

Allergic Rhinitis in Relation to Food Allergies

Pointers to future research

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حساسية الأنف وعلاقتها بحساسية الغذاء مؤشرات للبحث في المستقبل

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ABSTRACT: Allergic rhinitis is a ubiquitous type of allergic reaction which results in significant costs to affected patients and their families. Although allergic rhinitis can coexist with other atopic conditions, the role of food allergies in the development of allergic rhinitis has not been well studied. This article explores relevant literature on this subject in order to identify gaps in the available body of knowledge and elucidate scope for further research.

Keywords: Allergic Reactions; Respiratory Hypersensitivity; Allergic Rhinitis; Food Allergies; Allergens.

المخلص: تعتبر حساسية الأنف نوع من الحساسية واسعة الانتشار والتي ينتج عنها الكثير من التكاليف المادية والصحية على المريض المصاب وعائلته. بالرغم من أن حساسية الأنف يمكن أن تكون مصاحبة لأنواع أخرى من حالات التأتب، إلا أنه لم تتم دراسة دور حساسية الغذاء كسبب مؤدي لحدوث حساسية الأنف بصورة كافية إلى الآن. تهدف هذه الورقة العلمية إلى البحث في المقالات المنشورة ذات الصلة بنفس الموضوع بغرض التعرف على المعلومات المتاحة حالياً وتحديد الفجوة المعرفية وفتح المجال للمزيد من البحوث والدراسات المستقبلية.

الكلمات المفتاحية: التفاعل التحسسي؛ فرط الحساسية الرئوي؛ الحساسية الأنفية؛ حساسية الغذاء؛ المواد المثيرة للحساسية.

ALLERGIC RHINITIS IS ONE OF THE MOST common diseases worldwide and usually persists throughout the lifetime of the affected patient. Although allergic rhinitis is not associated with significant morbidity or mortality, the burden and cost of this disease are substantial.¹ This condition is not only associated with impaired quality of sleep and cognitive function but is also a significant contributor to reduced work performance and increased school absenteeism, with resulting indirect costs greater than those incurred by asthma.² Although allergic rhinitis is an organ-specific disorder, it frequently coexists with other allergic manifestations like asthma and eczema. The presence of rhinitis is a significant risk factor for asthma and the coexistence of rhinitis is associated with poor asthma control.³ Similarly, allergic rhinitis is the most common concomitant allergic disease associated with eczema.⁴

One suggested mechanism to explain the connection between common atopic disorders such as eczema, asthma and allergic rhinitis is atopic march, which proposes that the allergic disease progresses from atopic dermatitis to asthma and, subsequently, to allergic rhinitis.⁵ Pols *et al.* observed that the prevalence of the coexistence of all three atopic diseases was 9.8 times higher than that which would be expected by chance;

moreover, the relative risk for the occurrence of asthma and eczema in patients with allergic rhinitis was 6.20 (95% confidence interval: 5.30–7.27).⁶ Similarly, the link between food allergies, asthma and eczema has been well-studied.^{7,8} However, the same cannot be said of the relationship between food allergies and allergic rhinitis. This article explores the available body of knowledge on food allergies and allergic rhinitis in order to elucidate potential pointers for future research.

Pathogenesis of Food Allergies

Adverse food reactions encompass all abnormal clinical responses to the ingestion of food and can result from either an intolerance or allergy [Figure 1].⁹ The former refers to an adverse reaction to an inherent property of the food item (i.e. toxic contamination) and is beyond the scope of this article. In contrast, a food allergy is an abnormal immunological response which may or may not be mediated by immunoglobulin E (IgE).⁹ When the gastrointestinal barrier breaks down—either due to increased permeability, as in infants, or due to an inflammatory process—sensitisation to the allergenic antigens occurs. Occasionally, sensitisation can occur via the respiratory tract or skin, bypassing the gastrointestinal

