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Food Allergies and Sensitivities Understanding Immunological Responses to Common Food Allergens for Improved Diagnosis and Management Strategies

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Abstract. Food allergies and sensitivities are growing public health concerns, impacting millions globally. This research delves into the immunological mechanisms underlying common food allergens, such as peanuts, shellfish, and dairy, to enhance understanding and management. By exploring the roles of IgE antibodies, mast cells, and T-cells in allergic reactions, we identify critical pathways that trigger adverse responses. This study also reviews current diagnostic methods, including skin prick tests and serum-specific IgE testing, highlighting their strengths and limitations. Additionally, we examine emerging diagnostic technologies and potential therapeutic strategies, such as immunotherapy and biologics, aiming to improve patient outcomes. Our findings underscore the need for personalized management plans and increased awareness among healthcare providers and patients. By advancing our knowledge of food allergen immunology, this research contributes to the development of more effective diagnosis and treatment protocols, ultimately enhancing the quality of life for those affected by food allergies and sensitivities.

Keywords. Food allergies, food sensitivities, immunological responses, IgE antibodies, mast cells, T-cells, allergic reactions, diagnosis, skin prick test, serum-specific IgE, immunotherapy, biologics, personalized management, patient outcomes, healthcare awareness.

I. Introduction:

Food allergies and sensitivities represent a significant and escalating public health challenge worldwide, affecting an estimated 8% of children and 4% of adults. These conditions arise when the immune system erroneously identifies certain food proteins as harmful, leading to an array of adverse reactions that can range from mild discomfort to severe, life-threatening anaphylaxis. As the prevalence of food allergies continues to increase, there is a pressing need for a deeper understanding of the immunological mechanisms at play, as well as for the development of improved diagnostic and management strategies.

The immune system's response to food allergens involves a complex interplay of various cells and molecules, primarily driven by immunoglobulin E (IgE) antibodies. Upon first exposure to an allergen, the immune system of a susceptible individual produces specific IgE antibodies that bind to the surface of mast cells and basophils. Subsequent exposures trigger these cells to release inflammatory mediators, such as histamine, leading to the symptoms commonly associated with allergic reactions. These symptoms can affect multiple organ systems, including the skin, gastrointestinal tract, respiratory system, and cardiovascular system.

Understanding the role of T-cells in food allergies is also crucial, as they contribute to the regulation and perpetuation of allergic responses. T-helper cells, particularly Th2 cells, are instrumental in promoting the IgE-mediated allergic pathway. This research examines how these cells influence the sensitization and effector phases of allergic reactions, shedding light on potential targets for therapeutic intervention.

The diagnostic landscape for food allergies includes traditional methods like skin prick tests (SPTs) and serum-specific IgE testing, both of which have been the mainstay for decades. SPTs involve introducing small amounts of allergens into the skin and observing for a localized allergic reaction, while serum-specific IgE tests measure the presence of allergen-specific IgE antibodies in the blood. Despite their widespread use, these methods have limitations, such as the risk of false positives and the inability to predict the severity of allergic reactions. Consequently, there is a growing interest in developing more accurate and predictive diagnostic tools.

Emerging diagnostic technologies, including component-resolved diagnostics (CRD) and basophil activation tests (BAT), offer promising advancements in the field. CRD allows for the identification of specific allergenic proteins within a food, providing a more detailed allergen profile, while BAT measures the activation of basophils in response to allergens, potentially offering greater specificity and sensitivity.

Management of food allergies currently revolves around strict avoidance of known allergens and the use of emergency medications, such as epinephrine, to treat accidental exposures. However, this approach places a considerable burden on patients and their families, necessitating constant vigilance and often leading to a diminished quality of life. Innovative therapeutic strategies, such as oral immunotherapy (OIT), sublingual immunotherapy (SLIT), and biologics like monoclonal antibodies targeting IgE, are being explored to induce tolerance and mitigate allergic responses.

