive diagnostic method but requires careful medical supervision due to potential risks [226]. Although IgG testing may provide insight into general immune responses, it is not specific enough to diagnose food allergies reliably. Instead, a combination of skin prick testing and oral provocation tests should be employed to accurately identify food allergies, as these methods directly evaluate sensitization and clinical reactions to specific food allergens.

Once the diagnosis of food allergy is confirmed, the European Academy of Allergy and Immunology recommends a comprehensive approach to managing the patient's condition. The primary goal of food allergy management is to minimize the risk of allergic reactions, ensure patient safety, and improve quality of life. One of the fundamental aspects of this process is allergen avoidance and dietary recommendations. Upon identification of a specific food allergen, an individualized diet plan should be developed to exclude the offending food or group of foods containing the allergen. This plan must be formulated in collaboration with a qualified nutritionist who can ensure the diet remains balanced and provides all essential nutrients necessary for the patient's health. This consideration is especially critical for children, whose nutritional needs must be met carefully to prevent deficiencies in trace elements and vitamins. Furthermore, educating the patient and their family on how to accurately read food labels is crucial, as many common ingredients may contain hidden allergens. Patients must learn to identify potentially dangerous additives such as preservatives, colourings, or emulsifiers that could trigger allergic reactions.

Providing patients with a written action plan is another vital element in managing food allergies. This plan clearly outlines the steps to be taken in the event of accidental allergen ingestion or the onset of an allergic reaction. Such instructions are particularly important for individuals at risk of severe reactions like anaphylaxis. The action plan should detail emergency procedures, including the administration of antihistamines, the use of epinephrine auto-injectors, and the prompt contact of medical professionals or emergency services when necessary. It is equally important that this plan is accessible to caregivers, family members, teachers, and food service employees who may be responsible for the patient's care or in environments where exposure to allergens is possible.

Education on recognizing symptoms and appropriate medication use is essential for empowering patients and their families. Food allergy symptoms can manifest diversely, including itching, skin rashes, swelling of the lips or throat, abdominal pain, nausea, vomiting, and in severe cases, respiratory difficulties and anaphylactic shock. Patients should be trained to promptly identify these signs and take immediate action to prevent complications. This training includes familiarization with prescribed medications such as antihistamines and corticosteroids, as well as hands-on instruction in the use of epinephrine auto-injectors to ensure patients are prepared to respond effectively during emergencies.

Psychological support plays an important role in the comprehensive care of patients with food allergies. The dietary restrictions and constant vigilance required to avoid allergens can lead to significant stress and anxiety, adversely affecting social life, daily habits, and overall well-being. Psychological counselling can assist patients in adapting to lifestyle changes, boosting self-esteem, reducing anxiety, and developing effective coping strategies. For children, particularly in

educational settings, specialized psychological support is crucial to help them understand their limitations and mitigate potential social challenges arising from their allergies.

In cases where allergen avoidance and conventional medication are insufficient, immunotherapy and biologic drugs may be considered. Immunotherapy involves the gradual introduction of small allergen doses to promote immune tolerance and decrease sensitivity over time. This treatment is primarily applied to allergies to specific foods such as milk or eggs and must be conducted under close medical supervision. Additionally, biologic agents like omalizumab, which target immune molecules responsible for allergic reactions, can be used to manage severe and chronic food allergies, especially in patients who do not respond adequately to standard therapies. These advanced treatments offer promising options to reduce the frequency and severity of allergic episodes and improve patients' quality of life.

Thus, food allergy management is a multifaceted process that includes not only medical treatment, but also aspects of education, psychological support and innovative therapeutic methods. A comprehensive approach can significantly improve the quality of life of patients, minimise the risk of complications and provide social and emotional support for patients with food allergies. The EAACI guidelines provide comprehensive and evidence-based recommendations for the diagnosis and management of food allergy. These guidelines emphasise the importance of a comprehensive approach that includes accurate diagnosis, individualised management and patient education to improve quality of life and reduce the risk of serious reactions.

Conclusions and recommendations

The monograph Allergy and Intolerance to Substances Added to Foods covers important aspects related to food allergy and food intolerance, in particular in the context of substances added to foods – dyes, preservatives, sweeteners, emulsifiers, etc. In the conclusions, the authors emphasise the need for a clear distinction between the concepts of food allergy and food intolerance. A food allergy is a reaction of the immune system that occurs in response to the presence of allergens in food, most often of a protein nature. Such a reaction can occur instantly and can be life-threatening, up to and including anaphylactic shock. In contrast, food intolerance is not related to the immune system, and its mechanisms often depend on enzyme deficiencies (e.g. lactase) or sensitivity to chemical compounds contained in food or added to it during production. Intolerance mostly manifests itself gradually, usually within a few hours of eating the product, and is rarely life-threatening, but still has a significant impact on the quality of life.

The intolerance to sugars, including lactose, fructose and sorbitol, is discussed separately. Lactose intolerance is one of the most common forms of enzyme deficiency. It is caused by a deficiency of lactase, an enzyme that breaks down lactose into glucose and galactose. As a result, undigested lactose enters the large intestine, where it is fermented by the microflora, causing bloating, abdominal pain, and diarrhoea. Diagnostics include a hydrogen breath test, fecal carbohydrate analysis in children, and genetic tests. Treatment involves limiting or eliminating dairy products, taking lactose-enzyme preparations, or consuming lactose-free milk. Intolerance to fructose and sorbitol manifests itself similarly, but the mechanisms are somewhat different, involving the transport of substances through the intestinal wall. The book also focuses on celiac disease and gluten enteropathy. This is an autoimmune disease that occurs in genetically predisposed individuals in response to the consumption of the protein gluten, which is found in wheat, rye, and barley. It affects the lining of the small intestine, leading to malabsorption of nutrients, vitamin deficiencies and anaemia. Symptoms in children include diarrhoea, growth retardation, emotional disorders; in adults, chronic fatigue, osteoporosis, and infertility. Diagnosis is based on serological tests (antigliadin, anti-endomysial, tissue transglutaminase antibodies) and is confirmed by histological analysis of a small intestine biopsy. The only effective treatment is a strict gluten-free diet that must be followed for life. The authors emphasise the importance of following this diet even in the absence of symptoms, as dietary disorders cause irreversible damage to the intestines.

