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Vegetable Allergies: From Molecular Mechanisms to Clinical Management

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VEGETABLE ALLERGIES: FROM MOLECULAR MECHANISMS TO CLINICAL MANAGEMENT

This book is devoted to vegetable allergies, providing a comprehensive overview from molecular mechanisms to clinical management. The research explores the pathogenesis, epidemiology, and clinical phenotypes of allergic reactions to various vegetable families. The book reviews modern diagnostic approaches, emphasizing molecular allergology and component-resolved diagnostics. The study also provides evidence-based suggestions for the prevention, treatment, and dietary management of patients. Furthermore, it highlights the challenges of cross-reactivity and the impact of food processing, offering a personalized approach to integrating scientific advancements into practical clinical allergology.

Maria Zofia Lisiecka is a PhD in Medicine and has individual specialist medical practice. 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 2026. Her studies demonstrate a consistent integration of clinical observation with immunological diagnostics, contributing to the development of personalized allergy treatment strategies.

Philippe Houpline is Doctor of Biological Sciences and biotechnologist at the National Medical Institute of the Ministry of the Interior and Administration. His scientific work focuses on the intersection of biotechnology, microbiology, and biomedical research, with particular attention to pathogenic microorganisms and the development of innovative diagnostic and therapeutic approaches. His research interests include the expression and characterization of recombinant proteins, the study of antigenic structures, and the application of molecular biology techniques to improve infectious disease diagnostics. He is also engaged in interdisciplinary research that integrates biological sciences with medical practice, contributing to advancements in immunology, vaccine development, and public health. His work reflects a commitment to translating fundamental research into practical clinical solutions, while his appreciation for nature further informs his interest in the complexity of biological systems.

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Foreword

Food allergy represents one of the fastest-growing and most complex challenges in modern medicine, affecting millions of individuals globally. Within this expanding landscape of immunological diseases, allergic reactions to vegetables have gradually emerged from the shadows of more commonly researched triggers like milk and peanuts to assume a critical clinical role. This shift is inextricably linked to evolving global dietary patterns, advanced agricultural practices, and the intricate realities of our modern environment. This comprehensive book offers a profound, scholarly investigation into the multifaceted world of vegetable allergies, bridging the gap between foundational molecular immunology and practical clinical management.

The scientific understanding of vegetable allergies has undergone a remarkable historical evolution. Early clinical observations in the first half of the twentieth century documented adverse reactions to plant-based foods, yet their exact immunological nature remained obscured. The conceptual breakthroughs of the nineteen sixties, which elucidated immunoglobulin-mediated hypersensitivity, laid the essential groundwork for interpreting these biological responses. Subsequently, the discovery of pollen-food syndrome in the late twentieth century illuminated the complex cross-reactivity between inhaled pollen and ingested vegetable proteins. Today, we exist within the molecular era, a period that has fundamentally revolutionized diagnostic accuracy through the precise identification of specific allergenic proteins and the advent of component-resolved diagnostics.

Despite these tremendous scientific strides, significant clinical challenges persist in the daily management of vegetable allergies. Diagnostic uncertainty frequently arises due to the limitations of traditional skin prick tests and the unpredictable nature of labile plant proteins. Furthermore, the culinary processing of vegetables introduces a dynamic variable, as thermal treatment can either safely inactivate thermolabile allergens or dangerously concentrate thermostable proteins, confounding both patients and physicians. The heavy economic burden and the profound impact on the psychological well-being of patients, who must navigate strict dietary restrictions and social anxieties, underscore the urgent necessity for a more nuanced, multidisciplinary approach to patient care.

At the core of this monumental study is the commitment to precision medicine and interdisciplinary collaboration. By meticulously analyzing the botanical taxonomy and specific allergenic profiles of diverse vegetable families, the authors provide an unprecedented depth of coverage. The integration of molecular allergology into every section ensures that allergenic proteins are understood not merely as abstract concepts, but as specific molecules with defined structures, epitopes, and direct clinical implications. This granular perspective empowers healthcare professionals to differentiate between harmless cross-sensitization and life-threatening systemic risks, thereby optimizing elimination diets and emergency protocols.

The ultimate purpose of this book is not solely to document the pathophysiological mechanisms of vegetable allergies, but to translate this complex science into actionable, evidence-based clinical practice. It seeks to articulate how the rich legacy of immunological research continues to shape modern therapeutic strategies, including allergen avoidance, pharmacotherapy, and emerging immunotherapeutic interventions. By bridging theoretical insight with a critical examination of real-world clinical scenarios, this book serves as an indispensable resource for allergists, dietitians, and primary care physicians. It reaffirms the enduring importance of rigorous scientific inquiry in alleviating patient suffering and invites a vital re-examination of how precision

diagnostics can foster safe, individualized, and highly effective patient care in a rapidly evolving medical landscape. Ultimately, this comprehensive guide will not only enrich the academic community but also transform the daily lives of countless individuals globally, ensuring that future generations can navigate nutritional needs with absolute confidence, safety, and a vastly improved overall quality of life.

Introduction

Growing significance of vegetable allergies in modern medicine

Food allergy is one of the fastest-growing problems in modern medicine, affecting approximately 220-250 million people worldwide, according to the World Allergy Organisation (De Martinis *et al.*, 2020). In this growing pattern of allergic diseases, vegetable allergies are taking on a special and increasingly substantial role. Although historically overshadowed by more researched allergens such as milk, eggs and peanuts, allergic reactions to vegetables have become a significant clinical problem, particularly in the context of changing dietary patterns, the growth of global food trade and the development of agricultural practices.

Epidemiological data show an alarming trend towards an increase in the prevalence of vegetable allergies in various geographical regions. European studies show that vegetable allergies affect approximately 1.5-2.5% of the general population, with higher rates observed in certain subgroups, especially in individuals with pollen allergies due to cross-reactivity (Spolidoro *et al.*, 2024). North American data show comparable prevalence rates, although there are regional differences depending on dietary habits and environmental influences (Gupta *et al.*, 2019). Notably, the incidence is rising most sharply in urban populations and among young people, demographic shifts that require close attention from healthcare professionals and health officials. The clinical and economic burden of vegetable allergies exceeds simple prevalence statistics. These conditions significantly impact quality of life by imposing dietary restrictions that affect social interaction, nutritional status, and psychological well-being. Parents of children with vegetable allergies report increased levels of stress and anxiety about adequate nutrition during critical periods of development (Cao *et al.*, 2021). The economic burden of food allergies exceeds 24 billion USD annually in the United States alone, with vegetable allergies accounting for a measurable portion of this amount (Bilaver *et al.*, 2023).

Historical evolution of vegetable allergy research

Scientific research on vegetable allergies has gone through several key stages. Initial clinical observations in the 1920s-1930s documented adverse reactions to vegetables, although their immunological nature remained unclear (Smith, 2016). A conceptual breakthrough occurred in the 1960s with the elucidation of IgE-mediated hypersensitivity mechanisms, which provided an immunological basis for the interpretation of allergic reactions to food proteins (Platts-Mills *et al.*, 2016). The discovery of pollen-food syndrome in the 1980s-1990s was a key breakthrough: researchers established cross-reactivity between pollen allergens and vegetable proteins, which explained the oral symptoms in patients with seasonal rhinitis (Ortolani *et al.*, 1988). The molecular era of the 2000s revolutionised diagnostics through the identification of specific allergenic proteins and the introduction of component-specific diagnostics (Calamelli *et al.*, 2019).

Modern challenges and issues

Despite significant progress, key problems remain in the treatment of vegetable allergies. Diagnostic uncertainty arises due to the suboptimal positive predictive value of skin prick tests and specific IgE measurements, which can lead to clinically insignificant sensitisation or false-negative results for labile proteins (Cox *et al.*, 2019). Threshold doses for reactions vary significantly between patients and depend on cofactors (pollen, physical activity, alcohol, medication), making it difficult to establish safe consumption levels (Bartra *et al.*, 2023). Food processing unpredictably alters

allergenicity: thermolabile allergens are inactivated, while thermostable allergens are preserved or concentrated (Gonzalez *et al.*, 2025). Therapeutic options remain limited, with oral immunotherapy for vegetable allergens still in the research phase (Mori *et al.*, 2021). Global inequalities in access to molecular diagnostics and cultural differences in vegetable consumption require individualised treatment approaches.

Basis of the complex piece

The creation of a comprehensive textbook on vegetable allergies is driven by several key factors. First, rapid advances in molecular research of plant allergens and cross-reactivity mechanisms, transforming diagnostic and therapeutic approaches, were noted (Dall'Antonia *et al.*, 2014). Second, the development of precision medicine creates opportunities for individualised treatment based on genetic markers, microbiome characteristics and molecular biomarkers (Kostara *et al.*, 2020; Bunyavanich and Berin, 2019). At the same time, existing medical literature on vegetable allergies remains fragmented across numerous specialisations and journals. Most textbooks on allergology devote limited attention to vegetable allergies, while specialised reviews focus only on specific aspects of the problem. The lack of a comprehensive resource that integrates interdisciplinary perspectives and current scientific advances creates a critical gap in medical education and clinical practice that this book aims to fill.

Structure and philosophy of the book

The textbook is structured following the principle of a sequential transition from fundamental knowledge to clinical application. The introductory section lays the immunological and molecular foundations for determination of vegetable allergies, including mechanisms of development, classification of allergens, epidemiology, and risk factors. Subsequent chapters systematically review individual vegetables and their families, covering allergenic profiles, clinical manifestations, diagnosis, and treatment. The guiding principles are evidence-based medicine with gradation of recommendations, a personalised approach to each patient, interdisciplinary collaboration and patient education. Each section contains clear learning objectives, clinical cases, algorithms and tables for practical application, as well as summary blocks of key points.

Methodological principles and standards of evidence-based

The validity of the analysis is based on the principles of evidence-based medicine. Recommendations are based on a systematic assessment of randomised controlled trials, systematic reviews and meta-analyses, and observational studies using standardised quality assessment tools. The literature search covered major medical databases (PubMed, EMBASE, Cochrane Library, Web of Science) with an emphasis on publications from the last decade and the inclusion of fundamental works. The limitations of evidence-based practice are marked. The text combines theoretical depth with practical applicability through clinical algorithms, step-by-step recommendations, and real-world clinical scenarios.

Distinctive features and innovations

This textbook has several key features. First, its exclusive focus on vegetables provides unprecedented depth of coverage of botanical relationships, cross-reactivity patterns, and the effects of food processing, which is not possible in general texts on food allergies. Secondly, molecular allergology is integrated into all sections – allergenic proteins are considered as specific molecules

with known structures, epitopes and clinical significance, which increases the accuracy of diagnosis and analysis of cross-reactivity. Thirdly, clinical orientation ensures practical applicability through decision-making algorithms, analysis of typical errors and the experience of clinicians, answering specific questions of practice. Fourthly, the interdisciplinary and global approach encompasses the contributions of allergists, immunologists, dieticians and other specialists, incorporates regional epidemiological differences and adapts recommendations to different healthcare systems.

Efficient use guidelines

The textbook is intended for various categories of readers. Medical students will benefit from studying the chapters sequentially, especially the immunological mechanisms, pathophysiology, and clinical vignettes. Allergy residents and fellows should prioritise diagnostic algorithms, molecular allergy, and critical evaluation of the evidence base. Practising allergists can use the textbook as a reference for unusual cases and to update their knowledge of molecular diagnostic approaches. Primary care physicians will find the sections on clinical manifestations, primary assessment algorithms, and referral criteria useful.

Development of critical thinking and lifelong learning

Readers should critically evaluate the information presented, recognising the limitations of the evidence base and the dynamic nature of medical knowledge. Many aspects of the management of vegetable allergies are based on observational studies or expert consensus rather than randomised controlled trials. The individual circumstances of the patient require adaptation of general recommendations, accounting for comorbidities, cultural factors, and resource availability. Maintaining clinical competence requires continuing medical education through reading professional journals, participating in professional conferences, and conducting clinical research.

Concluding remarks

The field of vegetable allergy is undergoing rapid development. Molecular allergology provides more accurate diagnostics, immunotherapeutic approaches create prospects for tolerance induction, and further research of mechanisms creates a basis for preventive strategies. This textbook systematises current knowledge, acknowledging the existence of gaps that will be filled by future research. The aim is to improve diagnosis, optimise treatment, and contribute to improving the quality of medical care for patients with vegetable allergies.

CHAPTER 1.

Basics of vegetable allergies

Vegetable allergies are a complex and multifaceted group of immunologically mediated reactions to protein components of vegetable crops, which are becoming increasingly clinically significant in modern medical practice. This fundamental section lays the scientific foundation for the interpretation of the pathophysiological mechanisms, molecular basis, and epidemiological patterns of vegetable allergies, creating a conceptual basis for further study of the diagnostic and therapeutic aspects of these diseases. Basic principles of immunological reactions to vegetable allergens, their classification, prevalence and risk factors are necessary for clinicians of various specialities who encounter patients suffering from these conditions.

Current research shows that vegetable allergies are not a simple category of food allergies but represent a heterogeneous group of diseases with unique immunological characteristics, specific patterns of cross-reactivity, and distinct clinical manifestations. Molecular allergology has revolutionised the concept of these conditions, which can be used to identify specific allergenic proteins, elucidate the mechanisms of cross-reactivity, and develop more accurate diagnostic approaches. This evolution of knowledge requires a systematic rethinking of traditional approaches to the diagnosis and treatment of vegetable allergies, making this section particularly relevant to modern clinical practice.

1.1 Mechanisms of vegetable allergy development

In contrast to classic food allergens such as milk or eggs, vegetable allergens are often characterised by a high degree of structural homology with pollen allergens, which accounts for unique mechanisms of sensitisation and clinical manifestations. The fundamental mechanism of most vegetable allergies is IgE-mediated type I hypersensitivity, which develops through a complex cascade of immunological reactions, including phases of sensitisation and efferent reactions.

The process of sensitisation to vegetable allergens can occur through several anatomical pathways, each with unique characteristics and clinical consequences. Primary sensitisation through the gastrointestinal tract has traditionally been considered the main mechanism, especially in young children, when an immature immune system and increased intestinal barrier permeability facilitate the presentation of food antigens to immunocompetent cells (Järvinen *et al.*, 2013). However, studies show that for many vegetable allergens, primary sensitisation occurs via the respiratory route due to the inhalation of pollen allergens that are structurally similar to vegetable proteins. This phenomenon, known as oral allergy syndrome or pollen-food syndrome, is a secondary food allergy that develops in individuals who are already sensitised to pollen.

The development of IgE-mediated responses to vegetable allergens is initiated by the presentation of allergenic peptides by dendritic cells and other antigen-presenting cells of the intestinal mucosa or respiratory tract to naive CD4+ T lymphocytes. The differentiation of these cells towards the Th2 phenotype under the influence of a specific cytokine microenvironment, including IL-4, IL-5 and IL-13, is a critical step that determines the development of an allergic response instead of tolerance (Poulsen and Hummelshoj, 2007). Activated Th2 cells secrete IL-4 and IL-13, which stimulate B lymphocytes to switch antibody class from IgM to IgE through a process that requires the interaction of CD40-CD40L and specific transcription factors. The specific IgE antibodies formed circulate in the bloodstream and bind to high-affinity FcεRI receptors on the surface of mast cells and basophils, sensitising the body to repeated contact with the allergen.

When a vegetable allergen re-enters the body, cross-linking of surface-fixed IgE antibodies occurs, activating mast cells and basophils, followed by degranulation and release of inflammatory mediators. Primary mediators, including histamine, tryptase, heparin, and chemotactic factors, cause immediate clinical manifestations of an allergic reaction within minutes of contact with the allergen. The secondary phase of the allergic reaction, which develops 4-12 hours after the initial contact, is mediated by newly synthesised mediators, including leukotrienes, prostaglandins, thromboxane, and numerous cytokines. These mediators provide prolonged inflammatory responses, including chemotaxis of eosinophils, neutrophils, and other inflammatory cells, which can lead to prolonged clinical manifestations even after allergen elimination. Notably, vegetable allergens can be modified during culinary processing, which alters their antigenic structure and, accordingly, the nature of the immune response.

The normal physiological response of the immune system to food antigens, including vegetable proteins, is the development of oral tolerance, a state of active immunosuppression that ensures the absence of pathological immune reactions to constantly consumed food components. This complex process involves several mechanisms that act at different levels of the immune system and ensure the maintenance of homeostasis under conditions of constant antigenic load from food products (Commins, 2015).

Although IgE-mediated hypersensitivity is the most common and clinically relevant mechanism of vegetable allergies, there are other immunopathological mechanisms that can lead to clinically relevant reactions to vegetable components. T-cell-mediated delayed-type hypersensitivity can manifest as systemic reactions 24-72 hours after consumption of specific vegetables. This mechanism is more common in patients with atopic dermatitis, where vegetable antigens can trigger exacerbations of skin manifestations through the activation of Th1 and Th17 immune responses (Papapostolou *et al.*, 2022). Food protein-induced enterocolitis syndrome (FPIES) is a specific form of non-IgE-mediated food allergy that can develop in response to certain vegetable proteins, especially in infants and young children. This syndrome is characterised by prolonged vomiting, diarrhoea and possible development of dehydration and shock without the involvement of IgE antibodies. The pathogenic mechanisms of FPIES include T-cell activation and local inflammation of the intestinal mucosa with the release of pro-inflammatory cytokines, including TNF-α and interferon-γ (Zhang *et al.*, 2021).

Mixed mechanisms may combine elements of IgE-mediated and cell-mediated hypersensitivity, complicating diagnosis and treatment. Eosinophilic oesophagitis associated with the consumption of certain vegetables may involve both IgE-dependent and Th2-mediated non-IgE-dependent mechanisms, leading to chronic inflammation of the oesophagus with characteristic eosinophilic infiltration. Recognition of these alternative mechanisms is substantial for clinicians, as standard allergy tests may be negative despite the presence of clinically significant reactions to vegetable components.

1.2 Classification of vegetable allergens

The current classification of vegetable allergens is based on a scientifically sound nomenclature system developed by the Subcommittee on Allergen Nomenclature of the International Union of Immunological Societies (IUIS), which provides a unified approach to the identification and designation of allergenic proteins in the international scientific community. According to this system, each allergen is given a unique designation consisting of the first three letters of the generic name of the plant, the first one or two letters of the species name, and an Arabic numeral indicating the

order in which the allergen was discovered within that species. For example, the main allergen in carrots is designated as Dau c 1 (*Daucus carota*), and the main allergen in celery is designated as Api g 1 (*Apium graveolens*). This systematisation not only ensures the accuracy of scientific communication but can also predict potential cross-reactions between allergens of different vegetable species based on structural homology and phylogenetic proximity. Notably, the nomenclature reflects not only the taxonomic relationships between plants, but also the functional characteristics of allergenic proteins, their localisation in plant tissues and their biological role in the life of the plant organism. This systematic approach is relevant for vegetable allergens, as many of them are protective plant proteins expressed in response to stress factors or pathogenic organisms. In addition to the basic nomenclature, there are additional classification systems that group allergens according to their structural and functional characteristics. Classification by protein families can be used to predict cross-reactivity and determine the evolutionary relationships between allergens. Of particular importance for vegetable allergens are the families of profilins, pathogen-related proteins (PR proteins), thaumatin-like proteins, and other structurally conserved protein groups that are widely represented in the plant world (Breiteneder and Radauer, 2004).

1.2.1 Botanical taxonomy and cross-reactivity of vegetable allergens

The botanical taxonomy of vegetable crops serves as a fundamental basis for determination of cross-reactivity patterns and predicting potential allergic reactions in patients sensitised to specific vegetable allergens. The main characteristics of the most relevant botanical families are presented in Table 1.

Table 1. Main characteristics of the most relevant botanical families

Relatives	Main vegetables	Main allergens	Cross-reactivity	Thermal stability
Umbellifers (Apiaceae)	Carrots, celery, parsley, dill, parsnips, fennel	Profilins, PR-10 proteins, glycoproteins	Birch pollen, wormwood pollen, other members of the family	Thermolabile (profilins, PR-10); glycoproteins may be stable
Cruciferous (Brassicaceae)	Cabbage, broccoli, cauliflower, radish	2S-albumins, profilins, Bet v 1-like proteins, LTP, defensins, glucosinolates, isothiocyanates	Birch pollen, other cruciferous plants, and LTP cross-pollination with fruit	Variable: profilins are thermolabile, LTPs are thermostable; heating can either reduce or increase the allergenicity of individual epitopes
Solanaceae	Tomatoes, potatoes, aubergines, peppers	Profilins, Bet v 1-like proteins, PR proteins, glycoalkaloids (solanine, chaconine, tomatine)	Birch pollen, wormwood pollen; latex; other nightshades	Thermolabile profiles; glycoalkaloids are stable (higher concentrations in unripe fruits and green potatoes)
Gourd (Cucurbitaceae)	Cucumbers, courgettes, pumpkins, melons, watermelons	Profilins, tauatin-like proteins (TLP)	Pollen from grasses, birch trees, latex, and other pumpkin plants	Thermolabile; cooking/baking significantly reduces allergenicity
Relatives	Main vegetables	Main allergens	Cross-reactivity	Thermal stability

Source: *based on M.G. Terán et al. (2023), M. Słowianek et al. (2020), H. Breiteneder and C. Radauer (2004), L.R. Offermann et al. (2016), Z. Han and R. Schneiter (2024), S.P. Commins (2015), L.K. Poulsen and L. Hummelshoj (2007).*

The molecular mechanisms of cross-reactivity between pollen and vegetable allergens are based on the structural homology of specific protein domains that provide binding to identical IgE antibodies. Profilin, PR proteins, and other pan-allergens show a high degree of conservation

among different plant species, which explains the broad patterns of cross-reactivity between birch pollen and numerous vegetables, including carrots, celery, parsley, and other members of the Umbelliferae family (Terán *et al.*, 2023). The molecular basis of cross-reactivity is critical for the interpretation of clinical manifestations and diagnostic results of allergy testing.

Interpretation of the botanical classification of vegetables can be used by clinicians to predict potential cross-reactions in patients with established allergies to specific vegetables or pollen allergens (Słowianek *et al.*, 2020). Patients sensitised to birch pollen are at increased risk of developing oral allergy syndrome when consuming raw vegetables due to shared profilins and PR-10 proteins. However, heat treatment can significantly alter the allergenicity of thermostable proteins, as heating reduces immunoreactivity, while thermostable allergens retain their activity even after cooking. This knowledge is critical for development of individualised dietary recommendations and assessing the risk of severe reactions in sensitised patients.

1.2.2 Clinical classification of vegetable allergens

The clinical classification of vegetable allergens according to the nature and severity of the reactions they cause is fundamental for the practical management of patients and risk assessment. The main characteristics are presented in Table 2.