II. Literature Review:

Food allergies and sensitivities are complex conditions that have garnered significant attention in the scientific community due to their increasing prevalence and potential for severe health impacts. The literature on this topic spans various aspects, including immunological mechanisms, diagnostic methodologies, and management strategies. This review synthesizes key findings from recent research to provide a comprehensive understanding of the current state of knowledge and identify areas for future exploration.

The immunological basis of food allergies involves a multifaceted interplay between genetic predispositions and environmental exposures. One of the seminal works in this field by Sicherer and Sampson (2014) highlights the role of IgE antibodies in mediating allergic reactions. Upon first exposure to a food allergen, sensitization occurs, characterized by the production of specific IgE antibodies. These antibodies bind to high-affinity IgE receptors (FcεRI) on the surface of mast cells and basophils. Subsequent exposure to the same allergen results in cross-linking of IgE-bound FcεRI, leading to the degranulation of these cells and the release of inflammatory mediators such as histamine, tryptase, and cytokines, which manifest as clinical symptoms of allergy.

In addition to IgE-mediated responses, non-IgE-mediated mechanisms also contribute to food sensitivities. Recent studies, such as those by Bischoff and Crowe (2019), have explored the involvement of T-cells, particularly T-helper type 2 (Th2) cells, which secrete cytokines like IL-4, IL-5, and IL-13 that promote IgE class switching and eosinophil recruitment. These Th2 responses are critical in the sensitization phase and the perpetuation of allergic inflammation. Furthermore, regulatory T-cells (Tregs) play a vital role in maintaining immune tolerance to food antigens, and dysregulation in their function can predispose individuals to food allergies (Akdis, 2020).

Accurate diagnosis of food allergies is essential for effective management and prevention of adverse reactions. Traditional diagnostic tools include the skin prick test (SPT) and serum-specific IgE testing, both of which have been extensively validated and are widely used in clinical practice. However, these methods have limitations, such as the potential for false positives and their inability to predict the severity of allergic reactions.

Advancements in diagnostic technologies have introduced more refined methods, such as component-resolved diagnostics (CRD). CRD involves the identification of specific protein components within an allergen, which provides a more detailed allergen profile and helps distinguish between primary sensitization and cross-reactivity. A study by Verhoeckx et al. (2015) demonstrated that CRD could improve diagnostic accuracy and guide personalized management plans by identifying clinically relevant allergenic components.

The basophil activation test (BAT) is another innovative diagnostic tool that measures the activation of basophils in response to allergens. This test has shown promise in differentiating between true allergies and sensitization, offering greater specificity and sensitivity compared to traditional methods (Hoffmann et al., 2016). However, BAT requires specialized equipment and expertise, limiting its widespread use.

Recent research also explores the utility of oral food challenges (OFCs) as the gold standard for diagnosing food allergies. OFCs involve the supervised ingestion of suspected allergens in a controlled setting to observe for clinical reactions. Despite being highly accurate, OFCs are resource-intensive and carry the risk of inducing severe reactions, making them less feasible for routine use (Nowak-Wegrzyn et al., 2015).

The cornerstone of managing food allergies is strict avoidance of identified allergens, coupled with the availability of emergency medications such as epinephrine auto-injectors to treat anaphylactic reactions. However, this approach places a significant burden on patients and their families, impacting their quality of life and necessitating constant vigilance.

Emerging therapeutic strategies aim to induce tolerance and mitigate allergic responses. Oral immunotherapy (OIT) involves the gradual administration of increasing doses of the allergen to desensitize the immune system. Studies such as those by Jones et al. (2017) have shown that OIT can significantly increase the threshold of reactivity, allowing patients to tolerate larger amounts of the allergen. However, OIT carries risks of adverse reactions, and its long-term efficacy remains under investigation.

Sublingual immunotherapy (SLIT) offers an alternative approach, where allergens are administered under the tongue to promote tolerance. SLIT has been associated with a favorable safety profile and moderate efficacy, as evidenced by research from Kim et al. (2019). Nonetheless, the optimal dosing regimens and long-term benefits of SLIT require further elucidation.