The chapter on substances added to food is based on the Statham tables. It provides a classification of additives: colouring agents (e.g. tartrazine, azorubin), preservatives (benzoates, sulphites), thickeners and gelling agents (guar gum, xanthan gum), sweeteners (aspartame, saccharin), antioxidants, stabilisers, emulsifiers, and flavour enhancers (monosodium glutamate). Many of these substances, especially in case of excessive or prolonged consumption, can cause adverse reactions, including skin rashes, headaches, behavioural disorders in children, including manifestations similar to attention deficit hyperactivity disorder (ADHD). The side effects of food additives range from mild – skin reactions, itching, hives – to more severe, such as asthma exacerbation, migraines, or even anaphylactic shock in the case of severe individual reactions. The authors emphasise that many reactions are nonspecific and often not immediately associated with the use of certain supplements. This makes diagnosis difficult, as standard allergy tests do not always provide a clear answer. That is why it is important to keep a dietary diary, conduct elimination diets and provocative tests under medical supervision.

Considerable attention is also paid to the impact of food processing on its structure and potential symptoms. Freezing, heating, sterilisation, pasteurisation, drying – all these processes can change the structure of proteins, polysaccharides and other food components, sometimes increasing or decreasing the ability to cause allergic reactions. For example, some allergens are destroyed by heating, while others, on the contrary, become more active. This has practical implications for the management of patients with food allergies and intolerances – for example, some patients can tolerate boiled carrots but not raw carrots. A separate chapter is devoted to the assessment of immunoglobulin G (IgG) levels as a method of diagnosing food allergy. The book presents a position paper from the European Academy of Allergy and Clinical Immunology (EAACI), which emphasises that the presence of specific IgG or IgG4 to food proteins does not indicate a pathological reaction, but rather a physiological response to food contact. In other words, a positive IgG test often only reflects the fact of consumption of a product, not hypersensitivity to it. Using such tests as the basis for diagnosing food allergies or prescribing restrictive diets is incorrect and can be harmful to health, in particular through the development of nutritional deficiencies. EAACI strongly discourages the use of IgG tests as a tool in the diagnosis of food allergy or intolerance.

In light of the above conclusions, the authors of the book provide recommendations for further research and practice in the field of nutrition, allergology and food production. Firstly, large-scale studies are needed to assess the prevalence of food reactions to additives in different age and social groups. It is also important to improve diagnostic methods: more specific tests are needed to distinguish true allergic reactions from intolerance or nonspecific side effects. Standardised protocols for elimination-provocation testing need to be developed, and accessible educational programmes for doctors, nutritionists, pharmacists, and consumers need to be created. Collaboration with food producers is also important. It is necessary to promote the development of safe products that use natural or well-researched substances that have a minimal risk of causing negative reactions. Manufacturers should take a responsible approach to product labelling, indicating not only the presence of potentially dangerous additives, but also the sources of proteins (milk, egg, gluten) that are common allergens. The need to develop individualised approaches to nutrition, especially for patients with multiple intolerances or complex allergic conditions, is also worth noting.

In practical terms, it is important for the authors to emphasise the importance of an interdisciplinary approach: an allergist, gastroenterologist, immunologist, nutritionist, and, if necessary, a psychologist should work together as a team. The modern approach to patients with food allergies or intolerances involves not only identifying the irritant but also understanding the patient's emotional background, habits, lifestyle, and comorbidities. In general, the book forms a holistic view of the complex interaction between food, technological processes and the human body. It calls for a well-founded and scientifically supported approach in both medicine and the food industry. Further development in this area should be based on evidence, multidisciplinary analysis and the preservation of the core value of human health.

Recommendations for further research and practical steps in the field of food allergy and intolerance. Given the urgency of the problem of food allergy and intolerance, it is advisable to direct further research to a deeper understanding of the mechanisms of the body's immune response to various foods, as well as to the development of innovative methods of early diagnosis, including molecular diagnostics and genetic testing. It is important to implement interdisciplinary research that combines data from immunology, gastroenterology, nutrition and psychosomatics, as a

growing body of research shows that food allergies are linked to the patient's psycho-emotional state. It is also recommended to conduct epidemiological studies to clarify the prevalence of food allergies among different age and social groups, which will allow for better adaptation of preventive measures and individualised treatment approaches.

In practical terms, it is advisable to create multidisciplinary teams of allergists, gastroenterologists, psychologists, nutritionists and educators to provide comprehensive care to patients, especially children. Educational programmes for parents and educators should be promoted to identify and prevent food allergies, develop skills in reading food labels, keeping a food diary and creating a safe diet. It is also important to promote the development of adapted menus in educational and medical institutions, taking into account the needs of people with proven food allergies or intolerances. It is recommended to introduce psychological support for children and the families, which will reduce anxiety, improve compliance with dietary recommendations and improve quality of life. Overall, addressing food allergies requires a systematic approach that includes both medical and sociopsychological aspects.

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