Table 2. Clinical classification and characteristic of vegetable allergens

Allergen type	Thermal stability	Reaction type	Protein sample	Clinical manifestations
Allergens causing localised reactions	Thermolabile	Predominantly oral allergy syndrome (OAS)	Profilins, PR-10 proteins	Itching, swelling of the lips, tongue, mouth and throat; rarely progressing to systemic manifestations; cooked vegetables are usually tolerated
Allergens that cause systemic reactions	Thermostable	Systemic reactions, including anaphylaxis	LTP (lipid transfer proteins), some tauatin-like proteins, and specific glycoproteins	Generalised urticaria, angioedema, bronchospasm, hypotension, anaphylactic shock; reactions are possible even with minimal amounts or aerosol contact; activity persists after heat treatment.
Allergens with variable manifestations	Variable	Local and/or systemic reactions depending on cofactors	PR proteins (individual representatives), some glycoproteins	From mild oral symptoms to systemic reactions; severity depends on individual sensitivity, allergen dose and cofactors (physical exertion, alcohol, NSAIDs)

Source: *based on M. De Martinis et al. (2020), G.C.I. Spolidoro et al. (2024), M.G. Terán et al. (2023), H. Breiteneder and C. Radauer (2004), Z. Han and R. Schneiter (2024), N. Papapostolou et al. (2022), S. Zhang et al. (2021).*

1.3. Epidemiology and statistics

Epidemiological studies of food allergies, particularly to vegetables, show significant variations in prevalence and patterns of sensitisation between different geographical regions, age groups and populations, reflecting the complex interaction of genetic factors, environment, dietary habits, and methodological approaches. According to European reviews, the prevalence of food allergies, determined based on self-reported data, ranges from less than 1% to more than 10% depending on the country, age, and specific food products (Arens *et al.*, 2025). Data combining medical history, skin test results, and provocation tests indicate that the actual prevalence of clinically significant vegetable allergies is lower than self-reported rates but is in the low single digits.

1.3.1 Geographical differences in the prevalence of vegetable allergies

Regional characteristics of the prevalence of vegetable allergies are presented in Table 3.

Table 3. Geographical differences in the prevalence and characteristics of vegetable allergies

Region	Prevalence	Main allergens	Dominant mechanisms	Peculiarities
Northern and Central Europe	Low single-digit values (clinically confirmed)	Carrots, celery	Profilins, PR-10 proteins; oral allergy syndrome	High sensitivity to birch pollen; cross-reactions
North America	Adults: 1.2-3.1 %; children: 0.5-1.5%	Tomatoes, other nightshades	Profiles, PR proteins	Association with sawdust allergic rhinitis; consumption of raw vegetables
Asia	Vegetables: ~3.0 %; fruits: ~5.6 %	Local vegetable crops	Cross-reactivity with wormwood pollen, Japanese cedar	Low frequency of birch-dependent reactions; urbanisation increases the risk
Mediterranean	Variable; higher proportion of severe reactions	Celery, tomatoes, parsley	LTP-mediated sensitisation	Frequency of systemic reactions; consumption of raw vegetables

Source: *based on G.C.I. Spolidoro et al. (2024), R.S. Gupta et al. (2019), M.G. Terán et al. (2023), M. Słowianek et al. (2020), Z. Han and R. Schneiter (2024), H. Breiteneder and C. Radauer (2004), J. Bartra et al. (2023).*

1.3.2 Age distribution and gender differences

Adolescence and young adulthood represent another critical period for the development of vegetable allergies, especially in the context of oral allergy syndrome. During this period, sensitisation to pollen allergens is established, which can lead to secondary cross-reactivity with vegetable allergens. Hormonal changes characteristic of puberty can modulate the immune response and influence the clinical manifestations of allergy. Lifestyle changes, including increased consumption of raw vegetable salads and other foods popular among adolescents, may increase exposure to allergens and the risk of clinical reactions in already sensitised individuals.

The age distribution of vegetable allergies shows characteristic patterns that distinguish these allergies from classic childhood food allergies (Table 4).

Table 4. Age distribution and gender differences in the prevalence of vegetable allergies

Age groups	Prevalence	Prevalent mechanisms	Clinical peculiarities
0-3 years	<0.5%	Non-IgE-mediated reactions (FPIES)	Rare; atypical manifestations
3-12 years	0.8-1.5%	Mixed mechanisms	Part of the atopic march
15-30 years	Peak incidence of oral allergy syndrome	IgE-mediated (profilins, PR-10)	Associated with respiratory allergic rhinitis
Adults	1.2-3.1%	IgE-mediated; less commonly LTP	Chronic course

Source: *based on K.M. Järvinen et al. (2013), S. Zhang et al. (2021), N. Papapostolou et al. (2022), M.G. Terán et al. (2023), L.K. Poulsen and L. Hummelshoj (2007), S.P. Commins (2015), E. Stephen-Victor and T.A. Chatila (2019), J. Bartra et al. (2023).*

Gender differences in the prevalence of vegetable allergies are statistically significant, with women showing a higher prevalence than men, with a ratio of 1.5:1 to 2:1 (Jensen-Jarolim and Untersmayr, 2008). This phenomenon can be partly explained by hormonal influences on the immune system, differences in the frequency of seeking medical help, or sociocultural factors. Gender differences are particularly pronounced in adolescence and young adulthood, which coincides with a period of hormonal changes. Pregnancy can modify the clinical manifestations of vegetable allergies, with reports of both improvement and deterioration of symptoms.

1.3.3 Temporal trends and comorbidity

Longitudinal epidemiological observations indicate a gradual increase in the prevalence of food allergies, including vegetable allergies, in most developed countries over the past two decades. In European populations, self-reported food allergies have increased from approximately 6% in the early 2000s to over 14% after 2015 (Spolidoro *et al.*, 2022). This increase reflects both a real increase in incidence and improvements in diagnostic methods, increased clinical vigilance, and growing public awareness. Particularly rapid growth has been observed among urban populations and in countries undergoing rapid urbanisation. The "western lifestyle" hypothesis offers an explanation through changes in early microbial exposure, dietary habits, and air pollution (Ozdemir *et al.*, 2024). Climate change may also contribute to the increase in prevalence through the lengthening of the pollen season and increased pollen concentrations in the air.

The comorbidity of vegetable allergies with other allergic diseases is high (Table 5).

Table 5. Comorbidity of food allergies with other atopic diseases

Concomitant disease	Prevalence among patients with food allergies	Clinical significance
Atopic dermatitis	~48 %	Part of the atopic march; triggers of exacerbations
Bronchial asthma	~46 %	Increased risk of systemic reactions
Allergic rhinitis	~39 %	The basis for oral allergy syndrome due to cross-reactivity
Multiple food allergies	Significant proportion	Nuts, fruits, grains; cross-reactivity due to shared protein families

Source: *based on C. Warren et al. (2024), E. Sharma and J. Vitte (2024).*

1.3.4 Severe reactions and the role of cofactors

Although most allergic reactions to vegetables are mild or moderate, some patients may experience severe systemic reactions, including anaphylaxis. Data from the European Anaphylaxis Registry (EAACI) show that plant-based foods account for a significant proportion of food-induced anaphylaxis in adults, especially in Mediterranean countries with high LTP sensitisation. The most common severe reactions are described for celery, tomatoes, and parsley (Dölle-Bierke *et al.*, 2023). Fatal cases of anaphylaxis remain rare, with the overall mortality rate from food anaphylaxis estimated at 0.03-0.3 cases per million population per year (Anagnostou *et al.*, 2022).

A significant epidemiological observation is the role of cofactors in increasing the risk of severe reactions. Physical exertion during sensitisation to LTP can induce food-dependent anaphylaxis (FDEIA), especially in Mediterranean populations. Cofactors such as physical exertion, alcohol, NSAIDs, and acute infections are involved in approximately 15-30% of all cases of food anaphylaxis, significantly increasing the risk of systemic manifestations (Shin, 2020).

1.3.5 Economic burden and impact on quality of life

The economic burden of vegetable allergies is significant, although often underestimated. Direct medical costs include diagnosis, consultations, medication (adrenaline auto-injectors), emergency care and hospitalisation. Estimated annual direct costs per patient range from 500 to 2,000 US dollars, depending on severity (Bilaver *et al.*, 2019). Indirect costs, such as lost productivity, missed work/school days, specialised nutrition, and work schedule changes, may exceed direct medical costs.

The impact on quality of life is significant and complex. Patients report significant limitations in social activities, especially those related to eating outside the home. Constant vigilance

regarding accidental contact with allergens creates significant psychological stress for patients and their families. Parents of children with vegetable allergies often experience increased anxiety, depression, and social isolation. Adolescence is particularly challenging, as the desire for social integration conflicts with the need to adhere to dietary restrictions. These psychosocial aspects underscore the need for a comprehensive approach to patient management that includes not only medical treatment but also psychological support and educational programmes.

1.4 Risk factors and aetiology

The aetiology of vegetable allergies is multifactorial, involving complex interactions between genetic predisposition, epigenetic modifications, environmental factors, dietary patterns, and gut microbiota. Determination of these risk factors can identify vulnerable populations and develop preventive strategies.

1.4.1 Genetic and epigenetic factors

Genetic factors are fundamental in determining an individual's susceptibility to developing vegetable allergies. A family history of atopic diseases significantly increases the risk of developing vegetable allergies in a child, with a relative risk of 2.5 to 5.0 depending on the specific phenotype of the parental allergy (Arnau-Soler *et al.*, 2024). Twin studies demonstrate concordance in the development of food allergies in 60-80% of monozygotic twins compared to 20-30% in dizygotic twins, indicating a significant genetic component. Genome-wide association studies (GWAS) have identified numerous loci associated with an increased risk of food allergies, including polymorphisms of epithelial barrier genes (filaggrin FLG), HLA class II (HLA-DQ and HLA-DR alleles), Th2-response cytokines (IL-4, IL-13, IL-5 and their receptors) and toll-like receptors (TLR) (Kanchan *et al.*, 2021; Ashley *et al.*, 2017).

Epigenetic mechanisms, including DNA methylation, histone modifications, and regulatory non-coding RNAs, can modify genetic susceptibility and mediate the influence of environmental factors on the development of vegetable allergies. Maternal nutrition during pregnancy, exposure to pollutants, and other prenatal factors can induce epigenetic changes in the foetus that influence future immune responses (Arnau-Soler *et al.*, 2024). These modifications can be transmitted across generations, partially explaining the transgenerational effects and familial clustering of allergic diseases. Regulatory T cells (Tregs), which secrete the immunosuppressive cytokines IL-10 and TGF-β, are central in maintaining oral tolerance. Disruption of oral tolerance mechanisms can occur due to genetic predisposition, epigenetic modifications, intestinal microbiota imbalance, and changes in intestinal barrier permeability.

1.4.2 Early dietary factors

The age at which vegetables are introduced into an infant's diet is a critical factor influencing the development of tolerance or sensitisation. Traditional recommendations to delay the introduction of potentially allergenic foods until 12-24 months have been refuted by studies showing that early introduction (4-7 months) may promote tolerance (Scarpone *et al.*, 2023; Borowitz, 2021). Delaying the introduction of vegetables beyond this "critical window" may increase the risk of allergic sensitisation. Gradual introduction of small amounts with a gradual increase in the volume and variety of vegetables is more favourable than sudden introduction of large amounts (Covington *et al.*, 2025). Heat-treated vegetables may be a better choice for initial introduction, as denaturation of thermostable allergens may reduce allergenic potential.

Maternal nutrition during pregnancy and lactation is essential for the development of the child's immune system. A diet rich in a variety of fruits and vegetables is associated with a lower risk of atopic diseases in children, possibly due to transplacental transfer of immunomodulatory factors or epigenetic programming (Adineh *et al.*, 2024). Breastfeeding may promote tolerance through the transfer of maternal antibodies, immunomodulatory cytokines, and components that support a healthy gut microbiota, although the protective effect depends on duration, exclusivity, and maternal diet. Consumption of a variety of vegetables by the mother during lactation may induce tolerance through exposure to low doses of vegetable antigens via breast milk. A varied family diet with a wide range of vegetables introduced at an early age may promote tolerance, whereas a monotonous diet may increase the risk of sensitisation.

1.4.3 Ecological factors

Environmental pollution, especially atmospheric pollution and exposure to diesel exhaust particles, has been shown to be associated with an increased risk of allergic diseases. Diesel exhaust particles can act as adjuvants, enhancing the Th2-mediated immune response (Reinmuth-Selzle *et al.*, 2017). Epidemiological studies show a higher prevalence of food allergies among residents of densely populated urban areas with high levels of air pollution compared to rural areas.

Exposure to pollen allergens is a critical risk factor for the development of vegetable allergies through cross-reactivity mechanisms. Geographical regions with high concentrations of birch pollen show a higher prevalence of oral allergy syndrome associated with vegetables of the Umbelliferae family (Popescu, 2015). Climate change leads to a longer pollen season, higher pollen concentrations in the air, and a possible increase in the allergenicity of pollen grains. Occupational exposure among food industry workers, cooks, and agricultural workers is associated with an increased risk of sensitisation due to repeated inhalation exposure to aerosol particles and skin contact with vegetable juices (Fukutomi, 2019).

The hygiene hypothesis explains the increase in the prevalence of allergic diseases due to reduced early microbial exposure. Children growing up in rural environments with regular contact with animals and a variety of microbes show a lower risk of developing allergic diseases compared to their urban peers (von Mutius, 2010). Early contact with microbial agents promotes the maturation of the immune system towards a balanced Th1/Th2 response and the development of effective regulatory mechanisms.

1.4.4 Microbiota and medication factors

The composition and diversity of the gut microbiota in early childhood a critical factor influencing the development of immune tolerance. Studies show significant differences in the gut microbiome between children with food allergies and healthy peers, including reduced colonisation by Bifidobacterium and Lactobacillus species (Farnetano *et al.*, 2024). Normal gut microflora produces short-chain fatty acids (butyrate, propionate), which have immunomodulatory properties and promote the differentiation of regulatory T cells.

Intestinal dysbiosis caused by antibiotic therapy during critical periods of immune development, especially in the first year of life, is associated with an increased risk of food allergies. Epidemiological data indicate that each course of antibiotics in early childhood increases the risk of food allergy by 10-15%, with a cumulative effect with repeated courses. The type of antibiotic also matters, with the highest risk associated with broad-spectrum antibiotics. Pre- and probiotic interventions show potential for modulating risk, although results remain inconclusive (Li *et al.*, 2025).

Long-term use of proton pump inhibitors and H2 antagonists, especially in infants, is associated with an increased risk of food allergies due to impaired protein digestion and increased allergenicity (Robinson and Camargo Jr, 2018). The use of paracetamol in early childhood is associated with an increased risk of allergic diseases in some studies, although the mechanisms remain unclear (Beasley *et al.*, 2008). In contrast, vaccination is not associated with an increased risk of allergic diseases, and some vaccines may even demonstrate protective effects through stimulation of the Th1 response (Navaratna *et al.*, 2021).

1.4.5 Socio-cultural and psychosocial factors

Socioeconomic status shows complex associations with the risk of developing vegetable allergies. Higher socioeconomic status is associated with an increased risk of allergic diseases, which may reflect a "Western lifestyle" with excessive hygiene and reduced microbial exposure (Warren *et al.*, 2022). At the same time, higher levels of education and income may provide better access to a varied diet. Compared to rural areas, urban environments are associated with an increased risk of food allergies due to the cumulative effects of air pollution, reduced microbial diversity, and reduced contact with the natural environment (Warren *et al.*, 2020).

Cultural food traditions and ethnicity influence both patterns of exposure to vegetable allergens and genetic susceptibility to developing specific types of allergic reactions. Populations with traditionally high consumption of certain vegetables may demonstrate either increased tolerance due to early exposure or higher rates of sensitisation due to greater allergen exposure. Migration and changes in traditional eating habits are associated with changes in food allergy patterns.

Psychosocial stress, including maternal stress during pregnancy and stressful events in early childhood, can modify the risk of developing allergic diseases through effects on the immune system and intestinal barrier function. Chronic stress is associated with an imbalance in the Th1/Th2 response towards Th2 dominance and may disrupt the integrity of the intestinal epithelium. Maternal depression and anxiety during pregnancy are associated with an increased risk of atopic diseases in offspring through neuroimmune mechanisms and epigenetic modifications.

1.4.6 Generalisation: Multifactoriality and clinical significance

The aetiology of vegetable allergies is the result of a complex interaction of multiple risk factors acting at different stages of development, from the prenatal period to adulthood. Genetic predisposition determines the baseline risk, which is modified by epigenetic mechanisms under the influence of maternal nutrition, stress and environmental factors. The critical window for inducing oral tolerance in early childhood (47 months) represents a significant opportunity for preventive interventions through the early introduction of a variety of vegetables. The gut microbiota is central in the development of immune tolerance, and its disruption through antibiotic therapy or other factors increases the risk of sensitisation. Environmental factors, including air pollution, pollen exposure and urbanisation, contribute to the increasing prevalence of vegetable allergies in developed countries. Determination of these risk factors can identify vulnerable populations, develop prevention strategies, and educate parents and healthcare professionals on optimal approaches to introducing vegetables into children's diets, thereby improving clinical outcomes and quality of life for patients with vegetable allergies.

CHAPTER 2.

Diagnosis and clinical manifestations

2.1 Symptoms of allergic reactions

The clinical manifestations of allergic reactions to vegetables range from mild localised reactions to life-threatening systemic conditions. The most common manifestation is oral allergy syndrome, which occurs within minutes of eating fresh raw vegetables. Patients describe burning, itching, and tingling of the lips, tongue, palate, and throat. Objective signs include mucosal erythema, mild swelling of the lips and tongue. Pathophysiologically, this is conditioned by local degranulation of mast cells in contact with labile allergenic proteins, which are rapidly destroyed by saliva and gastric juice (Alessandri *et al.*, 2020). It is characterised by rapid regression of symptoms within 5-30 minutes after stopping contact with the allergen. The intensity varies depending on the variety of vegetables, freshness, and storage method due to different concentrations of labile allergens.

Skin manifestations are represented by urticaria and angioedema. Urticaria is characterised by erythematous raised papules with clear borders and intense itching resulting from swelling of the surface layers of the dermis. Elements have different sizes, can merge, usually appear on the face, neck, torso within a few minutes to two hours after exposure, and exist for up to 24 hours (Oakley, 2021). Angioedema is a deeper swelling of the subcutaneous tissue and mucous membranes with a painful feeling of bursting, most often in the periorbital area, lips, tongue. Especially dangerous is angioedema of the upper respiratory tract with the risk of obstruction and asphyxia, which requires immediate administration of epinephrine. Exacerbation of atopic dermatitis as a delayed reaction is observed in children with increased erythema, dryness, lichenisation in typical locations 6-48 hours after eating causative vegetables (Memon and Tiwari, 2023).

Gastrointestinal symptoms range from mild dyspeptic disorders to severe systemic reactions. Nausea occurs within 30 minutes to 2 hours, vomiting can be repeated with spasmodic abdominal pain. Diarrhoea develops within 1-4 hours, is characterised by watery stools with an admixture of mucus, and may be profuse with a risk of dehydration (Nowak-Węgrzyn *et al.*, 2017). Food protein-induced enterocolitis syndrome (FPIES) is a non-IgE-mediated reaction in infants with delayed onset after 1-4 hours, classically manifested by repeated vomiting, lethargy, pallor, hypotension, and in severe cases hypovolemic shock. Diagnosis is complicated by negative standard allergy tests due to T-cell mechanisms.

Respiratory symptoms as isolated manifestations are rare, more often occurring when cross-reacting with pollen allergens or inhaled exposure during cooking vegetables. Rhinitis is manifested by itchy nose, sneezing, rhinorrhoea. Bronchospasm with wheezing, coughing, shortness of breath most often occurs during inhalation exposure to aeroallergens in food industry workers (Roberts and Lack, 2003).

Systemic anaphylaxis is the most severe manifestation with an acute onset and rapid progression of polysystemic symptoms. Clinical presentation: prodromal symptoms (generalised itching, feeling hot, anxiety), generalised urticaria, angioedema, difficulty breathing, abdominal cramps, vomiting. Cardiovascular collapse is manifested by tachycardia, hypotension, dizziness, and can progress to loss of consciousness. The World Allergy Organisation's diagnostic criteria include acute skin/mucosal lesions with respiratory and/or cardiovascular symptoms (Cardona *et al.*, 2020). The Ring and Messmer classification distinguishes four degrees from generalised skin symptoms to cardiac arrest (Dewachter and Savic, 2019).

Atypical manifestations include contact urticaria with skin contact during cooking vegetables (Apiaceae, Solanaceae, Alliaceae) and food-dependent physical activity anaphylaxis, where symptoms occur only when eating certain vegetables is combined with physical activity for 2-4 hours (Feldweg, 2017). The variability of symptoms depends on the method of preparation (heat treatment denatures labile allergens), the amount of product, concomitant factors (alcohol, NSAIDs, infections, physical exertion) and individual characteristics (age, asthma, use of beta-blockers).

A detailed allergic history is the foundation of diagnosis. A structured survey should include symptom characteristics, temporal association with exposure, exposure to cooking, concomitant factors, and family history of atopy. A food diary with a record of products, time, quantity, and symptoms allows identifying causal relationships, especially with delayed reactions.

2.2 Methods for diagnosing vegetable allergies

Diagnosis of vegetable allergies requires an integrative approach that combines a detailed medical history with *in vivo* and *in vitro* methods. The systematic survey should cover the identification of suspected vegetables, the detailed characterisation of symptoms by organ systems, the time connection (IgE-mediated reactions – minutes to two hours, non-IgE-mediated reactions – hours to days), the minimum amount of product that causes symptoms, and the impact of food processing. Thermolabile allergens (profilins, some PR proteins) are denatured by temperature treatment, so reactions occur only on raw vegetables, while thermolabile allergens retain their allergenicity after cooking or frying (Haidar *et al.*, 2025). Information about concomitant factors (physical activity, alcohol, NSAIDs), family and personal atopic history increases the pre-test likelihood of allergies.

Skin prick tests are the main method of *in vivo* diagnosis due to their speed, safety, and high negative prognostic value. Commercially standardised extracts have limitations due to the destruction of labile allergens during production. The prick-to-prick method with native fresh vegetables solves this problem by demonstrating higher sensitivity to labile allergens (Rancé *et al.*, 1997; Ansotegui *et al.*, 2020). The procedure includes applying an allergen drop to the forearm, puncturing the epidermis with a special lancet, with mandatory positive (histamine 10 mg/mL) and negative controls. Results are evaluated after 15-20 minutes, and a papule ⩾3 mm is considered positive. A positive test confirms sensitisation, but not necessarily a clinical allergy. False positive results occur with dermatographism, too concentrated extracts, false negative – with the use of antihistamines (withdrawal in 3-7 days), insufficient skin reactivity, outdated extracts. Contraindications: a history of severe reactions, uncompensated asthma, active urticaria, pregnancy. Precautions include styling for anaphylaxis with epinephrine, monitoring 20-30 minutes after testing.

Determination of specific serum IgE provides an objective assessment of sensitisation without discontinuation of antihistamine therapy and without the risk of systemic reactions. ImmunoCAP is the most proven method with high sensitivity, specificity, and inter-laboratory reproducibility. Levels ⩾0.35 kU/L are typically positive, >0.70 kU/L is clinically relevant, and >17.5-100 kU/L is associated with a high probability of reactions. However, the correlation between IgE levels and clinical reactivity is imperfect due to the significant overlap between tolerant and allergic patients. Limitations include asymptomatic sensitisation in cross-reactivity, inability to differentiate from asymptomatic sensitisation without challenges, and low sensitivity to labile allergens (Popescu and Vieru, 2018).