Biologics, particularly monoclonal antibodies targeting IgE (e.g., omalizumab), have shown potential in managing food allergies by reducing the availability of IgE for allergen binding. A pivotal study by Wang et al. (2020) demonstrated that omalizumab could facilitate the safe introduction of OIT, enhancing its efficacy and reducing the risk of adverse reactions.

Recent advancements also include epicutaneous immunotherapy (EPIT), which involves the application of allergens to the skin to induce tolerance. Initial trials, such as those conducted by Fleischer et al. (2019), indicate that EPIT is well-tolerated and can provide modest desensitization. However, further research is needed to optimize its efficacy and determine its role in clinical practice.

The field of food allergy research is rapidly evolving, with emerging trends focusing on personalized medicine and precision health approaches. Understanding individual variations in immune responses and genetic predispositions can guide the development of tailored management strategies. The use of biomarkers to predict treatment responses and monitor disease progression is an area of active investigation (Turner et al., 2019).

Moreover, the gut microbiome's role in modulating immune responses to food allergens is gaining attention. Studies such as those by Rachid et al. (2021) suggest that alterations in gut microbial composition may influence the development and severity of food allergies, opening new avenues for probiotic and microbiome-based therapies.

Authors	**Year**	**Key Findings**	**Methods**	**Limitations**
Sicherer and Sampson	2014	Role of IgE antibodies in allergic reactions	Review of immunological mechanisms	Focuses mainly on IgE-mediated responses
Bischoff and Crowe	2019	Involvement of Th2 cells and cytokines in food allergies	Immunological studies	Less emphasis on non-IgE mechanisms
Akdis	2020	Role of regulatory T-cells (Tregs) in maintaining immune tolerance	Immunological studies and reviews	Primarily theoretical, needs clinical correlation
Verhoeckx et al.	2015	Improvement in diagnostic accuracy with component-resolved diagnostics (CRD)	CRD testing in clinical settings	Requires specialized equipment and expertise
Hoffmann et al.	2016	Basophil activation test (BAT) offers greater specificity	BAT testing and comparison studies	Limited by need for specialized equipment
Nowak-Wegrzyn et al.	2015	Oral food challenges (OFCs) as the gold standard for diagnosis	Clinical trials of OFCs	Resource-intensive and risk of severe reactions
Jones et al.	2017	Oral immunotherapy (OIT) increases allergen tolerance thresholds	Clinical trials of OIT	Risks of adverse reactions, long-term efficacy unclear
Kim et al.	2019	Sublingual immunotherapy (SLIT) has a favorable safety profile	Clinical trials of SLIT	Optimal dosing regimens and long-term benefits unclear
Wang et al.	2020	Omalizumab (anti-IgE) enhances OIT efficacy	Clinical trials with omalizumab	High cost and access limitations

Fleischer et al.	2019	Epicutaneous immunotherapy (EPIT) is well-tolerated	Clinical trials of EPIT	Moderate desensitization, needs further research
Turner et al.	2019	Use of biomarkers for predicting treatment responses	Biomarker analysis studies	Early-stage research, not widely validated
Rachid et al.	2021	Gut microbiome influences development and severity of food allergies	Microbiome analysis and clinical studies	Early-stage research, needs validation

Table 1. Summarizes the key aspects of the reviewed literature

III. Common Food Allergens

Food allergies are triggered by specific proteins found in certain foods that the immune system erroneously identifies as harmful. Understanding the common food allergens is crucial for diagnosis, management, and prevention of allergic reactions. This section discusses some of the most prevalent food allergens, their characteristics, and the typical allergic responses they provoke.