Molecular allergodiagnostics allows determining IgE for individual allergenic proteins instead of whole extracts, providing a detailed molecular sensitisation profile. ImmunoCAP ISAC is a

multiplex system for simultaneous detection of IgE up to >110 components (Matricardi *et al.*, 2016). PR-10 proteins (Api g 1, Dau c 1) – homologues of Bet v1, thermolabile, are associated with mild oral allergy syndrome. Profilins (Api g 4, Dau c 4) – actin-binding proteins 12-15 KDA, highly stable, clinical significance is limited to oral symptoms. nsLTP (Lyc e 3 in tomatoes), a 9 kDa heat-resistant protein that is resistant to digestion, is associated with a high risk of systemic reactions, including anaphylaxis, even after heat treatment. The results allow differentiating primary sensitisation from cross-reactivity, predicting the severity of reactions, and guiding recommendations for elimination and the possibility of using heat-treated products. Limitations: high cost, limited availability, and the need for expert interpretation.

Oral challenge tests are the gold standard for definitive confirmation of clinical reactivity and dose threshold determination. Protocols include open-label, single-blind, and double-blind placebo-controlled tests (DBPCFC), the latter being the most objective (Sampson *et al.*, 2012). Preparation: withdrawal of antihistamines for 3-7 days, controlled asthma (FEV1 >70%), no infections and fever. The initial dose is determined by anamnesis: 1-10 mg of protein for severe reactions, 100-500 mg for moderate reactions, 1-2 g for low probability. Typical protocol: 6-10 doses, doubling every 15-30 minutes to the age portion or objective symptoms. Discontinuation criteria: urticaria, angioedema, wheezing, vomiting, blood pressure reduction >20%, FEV1 reduction >20%. Absolute need for controlled conditions with stacking for anaphylaxis (epinephrine 0.01 mg/kg IV, antihistamines, corticosteroids, beta-2 agonists, intubation equipment, oxygen, venous access) and trained personnel. Follow-up 2+ hours with a negative result, until complete stabilisation with a positive one. Contraindications: history of anaphylactic shock, uncompensated asthma (FEV1 <70%), acute infections, pregnancy, use of beta-blockers/ACE inhibitors.

Additional methods include the basophilic activation test (BAT), which evaluates CD63/CD203c expression after incubation with the allergen *in vitro* by flow cytometry, has advantages in testing native allergens without standardised extracts (Hoffmann *et al.*, 2015). Limitations: high cost, non-responder phenomenon of 5-10%, lack of standardisation. Atop patch tests for non-IgE-mediated reactions have insufficiently proven value for vegetable allergies. Elimination-challenge diets are useful in difficult cases: complete elimination for 2-4 weeks, gradual re-introduction at intervals of 3-7 days.

Integrative approach: diagnosis is based on the consistency of anamnesis, clinical manifestations, and results of multiple methods. With a high pre-test probability and positive skin/serological tests, the diagnosis is confirmed without challenges. If there is a discrepancy, molecular diagnostics with possible challenges is indicated. With a low probability and negative tests, an allergy is unlikely. Positive tests without a history of reactions require challenge to differentiate asymptomatic sensitisation from true allergies.

2.3 Differential diagnosis

Differential diagnosis of vegetable allergies requires systematic exclusion of conditions that mimic allergic reactions. A fundamental differentiation is made between true immunologically mediated reactions and non-allergic food hypersensitivity. Pharmacological reactions to biogenic amines (histamine, tyramine in tomatoes, spinach) cause histamine-like symptoms (redness, itching, headache) due to direct action without IgE (Maintz and Novak, 2007). Differences: dose dependence, lack of reactions with small amounts, negative allergic tests. Toxic reactions from contamination with pesticides, heavy metals, and microbial toxins occur in several individuals, are characterised by an epidemiological connection, and negative allergological tests.

Irritable bowel syndrome is the most common differential diagnosis. It is characterised by chronic abdominal pain associated with changes in bowel movements, flatulence according to Roman IV criteria (symptoms ⩾1 day/week for 3 months, onset ⩾6 months ago). Pathophysiology: visceral hypersensitivity, impaired motility, changes in the microbiota without structural abnormalities. Many patients report an increase after FODMAP-rich vegetables (onions, garlic, cauliflower, mushrooms, asparagus) due to fermentation with gas production and osmotic effect. Differences: chronic course of months to years, absence of atopic manifestations, variability depending on stress, negative allergological tests, improvement with a low-FODMAP diet without complete elimination (Nathani *et al.*, 2025).

Celiac disease is an autoimmune disease caused by gluten in HLA-DQ2/DQ8 carriers, characterised by atrophy of the villi of the small intestine. Clinically variable from classical malabsorption to atypical forms. Diagnosis: antibodies to tissue transglutaminase IgA (sensitivity/specificity >95%), to endomysium, deamidated gliadin peptides, consideration of total IgA (selective deficiency in 2-3%), endoscopic duodenal biopsy according to Marsh-Oberhuber, HLA-DQ2/DQ8 testing (negative practically excludes celiac disease). Non-celiac gluten sensitivity is diagnosed by exclusion after negative celiac disease and allergy tests due to DBPCFC challenge (MedlinePlus Genetics, 2020).

Inflammatory bowel diseases (Crohn's disease, ulcerative colitis) are manifested by an exacerbation after vegetables due to mechanical irritation with coarse fibres without an allergic mechanism. Crohn's disease: transmural granulomatous inflammation of any part of the digestive tract, segmental, with chronic diarrhoea often with blood, abdominal pain, weight loss, perirectal complications. Ulcerative colitis: diffuse superficial inflammation of the colon from the rectum proximally, bloody diarrhoea, faecal urgency, tenesmus. Diagnosis: faecal calprotectin/lactoferrin >50-100 µg/g, endoscopic changes (ulcers, pseudopolypes in UC; segmental lesions, paving stones in Crohn's disease), histological confirmation of chronic inflammation, non-caseating granulomas in Crohn's disease (Hong and Baek, 2024).

Eosinophilic gastrointestinal disorders are characterised by pathological eosinophilic infiltration without other causes of eosinophilia, a mixed Ige/non-IgE mechanism, and frequent association with food triggers. Eosinophilic oesophagitis: dysphagia, food impaction in adults, reflux symptoms in children, >15 eosinophils/field of view on oesophageal biopsy without PPI response (Dellon *et al.*, 2018). Endoscopic signs: linear furrows, white exudates, ring-shaped constrictions. Elimination diets lead to an improvement of 70-80%, vegetables are less likely to cause compared to milk, wheat, eggs. Differentiation: histological confirmation of eosinophilia, chronic progressive course, the need not only for diet but also for pharmacotherapy.

Infectious causes: bacterial toxicoinfections (Salmonella, Campylobacter, E. coli O157: H7) are manifested by acute diarrhoea, often with blood, abdominal pain, fever a few hours or days after contaminated vegetables. Epidemiology: disease clusters, association with outbreaks (E. coli with spinach, Salmonella with tomatoes). Diagnostics: microbiological examination of faeces, PCR. Parasitic infestations (Giardia, Cryptosporidium) through contaminated vegetables are manifested by chronic diarrhoea, malabsorption. Viral gastroenteritis (noroviruses, rotaviruses): acute watery diarrhoea, vomiting, short incubation period of 12-48 hours, self-limiting course of 1-3 days. Differentiation from allergies: acute onset in a pre-tolerant person, systemic symptoms of infection (fever, myalgia), epidemiological relationship, positive microbiology, negative allergological tests (Interagency Food Safety Analytics Collaboration, 2024). Psychogenic disorders with fixation on food triggers: somatisation disorder, ARFID in children, orthorexia in adults manifest as self-di-

agnosed multiple allergies without confirmation. Signs: discordance of subjective complaints and objective results, disproportionately restrictive diet, positive open but negative double-blind provocations, concomitant anxiety/depressive disorders (Teufel *et al.*, 2007; De Toro *et al.*, 2020). Management requires a multidisciplinary approach with psychologists, cognitive behavioural therapy.

Mastocytosis and mast cell activation syndrome are rare but important differential diagnoses with allergy-like symptoms but from abnormal proliferation or spontaneous degranulation of mast cells without IgE. Mastocytosis: cutaneous (more common in children, may regress) and systemic (adults, chronic progressive) with bone marrow infiltration (Valent *et al.*, 2017). Criteria: large-multifocal dense mast cell infiltrates in biopsies; small-atypical morphology, KIT D816V mutation, CD25/CD2 expression, basal tryptase >20 ng/mL. Mast cell activation syndrome: episodic symptoms of degranulation, increased tryptase during episodes (basal +20% +2 ng/mL), response to mast cell stabilisers. Differentiation: unpredictable episodes without a clear link to products, multiple non-specific triggers, basal tryptase between episodes, negative allergy tests.

Differentiation algorithm: detailed medical history determines the nature of symptoms, association with exposure, time profile, and atopic history. In acute episodic symptoms after eating, an allergy is suspected-skin tests/specific IgE, positive ones confirm sensitisation but require correlation with anamnesis or challenging. With chronic symptoms without a clear connection, functional disorders, IBD, and psychosomatics are suspected. Negative allergy tests refer to non-IgE-mediated reactions or non-immunological causes. For chronic gastrointestinal symptoms: celiac disease screening (anti-tTG), IBD (faecal calprotectin), if necessary, endoscopy with biopsy. Elimination-challenge diets with uncertain results. Psychological assessment in case of discordance of subjective/objective findings.

2.4 Cross-allergic reactions

Cross-reactivity is a critical phenomenon in the understanding of vegetable allergies, since most reactions in adults are secondary to pollen sensitisation. The molecular basis consists of structural homology between allergenic proteins of different origins, where IgE to the primary allergen recognises similar epitopes on homologous proteins. Linear epitopes (a sequence of amino acids) can be preserved after denaturation, conformational (three-dimensional structure) are destroyed during heat treatment, pH changes, and digestion (Sharma and Vitte, 2024). Conserved functional domains of proteins (profilins, PR proteins) are preserved between phylogenetically distant species due to important biological functions. Sequence homology >50-70% is associated with a high probability of cross-reactivity.

Pollen-food allergy syndrome affects 50-90% of adults with polyposis, depending on the region and the specifics of sensitisation, usually manifests as oral allergy syndrome after fresh raw vegetables. Birch-nut-fruit syndrome: sensitisation to Bet v 1 (PR-10 protein of 17 kDa birch pollen) with cross-reactions to Apiaceae (celery, carrot via Api g 1, Dau c 1 with 57-58% homology), Solanaceae (potato), Rosaceae fruits, nuts. PR-10 proteins are highly stable, rapidly denatured in the stomach and during heat treatment, so clinical manifestations are limited to mild oral symptoms, and patients often tolerate heat-treated vegetables (Skypala *et al.*, 2013). Wormwood-food syndrome is associated with wormwood Art v 1 with reactions mainly to Apiaceae, predominant in Central Europe, often more severe reactions due to additional sensitisation to celery profilins and nsLTP. Ambrosia-melon syndrome: Ambrosia with reactions to Cucurbitaceae (cucumbers, zucchini) due to profilins, common in North America. May polyposis is associated with reactions to tomatoes through profilins, low clinical significance.

Panallergens are protein families widely distributed in plants that are responsible for multiple cross-reactions. Profilins are actin-binding proteins of 12-15 kDa, present in almost all plants, 70-85% consistent homology between species. Vegetable profilins (Api g 4, Dau c 4, Lyc e 1) cross-react with pollen profilins (Bet v 2, Phl p 12, Art v 4) (Sánchez-Salguero, 2014; Rydzyńska *et al.*, 2025). Highly resistant to heat treatment (>60-70°C) and digestion, so sensitisation is associated with mild oral symptoms. Clinical significance is often overestimated-positive IgE may reflect asymptomatic cross-reactivity. Practical: patients can consume heat-treated vegetables, avoiding excessive restrictions on multiple sensitisation to different vegetables, which actually reflects a single sensitisation to profilin.

PR proteins are divided into 17 families. PR-10 (Bet v 1 homologues) – most clinically significant in Northern/Central Europe, β-leaf structure, thermolabile, sensitive to acidic pH, associated with mild oral allergy syndrome although there are reports of systemic reactions. nsLTP (PR-14) are small thermostable proteins of 9 kDa concentrated in the skin, the compact structure with four disulphide bonds makes them resistant to heat treatment (>100°C) and pepsin digestion, so sensitisation is associated with a high risk of systemic reactions including anaphylaxis even after heat treatment (Han and Schneiter, 2024). Lyc e 3 tomatoes are associated with severe reactions, especially in the Mediterranean, where primary sensitisation to Ole e 7 olives leads to cross-reactions. Geographical variability: PR-10 dominates Northern Europe (birch-associated syndrome, mild symptoms), nsLTP in the Mediterranean (more severe systemic reactions, often food-dependent physical activity anaphylaxis).

Latex-fruit-vegetable syndrome: latex allergy with reactions to avocados, bananas, chestnuts, kiwis, tomatoes, potatoes, peppers due to hevein-like proteins or chitinases (PR-3, PR-4, PR-8). 30-50% of patients with latex allergies show reactions to related products (Wagner and Breitenederer, 2002). Class 1 chitinases are thermally stable and resistant to digestion, so latex-associated food allergies can manifest themselves systemically. Cross-reactivity in botanically related families is expected (Apiaceae among themselves, Solanaceae are less predictable). Between distant species, it is mediated by panallergens, especially profilins.

Molecular diagnostics can differentiate primary sensitisation from cross-reactivity. Marker allergens indicate primary sensitisation (Bet v 1 for birch), cross-reactive ones reflect secondary sensitisation (Api g 1 at high Bet v 1 = cross-reactivity; high Api g 1 at low Bet v 1 = primary celery allergy with a higher risk of severe reactions). Sensitisation profiling to multiple components establishes a molecular profile: exclusively labile allergens (PR-10, profilins) = low risk of systemic reactions, possibility of heat treatment; stable (nsLTP) = complete elimination regardless of preparation (Dramburg *et al.*, 2023). Inhibition tests (ELISA inhibition) confirm common epitopes. Clinical validation through challenge tests remains the gold standard because *in vitro* cross-reactivity is not always clinically significant.

Practical significance of component diagnostics: individualisation of elimination diets (labile allergens – can be heat treatment, stable – complete elimination), foresight of the possibility of heat treatment avoiding unnecessary restrictions in birch-associated syndrome, risk assessment of anaphylaxis (nsLTP = high risk, possible appointment of epinephrine autoinjectors; labile = low risk, epinephrine is usually not required), planning challenges (labile allergens – test with fresh raw product then heat-treated; stable – start with heat-treated is safer).

The recommendations for clinicians are a balanced approach to the management of patients with multiple sensitisation. It is important to remember that the presence of specific IgE or positive skin tests does not always correspond to clinically significant allergies: asymptomatic sensitisation

to pan-allergens, especially profilins and PR-10 proteins, is common and does not require preventive exclusion of products that the patient tolerates well. Geographical features of sensitisation are key to interpreting the results (birch pollen in Northern Europe, wormwood in Central Europe, ragweed in North America, nsLTP sensitisation in the Mediterranean countries). Clinical history remains a crucial criterion for risk assessment, so regular consumption of heat-treated tomatoes without reactions confirms tolerance, regardless of positive IgE. In children, dynamic monitoring should be carried out considering the possibility of forming tolerance to thermolabile allergens, while sensitisation to thermolabile proteins is more often preserved. Effective patient management involves interdisciplinary interaction between an allergist, dietitian, and gastroenterologist, which allows balancing safety by reasonably eliminating really dangerous products while maximising the nutritional usefulness of the diet and the quality of life of the patient.

CHAPTER 3.

Allergy to solanaceous vegetables

Solanaceae are an integral part of world cuisine, but they pose a significant allergic problem for a certain category of patients. The family Solanaceae includes more than 2,000 species, including tomatoes (*Solanum lycopersicum*), potatoes (*Solanum tuberosum*), eggplants (*Solanum melongena*), and various types of peppers (Capsicum spp.). Allergic reactions range from mild local manifestations of oral allergy syndrome to severe systemic reactions, including anaphylaxis. According to recent epidemiological studies, the prevalence of allergy to Solanaceous vegetables in the general population is 1.5-3%, but among patients with pollinosis, this figure increases to 8-12% (Tomás-Pérez *et al.*, 2019). A special feature of Solanaceous allergy is a complex network of cross-reactivity with other botanical families, which significantly complicates diagnosis and therapeutic management.

3.1 Tomatoes (*Solanum lycopersicum*)

3.1.1 Molecular characteristics of tomato allergens

Tomatoes are one of the most common triggers of food allergies among Solanaceous vegetables (Fig. 1). To date, seven major allergens have been identified, which are officially registered in the WHO/IUIs Allergen Nomenclature Sub-committee database. Sola l 1 is a profilin with a molecular weight of 14 kDa, which is responsible for cross-reactivity with birch, grass, and wormwood pollen. This allergen is thermolabile and rapidly degrades when heat treated above 70°C, which explains the clinical phenomenon of tolerance to heat-treated tomatoes in patients with profilin-mediated allergies (Popescu, 2015; WHO/IUIs Allergen Nomenclature Sub-Committee, 2019d).

Figure 1. Tomatoes (*Solanum lycopersicum*)

The WHO/IUIs Allergen Nomenclature Sub-Committee database lists seven major tomato allergens belonging to different protein families and showing a wide range of thermal stability and clinical significance. Table 6 provides a brief description of their structure, stability, and role in cross-reactivity.

Table 6. Main allergens in tomatoes (*Solanum lycopersicum*) and their characteristics

No.	Allergen	Protein type / family	Molecular weight (kDa)	Basic properties	Thermal stability	Clinical significance / cross-reactivity
1	Sola l 1	Profilin	~14	Cross-reactivity with birch, grass, and wormwood pollen	Thermolabile (>70°C destructible)	Oral allergic syndrome in patients with pollen allergy
2	Sola l 2	β-phrasin / PR-10 protein	~17	Homologue Bet v 1 (Birch)	Thermolabile	Cross-reactivity with birch pollen
3	Sola l 3	nsLTP (lipid transporter protein)	~9	Main marker of severe systemic reactions	Highly stable (up to 100°C, proteases)	Severe systemic reactions, Mediterranean phenotype
4	Sola l 4	Polygalacturonase	~45	Cell wall enzyme	Moderately stable	May cause IgE-binding in sensitised vegetables

Table 6, Continued

No.	Allergen	Protein type / family	Molecular weight (kDa)	Basic properties	Thermal stability	Clinical significance / cross-reactivity
5	Sola l 5	Glycoprotein (CCD-positive)	~33	Contains carbohydrate determinants	Stable	Can give false positive sIgE results
6	Sola l 6	Glycoprotein (CCD-positive)	~35	Similar properties to Sola l 5	Stable	Can cause false positive results
7	Sola l 7	LTP homologue or PR-14 protein	~9	Possible marker of cross-reactivity	Highly stable	Rare, described in several patients

Source: *based on WHO/IUIs Allergen Nomenclature Sub-Committee (2019d).*

The combination of tomato allergens forms a complex molecular profile that explains the variety of clinical manifestations – from mild oral symptoms to severe systemic reactions. Understanding their structural features is essential for accurate diagnosis, interpretation of the results of component allergodiagnostics, and development of individual recommendations for product elimination.

3.1.2 Cross-reactivity and clinical syndromes

The cross-reactivity of tomatoes with aeroallergens forms a complex network, where profilins and PR-10 proteins play a leading role. Patients with pollinosis, in particular, those sensitised to birch, grasses and wormwood, often develop oral allergy syndrome to fresh tomatoes due to cross-reactivity of profilins. According to clinical and review studies, sensitisation to profilin in European pollen cohorts occurs in approximately 5-26% of patients, and in one study, 38% of patients with rhinitis/asthma had simultaneous sensitisation to grass and tomato pollen, with 92% of them to tomato profilin. In patients with birch pollinosis, approximately 9% report clinical reactions to tomatoes; a significant proportion of birch-associated cases are caused by PR-10 Sola l 4 protein (and not just Sola l 1 profilin) (Rodríguez del Río *et al.*, 2018).

Cross-reactivity is mainly associated with profilins (Sola l 1) and PR-10 proteins (Sola l 4), which have a high degree of homology with Bet v 1 and Bet v 2, so OAS is more common in patients with birch, grass, and wormwood pollinosis. Cases of cross-reactivity between tomatoes and other representatives of Solanaceae (potatoes, eggplants, peppers) are also described, but the frequency of such reactions varies and does not have consistently confirmed epidemiological indicators. LTP-mediated tomato allergy is the greatest clinical challenge, as it is associated with severe systemic reactions, including generalised urticaria, angioedema, bronchospasm, and anaphylaxis. In Mediterranean countries, LTP sensitisation is the leading cause of food anaphylaxis in adults. An important feature of LTP-mediated reactions is the phenomenon of cofactor anaphylaxis, when systemic reactions occur only when exposed to additional factors, such as exercise, nonsteroidal anti-inflammatory drugs (NSAIDs), alcohol, or acute infections (Jara-Toro *et al.*, 2020).

Oral allergy syndrome (OAS), or pollen-food allergy syndrome (PFAS), is characterised by itching, tingling, burning, and moderate swelling of the lips, tongue, palate, or pharynx within 5-15 minutes of eating raw tomatoes. Symptoms are usually limited and disappear within 30-60 minutes.

3.1.3 Diagnostic approaches and clinical phenotypes

Diagnosis of tomato allergy requires a comprehensive approach. Due to the variability of commercial extracts, skin prick tests (SPT) with them show low and unstable sensitivity, which can lead

to false negative results. But the prick-to-prick test with fresh tomatoes has a significantly higher diagnostic information content, since it preserves the natural profile of allergens, including thermolabile components (PR-10, profilins).

Component resolved diagnosis (CRD) allows differentiating clinically significant mechanisms of sensitisation to tomatoes. sIgE to rSola l 1 (profilin) indicates profilin-mediated reactivity, usually manifested by mild oral symptoms with preserved tolerance to heat-treated tomatoes. Sige-positive rSola l 3 (LTP) is a marker of high risk of systemic reactions, including anaphylaxis. Currently, sIgE thresholds predicting response severity for Sola l 3 are not standardised, and clinical risk determination should be based on a combination of medical history, CRD results, and challenge tests (Włodarczyk *et al.*, 2022).

Based on the molecular sensitisation profile, four main phenotypes of tomato allergy are distinguished (Table 7)

Table 7. Phenotypes of tomato allergy

Phenotype	Key features confirmed
Profilin-associated PFAS (Sola l 1)	Mild oral symptoms; tolerance to cooked food; association with pollinosis.
LTP-mediated systemic allergy (Sola l 3)	High risk of systemic reactions / anaphylaxis; thermal stability; reactions to all forms of tomatoes.
Latex-fruit syndrome (chitinase / gevein-like proteins)	Cross-reactivity with latex, often accompanied by reactions to banana/avocado/chestnut.
Isolated tomato allergy without cross-reactivity	Sensitisation to unique tomato proteins; clinically rare.

Source: *based on K. Włodarczyk et al. (2025).*

Isolation of profilin-associated, LTP-mediated, latex-associated, and isolated phenotypes helps to clearly differentiate the mechanisms of allergic response and choose individual patient management tactics. This approach improves diagnostic accuracy, avoids unjustified dietary restrictions, and helps to reduce the risk of severe systemic reactions in high-risk groups.

3.2 Potato (*Solanum tuberosum*)

3.2.1 Allergenic components of potatoes

Potatoes are one of the most important agricultural crops, but allergies to them remain relatively rare, since heat treatment significantly reduces allergenicity (Fig. 2). Four main allergens were identified. Sol t 1 is patatin, a glycoprotein with a molecular weight of 40-43 kDa, which accounts for up to 40% of total potato protein (*Solanum tuberosum*) and is considered the main clinically significant allergen of this vegetable. Potato profilin, known as Sol t 4, is a pan-allergen structurally homologous to tomato Sola l 1 and birch Bet v 2, and is responsible for cross-reactivity with pollen allergens. Sol t 2 is described as a less common allergen with limited clinical significance.

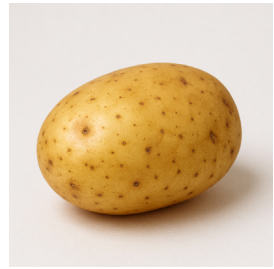

Figure 2. Potato (*Solanum tuberosum*)

Several proteins have been identified in potatoes that can cause IgE-mediated reactions of varying severity. These allergens belong to different protein families, from reserve proteins to pan-allergens, and are characterised by significant variability in stability and clinical significance. Table 8 shows the main identified potato allergens registered in international databases.

Table 8. Main allergens in potatoes (*Solanum tuberosum*) and their characteristics

No.	Allergen	Protein type / family	Molecular weight (kDa)	Basic properties	Thermal stability	Clinical significance / cross-reactivity
1	Sol t 1	Patatin (glycoprotein, reserve protein)	40-43	It makes up to 40% of the total tuber protein; the main allergen of potatoes	Highly stable (retains IgE binding after heating)	Often causes skin and respiratory symptoms in food and occupational allergies
2	Sol t 2	Unspecified protein (alternative isoform of reserve protein)	~22	Less common allergen	Moderate	Limited clinical significance
3	Sol t 3	Cysteine proteinase inhibitor (PR-like protein)	20-22	Resistant to proteolytic enzymes and heat	High	Potentially associated with systemic reactions
4	Sol t 4	Profilin (pan-allergenic)	~14-15	Homologue of Sola l 1 (tomato), Bet v 2 (birch); causes cross-reactivity with pollen	Thermolabile	Oral allergic syndrome in patients with pollen sensitisation

Source: *based on F. Carolino et al. (2016) and WHO/IUIs Allergen Nomenclature Sub-Committee (2019a).*

The allergenicity of potatoes significantly depends on the processing method. Cooking leads to partial denaturation of profilin and a decrease in its allergenicity by 70-80%, while patatin exhibits intermediate thermal stability, losing only 30-50% of its IgE binding capacity after 20-30 minutes of boiling. Potato starch should contain less than 0.5% protein according to international standards, but this may be sufficient to provoke symptoms in some patients (Seppälä *et al.*, 2001).

3.2.2 Clinical manifestations and occupational allergies

Clinical manifestations range from oral allergy syndrome to severe systemic reactions. The most common form is OAS in patients with pollinosis when eating raw or undercooked potatoes. Gastrointestinal symptoms (nausea, vomiting, abdominal pain, diarrhoea) develop 1-6 hours after use. Anaphylaxis is rare (less than 5%), but isolated cases of severe reactions have been described. Patients with tomato allergies have an increased risk of developing potato allergies – approximately 30-35% show positive skin test results, although only 10-15% develop clinically significant reactions (Gungor *et al.*, 2016).

Occupational allergy to potatoes is most often manifested in workers who regularly come into contact with raw potatoes, especially in the field of public catering and the food industry. Typical are contact urticaria or contact allergic dermatitis, which occurs after repeated skin exposure to potato protein components. Employees of potato washing, cleaning, and processing enterprises also have the described respiratory symptoms caused by inhalation of potato juice aerosols and organic dust. The development of specific IgE to potato allergens has been confirmed in some sensitised workers, but the incidence of clinically significant occupational allergies remains low and varies significantly between production conditions. Therefore, the diagnosis should be based on

anamnesis, prick-to-prick testing with raw potatoes and sIgE determination, and, if necessary, on controlled challenge tests (Lukács *et al.*, 2016).

3.2.3 Differential diagnosis

An important aspect is the differentiation between true IgE-mediated allergies and intolerances. Starch intolerance can be caused by malabsorption due to amylase deficiency, which leads to gastrointestinal symptoms due to fermentation by the intestinal microbiota. The high glycaemic index of potatoes can cause reactive hypoglycaemia. Solanine and other glycoalkaloids accumulated in green or sprouting potatoes can cause toxic reactions with nausea, vomiting, and neurological symptoms that are not immunologically mediated (Zuvarov *et al.*, 2025).

3.3 Eggplant (*Solanum melongena*)

3.3.1 Epidemiology and allergenic profiles

Eggplant allergy is rare, but it is more often described in regions with high consumption of this product (South Asia, the Middle East, the Mediterranean) (Fig. 3). In clinical practice, eggplant is more likely to cause symptoms in patients with pre-existing sensitisation to other Solanaceous or pollen allergens. The main immunologically significant allergen is profilin *Sola m 1*, which causes cross-reactivity, in particular, with ragweed and birch pollen. Eggplant also describes a heat-resistant protein of the nsLTP family (~9 kDa), which may be associated with more systemic reactions. An important feature of eggplant is that it can contain elevated concentrations of histamine (approximately 15-35 mg/kg, depending on the variety and storage conditions), which can cause pseudoallergic reactions in patients with histamine intolerance and clinically mimic IgE-mediated allergies (Mait *et al.*, 2020).

Figure 3. Eggplant (*Solanum melongena*)

3.3.2 Clinical manifestations and association with nickel allergy

Clinical manifestations of eggplant allergy can range from mild local symptoms to systemic reactions. The most common is oral allergy syndrome, which is manifested by itching, tingling, or burning of the oral mucosa and lips shortly after consuming the product (usually within the first minutes). Some patients may experience skin symptoms such as urticaria or angioedema. Gastrointestinal symptoms (nausea, abdominal pain, diarrhoea) are described mainly in patients with more severe sensitisation or concomitant histamine intolerance.

Anaphylaxis when eating eggplant is rare, but can occur in patients with sensitisation to stable proteins, mainly nsLTP, which can cause systemic reactions regardless of heat treatment (Bheemanapalli and Veldur, 2009).

In some patients with systemic nickel allergic syndrome (SNAS), the use of products containing food-grade nickel can provoke exacerbation of skin manifestations (eczematous rash, exacerbation of contact dermatitis) and gastrointestinal symptoms. Solanaceous vegetables, including eggplant, are considered foods that may contain nickel in moderate concentrations, and

therefore can cause symptoms in sensitive patients. SNAS is most commonly described in people with a history of contact allergic dermatitis to nickel, mainly in women. In such patients, a diet restricted to nickel-containing foods may reduce the frequency and intensity of symptoms (Ahlström *et al.*, 2019).

3.3.3 Diagnostics and practical recommendations

Diagnosis of eggplant allergy is based on a detailed allergic history, skin testing (SPT or prick-to-prick with fresh product) and determination of specific IgE with interpretation in the context of the clinic, since there are no universal thresholds for sIgE, and prick-to-prick sensitivity for eggplant is not validated; in case of doubt, controlled oral challenge remains the "gold standard". The differential diagnosis should take into account pseudoallergic reactions to dietary histamine, which are evaluated using a short-term (approximately 2-4 weeks) low-histamine diet followed by controlled reintroduction, as well as systemic nickel allergic syndrome, for which nickel patch testing is used and, if necessary, the response to a nickel-restricted diet is evaluated or oral challenge is performed in specialised conditions. The elimination diet for eggplant allergy requires complete elimination of all forms of this vegetable. Eggplant is widely used in Mediterranean, Middle Eastern, and Asian cuisine (moussaka, babaganush, ratatouille). Patients with LTP sensitisation may need to limit other LTP-containing products. For systemic nickel allergy, a low-nickel diet is recommended, limiting not only eggplant, but also other foods with a high nickel content (Ukleja-Sokołowska *et al.*, 2018).

3.4 Bell pepper (*Capsicum annuum*)

3.4.1 Allergens and irritants

Bell pepper presents a unique diagnostic challenge due to the coexistence of true allergenic proteins and irritant substances (Fig. 4). Allergenic components include profilin (Cap a 2) and thaumatin-like protein (Cap a 1). The presence of the Cap a 7 – gibberellin-regulated protein (snakin) allergen with a molecular weight of approximately 10-12 kDa has also been officially confirmed, which may be a marker of more severe systemic reactions to sweet/bell peppers (WHO/IUIS Allergen Nomenclature Sub-Committee, 2023). Capsaicin and other capsaicinoids are alkaloids that elicit nonimmunological responses by activating TRPV1 receptors. Sweet peppers contain minimal concentrations of capsaicin (0-50 Scoville units), while spicy varieties contain significant amounts (2,500-350,000 units).

Figure 4. Bell Pepper (*Capsicum annuum*)

Non-allergic reactions to capsaicin are clinically different: they occur at the first contact without prior sensitisation, depend on the concentration, quickly regress after discontinuation of exposure, and are not accompanied by systemic manifestations. True allergies require prior sensitisation, can occur at minimal doses, are accompanied by the production of specific IgE, and can manifest as systemic reactions (Takei *et al.*, 2022).

3.4.2 Occupational risks and diagnostics

Occupational allergy to pepper (Capsicum) is observed in workers of greenhouses, food industry, and cooks: after repeated contact with fresh peppers, skin reactions are described – primarily irritating contact dermatitis ("chili burn") and contact urticaria – in food workers and other exhibited persons. Respiratory forms are manifested by occupational rhinitis and asthma: in a cross-sectional study of greenhouses working with sweet peppers (n = 472), working respiratory symptoms were 53.8%, and sensitisation to pepper components was 35.4% (pollen was the key allergen); in an 8-year follow-up in the same area, the cumulative incident rate was 9% for sensitisation, 19% for rhinitis, and 8% for asthmatic symptoms. In spice mill workers, "asthma-like" symptoms occurred in 17%, sensitisation (mainly to garlic, with cosensitisation to chili) – in 19%, and objective flow reversibility (a sign of asthma) – in 4%. Diagnosis is based on a detailed professional medical history, keeping a symptom diary with serial measurements at/outside work (for rhinitis – peak nasal inspiratory rate; for asthma – serial peak expiratory flow), skin prick tests and specific IgE for pollen / capsicum fruit or spice mixtures, and – if appropriate expertise is available – specific nasal or inhalation challenge tests to confirm occupational respiratory allergy (Patiwael *et al.*, 2010).

The diagnosis of pepper allergy requires differentiation between IgE-mediated allergies and irritant reactions. Prick-to-prick tests with fresh pepper are the method of choice. It is important to use the same pepper variety that caused the reaction, as allergenic profiles vary between sweet and spicy varieties. Determination of sIgE for bell pepper (f218) or chili pepper (f279) has moderate diagnostic value with a sensitivity of 60-75%. Allergenic profiles vary significantly between different pepper varieties and colours (Jensen-Jarolim *et al.*, 1998; Callero *et al.*, 2018).

3.5 Clinical cases and practical experience

Allergological problems of Solanaceous vegetables are characterised by significant clinical heterogeneity, covering a wide range of manifestations – from mild local reactions of oral allergy syndrome to severe systemic anaphylactic reactions. Molecular diagnostics can identify specific allergenic profiles, such as thermolabile profilins, which cause cross-reactivity with pollen and are manifested mainly by oral symptoms when eating raw vegetables, and thermostable lipid carrier proteins, which are associated with a high risk of systemic reactions regardless of the method of preparation of the product. Cross-reactivity between different members of the Solanaceae family, and with latex, birch, grass, and wormwood pollen, creates a complex diagnostic network that requires an individual approach to each patient.

Professional exposure to Solanaceous vegetables forms a separate category of risk for employees of greenhouses, the food industry and public catering, where prolonged contact with raw products can lead to the development of both skin and respiratory forms of allergies. Differential diagnosis between true IgE-mediated reactions and pseudoallergic conditions caused by histamine, capsaicin, nickel, or toxic glycoalkaloids remains critical for proper therapeutic management. Component diagnostics, combined with careful medical history collection, prick-to-prick testing, and controlled challenge tests, allows establishing an accurate diagnosis and develop rational dietary recommendations, avoiding unjustified restrictions.

The clinical case below illustrates an atypical presentation of potato allergy that occurred after heat treatment of the product, which contradicts the widespread clinical observation of reduced allergenicity during cooking.

3.5.1 Clinical case: Allergy to boiled potatoes in young children

The observation concerns two paediatric patients with acute allergic reactions to boiled potatoes, which is clinically unusual, since heat treatment usually significantly reduces the allergenicity of this product.

Case 1. A two-year-old girl who had previously consumed potatoes in various forms without any problems suddenly reacted with erythema and swelling of both cheeks after one spoonful of boiled mashed potatoes without adding milk. Symptoms developed within minutes of consumption and appeared twice, as the mother found it difficult to believe that this was a reaction to potatoes as a mono-ingredient. During the second exposure, the clinical picture was repeated with a similar intensity of manifestations. Laboratory testing revealed an increased level of potato-specific IgE, which was 16.0 kUA/L, which is significantly higher than the threshold of 0.35 kUA/L and confirms IgE-mediated sensitisation.

Case 2. A boy aged 18 months developed a facial rash and swelling of the upper lip after consuming a small amount of boiled mashed potatoes without adding milk. Symptoms occurred a few minutes after consuming the product. During serological examination, the level of specific potato IgE was 25.0 kUA/L, which indicates a pronounced sensitisation and a high probability of a clinically significant allergic reaction.

Clinical analysis. Both cases show several important clinical features. Firstly, reactions occurred to boiled potatoes in the form of mashed potatoes prepared without the addition of milk, which eliminates the possibility of allergies to cow milk proteins as an alternative diagnosis. Secondly, the first patient developed an allergy after a period of tolerance to potatoes, which may indicate a phenomenon of loss of tolerance or an accumulation of sensitisation after repeated exposures. Thirdly, high levels of specific IgE in both cases correlate with clinical manifestations and confirm the IgE-mediated response mechanism.

The preservation of allergenicity after heat treatment in these cases is most likely associated with sensitisation to thermostable potato components. Patatin, which makes up a significant part of potato protein, shows intermediate thermal stability and retains 50-70% of its IgE binding capacity even after prolonged boiling. The cysteine proteinase inhibitor Sol t 3 is characterised by even higher thermal stability. Sensitisation to these components can explain the development of symptoms even after sufficient heat treatment of the product.

Differential diagnosis. In these cases, it was important to exclude other possible causes of reactions. The absence of milk in the puree eliminates allergies to cow milk proteins. The immediate development of symptoms after use and the presence of high titres of specific IgE exclude starch intolerance, which has a non-immunological mechanism and is mainly manifested by delayed gastrointestinal symptoms. The use of fresh, high-quality potatoes without signs of greening eliminates a toxic reaction to solanine and other glycoalkaloids.

Therapeutic management. Both patients were prescribed complete elimination of potatoes in all forms from the diet. Considering the age of children and the risk of developing more severe reactions with repeated exposures, parents were advised to carefully study the composition of finished products for the presence of potato starch and other potato ingredients. Families were given a prescription for an epinephrine injector for emergency care in case of accidental use and the development of a systemic reaction, and detailed instructions on the recognition of anaphylaxis symptoms and the algorithm of actions.

A routine re-examination to assess the natural evolution of allergies was scheduled after twelve months to determine the dynamics of specific IgE levels. In the case of a significant decrease in

antibody titres, the possibility of a controlled oral challenge test in a specialised allergological hospital may be considered to assess the possibility of reintroduction of the product. It was explained to parents that spontaneous potato tolerance can develop with age in some children, especially if the allergy is not associated with pollinosis or multiplex food allergies.

Conclusions from the clinical case. These observations highlight that heat treatment does not always guarantee product safety for sensitised patients. Potato allergies can develop even after a period of asymptomatic consumption, which requires caution against new food reactions. High levels of specific IgE correlate with the clinical significance of sensitisation and should be considered when assessing the risk of severe reactions. Pediatric patients with confirmed allergies to boiled potatoes require a strict elimination diet and emergency therapy due to the risk of accidental exposure and the possibility of progression to systemic reactions.

CHAPTER 4.

Cruciferous and Allium Vegetables

4.1 Cabbage (*Brassica oleracea*)

Cabbage is one of the most common representatives of the cruciferous family (Brassicaceae) in the diets of populations in Europe and Asia (Fig. 5). Despite its widespread consumption, allergic reactions to cabbage are reported rarely, mostly as isolated cases of food or contact allergy. In most observations, sensitisation involves proteins from the family of nonspecific lipid transfer proteins (nsLTP) or profilins, which may be shared with other vegetables and pollen allergens. Occupational sensitisation to cabbage may occur among workers in the food industry or greenhouses, but remains sporadic. Differential diagnosis requires exclusion of irritant reactions caused by sulphur-containing compounds typical of cruciferous vegetables (Thermo Fisher Scientific, 2022).

Figure 5. Cabbage (*Brassica oleracea*)

4.1.1 Molecular characterisation of allergens

In the official WHO/IUIS Allergen Nomenclature, only one allergen has been registered for *Brassica oleracea*: Bra o 3, which belongs to the family of nonspecific lipid transfer proteins (nsLTP1) with a molecular weight of about 9 kDa. This protein is characterised by high thermostability and resistance to proteolytic digestion, which explains its ability to retain allergenic properties after culinary processing. Bra o 3 is the only clinically relevant cabbage allergen associated with systemic reactions, especially in patients with LTP-sensitisation syndrome, which is common in the Mediterranean region. Other potential proteins (2S albumins, profilins, thiol proteases) that may be present in related species of the Brassicaceae family (e.g., Brassica juncea, Brassica napus) currently have no official confirmation as cabbage allergens (Palacín *et al.*, 2006).

Glucosinolates and their derivatives – isothiocyanates – are characteristic bioactive compounds of cruciferous vegetables, including cabbage (*Brassica oleracea*). They are formed under the action of the enzyme myrosinase during mechanical damage or chewing of plant tissue. These substances are not true allergens, but may cause pseudoallergic or irritant reactions in sensitive individuals due to their local irritating effect and their ability to influence inflammatory mediators without involvement of IgE mechanisms. The best-studied representatives include sinigrin, glucobrassicin, and glucoraphanin – the precursor of sulforaphane – whose concentrations in cabbage usually range from 20 to 120 mg/100 g of raw mass depending on variety, growing conditions, and processing (Verkerk *et al.*, 2009).

4.1.2 Cross-reactivity

Cabbage allergy is often accompanied by cross-reactivity with other members of the cruciferous family (Brassicaceae), such as broccoli, cauliflower, Brussels sprouts, and Savoy cabbage. This is explained by the presence of shared allergenic proteins, particularly profilins and nonspecific

lipid transfer proteins (nsLTP), which have similar epitopes. Although exact rates of cross-reactivity between different Brassica species have not yet been established, *in vitro* studies using molecular tests (ImmunoCAP, ImmunoCAP ISAC) demonstrate substantial overlap of sensitisation within this genus. Patients with primary sensitisation to Bra o 3 (LTP) generally have a higher risk of systemic reactions, but may sometimes tolerate thermally processed cabbage, whereas sensitisation to thermostable proteins from other Brassicaceae genera is associated with a higher likelihood of reactions even after boiling (Scott *et al.*, 2012).

Pollen-food allergy syndrome (PFAS) may be observed in patients sensitised to cruciferous vegetables, including cabbage, particularly in regions of Northern Europe where birch pollen allergy (Bet v 1) is highly prevalent. In such cases, the PFAS mechanism is generally linked to cross-recognition of profilins and PR-10 family proteins between pollen and foods. At the same time, for cabbage the component convincingly characterised to date is mainly the lipid transfer protein Bra o 3, whereas the involvement of PR-10-like components in PFAS formation remains largely theoretical, and clinical reports of PFAS specifically associated with cabbage are limited to isolated cases and small case series (Palacín *et al.*, 2006).

4.1.3 Effect of culinary processing

Thermal processing may reduce the allergenicity of cabbage, but quantitative data remain limited. In clinical practice, cases have been described where reactions occurred only to raw cabbage with good tolerance of boiled cabbage, suggesting the presence of thermolabile proteins that are inactivated during cooking (Vovolis *et al.*, 2009; Scott *et al.*, 2012). The main cabbage allergen, Bra o 3 (nsLTP), is heat- and pepsin-stable, so its allergenicity usually persists after boiling or stewing (Palacín *et al.*, 2006).

Fermentation may cause partial proteolysis of proteins, but there are no convincing data that it reduces IgE reactivity specifically to Brassica allergens. Instead, prolonged lactic fermentation may be accompanied by accumulation of biogenic amines (including histamine), which sometimes causes intolerance but not IgE-mediated allergy (Doeun *et al.*, 2017). High-temperature cooking methods can inactivate thermolabile proteins, but nsLTPs remain stable; therefore, in patients with LTP-mediated sensitisation, reactions are possible regardless of the culinary method (Skypala *et al.*, 2021).

4.1.4 Occupational sensitisation

Occupational allergy related to processing cruciferous vegetables (Brassicaceae), including cabbage, has been described in food industry and vegetable storage workers. Most commonly, manifestations involve the respiratory tract – particularly occupational asthma and allergic rhinitis – arising from inhalation of aeroallergens generated during cutting, shredding, or heat processing of cabbage and cauliflower. Cases of contact urticaria and contact dermatitis related to direct hand contact with plant tissue have also been reported. The allergen Bra o 3 (nsLTP) has been identified as the main protein capable of causing IgE-mediated reactions to cabbage and may also participate in cross-reactivity with pollen allergens, particularly mugwort. Although exact epidemiological rates of occupational sensitisation to cabbage have not been established, published clinical cases confirm the possibility of both respiratory and contact forms of allergy in workers exposed over prolonged periods or at high intensity. Respiratory symptoms during cabbage cooking are often due to the irritant properties of volatile isothiocyanates, especially allyl isothiocyanate, which is released when cellular structures are damaged (Palacin *et al.*, 2007).

Differentiation between true occupational asthma and irritant-induced bronchoconstriction requires specific bronchial provocation testing with cabbage extract and measurement of sIgE (Zamir *et al.*, 2023).

4.1.5 Diagnostic approaches

Diagnosis of cabbage allergy is based on a combination of clinical history, skin testing, and measurement of specific IgE. The available literature does not include large-scale studies providing standardised sensitivity and specificity values for commercial cabbage extracts. However, in the study by A. Palacin *et al.* (2007), all patients with confirmed IgE-mediated cabbage allergy had positive skin prick tests and elevated levels of specific IgE to cabbage allergens. Prick-to-prick testing with fresh cabbage is considered more sensitive – especially in sensitisation to thermolabile components – than testing with extracts. The ImmunoCAP method allows detection of specific IgE to cabbage and its main allergen Bra o 3 (nsLTP). In clinical practice, the highest diagnostic value lies in the concordance between skin test results, specific IgE, and a typical history of reaction to the product; in doubtful cases, an oral food challenge under medical supervision is indicated.