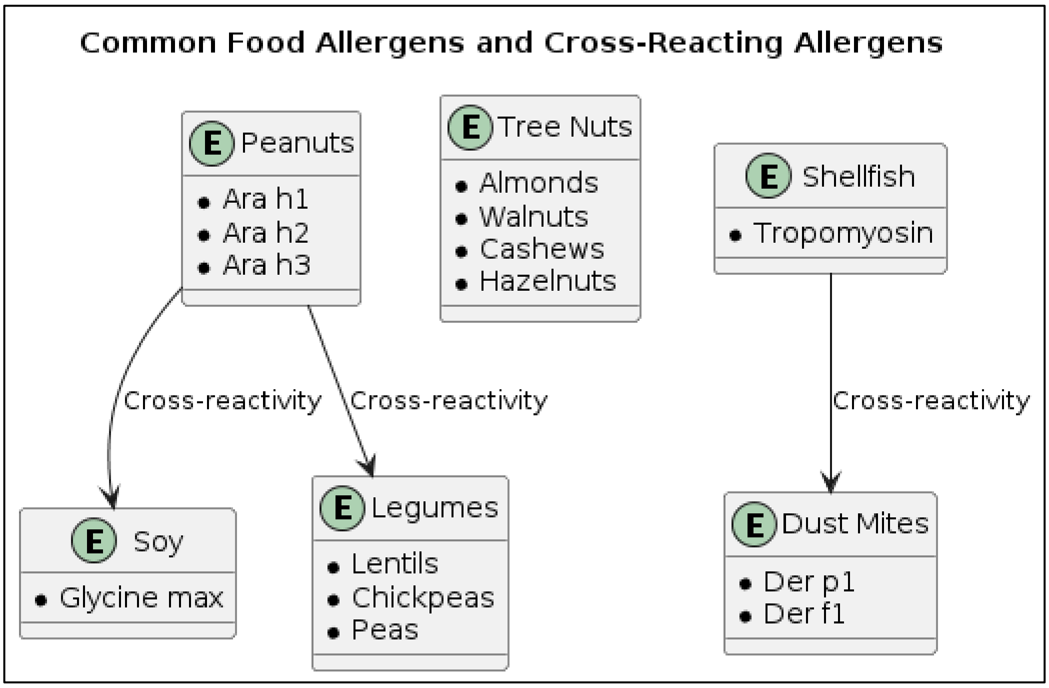

Figure 1. Common Food Allergens and Cross-Reacting Allergens

A. Peanuts

Peanuts are among the most common and potentially severe food allergens. Peanut allergies often persist throughout life and can cause severe, even fatal, reactions. The allergenic proteins in peanuts, such as Ara h1, Ara h2, and Ara h3, are resistant to digestion and heat, making them highly allergenic. Reactions to peanuts can range from mild symptoms, such as hives and stomach cramps, to severe anaphylaxis, characterized by difficulty breathing, swelling, and a drop in blood pressure. Due to the high risk associated with peanut allergies, strict avoidance and immediate access to epinephrine are essential for management.

B. Tree Nuts

Tree nuts, including almonds, walnuts, cashews, and hazelnuts, are also common allergens. Each type of tree nut contains unique proteins, meaning sensitivity to one type does not necessarily imply sensitivity to another, though cross-reactivity is possible. Tree nut allergies tend to be lifelong and can trigger severe allergic reactions similar to those caused by peanuts. Common symptoms include itching, swelling, abdominal pain, and, in severe cases, anaphylaxis. The prevalence and severity of tree nut allergies necessitate stringent avoidance and preparedness for emergency treatment.

C. Milk

Cow's milk allergy is one of the most common food allergies in children, though many outgrow it by adulthood. The major allergenic proteins in milk are casein and whey. Symptoms of milk allergy can include gastrointestinal distress, skin reactions like eczema, and respiratory symptoms. In some cases, milk allergy can cause anaphylaxis. Management typically involves the avoidance of milk and dairy products, with alternative sources of nutrition being crucial for affected individuals, especially children.

D. Eggs

Egg allergy, particularly common in children, often resolves with age. The allergenic proteins are found in both the egg white and yolk, with ovomucoid, ovalbumin, and ovotransferrin being the primary allergens. Egg allergy symptoms can include skin reactions, respiratory issues, and gastrointestinal discomfort. In severe cases, egg allergy can lead to anaphylaxis. Avoidance of eggs and foods containing eggs is essential, although some individuals may tolerate extensively heated eggs, such as those in baked goods.