Component-resolved diagnostics (CRD) using multicomponent platforms such as ImmunoCAP ISAC (Thermo Fisher Scientific, 2025c) or ALEX2 (Allergy Explorer 2, Macro Array Diagnostics) (van Hage *et al.*, 2017) makes it possible to identify sensitisation to individual allergenic proteins and assess the potential clinical relevance of reactions. For cabbage, the most studied component is Bra o 3, a nonspecific lipid transfer protein (nsLTP), sensitisation to which has been described as a potential marker of systemic reactions – by analogy with other plant LTPs (peach, hazelnut, peanut). The basophil activation test (BAT) may be useful in cases where skin test and specific IgE results do not match the clinical picture. BAT studies with plant allergens show high overall specificity, but values specific to cabbage extract have not yet been established. The oral food challenge (OFC) remains the "gold standard" for confirming food allergy according to international EAACI and AAAAI recommendations. Its performance requires specialised conditions because both local and systemic reactions are possible. OFC protocols involve stepwise administration of increasing doses of food over several hours, but standardised regimens specifically for cabbage have not been published (Santos *et al.*, 2025; Nowak-Wegrzyn and Spergel, 2017).

4.2 Radish (*Raphanus sativus*)

Radish (*Raphanus sativus*) is a common vegetable of the Brassicaceae family, especially in East Asian countries where it is traditionally used fresh and in fermented dishes (Fig. 6). In Europe and North America, overall consumption is lower, but it remains among popular root vegetables. Allergic reactions to radish are reported rarely and mostly as isolated cases; however, available clinical observations indicate that they more often occur in patients sensitised to plant panallergens, especially profilins and nsLTP, or in individuals with pre-existing pollen allergy.

Figure 6. Radish (*Raphanus sativus*)

4.2.1 Allergenic components and molecular characteristics

To date, no radish allergens have been officially registered in the WHO/IUIS database, and its allergen profile has been only partially studied. Isolated cases of IgE-mediated reactions to radish suggest that in some patients the source of sensitisation may be panallergens – primarily profilins and nonspecific lipid transfer proteins (nsLTP) – which are widely represented in the Brassicaceae family and underlie cross-reactivity with other plant foods and pollen allergens. In addition to protein components, radish contains significant amounts of glucosinolates such as glucoraphenin and glucoraphanin, which are converted into isothiocyanates under the action of the enzyme myrosinase. These compounds can cause irritant reactions of the mucous membranes and skin upon contact or mechanical damage to the flesh, independent of immunological mechanisms. Available data indicate that allergic reactions to radish are rare and occur more often in patients with existing pollen allergy or sensitisation to plant panallergens (Lee *et al.*, 2015).

4.2.2 Pollen-food allergy syndrome

Radish allergy (*Raphanus sativus*) is rare and is mainly described as isolated clinical cases. In some patients it arises against the background of pollen polysensitisation, which allows it to be considered a possible variant of pollen-food allergy syndrome (PFAS), although confirmed reports are much fewer than for classic "birch" triggers such as apple, carrot, or celery. Available publications describe IgE-mediated reactions to raw radish or Japanese white radish (daikon); in one case, a thermolabile ~18-kDa protein was identified that lost IgE binding after boiling, and in another case a clinical PFAS picture occurred after ingestion of raw Japanese radish (Abe *et al.*, 2021; Uesugi *et al.*, 2023). Convincingly characterised allergenic components of radish (profilins, PR-10, or LTP) have not yet been identified, underscoring the limited molecular data for this vegetable.

In Asian populations, PFAS associated with radish occurs sporadically, reflecting a different sensitisation structure dominated by allergens of Japanese cedar (Cryptomeria japonica), cypress, and mugwort. Reported clinical cases show a typical PFAS pattern: itching, tingling, or mild swelling of the lips, tongue, or palate within minutes after ingestion of raw radish. Systemic reactions, including urticaria, angioedema, or bronchospasm, are rare and usually associated with additional sensitisation to more stable plant allergens such as nsLTP (Uesugi *et al.*, 2023).

4.2.3 Cross-reactivity

Within Brassicaceae, radish may participate in cross-immunological responses with other members of this group – mustard, rapeseed, cabbage, and broccoli – linked to shared plant panallergens, particularly profilins and nonspecific lipid transfer proteins (nsLTP). The best documented clinical cross-reactivity is with mustard, whose allergens (Sin a 1, Sin a 3, Sin a 4) show homology with proteins of other crucifers and can provoke reactions in sensitised patients (Sirvent *et al.*, 2009; Fiocchi *et al.*, 2016). There are no data on the frequency of cross-sensitisation of radish specifically with other Brassicaceae, but isolated clinical cases indicate that such reactivity is possible and most often related to profilin- or LTP-sensitisation. Outside Brassicaceae, cross-reactions may occur in patients with LTP syndrome or profilin-dependent polysensitisation, in whom radish sometimes forms part of a broader reaction spectrum, although clinically significant manifestations are rare (Scheurer *et al.*, 2021).

4.2.4 Effect of thermal processing

Heat treatment may substantially change the allergenic potential of radish, but data on specific allergenic proteins in this vegetable remain limited. Clinical descriptions of patients allergic to raw *Raphanus sativus* note that boiling or stewing often reduces the severity of oral symptoms, consistent with the nature of thermolabile panallergens such as profilins or PR-10-like proteins, which degrade upon heating. At the same time, reactions are possible in patients sensitised to heat-stable components, particularly nsLTP-type proteins (known for heat resistance in many plant species), so full tolerance of thermally processed radish is not guaranteed (Lee *et al.*, 2015). Acid processing, such as pickling, may also reduce the irritant properties of raw radish, mainly by affecting glucosinolates and isothiocyanates, but the immunological significance of this effect has not been established. Drying radish, common in Asian culinary tradition (e.g., dried daikon), affects the concentration of bioactive and irritant compounds, including glucosinolates and their derivatives, and may alter tolerability in sensitive individuals.

4.2.5 Occupational sensitisation

Occupational sensitisation to radish (*Raphanus sativus*) is rarely described but has been confirmed in isolated clinical observations. It most often manifests in food service workers who have regular contact with raw radish. In particular, allergic contact dermatitis was reported in a waitress with positive patch tests to radish, as well as an IgE-mediated reaction in a restaurant worker who developed urticaria and anaphylaxis after contact with the fresh vegetable (Mitchell and Jordan, 1974). These cases indicate that radish can act as a rare occupational allergen in the food industry.

4.2.6 Diagnostic approaches

Diagnosis of radish allergy is complicated by the absence of standardised extracts; therefore, prick-to-prick testing with fresh radish is considered the most informative method, yielding positive results in patients and negative results in controls in reported cases. Measurement of specific IgE is possible only using individually prepared extracts or immunoblotting, because there are no official radish components and no commercial ImmunoCAP tests. Profilin-dependent cross-sensitisation is more often associated with mild oral symptoms, whereas reactions to heat-stable proteins are rarer but can be more severe (Lee *et al.*, 2015).

4.3 Onion (*Allium cepa*)

Onion (*Allium cepa*) is one of the most widely consumed vegetables globally, with annual production reaching 100 million tonnes (Fig. 7). Despite this, allergic reactions to onion are rare and are mainly described as isolated clinical cases. According to clinical observations, onion allergy accounts for less than 1% among individuals evaluated for suspected food allergy. The clinical significance of this type of allergy lies not in its frequency, but in the difficulty of differentiating true IgE-mediated reactions from irritant effects of sulphur-containing compounds, as well as in the possibility of occupational sensitisation among food industry workers and cooks (Armentia *et al.*, 2020).

Figure 7. Onion (*Allium cepa*)

4.3.1 Molecular characterisation of allergens

In onion (*Allium cepa*), several allergenic proteins have been identified to date. The best characterised include All c 3, a nonspecific lipid transfer protein (nsLTP) with a molecular weight of about 12 kDa, and All c 4, a profilin (~14 kDa). All c 3 is regarded as the main stable onion allergen capable of triggering systemic reactions, especially in patients from the Mediterranean region, where LTP sensitisation is common among food allergies. All c 4 underlies cross-reactivity with pollen profilins and predominantly causes symptoms of oral allergy syndrome. A possible role has also been described for alliinase (~56 kDa) as a potential occupational allergen among food industry workers, although data on its clinical significance are limited. At the same time, true allergens should be distinguished from irritant substances: the volatile compound syn-propanethial-S-oxide, which causes tearing when onions are cut, is not an allergen and acts via direct irritation of corneal nerve endings rather than through immunological mechanisms (Albanesi *et al.*, 2019).

4.3.2 Contact dermatitis versus food allergy

Contact dermatitis caused by onion (*Allium cepa*) is predominantly allergic in nature and belongs to type IV hypersensitivity reactions (Coombs and Gell classification), mediated by T lymphocytes. Clinically, it presents with erythema, itching, papules, or vesicles on the hands and fingers, typically 24-72 hours after repeated contact with raw onion or its juice. Lesions are most often observed in individuals who work with onions regularly – cooks, catering staff, and workers in the food industry. Patch tests with raw onion extract or crushed onion may be positive in such patients, confirming the allergic nature of the reaction, although the exact sensitivity and specificity of these tests are not currently standardised (Albanesi *et al.*, 2019; Bercovitch, 2007).

Food allergy is an IgE-mediated disease of type I hypersensitivity, characterised by symptom onset within minutes to an hour after ingestion of the causative product. Clinical manifestations range from local symptoms such as oral allergy syndrome with itching and swelling in the oral cavity, to systemic reactions – urticaria, angioedema, gastrointestinal symptoms, and in some cases anaphylaxis. The most common clinical phenotypes are isolated cutaneous or oral manifestations, while severe systemic reactions occur relatively rarely (Anvari *et al.*, 2019).

4.3.3 Occupational risks and respiratory sensitisation

Occupational onion allergy (*Allium cepa*) is relatively rare but clinically significant among cooks, food industry workers, and catering staff. It most often presents as allergic rhinitis, conjunctivitis, or bronchial asthma developing after prolonged inhalational exposure to vapours and aerosols generated during cutting or thermal processing of onion. Pathogenesis involves IgE-mediated sensitisation to onion protein components, particularly alliinase and the lipid transfer protein (All c 3), which have been described as potential inhalant allergens. Symptoms usually develop gradually – after months or years of occupational contact – and include cough, nasal itching, rhinorrhoea, tearing, and chest tightness. To differentiate IgE-mediated occupational asthma from non-immunological irritant-induced bronchoconstriction, specific bronchial provocation testing may be used (Albanesi *et al.*, 2019; Vandenplas *et al.*, 2014).

4.3.4 Effect of heat treatment and oral allergy syndrome

Heat treatment substantially affects onion allergenicity. The profilin All c 4 is a thermolabile protein and therefore usually loses immunological activity during boiling or frying, which explains tolerance of cooked onion in most patients with profilin-associated allergy. In contrast, All c 3,

which belongs to the lipid transfer protein family (nsLTP), is highly thermostable and may retain allergenic properties even after culinary processing, particularly with short heating or frying. Dried or powdered onion may contain more concentrated protein allergens; however, the clinical significance of this phenomenon remains insufficiently studied.

Oral allergy syndrome after ingestion of raw onion occurs mainly in patients with hay fever to birch or grass pollen and is driven by profilin cross-reactivity. Symptoms are usually limited to itching, tingling, or mild swelling of the oral mucosa and resolve quickly without systemic manifestations (Popescu, 2015).

4.3.5 Cross-reactivity and hidden sources

Within the Alliaceae family, onion (*Allium cepa*) shows marked cross-reactivity with closely related species – garlic (*Allium sativum*), leek, shallot, and chives. This is explained by a high degree of structural homology among their major allergens – nsLTPs, profilins, and alliinase. In most patients, sensitisation is cross-reactive and involves multiple Allium species, complicating elimination of these foods. Outside the family, isolated cases of reactivity between onion and asparagus have been described, likely due to shared LTP or PR proteins, but such observations remain sporadic (Popescu, 2015).

Onion is a frequent "hidden" ingredient in industrial products, including soup concentrates, sauces, meat products, snacks, and ready meals, where it may be labelled as "natural flavourings", "vegetable extracts", or "flavour enhancers". This creates a risk of inadvertent ingestion for sensitised individuals and requires careful label scrutiny.

4.3.6 Diagnostic approaches

Diagnosis of onion allergy is based on a combination of skin testing, measurement of specific IgE, and ancillary methods. Skin prick tests with commercial extracts (ImmunoCAP f48) or prick-to-prick testing with fresh onion are used for primary confirmation of sensitisation, with fresh material often providing higher diagnostic informativeness due to the presence of thermolabile proteins absent from standardised extracts. Patch tests are used when allergic contact dermatitis is suspected in food industry workers and can confirm type IV reactions. Measurement of specific IgE to onion (f48) is available in laboratory systems, but its clinical accuracy has not been validated in large studies. Component diagnostics with sIgE to All c 3 (nsLTP) may be useful for identifying patients with a potential risk of systemic reactions, although data are limited. The basophil activation test (BAT) may be used as an additional method to confirm an IgE-mediated mechanism, especially when standard test results are conflicting; however, there are currently no onion-specific data on its effectiveness.

4.4 Garlic (*Allium sativum*)

Garlic (*Allium sativum*) is one of the most widespread representatives of the Alliaceae family, with global production exceeding 30 million tonnes per year. It is widely used as a food, seasoning, and phytotherapeutic agent (Fig. 8). Allergic reactions to garlic are rare and are described mainly as isolated cases of IgE-mediated allergy or occupational contact dermatitis. Increased risk of sensitisation is observed among individuals who regularly handle raw garlic – cooks, workers in the food industry, and spice production. The clinical significance of this allergy lies in the diversity of sensitisation routes (cutaneous, inhalational, or ingestion) and the extensive use of garlic in foods and medicinal products, which complicates allergen avoidance.

Figure 8. Garlic (*Allium sativum*)

4.4.1 Main allergenic components

Several protein components potentially acting as allergens have been identified in garlic, with alliinase (alliin lyase) considered the main one. This enzyme has a molecular weight of about 56 kDa, catalyses the conversion of alliin to allicin when garlic cells are damaged, and shows high immunogenicity. Sensitisation to alliinase has been confirmed both in patients with food allergy and among workers with occupational exposure to raw garlic. In addition, the presence of proteins related to nsLTPs and profilins has been described in garlic, potentially accounting for cross-reactivity with other Alliaceae members (particularly onion), although the molecular characterisation of these components is still incomplete (Kao *et al.*, 2004).

Allicin is the main biologically active compound of garlic, formed by enzymatic cleavage of alliin under the action of alliinase when cells are damaged. This compound is not a true allergen; however, it can cause irritation of mucous membranes and skin by activating TRPA1 receptors and inducing release of inflammatory mediators, including histamine, via a non-immunological mechanism. Alliin content in fresh garlic averages 6-14 mg/g, and mechanical crushing can yield up to 70-80% of the theoretically possible allicin, depending on variety, temperature, and humidity (Prati *et al.*, 2014).

4.4.2 Contact dermatitis: Mechanisms and clinical manifestations

Contact dermatitis is the most common clinical form of garlic allergy (*Allium sativum*). In most cases, it is allergic contact dermatitis (type IV), mediated by a T-cell response, presenting with erythema, vesicles, and lichenification on the hands after repeated contact with raw garlic. Irritant dermatitis caused by allicin has a faster onset and is not accompanied by immune sensitisation. Patch testing with garlic extract is the main method for differentiating allergic from non-immune reactions (Li *et al.*, 2022).

4.4.3 Occupational sensitisation

Occupational allergy to *Allium sativum* is described mainly among cooks and workers in the food and pharmaceutical industries. It most often presents as contact dermatitis, allergic rhinitis, or respiratory hypersensitivity. In some cases, occupational asthma has been reported, with cough, dyspnoea, and wheezing during work with garlic and symptom improvement away from work. Sensitisation is confirmed by positive skin tests or the presence of specific IgE to garlic protein components, particularly alliinase (All s Alliin lyase). Diagnosis of occupational asthma is established using serial spirometry or a specific bronchial provocation test in a specialised centre (Cullinan *et al.*, 2020; Lembo *et al.*, 1991).

4.4.4 Effect of heat treatment

Fresh garlic contains the highest amount of protein components, with alliinase as the main allergen. Heat treatment (boiling, frying) reduces its immunogenicity, but some protein epitopes may remain stable with short heating. Dried and powdered garlic has a higher protein concentration per

unit mass, potentially preserving allergenic potential. Fermented black garlic has a lower protein content due to enzymatic degradation, but clinical tolerance has not been demonstrated. Garlic oil, by contrast, contains almost no protein allergens, but can cause irritant or pseudoallergic reactions due to volatile sulphur-containing compounds (Hellu *et al.*, 2023).

4.4.5 Allergy versus pseudoallergic reactions

Differentiation of IgE-mediated allergy from non-immune reactions to garlic is important for correct diagnosis. True allergy is characterised by rapid symptom onset after minimal amounts, dose-independence, reproducibility of reactions, and positive skin tests or specific IgE. Pseudoallergic reactions caused by allicin and other sulphur-containing compounds are dose-dependent, manifest as local burning or mucosal irritation without systemic symptoms, and are not accompanied by positive allergy testing. Garlic intolerance is often due to fructans (FODMAPs), which cause gastrointestinal symptoms via osmotic mechanisms rather than an allergic reaction (Santos *et al.*, 2023).

4.4.6 Cross-reactivity

Within Alliaceae, garlic (*Allium sativum*) shows marked cross-reactivity with closely related species – onion, leek, shallot, and chives. The molecular basis is high homology of alliinases, profilins, and lipid transfer proteins, explaining frequent clinical intolerance to several Allium species in sensitised patients. Outside this family, sporadic cases of cross-reactivity with other liliaceous plants (asparagus, tulips, lilies) are possible, mainly in patients with LTP syndrome or occupational sensitisation in plant-related work (Armentia *et al.*, 2020).

4.4.7 Hidden sources and diagnosis

Garlic is a common ingredient in processed foods – sauces, soup concentrates, meat products, marinades, and spice mixes – where it is often labelled as “spices” or “natural flavourings”, which can complicate identification of the allergen source. Garlic extracts and capsules are also present in dietary supplements and may provoke unexpected reactions in sensitised individuals. Diagnosis of garlic allergy is based on a combination of skin tests (especially prick-to-prick with fresh product), measurement of specific IgE to garlic (ImmunoCAP f47), and in complex cases the basophil activation test. The most informative component is considered to be alliinase, the main garlic allergen (Hellu *et al.*, 2023).

4.5 Clinical observations and practical experience

4.5.1 Clinical case: LTP syndrome with a severe reaction to raw cabbage

Patient M., 34 years old, presented after an episode of generalised urticaria, facial angioedema, and breathing difficulty that developed 20-30 minutes after eating a salad containing raw white cabbage. Over the preceding years, she had tolerated boiled cabbage in soups and vegetable dishes well, suggesting possible involvement of thermolabile proteins or heat-induced modification of more stable structures. Testing revealed sIgE to white cabbage of 8.2 kUA/L. Component-resolved diagnostics confirmed marked sensitisation to Bra o 3 (nsLTP) at 12.5 kUA/L with no sensitisation to the profilin Bra o 4, which is consistent with the clinical course and atypical for profilin-mediated reactivity. Additional sensitisation was detected to Pru p 3 (peach) at 15.8 kUA/L, as well as nsLTPs from tomato (8.7 kUA/L) and apple (6.3 kUA/L), forming a typical LTP-syndrome pattern with a high risk of systemic reactions to multiple plant-derived foods.

Case interpretation. An LTP syndrome diagnosis was established, with primary sensitisation to peach nsLTP (Pru p 3) and secondary cross-reactivity to cabbage, tomato, and apple LTPs. Tolerance to boiled cabbage is explained by partial denaturation of Bra o 3 during prolonged heat treatment, whereas in raw form this thermostable protein retains high allergenicity. The absence of profilin sensitisation rules out a link with pollen allergy and explains the negative history of seasonal respiratory symptoms. LTP syndrome is associated with an increased risk of severe systemic reactions and requires strict elimination measures.

Clinical recommendations. The patient was advised to completely avoid raw cruciferous vegetables (all types of cabbage, broccoli, cauliflower, Brussels sprouts, radish), peaches, nectarines, apricots, tomatoes, and apples. Cautious consumption of well heat-treated cruciferous vegetables was permitted (boiling for more than 15 minutes, stewing for more than 20 minutes), with monitoring of wellbeing and gradual introduction starting from minimal portions. An adrenaline auto-injector was issued with detailed instructions for use in the event of systemic symptoms. Baseline therapy with antihistamines and a short course of systemic corticosteroids were prescribed to control the acute phase. The patient was taught to read food labels to identify hidden allergen sources (soup concentrates, sauces, and processed meats often contain cabbage and Allium vegetables). After 6 months, provided the condition is stable and specific IgE levels decrease, an oral provocation test with boiled cabbage may be performed to determine the individual tolerance threshold.

CHAPTER 5.

Legumes and root vegetables

5.1 Pea (*Pisum sativum*)

Pea belongs to the group of legumes that play a significant role both in nutrition and in the structure of food allergies (Fig. 9). Although exact prevalence figures for pea allergy have not been established, estimates for legumes that are not included among "priority" allergens are ⩽0.5% in studies analysing cases of food allergy. This allergy most commonly manifests as an IgE-type reaction (type I hypersensitivity), but mixed or non-IgE-mediated mechanisms have also been described, particularly in children. The clinical relevance of this allergen is increasing due to the widespread use of pea protein in plant-based alternatives to meat and dairy products, creating additional challenges for diagnosis and allergy management (Abu Risha *et al.*, 2024).

Figure 9. Pea (*Pisum sativum*)

5.1.1 Molecular characterisation of allergens

Pea (*Pisum sativum*) contains several clinically significant allergenic proteins, including those officially recognised by WHO/IUIS: Pis s 1 (vicilin, 7S globulin), Pis s 2 (convicilin, 7S globulin), and Pis s 3 (nsLTP1, ~9.5 kDa). In addition, profilin and other potential allergenic components have been identified in peas, although they do not have separate IUIS designations. The main storage globulins of pea – vicilin, convicilin, and legumin – account for approximately 60-80% of the seed protein profile, show relative stability, and are involved in IgE binding; Pis s 1 is considered the main immunodominant allergen in some patients. Vicilin/convicilin show substantial structural homology with peanut Ara h 1, which explains the cross-reactivity between pea and peanut described in clinical studies. Pea profilin belongs to panallergens associated with pollen-food syndrome and predominantly oral symptoms. Pis s 3, as a representative of the nsLTP family, is thermostable and potentially capable of inducing systemic reactions in patients with LTP sensitisation. However, available data suggest that the clinical relevance of pea LTP may be lower than that of classic LTP foods (e.g., peach) (WHO/IUIS Allergen Nomenclature Sub-Committee, 2019c; Sanchez-Monge *et al.*, 2004; Asen *et al.*, 2023).

5.1.2 Cross-reactivity and molecular diagnostics

Pea (*Pisum sativum*) shows cross-sensitisation within the Fabaceae family, mainly with peanut, soy, and other legumes, due to homology of storage proteins, particularly 7S and 11S globulins. Co-sensitisation does not always imply clinically significant allergy: in peanut-allergic patients, IgE binding or positive skin tests to pea are often detected, but actual reactions occur much less frequently, highlighting the need to verify the diagnosis with oral food challenges. Molecular diagnostics can distinguish sensitisation to reserve proteins (vicilin/convicilin), which may be associated with more severe systemic reactions, from reactivity driven by panallergens such as profilin, which typically manifests as oral allergy syndrome. In patients with pollinosis,

sensitisation to pea may occur, but it more often presents clinically with mild symptoms when raw products are consumed. The basophil activation test can be useful in complex cases to assess the clinical relevance of sensitisation, complementing *in vivo* and *in vitro* testing (Abu Risha *et al.*, 2024; Smits *et al.*, 2023).

Soybean (Glycine max) and chickpea (Cicer arietinum) are of particular relevance within the spectrum of legume allergy because of their frequent consumption and well-defined storage proteins. The principal soybean allergens, Gly m 5 (7S globulin) and Gly m 6 (11S globulin), demonstrate structural similarity to pea vicilin and legumin, which may account for IgE cross-binding observed in sensitised individuals.Chickpea likewise contains 7S and 11S globulins with comparable structural features, providing a molecular basis for serological cross-reactivity with pea. However, the presence of immunological cross-reactivity does not necessarily indicate clinically significant allergy, and tolerance to individual legumes should be determined on the basis of clinical history and, where appropriate, supervised oral food challenge (Holzhauser *et al.*, 2009; Bar-El Dadon *et al.*, 2013; Abu Risha *et al.*, 2024).

5.1.3 Effect of processing

Thermal processing of peas reduces the allergenicity of thermolabile proteins, including profilins and some PR-10, which may lessen oral allergy syndrome symptoms in patients with pollen-food sensitisation, whereas the major storage globulins (vicilin, convicilin, legumin) remain largely heat-stable and retain immunoreactivity. Other technological methods, such as autoclaving, fermentation, and high hydrostatic pressure, can modify protein structure and partially reduce allergenicity, but the effect depends on processing parameters and protein fractions and does not ensure complete allergen inactivation. Fermentation may partially hydrolyse storage globulins, but the clinical relevance of such changes remains limited. Assessment of processing effects should be based not only on *in vitro* reductions in IgE binding but also on clinical reactivity, including challenge-test data.

5.1.4 Diagnosis and clinical phenotypes

Diagnosis of pea allergy is based on a detailed dietary history, measurement of specific IgE, and skin prick testing; when results are unclear, component diagnostics and supervised oral challenge are used as the gold standard (Taylor *et al.*, 2021). Positive sIgE and prick tests indicate sensitisation but do not predict reaction severity; interpretation should therefore be clinically grounded. Component diagnostics helps differentiate sensitisation to heat-stable storage globulins associated with systemic reaction risk from reactivity to heat-labile panallergens (especially profilin), which usually presents as isolated oral symptoms. Because storage proteins retain immunoreactivity after heat treatment, more severe reactions may occur to both raw and processed products, whereas symptom reduction is more commonly observed when thermolabile proteins are involved. Comorbid atopy, including allergic rhinitis and asthma, may influence clinical course and should be considered during risk assessment (Calamelli *et al.*, 2019).

5.1.5 Management

The cornerstone of pea allergy management is complete avoidance of the product and careful education about possible hidden sources in plant-based drinks, protein mixes, vegetarian products, and processed foods. Under EU legislation, pea (like most other legumes except peanut and soy) is not included in the list of mandatory allergens for labelling, so patients must check ingredient

lists carefully (Regulation (EU) No 1169/2011, 2011). In cases of severe or systemic reactions, carrying an adrenaline auto-injector and having a written anaphylaxis action plan are recommended in line with general food allergy guidance. Data on the natural development of tolerance in pea allergy are limited, and the course may vary widely depending on the sensitising protein type, particularly storage globulins, which are often associated with more persistent allergy. Oral immunotherapy for legumes is being studied as a potential treatment strategy, but for pea it remains experimental and requires further research (Popp *et al.*, 2020).

5.2 Common bean (*Phaseolus vulgaris*)

Common bean (*Phaseolus vulgaris*) is one of the most widely consumed legumes and an important protein source in many regions of the world; however, allergy to it is rare and has been described mainly in isolated clinical cases, including anaphylaxis and sensitisation to phaseolin (Fig. 10).

Figure 10. Common Bean (*Phaseolus vulgaris*)

5.2.1 Allergenic components and the role of lectins

Common bean contains several protein components that can trigger IgE-mediated reactions. The best characterised allergen is Pha v 3, an nsLTP1 of about 9 kDa, identified as a major allergen of green beans. The main seed storage protein is phaseolin, a 7S globulin with a molecular weight of approximately 45-50 kDa, accounting for up to half of the total protein content and considered a potential allergen; however, it is not Pha v 3, and its allergenic role is supported less robustly. Other globulin-group proteins have also been identified, capable of cross-reactivity with allergens from other legumes, including peanut, soy, and chickpea.

Beyond IgE-mediated mechanisms, raw or insufficiently heat-treated beans contain phytohaemagglutinin (PHA), which exerts a toxic rather than immune effect, causing nausea, vomiting, diarrhoea, and abdominal pain through mucosal injury and haemagglutination. This can mimic a food reaction but is not associated with production of specific IgE and does not lead to anaphylaxis. Proper heat treatment markedly reduces lectin toxicity, while the possibility of allergic reactions depends on individual sensitisation and the specific protein composition (WHO/IUIS Allergen Nomenclature Sub-Committee, 2023; German Federal Institute..., 2025).

5.2.2 Geographical features and occupational allergy

Allergy to common bean is generally considered rare, but manifestations may differ depending on region and dietary habits. In Mediterranean countries, allergic reactions to green beans have been reported, including anaphylaxis and contact-related symptoms with fresh pods, whereas sensitisation to dried beans is more often associated with cross-reactivity to other legumes such as peanut, chickpea, and soy. In patients with pollinosis, oral allergy syndrome-type reactions may occur when raw green beans are eaten, while cooked products are usually tolerated, except in individuals with component sensitisation. Occupational cases have been described among food workers and individuals with frequent contact with fresh beans, where reactions can present with respiratory symptoms, contact dermatitis, or asthma exacerbations due to inhalational and contact exposure to pod proteins and lectins (Menéndez Rivero *et al.*, 2025; Zacharisen and Kurup, 1998).

5.2.3 Cross-reactivity and differential diagnosis

Cross-reactivity among legumes is well described and is driven by structural relatedness of Fabaceae storage proteins, particularly 7S and 11S globulins. IgE binding has been demonstrated between bean proteins and other legumes, including peanut, soy, pea, chickpea, and lentil. Despite serological cross-reactivity, clinical reactions across different legumes are usually not universal, and most patients allergic to one legume tolerate others, indicating limited clinical relevance of cross-binding. The main bean storage protein phaseolin (7S globulin) shows substantial sequence and structural homology with peanut Ara h 1 and soy Gly m 5, explaining potential serological cross-reactivity; however, clinical expression depends on individual sensitisation and does not always align with *in vitro* data (Kasera *et al.*, 2011; Smits *et al.*, 2023).

Accurate differentiation between IgE-mediated allergy and non-immune reactions to beans is clinically critical. Insufficiently heat-treated beans can cause toxic gastrointestinal symptoms (nausea, vomiting, diarrhoea) due to lectins such as phytohaemagglutinin. These reactions are dose-dependent, result from direct intestinal mucosal injury, and are not accompanied by elevated specific IgE or typical skin/respiratory manifestations. In contrast, true IgE-mediated reactions may occur with small amounts, develop rapidly, include urticaria, angioedema, or systemic manifestations, and are accompanied by positive allergy testing (sIgE, skin tests). Non-immune symptoms related to fermentable carbohydrates (FODMAPs), causing bloating and GI discomfort without immune involvement, should also be distinguished (Sicherer and Sampson, 2018; Muraro *et al.*, 2014).

5.2.4 Effect of processing

Thermal processing of beans markedly reduces lectin toxicity, whereas its effect on protein allergenicity is less pronounced. Soaking and prolonged boiling reduce phytohaemagglutinin levels, but complete lectin inactivation requires boiling or autoclaving. Storage proteins, including 7S globulins, may partially retain immunoreactivity after heat treatment, which is important for patients with IgE-mediated sensitisation. In green beans, which contain fewer storage proteins and are often eaten raw, reactions are usually limited to oral symptoms in patients with pollinosis, whereas reactions to dried beans are more often reported after consumption of cooked beans and may be systemic due to the stability of storage proteins or incomplete lectin inactivation (Petrski and Minich, 2020; German Federal Institute…, 2025).

5.2.5 Diagnosis and management

Diagnosis of bean allergy relies on a careful history differentiating IgE-mediated reactions from non-immune toxic effects, measurement of specific IgE, skin testing (including prick-to-prick with fresh product, which may be more informative than commercial extracts), and, when needed, supervised oral challenge testing. Component diagnostics for beans is currently limited and not routinely used. Management includes avoidance of the triggering product and individual assessment of tolerance to other legumes, as serological cross-reactivity does not always correspond to clinical cross-reactivity. Patients with anaphylaxis or comorbid asthma are advised to carry an adrenaline auto-injector. Unwarranted elimination of all legumes without proven clinical reactivity is not recommended, to avoid unnecessary dietary restriction (Sicherer and Sampson, 2018; Santos *et al.*, 2023).

5.3 Carrot (*Daucus carota*)

Carrot is one of the most common vegetable triggers of food allergy, and the prevalence of sensitisation ranges from 1% to 25% depending on the geographic region and the presence of con-

comitant respiratory allergy (Ballmer-Weber and Hoffmann-Sommergruber, 2011) (Fig. 11). Carrot allergy shows marked geographic heterogeneity: in Central and Northern Europe it predominantly presents as pollen-food syndrome in patients allergic to birch pollen, whereas in the Mediterranean area systemic reactions associated with sensitisation to lipid transfer proteins are more often observed.

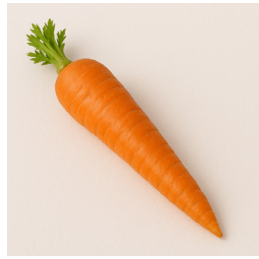

Figure 11. Carrot (*Daucus carota*)

5.3.1 Allergen profile and molecular characterisation

The allergen composition of carrot is heterogeneous and includes proteins from different structural families and with different sensitisation mechanisms. Their clinical impact depends not only on the protein type, but also on regional sensitisation patterns and cross-reactions. Table 9 provides a structured description of the main carrot allergens.

Table 9. Major carrot allergens (*Daucus carota*)

Allergen	Protein class	Mol. weight (kDa)	Stability (heat/ proteolysis)	Clinical manifestations	Geographic association
Dau c 1	PR-10 (Bet v 1-like)	~16-18	Heat-labile; rapidly degrades in the GI tract	Mainly oral allergy syndrome; rarely systemic	Central & Northern Europe (birch region)
Dau c 4	Profilin	~14	Heat-labile	Oral symptoms; cross-reactions with many plants	Not region-specific
Dau c 5	Isoflavone reductase-like	~33	Moderately stable	May be involved in systemic reactions, but data are limited	Not region-specific
Carrot nsLTP (not standardised as Dau c)	nsLTP type 1	~9	Highly heat-stable and proteolysis-resistant	Systemic reactions, including anaphylaxis	Mediterranean region

Source: *based on Hoffmann-Sommergruber et al. (1999); WHO/IUIS Allergen Nomenclature Sub-Committee (2019b).*

Clinical manifestations of carrot allergy depend not only on the product's protein profile but also on the type of prior sensitisation and regional patterns of pollen- and LTP-associated allergies. Serological cross-reactivity does not always correlate with symptoms, and the risk of systemic manifestations is determined by allergen stability and the influence of cofactors (physical exertion, NSAIDs, alcohol). Sensitisation profiles may change with age or migration, which should be considered during repeat testing and tolerance assessment. Therefore, interpretation of diagnostic results should be based not only on protein properties but also on the individual clinical presentation.

5.3.2 Pollen-food syndrome and cross-reactivity

Pollen-food syndrome (PFS) is the most common clinical manifestation of carrot allergy in Central and Northern Europe, affecting up to 50-70% of patients with birch pollen allergy. Pathogenetically, PFS is driven by cross-reactivity between pollen allergens and PR-10 proteins/profilins in plant foods. Clinically, itching, burning, and swelling of the lips, tongue, and palate develop within 5-15 minutes after consuming raw carrot, and symptoms usually resolve spontaneously within

15-60 minutes without systemic signs. Most patients with PFS tolerate heat-treated carrot well due to denaturation of heat-labile allergens at temperatures >60-70°C (Thermo Fisher Scientific, 2020).

The birch-mugwort-celery-carrot syndrome demonstrates complex cross-reactivity involving sensitisation to birch and mugwort pollen and to foods of the Apiaceae family (carrot, celery, parsley, fennel), as well as other vegetables and fruits. Molecular mechanisms include primary sensitisation to pollen allergens followed by secondary cross-reactivity. Patients with combined sensitisation to Bet v 1, profilins, and LTPs have a broader spectrum of food allergies and a higher risk of systemic reactions. Geographic variation is linked to exposure to different pollens: birch dominates in Northern Europe, whereas mugwort and grasses are more prominent in the Mediterranean region (Popescu, 2015).

5.3.3 Respiratory manifestations and occupational allergy

Respiratory manifestations of carrot allergy include rhinitis, conjunctivitis, and bronchospasm following inhalational contact with raw carrot particles during handling. Occupational cases of rhinitis and asthma have been described among chefs and food-industry workers, in whom symptoms arose due to inhalation of aerosol or vapours from raw carrot. Such reactions are rare and are usually reported as isolated case reports or small series; their frequency depends on exposure intensity and duration (Sánchez-Guerrero *et al.*, 2020; Moreno-Ancillo *et al.*, 2006).

Contact reactions to carrot are rare and may present as IgE-mediated contact urticaria when handling raw carrot, or as non-immune irritant dermatitis (Gómez *et al.*, 1996). Some furocoumarins typical of Apiaceae plants can cause phototoxic contact dermatitis when skin contact with juice is followed by UV exposure (Grosu Dumitrescu *et al.*, 2024).

5.3.4 Diagnosis of carrot allergy

Diagnosis includes a detailed history distinguishing reactions to raw versus heat-treated carrot, measurement of specific IgE, skin prick testing, component-resolved diagnostics, and, if necessary, an oral food challenge. Prick-to-prick testing with fresh carrot shows substantially higher diagnostic sensitivity than testing with commercial extracts; upon the investigation of B.K. Ballmer-Weber *et al.* (2001), sensitivity was 100% versus 26%, respectively, reflecting the lability of the major allergen Dau c 1 and loss of activity during extraction. Component diagnostics allows stratification of sensitisation: Dau c 1 (PR-10/Bet v 1-like) is primarily associated with PFS and reactions mainly to raw carrot; sensitisation to profilin Dau c 4 indicates broad polysensitisation and typically milder manifestations, often limited to OAS. Data on the clinically significant role of other proteins, including Dau c 5 (isoflavone reductase-like), remain limited, and carrot is not among the leading sources of food nsLTPs typically associated with systemic reactions (peach, apple, nuts). sIgE levels may help estimate the likelihood of clinical reactivity, but validated cut-offs specific to carrot have not yet been established (Ballmer-Weber *et al.*, 2001; Ballmer-Weber *et al.*, 2005).

5.3.5 Effect of culinary processing

Heat treatment substantially affects carrot allergenicity. The major allergen Dau c 1 (PR-10/Bet v 1-like) is heat-labile and largely loses immunoreactivity after heating, which explains better tolerance to cooked carrot in most patients with PFS. Profilins, like other labile panallergens, are also partially inactivated by heating. By contrast, nsLTPs show high heat and pepsin stability, consistent with their association with systemic reaction risk in sensitised patients, although carrot is not a major dietary source of LTP. The degree of allergenicity reduction depends not only on

temperature and duration of heating, but also on the food matrix (whole carrot, juice, purée) and processing methods, including pasteurisation, which reduces labile PR-10 proteins but does not affect heat-stable proteins (Pekař *et al.*, 2018; Jacob *et al.*, 2020).

5.3.6 Management

Management of carrot allergy should be based on the individual allergen profile and clinical history. In patients sensitised to PR-10/Bet v 1-like proteins typical of PFS, reactions are usually limited to oral symptoms and most often occur with raw carrot, whereas heat-treated carrot is usually very well tolerated. In contrast, in patients with a history of systemic reactions or sensitisation to heat-stable allergens (e.g., nsLTP, although carrot is not a leading dietary source), a more cautious preventive approach is required, including assessment of the need to carry an adrenaline auto-injector. Natural tolerance in PFS may persist or gradually form depending on control of pollen sensitisation, whereas with sensitisation to more stable proteins associated with systemic reactions, prolonged persistence of reactivity is more likely (Ballmer-Weber *et al.*, 2012).

5.4 Beetroot (*Beta vulgaris*)

Beetroot allergy (*Beta vulgaris*) is extremely rare and has mainly been described as isolated IgE-mediated reactions, including anaphylaxis (Tekeli *et al.*, 2023) (Fig. 12). Food-related manifestations occur much less frequently than respiratory symptoms triggered by inhalation of steam from cooked beetroot, and allergenic components remain insufficiently characterised. It is important to distinguish true IgE-mediated allergy from non-immune reactions, including betalain-related "beeturia" and metabolic intolerances. Overall diagnostic assessment should consider pseudoallergy and avoid unjustified dietary restrictions (Thermo Fisher Scientific, 2025b).

Figure 12. Beetroot (*Beta vulgaris*)

5.4.1 Allergenic components

Molecular characterisation of beetroot allergens remains incomplete; only Beta v 1 is officially registered in the WHO/IUIS database, although clinical studies suggest additional sensitising proteins exist (WHO/IUIS Allergen Nomenclature Sub-Committee, 2019a). Beta v 1 belongs to the PR-10 protein family (~17 kDa) and shows structural homology with the birch pollen allergen Bet v 1, explaining cross-reactivity in patients with pollinosis. Profilins have also been identified in beetroot, but their clinical significance remains unclear (Hofer *et al.*, 2016).

Betalains (including betanin), responsible for red and yellow beetroot pigmentation, are low-molecular-weight pigments rather than proteins and therefore are not considered true IgE-mediated allergens. They can cause the phenomenon of "beeturia" (red-coloured urine), classified as an idiosyncratic pigment-excretion effect rather than an immune reaction. There is no evidence of clinically significant adverse effects from betalain intake; they are considered safe as food colourants (Milton-Laskíbar *et al.*, 2021). Beetroot oxalates (~100 mg/100 g raw product) are not allergens, but at high intake they may reduce calcium bioavailability and potentially contribute to oxalate stone formation, which is a non-immune effect (Lisiewska *et al.*, 2011).

5.4.2 Cross-reactivity

Cross-reactivity in beetroot allergy may occur with other Amaranthaceae family members, including spinach and chard. This is supported by IgE-inhibition studies in which chard and beetroot extracts fully blocked IgE recognition of spinach proteins. Several IgE-binding proteins have been identified in beetroot pollen, including PR-10-type (Bet v 1-like) allergens, as well as Beta v 2 (profilin), a typical panallergen that may explain serological cross-reactivity with pollen allergens. As in other variants of pollen-food syndrome, clinical cross-reactivity is usually weaker than serological cross-reactivity, and not all sensitised patients develop symptoms after eating raw beetroot (Luoto *et al.*, 2008).

Cross-reactivity with pollen from goosefoot-family plants (Chenopodium album, Amaranthus retroflexus) is particularly relevant in Southern Europe, Central Asia, and some regions of North America (Amini *et al.*, 2011). Patients with primary sensitisation to goosefoot pollen may develop secondary food allergy, usually presenting as oral allergy syndrome. Heat treatment of beetroot substantially reduces reaction risk in pollen-linked cases due to denaturation of heat-labile PR-10 proteins and profilins.

5.4.3 Contact dermatitis and differential diagnosis

Contact reactions to beetroot during peeling or handling are typically irritant contact dermatitis, potentially driven by mechanical skin damage and irritant components, including oxalate crystals described in other Amaranthaceae plants as skin irritants. Allergic contact dermatitis is possible but is mainly reported as isolated cases and requires confirmation by standard patch testing with the suspected substance. Clinically, allergic reactions are delayed (24-48 hours) and present with erythema, vesicles, and itching, whereas irritant responses may occur immediately after contact (Modi *et al.*, 2009).

For differentiation, it is important to note that IgE-mediated reactions to beetroot have a different mechanism, with rapid symptom onset after ingestion and confirmation by specific IgE or skin prick testing. Beeturia (red urine after beetroot intake) is a benign pigment-excretion phenomenon without immunological basis. High oxalate content may contribute to metabolic or gastrointestinal symptoms with excessive intake but is not allergenic. With fermented beetroot products, histamine-mediated reactions are possible and should be distinguished from food allergy (Sauder and Rawla, 2023).

5.4.4 Reaction patterns and diagnosis

Clinical manifestations have mainly been described in isolated cases and range from mild local symptoms (oral itching, oropharyngeal discomfort) to rare systemic reactions, including anaphylaxis (Lopes de Oliveira *et al.*, 2011). In many patients, symptoms occur only with raw beetroot, consistent with heat lability of several plant allergens, including profilins. Skin manifestations such as urticaria or angioedema have been reported, but frequency is unknown and based on limited reports. Beeturia is not an allergic reaction (Milton-Laskíbar *et al.*, 2021). Gastrointestinal symptoms may occur both as part of food allergy and via non-immune mechanisms, including high oxalate content (Lisiewska *et al.*, 2011).

Symptoms more often arise after raw beetroot ingestion, consistent with pollen-food syndrome mechanisms in which heat-labile plant proteins are destroyed by cooking and become less immunogenic, while stable proteins may retain allergenicity after heating. However, reactions to cooked beetroot, including anaphylaxis, have also been reported (El-Hosni *et al.*, 2020). This

suggests possible heat-stable components in some patients. Rarely, sensitisation may also manifest with beetroot juices or concentrates containing higher amounts of soluble protein fractions, although systematic data are limited.

Diagnosis is complicated by the lack of standardised commercial extracts for skin testing and limited availability of beetroot-specific IgE assays; therefore, prick-to-prick testing with fresh product is most commonly used as a clinically practical initial assessment. Sensitivity and specificity data for beetroot are unavailable, and results may vary by cultivar and sample preparation. Commercial allergen components for beetroot are not currently available, limiting molecular diagnostics (Kleine-Tebbe and Jappe, 2017). In complex or conflicting cases, the gold standard remains a supervised oral food challenge under medical observation (Sicherer and Sampson, 2018).

5.4.5 Management

Management should be individualised and based on clinical risk assessment (Sicherer and Sampson, 2018). Patients with confirmed systemic reactions are advised strict elimination of beetroot and beet-containing products, including mixed dishes and products using beet colourants such as E162. In cases of local, mild oral symptoms related to pollen-food syndrome, heat-treated products may be consumed if tolerance is documented, as many heat-labile plant allergens are inactivated by cooking.

Unjustified elimination of other vegetables in the same family is not recommended, as serological cross-reactivity does not always correspond to clinical reactivity. Prescription of an adrenaline auto-injector is indicated for patients with anaphylaxis or high risk of systemic reactions according to international food allergy recommendations (Muraro *et al.*, 2014).

In patients with non-immune adverse reactions driven by beetroot components (e.g., high oxalate content or pigments), restriction rather than complete avoidance is usually appropriate, taking into account individual tolerance and the absence of an IgE-mediated mechanism.