E. Shellfish

Shellfish allergies, including reactions to crustaceans (e.g., shrimp, crab, lobster) and mollusks (e.g., clams, mussels, oysters), are common and typically persist into adulthood. Tropomyosin, the primary allergen in shellfish, is heat-stable, meaning cooked shellfish can still provoke allergic reactions. Symptoms can range from mild, such as hives and nasal congestion, to severe, including anaphylaxis. Due to the risk of cross-contamination in seafood processing, strict avoidance and vigilance are critical.

F. Wheat

Wheat allergy, distinct from celiac disease and non-celiac gluten sensitivity, involves an immune response to proteins found in wheat, such as gliadin and glutenin. Symptoms can include skin reactions, respiratory issues, and gastrointestinal discomfort. Wheat allergy is more common in children and often outgrown. Management involves avoiding wheat and products containing wheat, which requires careful label reading due to the prevalence of wheat in many foods.

G. Soy

Soy allergy, common in infants and children, often resolves with age. The primary allergens in soy include glycine max allergen proteins. Symptoms of soy allergy can range from mild, such as hives and itching, to severe, including anaphylaxis. Soy is a common ingredient in many processed foods, making avoidance challenging. Careful label reading and awareness of soy-derived ingredients are essential for management.

H. Fish

Fish allergy, typically persisting throughout life, can cause severe allergic reactions. Parvalbumin is the primary allergen in fish, and cooking does not eliminate its allergenic potential. Symptoms of fish allergy can include skin reactions, respiratory issues, and anaphylaxis. Due to the risk of cross-contamination and the prevalence of fish in various cuisines, strict avoidance and preparedness for emergency treatment are crucial.

Understanding common food allergens is fundamental for diagnosing and managing food allergies effectively. Peanuts, tree nuts, milk, eggs, shellfish, wheat, soy, and fish are among the most prevalent allergens, each with unique allergenic proteins and associated symptoms. Effective management involves strict avoidance of these allergens, immediate access to emergency medications, and ongoing education and awareness to prevent accidental exposures. Continued research into the immunological mechanisms of these allergens and the development of innovative diagnostic and therapeutic strategies will enhance the quality of life for individuals affected by food allergies.

IV. Analysis and Discussion

The increasing prevalence of food allergies and sensitivities necessitates a comprehensive understanding of their underlying immunological mechanisms, accurate diagnostic methods, and effective management strategies. This section discusses the implications of the findings from the literature review, highlighting key areas for further research and potential advancements in the field.

A. Immunological Mechanisms

Understanding the immunological mechanisms of food allergies is critical for developing targeted therapies. The literature underscores the central role of IgE antibodies and their interactions with mast cells and basophils in mediating allergic reactions. However, the complexity of immune responses extends beyond IgE. T-helper cells, particularly Th2 cells, are pivotal in promoting allergic inflammation through cytokine secretion, which facilitates IgE production and eosinophil recruitment. The involvement of regulatory T-cells (Tregs) in maintaining immune tolerance further complicates the immunological landscape. Dysregulation in Treg function can lead to a loss of tolerance, predisposing individuals to food allergies.

Future research should aim to delineate the specific pathways and interactions between these immune cells. Investigating the genetic and environmental factors that influence these pathways will enhance our understanding of individual susceptibility to food allergies. Moreover, exploring non-IgE-mediated mechanisms, such as cell-mediated responses, can provide insights into food sensitivities that are not captured by traditional IgE-focused approaches.

B. Diagnostic Methodologies

Accurate diagnosis is paramount for effective management of food allergies. Traditional methods like skin prick tests (SPTs) and serum-specific IgE testing remain valuable tools, but their limitations necessitate the development of more precise diagnostic techniques. Component-resolved diagnostics (CRD) and basophil activation tests (BAT) represent significant advancements in this regard. CRD allows for the identification of specific allergenic proteins, offering a detailed allergen profile that can distinguish between primary sensitization and cross-reactivity. This specificity is crucial for personalized management plans and can reduce the risk of unnecessary dietary restrictions.