5.5 Clinical observations and practical experience

5.5.1 Clinical case: Systemic IgE-mediated reaction to lentil in a child

A 6-year-old boy was brought in after an acute allergic reaction that developed within minutes after eating a small portion of a dumpling containing a filling with mashed cooked lentils. The clinical picture included erythema and facial swelling, angioedema of the upper and subsequently the lower lip, and generalised urticaria. Respiratory symptoms then developed, including expiratory dyspnoea, cough, and wheezing consistent with bronchospasm. The child had never eaten lentils before, and there was no history of allergic reactions to other legumes.

Laboratory testing with an ALEX panel showed a high level of specific IgE to lentil (35 kU/L). Sensitisation to other Fabaceae family members was also detected – soy, chickpea, beans, and peas – suggesting multisensitisation. However, the absence of a history of clinical reactions to these foods makes their clinical relevance currently uncertain and in need of confirmation.

5.5.2 Case interpretation

Primary sensitisation to lentil storage proteins (7S and 11S globulins), known for their heat stability and resistance to proteolysis, is the most likely mechanism. This is consistent with the severe systemic course even after minimal allergen intake. Multisensitisation to other legumes is explained by structural homology of storage proteins but does not confirm clinical allergy to them

without challenge tests. Given the history and reaction severity, there is a risk of recurrent anaphylactic manifestations with small amounts of allergen and with foods containing hidden lentils (vegan patties, sauces, soup concentrates, protein mixes).

5.5.3 Clinical recommendations

Complete avoidance of lentils in all forms was recommended, including processed products and dishes with possible plant-protein admixtures. Careful reading of food labels and avoidance of Asian and Indian dishes that commonly contain lentils were advised. Because of the high likelihood of cross-reactivity, tolerance to soy, beans, chickpea, and peas should be assessed under allergist supervision, prioritising controlled oral challenge tests in clinical settings. An adrenaline auto-injector was prescribed, and the parents were trained in anaphylaxis action protocols. Ongoing monitoring of specific IgE levels and repeat testing after 12 months were also recommended to assess sensitisation dynamics.

CHAPTER 6.

Cucurbit vegetables

The Cucurbitaceae family includes more than 800 species, among which cucumber, squash, pumpkin, melon and watermelon are common foods. Allergies to pumpkin vegetables are rare, but symptoms vary from mild oral allergy syndrome to rare systemic reactions. Epidemiological studies show that melon and other members of the Cucurbitaceae family are common triggers of OAS in patients with pollen sensitisation, and the frequency of such reactions among individuals with atopy can reach 10-15% or more. A substantial feature is the pronounced cross-reactivity between Cucurbitaceae species and pollen allergens, profilin and LTP, which causes wide variability in clinical manifestations (Carpio-Escalona *et al.*, 2023; López-Torrejón *et al.*, 2005).

6.1 Cucumber (*Cucumis sativus*)

6.1.1 Molecular characteristics and allergenic profiles

Cucumber is one of the most common vegetables of the Cucurbitaceae family, and its global production in 2021 exceeded 87 million tonnes (Vasić *et al.*, 2025) (Fig. 13). The only officially recognised allergen in cucumbers in the WHO/IUIS international database is profilin Cuc s 2, which belongs to the highly conserved actin-binding proteins of the panallergen family. Profilins have a molecular weight of approximately 14-15 kDa and show significant homology between different plant species, in particular with Bet v 2, Art v 4, Amb a 8 and Phl p 12, which explains the frequent reactions to cucumber in patients with hay fever. Due to the pronounced thermolability of profilins, their allergenicity decreases after heating above 70 °C for several minutes; therefore, clinical manifestations are usually limited to oral allergy syndrome (Allergome, 2013; Thermo Fisher, 2025b).

Figure 13. Cucumber (*Cucumis sativus*)

In addition to profilin, other proteins capable of causing allergic reactions were highlighted in cucumbers, including PR proteins (including Bet v 1-like proteins) and lipid transfer proteins (LTPs), which are well known as clinically significant allergens in other plant products, particularly those of the *Cucurbitaceae* family. However, their potential role in cucumber allergy is currently based mainly on structural and immunological homology with allergens from other plant species, as well as on isolated clinical observations; these proteins do not have the status of officially recognised allergens in the WHO/IUIS nomenclature. LTPs are thermostable, localised mainly in the skin and capable of being associated with severe reactions, especially in the Mediterranean region and in the presence of cofactors (physical exertion, NSAIDs, alcohol). Thaumatin-like proteins (PR-5) may also play a role in cross-reactivity, although their molecular characterisation in cucumber is limited (Hasnain *et al.*, 2017).

6.1.2 Sawdust-food syndrome and cross-reactivity

Pollen-food syndrome (PFAS) is the most common form of allergic reactions to cucumber and other members of the Cucurbitaceae family, as confirmed by clinical observations and review

publications, in which mild oropharyngeal symptoms predominate in patients with pollen sensitisation. Its development is caused by primary respiratory sensitisation to tree and weed pollen, followed by cross-reactivity with homologous proteins in plant products, mainly caused by profilins, in particular the officially recognised allergen Cuc s 2 in cucumbers, as well as probable Bet v 1-like proteins (PR-10), whose role is based on structural homology and limited experimental and clinical data (Vlaicu *et al.*, 2010). The most significant sources of such cross-reactivity are birch, mugwort, ragweed and grass pollen, whose profilins (Bet v 2, Art v 4, Amb a 8, Phl p 12) show a high degree of structural similarity to Cuc s 2, which explains the frequent reactions in patients with seasonal allergic rhinitis or hay fever (Matricardi *et al.*, 2016). Clinically, PFAS when eating raw cucumber usually manifests itself as a rapid onset of itching, tingling, or swelling in the mouth within a few minutes after contact with the product, and the symptoms resolve spontaneously within a short time. The severity of reactions may increase during the pollen season due to priming of the immune system and an active IgE-dependent response (Kato *et al.*, 2025).

Within the Cucurbitaceae family, significant cross-reactivity has been described between cucumber, melon, watermelon and squash, which is associated with the presence of common panallergens in this group of plants. At the same time, cross-reactivity is often incomplete: some patients react exclusively to cucumber or only to certain members of the family, reflecting differences in the composition and stability of protein components (Asero, 2000).

In addition to pollen sensitisation, cross-allergic reactions to cucumber are also possible in patients with latex allergy, leading to the development of latex-fruit syndrome: some patients with latex allergy may react to cucumber due to cross-reactions mediated by profilins, chitinases and thaumatin-like proteins. This mechanism is clinically significant, particularly for healthcare workers and patients who have repeated or prolonged contact with latex (Vlaicu *et al.*, 2011).

6.1.3 The influence of variety, cultivation methods and processing on allergenicity

The allergenicity of cucumbers can vary significantly depending on the variety, growing conditions and degree of stress, as the expression of PR proteins (in particular PR-10 and profilins) in plants changes under the influence of biotic and abiotic factors. Growing in greenhouses or under conditions of increased stress can enhance the synthesis of these proteins, which can alter the allergenic profile of the fruit (Lopes de Oliveira *et al.*, 2011).

Heat treatment generally significantly reduces the allergenicity of plant products by denaturing thermostable panallergens, which is a well-established property of profilins and Bet v 1-like proteins (PR-10), which rapidly lose their IgE-binding capacity during heating and under the action of digestive enzymes. In the context of cucumber, this effect is mainly associated with the officially identified profilin Cuc s 2, while the possible contribution of PR-10-like proteins is considered only probable and is based on homology with corresponding allergens from other plants. At the same time, lipid transfer proteins (LTPs) are known for their high thermal and proteolytic stability and remain clinically significant allergens in other plant products; However, for cucumber, LTPs do not have the status of officially identified allergens in the WHO/IUIS nomenclature, and their role in clinical reactions is considered only as potential (Dramburg *et al.*, 2023).

The acidic environment during marinating or fermentation can also reduce the allergenicity of the product due to structural changes and partial degradation of sensitive PFAS-type proteins (primarily profilins and Bet v 1-like proteins/PR-10), which has been demonstrated mainly in *in vitro* experimental models (assessment of IgE binding/immunoreactivity and protein stability after

technological processing); however, *in vivo* clinical data on cucumber are limited and mostly consist of isolated observations. At the same time, LTPs generally remain relatively resistant to acid and enzymatic treatment, which has also been predominantly confirmed *in vitro* and extrapolated from data for other plant matrices and LTP syndrome (Haidar *et al.*, 2025).

Peeling cucumbers may reduce the risk of reactions, as the skin of Cucurbitaceae has been shown to contain higher concentrations of LTP and other stable allergens than the flesh. Some patients with raw cucumber allergy may tolerate peeled or processed products, especially if their sensitisation is related to thermolabile proteins (Gandolfo-Cano *et al.*, 2018).

6.2 Zucchini (*Cucurbita pepo*)

Zucchini (*Cucurbita pepo*) is a common food, especially in Europe and the Mediterranean region, and allergy to it can range from mild oral allergy syndrome to systemic reactions, including anaphylaxis (Reindl *et al.*, 2000; Asero *et al.*, 2012) (Fig. 14).

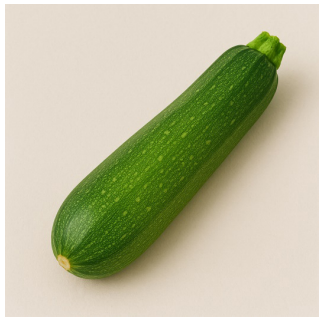

Figure 14. Zucchini (*Cucurbita pepo*)

6.2.1 Molecular characteristics and allergenic profiles

Several IgE-binding proteins in zucchini have been described in open sources, but none of them have been included in the official WHO/IUIS nomenclature as *Cucurbita pepo* allergens. The most frequently mentioned is profilin, designated in the Allergome database as Cuc p 2, which is classified as an IgE-binding molecule but does not have the status of an official WHO/IUIS allergen. Other proteins identified by the IgE-binding method probably correspond to the 15-17 kDa and 40-42 kDa fractions, which correspond to the profiles of possible profilins, chitinases and storage proteins (Allergome, 2013). The profilin described in zucchini (~14-15 kDa) has high homology with plant and pollen profilins, causing cross-reactions with birch, mugwort, ragweed, and grass pollen. Similar to other profilins, it is thermolabile; therefore, clinical manifestations are usually limited to symptoms of pollen-food syndrome. Chitinase-like proteins (approximately 30 kDa) described in zucchini demonstrate partial thermostability and potential cross-reactivity with latex and fruits associated with latex-fruit syndrome (Kahn *et al.*, 2016).

Lipid transport proteins (nsLTP, ~9-10 kDa) have also been described in *Cucurbita* species. These proteins are thermostable and may be more abundant in the outer tissues of the fruit (particularly in the skin). Their clinical significance has regional characteristics and is most often considered in the context of LTP syndrome (mainly in the Mediterranean region), where nsLTPs are associated with the risk of systemic reactions and may demonstrate cross-reactivity with LTPs from other plants, in particular with peach Pru p 3 (Gandolfo-Cano *et al.*, 2018). It is worth noting that *Cucurbita* storage proteins (in particular 11S globulins) are primarily associated with the allergenic potential of seeds (pumpkin/squash seeds) and products containing them (pastes, mixtures, baked goods, seed toppings), rather than the pulp of the fruit; in this limited context, cross-reactivity with storage proteins of other plant seeds may be discussed (WHO/IUIS Allergen Nomenclature Sub-Committee, 2020).

6.2.2 Clinical manifestations and diagnostic features

Oral allergy syndrome is the most commonly described manifestation of zucchini allergy, predominantly in patients with pollen sensitisation. Typical symptoms include itching, burning, or mild swelling of the oral mucosa, occurring within minutes of eating raw zucchini and usually resolving spontaneously within an hour. In some patients, oral manifestations may be accompanied by urticaria, angioedema, rhinoconjunctivitis, or gastrointestinal symptoms. Systemic reactions, including anaphylaxis, have been described in the literature but are less common; they are more often associated with sensitisation to stable plant proteins, primarily LTP or class I chitinases, which are widespread among various vegetables and fruits. As with other LTP-associated food allergies, severe reactions can be triggered by cofactors (physical exertion, NSAIDs, alcohol) and concomitant bronchial asthma. Contact reactions when handling raw courgettes – IgE-mediated contact urticaria or allergic contact dermatitis – are mainly described in occupational groups (cooks, food industry workers) (Reindl *et al.*, 2000; Asero *et al.*, 2018).

Skin prick tests with zucchini extracts have shown moderate diagnostic value, whereas prick-to-prick tests with fresh produce usually have higher sensitivity, especially in patients with cross-reactions to profilins or PR proteins. Determination of sIgE to whole zucchini extract (e.g., ImmunoCAP f225) may be informative, but sIgE levels do not always correlate with clinical reactivity, which is typical for vegetable allergens. Molecular diagnostics does not have official components for zucchini, but assessment of sensitisation to cross-reactive proteins (LTP, profilin, PR-10, class I chitinases) can help predict the risk of systemic reactions. A basophil activation test can serve as an additional method for confirming clinically significant reactivity in complex cases (Asero *et al.*, 2012).

6.2.3 Cross-reactivity and geographical characteristics

Within the Cucurbitaceae family, significant cross-reactivity has been described between zucchini, pumpkin, cucumber, melon and watermelon, as confirmed by immunoblotting and inhibition tests. However, individual clinical reactivity can vary significantly, so the tolerability of each product needs to be assessed separately. Cross-reactivity with pollen allergens – primarily birch, mugwort, ragweed, and grasses – forms the basis of pollen-food syndrome and is characterised by seasonal exacerbation of symptoms during the flowering periods of the respective plants. Zucchini has also been described as part of the spectrum of foods associated with latex-fruit syndrome, especially in patients with latex sensitisation, which may cause cross-reactions with avocado, banana, chestnut and other plant products (Figueredo *et al.*, 2000; Gandolfo-Cano *et al.*, 2018).

In the Mediterranean region, allergies to plant products of the Cucurbitaceae family, including zucchini, are more often associated with LTP syndrome, which is characterised by the risk of systemic reactions and lower temperature lability of allergens. This is further facilitated by the traditional consumption of raw or minimally processed pumpkin, particularly courgette flowers. In Central and Northern Europe, clinical manifestations are predominantly associated with profilin- and PR-10-mediated sensitisation in patients with birch pollen allergy, which more often leads to oral allergy syndrome. In North America, zucchini allergy is less commonly described and is usually considered in the context of general allergy to plant products or PFAS, without distinguishing a specific regional phenotype (Scheurer *et al.*, 2021; Reindl *et al.*, 2000). Thus, the geographical characteristics of sensitisation are of direct practical importance for assessing individual risk: they determine the possible molecular phenotype of the allergy (LTP vs profilin/PR-10), the expected

severity of reactions and the appropriateness of strict elimination recommendations or, conversely, the possibility of safe consumption of heat-treated products.

6.2.4 The impact of heat treatment and the hidden presence

Cooking at high temperatures causes rapid loss of immunoreactivity in PFAS-type proteins, especially profilins. As a result, even brief boiling or frying significantly reduces the ability of these proteins to bind specific IgE. Baking also effectively destroys these proteins, but some allergens may remain in the skin, where their concentration is usually higher than in the flesh. In contrast, nsLTP family proteins are characterised by high thermal and peptide resistance, which means that standard cooking methods do not usually result in a complete loss of their immunoreactivity, and clinical reactions may persist even after intense heating (Scheurer *et al.*, 2021).

Peeling the fruit can significantly reduce the allergenic load, as the most stable proteins, including LTP, are in the skin. In clinical practice, some patients with LTP-mediated allergies tolerate peeled or well-cooked pulp, although others remain reactive, requiring individual tolerance testing (Asero *et al.*, 2012).

Zucchini flowers, traditionally used in Mediterranean cuisine, contain similar plant proteins and may be a clinically significant allergen; there are reported cases of patients reacting to the flowers but tolerating the fruit, or vice versa. Zucchini may be hidden in soups, sauces, mixed vegetable dishes, and baby food, where it is often used as an ingredient in vegetable purées. In the European Union, zucchini is not one of the 14 food allergens that must be labelled, so its presence in dishes is not always indicated.

6.3 Pumpkin (*Cucurbita maxima*)

Pumpkin (*Cucurbita maxima*) is one of the most cultivated members of the Cucurbitaceae family, with global production of approximately 23-28 million tonnes per year, widely used in food, dietary products, seed processing and oil extraction (Food and Agriculture Organisation of the United Nations, 2025) (Fig. 15). Pumpkin allergy is characterised by significant clinical variability, ranging from oral allergy syndrome to severe systemic reactions, including anaphylaxis, most often associated with seed consumption (Gawryjołek *et al.*, 2021). It is necessary to distinguish between allergies to the flesh and to the seeds, as their allergenic profiles are different.

Figure 15. Pumpkin (*Cucurbita maxima*)

6.3.1 Molecular characteristics and allergenic profiles

Two primary allergens are officially registered in the WHO/IUIS Allergen Nomenclature for *Cucurbita maxima*: Cuc ma 4 (11S globulin, legumin) and Cuc ma 5 (2S albumin), both identified in seeds according to the WHO/IUIS Allergen Nomenclature Sub-Committee (WHO/IUIS Allergen Nomenclature Sub-Committee, 2020a; WHO/IUIS Allergen Nomenclature Sub-Committee, 2020b). Other proteins, such as profilin-like components or chitinases, have been described in experimental studies for Cucurbitaceae, but do not have an approved nomenclature status for pumpkin (Bueno-Díaz *et al.*, 2021).

Profilin-like proteins in pumpkin seeds (~14 kDa) have been demonstrated to be IgE-bound components with complete inhibition by recombinant birch profilin, indicating their involvement in pollen-food syndrome and predominantly oral symptoms. The thermolability of profilins explains the mild clinical course in most patients. Pumpkin seed proteins – 2S albumin (Cuc ma 5) and 11S globulin (Cuc ma 4) – are of greatest clinical significance. 2S albumins are thermostable and resistant to proteolysis, which explains their ability to cause severe reactions, including anaphylaxis. 11S globulin shows structural homology with globulins from other seed and nut species, leading to possible cross-reactivity. 11S globulin Cuc ma 4 is the main storage protein in seeds and a substantial marker of sensitisation, especially in patients with multiple food allergies to seeds or nuts. Heat treatment can alter the allergenicity of storage proteins, in some cases increasing their immunogenicity at moderate temperatures or decreasing it with intense roasting (Chatain *et al.*, 2017).

Data on chitinases and thaumatin-like proteins in the context of clinically significant pumpkin allergy are limited: although these proteins are widespread among plants and are involved in cross-reactivity within latex-fruit syndrome, their allergenic status for *Cucurbita maxima* has not been confirmed by the WHO/IUIS and has not been clinically characterised (Blanco *et al.*, 1994; Gromek *et al.*, 2024).

6.3.2 Clinical manifestations and occupational sensitisation

Oral allergy syndrome is the main clinical form of pumpkin pulp allergy, most often in patients with pollen sensitisation, and is manifested by rapid itching, tingling or swelling in the oral cavity after consuming the raw product, with a tendency to regress spontaneously. Skin manifestations are usually limited to contact urticaria when working with fresh pumpkin, while gastrointestinal and respiratory symptoms are less common and occur mainly in sensitised individuals or when pumpkin or seed particles are inhaled. Systemic reactions and anaphylaxis are uncommon and more often associated with the consumption of pumpkin seeds, which contain thermostable reserve proteins – 2S albumins and 11S globulins. Risk factors for severe reactions include uncontrolled asthma, a history of previous systemic manifestations, and the presence of cofactors such as physical exertion, NSAID use, or alcohol consumption (Hagendorens *et al.*, 2009; Muraro *et al.*, 2022).

Occupational allergies are reported among workers exposed to fresh pumpkin, dust, or seed processing products, and manifest as contact dermatitis, urticaria, occupational rhinitis, and, less commonly, asthma. Although the biochemical differences between pumpkin varieties have not been sufficiently studied, clinical observations indicate that some patients can tolerate the pulp but react to seeds or products with a higher content of stable proteins (La Shell *et al.*, 2010).

6.3.3 Features of pumpkin seed and oil allergies

Allergy to pumpkin seeds differs from allergy to pulp and is more often associated with severe reactions due to the presence of thermostable reserve proteins – 2S albumins and 11S globulins. Clinical cases have described anaphylaxis after consuming seeds while being fully tolerant to the pulp, confirming the difference in allergenic profiles. Cross-sensitisation with other seeds, such as sunflower, sesame or flax, is due to the structural similarity of reserve proteins and is individual in nature, therefore requiring personalised testing (Patel and Bahna, 2016).

Cold-pressed pumpkin seed oil may contain trace amounts of protein and cause reactions in sensitised patients, whereas highly refined oil is generally better tolerated due to its minimal protein content. This is true for highly refined oils, as it is the “less refined/cold-pressed” oils that may

retain protein impurities and pose a risk to patients with food allergies (Anaphylaxis UK, 2023). Cosmetic products containing unrefined seed oil may cause contact reactions, including protein dermatitis, especially when applied to large areas of skin (Fritsch *et al.*, 1997; Thermo Fisher Scientific, 2025a).

6.3.4 The impact of preparation and hidden presence

Heat treatment of pumpkin pulp reduces the clinical significance of thermolabile PFAS-type allergens; therefore, cooked, baked and intensively processed foods (especially purées) are usually better tolerated than raw products. However, complete loss of allergenicity is not guaranteed (Gawryjołek *et al.*, 2021).

In contrast to the flesh, pumpkin seeds retain high allergenicity due to thermostable 2S albumins and 11S globulins, which can remain active even after roasting. This explains the reported cases of severe reactions, including anaphylaxis, even though the flesh may be well tolerated. Seeds and seed oil may be hidden ingredients in bread, muesli, bars, salads, sauces and dressings (Bueno-Díaz *et al.*, 2021).

In cosmetics, pumpkin oil and extracts are used in creams, masks and hair products, and may cause contact reactions in sensitive individuals; they are labelled as *Cucurbita maxima* seed oil, *Cucurbita pepo* seed extract or pumpkin seed oil (Sousa *et al.*, 2025).

Pumpkin is often used in baby food as a product that is generally well tolerated, and heat treatment in industrial baby food production reduces the content of thermolabile plant proteins, which potentially reduces the immunoreactivity of the product. According to paediatric recommendations for the introduction of complementary foods, pumpkin is not a priority food allergen and can be introduced at the standard time for complementary feeding. Allergic reactions in infants are rarely reported and are usually mild, manifesting mainly as skin (perioral erythema, rash) or gastrointestinal symptoms (Fewtrell *et al.*, 2017).

6.4 Clinical cases and practical experience

The clinical case below illustrates that pumpkin seed allergy, described in the literature as rare and isolated, can result in significant and potentially dangerous reactions. It highlights the importance in clinical practice of taking a detailed dietary history, including seeds and foods that are not traditionally considered common food allergens but may be clinically significant in sensitised individuals (Alsukait and Alangari, 2019).

A 4-year-old girl with an atopic background (bronchial asthma) experienced repeated episodes of systemic reactions within minutes after eating pumpkin seeds, including urticaria, angioedema of the eyelids and lips, a feeling of tightness in the throat, vomiting, and general discomfort. The symptoms regressed spontaneously within two hours, but the clinical picture was typically IgE-mediated and met the criteria for anaphylaxis. Notably, the patient tolerated other foods well, including pumpkin flesh, which highlights the difference in allergenic potential between the seeds and the flesh of the plant.