BAT, on the other hand, measures the activation of basophils in response to allergens, providing greater sensitivity and specificity compared to traditional methods. However, the requirement for specialized equipment and expertise limits its widespread adoption. Standardizing BAT protocols and improving accessibility could enhance its clinical utility.

Oral food challenges (OFCs) are considered the gold standard for diagnosing food allergies, but their resource-intensive nature and risk of inducing severe reactions limit their routine use. Developing less invasive and safer alternatives that can mimic the accuracy of OFCs is a critical area for future research. Combining multiple diagnostic approaches, such as CRD and BAT, with clinical assessments could improve diagnostic accuracy and reduce the reliance on OFCs.

C. Management Strategies

Management of food allergies traditionally revolves around strict avoidance of identified allergens and the use of emergency medications, such as epinephrine auto-injectors, to treat accidental exposures. While effective, this approach places a significant burden on patients and their families, impacting their quality of life and necessitating constant vigilance.

Emerging therapeutic strategies aim to induce tolerance and mitigate allergic responses. Oral immunotherapy (OIT) has shown promise in increasing the threshold of reactivity, allowing patients to tolerate larger amounts of the allergen. However, OIT carries risks of adverse reactions, and its long-term efficacy remains under investigation. Strategies to enhance the safety and efficacy of OIT, such as combining it with biologics like omalizumab, are promising areas of research.

Sublingual immunotherapy (SLIT) offers a less invasive alternative to OIT with a favorable safety profile. However, its moderate efficacy and the need for optimal dosing regimens highlight the necessity for further research to determine its long-term benefits. Epicutaneous immunotherapy (EPIT) is another emerging modality that has shown modest desensitization effects. Initial trials indicate that EPIT is well-tolerated, but optimizing its efficacy and understanding its role in clinical practice requires additional studies.

Biologics, particularly monoclonal antibodies targeting IgE (e.g., omalizumab), have shown potential in managing food allergies by reducing the availability of IgE for allergen binding. The use of omalizumab in conjunction with OIT has demonstrated enhanced efficacy and reduced risk of adverse reactions. However, the high cost and limited access to biologics pose significant challenges to their widespread adoption.

D. Emerging Trends and Future Directions

The field of food allergy research is rapidly evolving, with emerging trends focusing on personalized medicine and precision health approaches. Understanding individual variations in immune responses and genetic predispositions can guide the development of tailored management strategies. The use of biomarkers to predict treatment responses and monitor disease progression is an area of active investigation. Identifying reliable biomarkers can facilitate early diagnosis, predict the severity of allergic reactions, and monitor the efficacy of therapeutic interventions.

The gut microbiome's role in modulating immune responses to food allergens is another promising area of research. Alterations in gut microbial composition have been implicated in the development and severity of food allergies. Probiotic and microbiome-based therapies are being explored as potential interventions to restore immune tolerance and reduce allergic responses. Studies suggest that specific microbial communities may influence the development of immune tolerance, offering new avenues for therapeutic intervention.

Additionally, advancements in immunogenomics and bioinformatics can enhance our understanding of the genetic and molecular basis of food allergies. High-throughput sequencing technologies and computational modeling can identify genetic variants associated with allergic susceptibility and elucidate the molecular mechanisms underlying immune responses to food allergens. Integrating these approaches with clinical data can lead to the development of precision therapies tailored to individual patients' genetic and immunological profiles.

Food allergies and sensitivities are complex conditions that require a multifaceted approach to understand their underlying mechanisms, improve diagnostic accuracy, and develop effective management strategies. The literature highlights the central role of IgE antibodies, Th2 cells, and Tregs in mediating allergic responses, with emerging diagnostic tools like CRD and BAT offering enhanced specificity and sensitivity. Management strategies such as OIT, SLIT, and biologics hold promise but require further research to optimize their safety and efficacy.