The diagnosis was based on a clear temporal relationship between product consumption and symptom development, as well as on the results of skin prick-to-prick testing, which revealed a positive reaction to pumpkin seeds (9 mm wheal with histamine control 8 mm). The presence of a specific clinical history together with a positive test made oral food provocation inappropriate and potentially dangerous (Calvani *et al.*, 2019). Thus, the diagnosis of IgE-mediated anaphylaxis

to pumpkin seeds was confirmed, a condition that, according to the literature, has been described only in isolated cases and is rare in childhood (Chatain *et al.*, 2017).

Management of this patient is consistent with contemporary principles for the treatment of food anaphylaxis and includes complete elimination of pumpkin seeds from the diet, noting potential hidden sources in baked goods, salads, or snack mixes. The family has been advised to strictly avoid the product and to learn to recognise the early signs of anaphylaxis. The patient was prescribed an age-appropriate dose of an adrenaline auto-injector with detailed instructions on how to use it in case of accidental contact (Cardona *et al.*, 2020). This approach is crucial, as even mild previous reactions do not exclude the possibility of severe anaphylaxis upon subsequent exposure. This clinical case highlights the need to consider seed allergies in children with systemic reactions of unknown origin and the importance of raising awareness of potential "hidden" food triggers that can have a significant clinical impact despite their rarity (Alsukait and Alangari, 2019).

CHAPTER 7.

Prevention and treatment

7.1 Allergen avoidance strategies

Eliminating causative allergens remains the cornerstone of food allergy management, but the modern approach requires a personalised strategy that accounts for the molecular profile of sensitisation, individual tolerance and the potential risks of nutrient deficiency. In contrast to traditional recommendations for complete elimination, data demonstrate the possibility of a differentiated approach depending on the type of sensitising proteins and cooking methods (Santos *et al.*, 2025). The personalisation of elimination measures is based primarily on the determination of the class of sensitising proteins (thermostable PR-10 proteins and profilins vs thermostable lipid-transfer proteins).

7.1.1 Primary prevention of food allergies

The concept of primary prevention has undergone a radical revision over the last decade. According to the 2020 EAACI recommendations, it is advisable to start introducing vegetable complementary foods at four to six months of age, regardless of the presence of atopic diseases in the family, as delaying the introduction of potentially allergenic foods does not provide a protective effect. The exception is infants with active moderate to severe atopic eczema, for whom a prior consultation with an allergist is recommended before introducing highly allergenic vegetables (Halken *et al.*, 2021). This is due to the increased permeability of the skin barrier and the higher risk of early food sensitisation in this category of children.

Breastfeeding during the first four to six months of life is considered a basic component of primary prevention, but there is no convincing evidence of its specific protective effect against vegetable allergies. Elimination diets in pregnant or breastfeeding mothers are not recommended, as they are not effective in preventing the development of allergies and may lead to nutrient deficiencies. For high-risk children, it is advisable to introduce new vegetables in a controlled manner, with an interval of two to three days between products (Halken *et al.*, 2021; Abrams *et al.*, 2023).

7.1.2 Secondary prevention and principles of an elimination diet

After verification of the diagnosis, the key task is to develop a personalised elimination diet that minimises exposure to the causative allergen while maintaining the nutritional adequacy of the diet. Modern data from molecular allergology can be used for a differentiated approach that incorporates the thermostability of sensitising proteins. Patients with isolated sensitisation to thermolabile profilins often tolerate heat-treated vegetables even in the presence of clinical reactions to fresh products.

More than 80% of patients with Sola l 1-mediated tomato allergy successfully tolerate tomato sauce after heat treatment at over 90°C for fifteen minutes. In such cases, it is possible to include heat-treated vegetables after a controlled provocation test (Skypala *et al.*, 2021).

Conversely, sensitisation to lipid transfer proteins requires complete elimination of all forms of the allergenic product. LTP proteins are characterised by high thermal stability and the ability to retain allergenicity after various cooking methods. Patients sensitised to Pru p 3 often show reactions to tomatoes due to cross-reactivity with Sola l 3, requiring complete elimination of fresh and processed tomato products (Asero *et al.*, 2021).

7.1.3 Identification of hidden allergens and reading labels

Vegetable ingredients are widely used as functional additives, creating a risk of unpredictable exposure. According to Regulation (EU) No 1169/2011 of the European Parliament and of the Council (2011), celery is subject to mandatory declaration, but other vegetable allergens are not always explicitly indicated on labels. Patients should emphasise terms such as "vegetable broth", "vegetable extracts", "natural colourings", or "vegetable protein", which may potentially include causally significant allergens. Cross-contamination during production poses an additional risk for highly sensitive patients. Warnings such as "may contain traces of celery" are substantial, especially for patients with a history of anaphylaxis, as individual sensitivity thresholds vary (Regulation (EU) No 1169/2011, 2011). It is worth noting that food labelling requirements may vary depending on the country and jurisdiction.

7.1.4 Safe eating outside the home and social adaptation

Dining in public catering establishments poses an increased risk due to limited control over the composition of dishes. Approximately one-third of allergic reactions to vegetables occur when eating outside the home. Patients are advised to inform staff in advance about their allergies and to use an allergy card for communication, especially when travelling (Stankovich *et al.*, 2023).

Cosmetics may contain vegetable extracts, and although absorption through intact skin is minimal, contact with damaged skin may cause reactions. Patients with severe allergies are advised to avoid cosmetics containing extracts of the causative allergen (Bruusgaard-Mouritsen *et al.*, 2020). The relevance of this issue is due to the use of plant extracts and enzymes in cosmetics.

7.1.5 Monitoring the effectiveness of elimination and prevention of nutrient deficiencies

Follow-up visits are recommended every six to twelve months to assess elimination effectiveness and nutrient status. Elimination of vegetables carries risks of deficiencies in vitamins A, C, K, folic acid, and minerals (Santos *et al.*, 2023). Consultation with a dietitian is recommended for patients who eliminate two or more vegetable groups to develop an individualised nutrient compensation plan. Periodic reassessment of the need for elimination is substantial, as spontaneous tolerance develops in 50-70% of children before adolescence (Kattan, 2016). Repeated challenge tests are recommended every one to two years when specific IgE levels decrease, or there are no reactions to accidental exposure.

7.2 Medication treatment

Pharmacological management of vegetable allergy involves emergency treatment of acute reactions and long-term strategies to modify the disease. The choice of therapeutic approach is determined by the severity of clinical manifestations, sensitisation profile and risk of systemic reactions.

7.2.1 Pharmacotherapy of acute allergic reactions

Second-generation antihistamines form the basis of symptomatic treatment for mild IgE-mediated reactions limited to skin manifestations or mild oral allergic syndrome. Drugs in this group are highly effective in relieving itching, urticaria and angioedema, with onset of action within 30-60 minutes and duration of effect up to 24 hours. The safety profile is characterised by minimal sedative effects due to low ability to cross the blood-brain barrier (Simons and Simons, 2008).

Antihistamines in this group do not prevent the development of systemic reactions and do not affect the course of anaphylaxis.

First-generation antihistamines have limited use due to their pronounced sedative and anticholinergic effects. Their parenteral forms can be used as adjunctive therapy for anaphylaxis in a hospital setting after epinephrine administration, especially in cases of severe skin manifestations. It is worth noting that antihistamines of any generation are not first-line treatments for anaphylaxis and should never delay or replace epinephrine administration (Elshehawy *et al.*, 2025).

Epinephrine remains the only pathogenetically justified and vitally necessary drug for the emergency treatment of anaphylaxis. The mechanism of action is mediated by stimulation of alpha-adrenoreceptors with a vasoconstrictor effect and beta-adrenoreceptors with bronchodilation and stabilisation of mast cell membranes. Epinephrine should be administered immediately at the first signs of anaphylaxis, as delayed administration is associated with an increased risk of fatal outcome. The recommended dosage for adults is 0.3 to 0.5 mg intramuscularly into the lateral surface of the thigh, for children, from 0.01 mg/kg body weight to a maximum of 0.3 mg (Shaker *et al.*, 2020). There are no contraindications to the use of epinephrine in anaphylaxis.

Epinephrine auto-injectors are the optimal method of administering the drug in non-hospital settings. All patients with vegetable allergies who have a history of anaphylaxis or are at high risk of developing it are advised to carry two auto-injectors at all times, as approximately 20% of anaphylaxis episodes require re-administration after 5-15 minutes (Muraro *et al.*, 2022). Patients and caregivers should receive regular training in the use of auto-injectors.

Systemic corticosteroids are traditionally prescribed as adjunctive therapy to prevent biphasic reactions, which occur in 4-23% of anaphylaxis cases 1-72 hours after the first episode. However, systematic reviews have found no convincing evidence of the effectiveness of corticosteroids in preventing biphasic reactions, which raises concerns regarding the routine prescription of these drugs (Dodd *et al.*, 2021). The decision should be made on an individual basis, incorporating the severity of the initial reaction and risk factors.

7.2.2 Long-term therapy and immunotherapy

Allergen-specific immunotherapy to pollen allergens demonstrates clinical efficacy in patients with pollen-food syndrome mediated by cross-reactivity between pollen proteins and thermostable vegetable proteins. Sublingual immunotherapy to birch pollen leads to a significant improvement in the tolerance of fresh vegetables in more than 50% of patients within 6-12 months of therapy through the induction of immunological tolerance (Kallen *et al.*, 2024). It is worth noting that ASIT to pollen allergens is only effective in sensitisation to class 2 thermostable proteins and does not affect reactions mediated by stable LTP-type allergens.

Oral immunotherapy to vegetable allergens is considered an experimental approach involving the controlled regular administration of gradually increasing doses of the causative allergen to induce desensitisation. The procedure carries a risk of allergic reactions of varying severity, including systemic reactions, which in a small proportion of patients may require the administration of epinephrine, so it can only be performed in specialised centres under the supervision of an experienced allergist. The available data are based mainly on studies of food immunotherapy in general, while the evidence base for oral immunotherapy specifically for vegetables remains limited; therefore, the method is not included in standard clinical recommendations and is used only for research purposes (Bégin *et al.*, 2020).

Biological therapy with monoclonal antibodies creates new prospects in the treatment of severe food allergies. Anti-IgE monoclonal antibodies block the binding of IgE to receptors on mast cells and basophils, which increases the threshold of tolerance to allergens and ensure the safe consumption of larger amounts of allergens (Wood *et al.*, 2024). Monoclonal antibodies to the interleukin-4 receptor block Th2-mediated allergic inflammation and can be used in eosinophilic oesophagitis associated with food allergies (Dellon *et al.*, 2022). The use of biological therapy for vegetable allergies remains largely experimental, but may be considered in patients at high risk of severe reactions or with concomitant severe atopic diseases, so the prescription of such therapy requires multidisciplinary assessment and careful patient selection.

7.3 Emergency care for anaphylaxis

Anaphylaxis is a severe, potentially life-threatening systemic allergic reaction characterised by rapid onset and involvement of multiple organ systems. Timely recognition and adequate treatment of anaphylaxis are critical to prevent fatal outcomes, as most deaths from anaphylaxis are associated with delayed administration of epinephrine or its non-use. Anaphylaxis can develop in patients with known allergies as well as upon first contact with an allergen.

7.3.1 Diagnostic criteria and clinical manifestations

The diagnosis of anaphylaxis is established clinically in the presence of one of three situations according to the NIAID/FAAN criteria. First, an acute onset of the disease within minutes or hours involving the skin and mucous membranes in combination with respiratory symptoms or hypotension. Second, two or more of the following symptoms after exposure to a suspected allergen: skin lesions, respiratory symptoms, hypotension, or persistent gastrointestinal symptoms. Third, hypotension after exposure to a known allergen for a given patient, defined as a systolic blood pressure below 90 mm Hg for adults or a decrease in systolic pressure of more than 30% from baseline for children (Sampson *et al.*, 2006).

The clinical manifestations of anaphylaxis are heterogeneous, but typically include skin symptoms in 80-90% of cases with generalised urticaria, itching, skin redness and angioedema. Respiratory symptoms are observed in 70% of cases and may manifest as dyspnoea, wheezing, stridor, a feeling of tightness in the throat, or difficulty swallowing due to laryngeal oedema. Gastrointestinal manifestations include nausea, vomiting, abdominal pain, and diarrhoea. Cardiovascular symptoms range from tachycardia and palpitations to hypotension and shock. Neurological symptoms may include dizziness, confusion, or syncope secondary to hypotension. It is worth noting that the absence of skin manifestations does not exclude the diagnosis of anaphylaxis, since 10-20% of cases may occur without urticaria or angioedema. In children, gastrointestinal symptoms may dominate over skin manifestations.

The severity of anaphylaxis varies from mild reactions with minimal symptoms to refractory shock and cardiac arrest. The classification by severity according to WAO criteria distinguishes five grades: the first degree is characterised by mild skin symptoms without systemic manifestations, the second degree includes moderate skin symptoms with mild respiratory or gastrointestinal manifestations, the third degree is manifested by pronounced respiratory symptoms or a decrease in blood pressure, the fourth degree is characterised by severe hypotension or respiratory failure requiring intensive care, and the fifth degree corresponds to cardiac arrest (Sampson *et al.*, 2006).

7.3.2 Emergency care algorithm

Initial actions in cases of suspected anaphylaxis include immediate cessation of exposure to the allergen, if possible, contacting emergency medical services, and assessing the patient's condition according to the ABC principle: airway patency, adequate breathing, and circulatory status. The patient should be placed in a horizontal position with the lower extremities elevated to improve venous return, except in cases of vomiting or severe respiratory symptoms, when a semi-sitting position is acceptable. Pregnant patients should be placed on their left side to prevent compression of the inferior vena cava.

Epinephrine intramuscularly into the lateral surface of the thigh is the first line of therapy and should be administered immediately when anaphylaxis is suspected, without delay for additional tests or other medications. The dosage for adults is 0.3-0.5 mg of a 1:1000 solution, for children 0.01 mg/kg of body weight, maximum 0.3 mg. Repeated administration of epinephrine is indicated if there is no improvement or if symptoms progress 5-15 minutes after the first dose. Approximately 20% of patients require a second dose, and 1-3% require three or more doses of epinephrine (Cardona *et al.*, 2020).

Additional therapy includes oxygen therapy with high-flow oxygen through a mask when oxygen saturation is below 92%, infusion therapy with crystalloid solutions for persistent hypotension at a rate of 5-10 ml/min for the first 5-10 minutes, and inhalation of short-acting beta-2 agonists for bronchospasm that does not respond to epinephrine. Antihistamines and corticosteroids may be prescribed as adjunctive therapy after epinephrine administration, but should not replace or delay its use. In cases of epinephrine-refractory anaphylaxis, especially in patients receiving beta-blockers, intravenous infusion of glucagon at a dose of 5-15 mcg/min may be required (Shaker *et al.*, 2020).

7.3.3 Observation and biphasic anaphylaxis

All patients with anaphylaxis require medical observation for at least four hours after symptom relief, and in cases of severe anaphylaxis or the presence of risk factors, the duration of observation should be 8-24 hours. Biphasic anaphylactic reactions are characterised by recurrence of symptoms without re-exposure to the allergen and occur in 4-23% of cases, typically 1-72 hours after the first episode. Risk factors for biphasic anaphylaxis include a delay in epinephrine administration of more than thirty minutes from the onset of symptoms, the need for repeated doses of epinephrine, the severity of the initial reaction with hypotension or respiratory failure, and the absence of corticosteroid administration (Lieberman, 2005).

Criteria for discharge include complete resolution of anaphylaxis symptoms, stable vital signs for at least 2 hours after the last dose of epinephrine, the ability to access medical care quickly in case of recurrence of symptoms, and the availability of epinephrine auto-injectors with confirmation of the patient's or caregivers' ability to use them. All patients should be provided with a written anaphylaxis action plan upon discharge and referred to an allergist within the next four weeks to verify the causative allergen and develop a long-term management strategy (Working Group of Resuscitation Council UK, 2021; Cardona *et al.*, 2020).

7.3.4 Action plan for anaphylaxis and patient education

An individual written action plan for anaphylaxis is a mandatory document for all patients at risk of anaphylaxis. The plan should include a list of known allergens, a list of anaphylaxis symptoms, step-by-step instructions for using an epinephrine auto-injector with indications for

administration, emergency contact numbers, and information about the need for medical observation after using epinephrine. The plan should be available to parents, teachers, colleagues, and others who are in regular contact with the patient. In addition, it should be reviewed regularly during follow-up visits.

Practical training in the use of epinephrine auto-injectors significantly improves patient readiness to respond appropriately to the onset of anaphylaxis. Studies show that less than half of patients prescribed auto-injectors can correctly perform the injection technique without prior training. Training should include practical demonstrations on training devices, discussion of common mistakes, and periodic review of skills during follow-up visits. Patients are advised to wear a medical bracelet or pendant with information about their allergy and the availability of epinephrine auto-injectors (Working Group of Resuscitation Council UK, 2021; Muraro *et al.*, 2022).

Psychosocial support is essential for the management of patients with a history of anaphylaxis, as anxiety about the possibility of a recurrent reaction can significantly impair quality of life. Patients and their families often need counselling on strategies for managing anxiety, adapting to social situations, and taking a balanced approach to avoiding risks without excessive restrictions. In cases of severe phobias or panic attacks, consultation with a psychologist or psychiatrist may be indicated to provide specialised care (Greiwe, 2023). Educational programmes and support promote treatment adherence and reduce unnecessary restrictions in daily life.

7.4 Dietary recommendations and alternatives

Developing a personalised diet for patients with vegetable allergies requires a balance between effectively eliminating causative allergens and ensuring that the diet is nutritionally adequate. The modern approach involves personalising dietary recommendations based on the molecular profile of sensitisation and individual tolerance to different forms of vegetable preparation. The goal of dietary recommendations is not only to avoid allergens, but also to support the healthy growth, development and quality of life of the patient.

7.4.1 Personalised diet based on molecular profile

Molecular diagnostics can be used for differentiation of elimination strategies depending on the type of sensitising proteins. Patients with isolated sensitisation to thermostable profilins or PR-10 proteins can often safely consume heat-treated vegetables, as these proteins are denatured at temperatures above 60-70°C. Boiling for 15-20 minutes, baking, or stewing usually removes the allergenicity of profilins, which reintroduces cooked foods in the diet. However, before expanding the diet, it is recommended to perform a controlled oral provocation test (Dramburg *et al.*, 2023).

Conversely, patients sensitised to lipid transfer proteins require complete elimination of all forms of the allergenic product. LTP proteins retain their structural stability after any culinary processing, including boiling, frying, baking and canning. Legume cupin proteins show partial thermolability, but standard processing may be insufficient to eliminate allergenicity without prior challenge testing (Santos *et al.*, 2023). The degree of allergenicity reduction depends on the temperature and duration of processing.

7.4.2 The effect of culinary processing on allergenicity

Different cooking methods affect the structure of vegetable proteins in different ways. Boiling in water leads to partial leaching of water-soluble allergens, but the effect is clinically significant only for thermolabile proteins. Baking at high temperatures can cause Maillard reactions, which alter

the antigenic properties of allergens in unpredictable ways. Marinating in an acidic environment can partially denature some proteins, but the effect varies depending on the specific allergen (Verhoeckx *et al.*, 2015).

Fermentation of vegetables leads to proteolytic degradation of proteins, which can reduce the allergenicity of certain products, although fermented soy products often retain significant residual allergenicity. Freezing does not affect the allergenicity of proteins (Bégin *et al.*, 2011). Thus, culinary processing cannot be considered a universal method for reducing the allergenicity of vegetables.

7.4.3 Food alternatives and practical tools

The identification of tolerable vegetables maximises the expansion of the diet while maintaining safety. Systematic testing of the tolerability of vegetables from different botanical families under the supervision of an allergist helps to compile an individual list of safe foods. Patients with pollen-food syndrome often tolerate exotic vegetables well without cross-reactivity with local pollen allergens. The expansion of the diet should be implemented gradually and under medical supervision.

Substitutions in popular dishes require recipe adaptations. Tomato sauces can be replaced with red pepper, pumpkin or beetroot-based sauces, sweet potatoes or Jerusalem artichokes can be used as an alternative to potatoes, and salads without traditional leafy vegetables can include cabbage or sprouted grains. Practical tools include sample menus, lists of safe foods with nutrient profiles, and adapted recipes (Santos *et al.*, 2025). The proposed substitutions are individualised and need to be adapted to specific sensitisation profiles.

7.4.4 Monitoring and reassessment of dietary restrictions

Consultations with a dietitian are recommended every 6-12 months to assess the actual diet and identify nutrient deficiencies. Children require regular monitoring of physical development. Laboratory assessment of critical micronutrient levels may be indicated in cases of clinical symptoms of deficiency (Sampson *et al.*, 2024).

Periodic reassessment of the need for restrictions is relevant, as natural tolerance develops in a significant proportion of patients. Indications for repeat provocation testing include a sustained decrease in specific IgE levels over time, no reactions to accidental exposure, or negative skin prick tests. Successful completion of the test can reintroduce the product with a gradual increase in portions, which significantly improves quality of life and reduces the risk of nutrient deficiencies (Santos *et al.*, 2025). This approach helps to optimise dietary restrictions and reduce their negative impact on patients' quality of life.

Conclusions and recommendations

This book systematically examines the problem of allergic diseases with an emphasis on food allergies, particularly allergies to vegetables, as a clinically significant yet insufficiently structured area of modern allergology. The main goal of the publication was to summarise scientific data and form a comprehensive overview of the mechanisms of development, clinical phenotypes, and approaches to the diagnosis and management of patients with vegetable allergies, which was consistently implemented in all sections of the book. Practical orientation of the material was emphasised, incorporating the needs of doctors of various specialities and students of higher medical education institutions.

In the process of preparing the book, the epidemiological features of vegetable allergies were analysed, and the spectrum of clinical manifestations was described, ranging from mild local reactions to severe systemic conditions, incorporating age and phenotypic characteristics. It summarises modern research on the molecular mechanisms of sensitisation, the role of major allergen families, and the patterns of cross-reactivity between food and inhalant allergens. Diagnostic approaches, including clinical assessment, traditional methods of allergy diagnosis, and a component-resolved approach, were emphasised. The principles of managing patients with different clinical phenotypes of allergic reactions are also systematised. This approach provides a comprehensive view of vegetable allergy as a multifactorial clinical condition.

A summary of the material presented addressed vegetable allergies as a heterogeneous group of conditions that differ significantly in terms of pathogenesis, clinical course and prognosis. This conceptualisation is relevant for a correct determination of clinical variability, reduction of the risk of overdiagnosis or underdiagnosis, and more rational use of modern diagnostic tools. The book complements existing theoretical and clinical knowledge and promotes the integration of molecular allergology into practical medicine. The use of a personalised approach can optimise both diagnostic and therapeutic tactics.

At the same time, certain limitations should be noted due to the limited amount of systematised clinical data on rare vegetable allergies, as well as the insufficient number of population studies in different regions. Promising areas for further scientific research include the accumulation of epidemiological data, further study of the molecular profile of vegetable allergens, improvement of component-resolved diagnostics, and deepening knowledge of the factors that determine the severity and prognosis of allergic reactions. Further development of these areas will contribute to improving the quality of diagnosis, treatment, and prevention of vegetable allergies in clinical practice.

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