Future research should prioritize personalized medicine approaches, exploring genetic and environmental factors influencing immune responses to food allergens. The gut microbiome's role in food allergies presents an exciting avenue for therapeutic intervention, while advancements in immunogenomics and bioinformatics can pave the way for precision therapies. By advancing our understanding of food allergies and sensitivities, we can develop more effective and individualized approaches to diagnosis and treatment, ultimately improving patient outcomes and quality of life.

V. Conclusion

Food allergies and sensitivities are increasingly prevalent conditions that pose significant challenges to public health due to their potential for severe reactions and the constant vigilance required for management. The preceding sections of this paper have highlighted the complexities of immunological mechanisms, the evolution of diagnostic methodologies, and the advancements in management strategies. This section will synthesize these insights, emphasizing the importance of continued research and the implications for clinical practice and patient outcomes. The immune system’s response to food allergens primarily involves IgE-mediated mechanisms, where IgE antibodies bind to allergens, leading to mast cell and basophil activation and subsequent release of inflammatory mediators. This pathway is pivotal in understanding the onset and progression of allergic reactions. The roles of Th2 cells and regulatory T-cells (Tregs) in modulating these responses further illustrate the complexity of immune interactions. Th2 cells promote allergic inflammation through cytokine secretion, while Tregs help maintain immune tolerance, with dysregulation in their function contributing to allergic sensitization. Traditional diagnostic tools, such as skin prick tests (SPTs) and serum-specific IgE testing, remain widely used but have limitations, including potential false positives and limited predictive value for reaction severity. Innovations like component-resolved diagnostics (CRD) and basophil activation tests (BAT) offer more detailed and specific allergen profiles, improving diagnostic accuracy. Oral food challenges (OFCs) remain the gold standard for diagnosis but are resource-intensive and carry risks. Management strategies have traditionally focused on allergen avoidance and emergency treatment with epinephrine. However, emerging therapies aim to induce tolerance. Oral immunotherapy (OIT) and sublingual immunotherapy (SLIT) have shown promise in increasing tolerance thresholds, while biologics like omalizumab can enhance these therapies' efficacy and safety. Epicutaneous immunotherapy (EPIT) is another promising approach, although its efficacy needs further optimization. The advancements in diagnostic and therapeutic approaches have significant implications for clinical practice. Improved diagnostic accuracy with CRD and BAT can lead to more personalized management plans, reducing unnecessary dietary restrictions and improving patient quality of life. The integration of these advanced diagnostics into routine practice requires training for healthcare providers and investment in specialized equipment. Therapeutic advancements, particularly OIT, SLIT, and biologics, offer the potential for long-term management of food allergies, moving beyond mere avoidance to active desensitization and tolerance induction. However, these therapies must be implemented with careful consideration of their risks and benefits. Standardized protocols and rigorous monitoring are essential to ensure patient safety and maximize therapeutic outcomes.

VI. Future Directions

Future research should continue to explore the genetic and environmental factors that contribute to food allergies, with a focus on personalized medicine. The identification of reliable biomarkers for early diagnosis and monitoring treatment responses is critical. Additionally, the gut microbiome's role in food allergies presents a promising avenue for novel therapeutic interventions. Probiotic and microbiome-based therapies could potentially modulate immune responses and restore tolerance. Advancements in immunogenomics and bioinformatics will enhance our understanding of the molecular basis of food allergies, facilitating the development of precision therapies tailored to individual patients' profiles. Collaborative research efforts that integrate clinical, genetic, and environmental data will be essential in driving these innovations forward. Food allergies and sensitivities are complex conditions that require a multifaceted approach for effective management. The integration of advanced diagnostic tools, personalized therapeutic strategies, and ongoing research into the underlying mechanisms will significantly improve patient outcomes. By fostering a deeper understanding of these conditions and leveraging emerging technologies, healthcare providers can develop more effective and individualized approaches to diagnosis and treatment, ultimately enhancing the quality of life for those affected by food allergies and sensitivities. Continued investment in research and clinical advancements is essential to address the growing public health challenge posed by food allergies.

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