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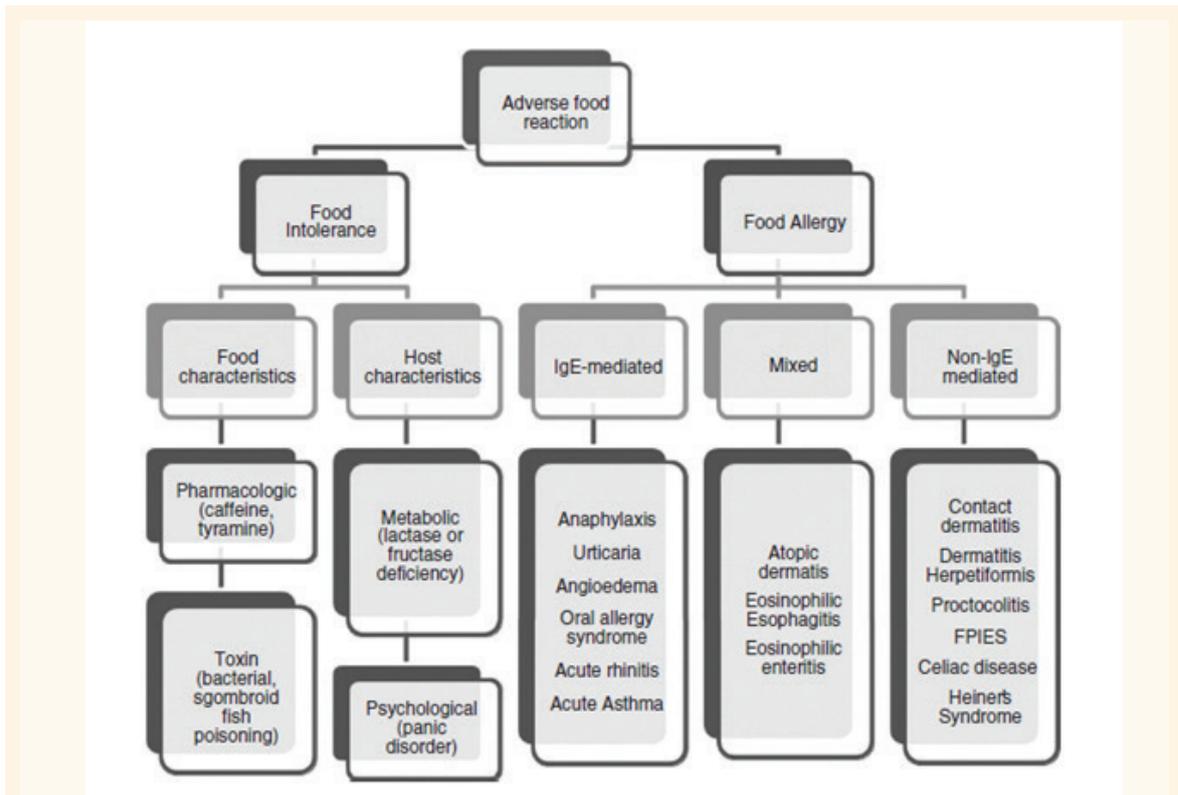


Figure 1: Classification of various food-related adverse reactions.

IgE = immunoglobulin E; FPIES = food protein-induced enterocolitis syndrome.

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barrier, as with oral allergy syndrome or pollen allergy syndrome.⁹ Food sensitisation is considered an important risk factor for developing respiratory allergies.

In the classic IgE-mediated pathway, which occurs among individuals who have been exposed to the allergen and have had an initial immune response, subsequent exposure to the allergen triggers IgE-mediated degranulation of mast cells and basophils, resulting in allergic symptoms.^{10–12} On the other hand, non-IgE-mediated food allergies, such as food protein-induced enterocolitis syndrome, food protein-induced proctocolitis and food protein enteropathy, are less common and are usually due to a chronic inflammation of the gastrointestinal tract; such conditions are mediated through allergen-specific T cells or eosinophils and primarily affect the gastrointestinal rather than respiratory tract.¹³

Allergic rhinitis is more frequently associated with a secondary rather than a primary food allergy. A secondary food allergy, also known as pollen food syndrome, involves cross-reactivity in patients with pollen allergies who develop allergic symptoms to certain types of food; it is a mild food allergy and has been associated with polyvalent airborne allergens.^{4,14} Although no specific genes have been identified, food allergies are at least in part genetically determined, with various studies confirming patterns of familial inheritance.^{15,16} Polymorphisms

in up to nine genes have been associated with the incidence or severity of food allergies, including the *CD14*, *forkhead box P3*, *signal transducer and activator of transcription 6*, *serine protease inhibitor kazal type 5* and *interleukin 10 genes*.¹⁷ However, most of these findings need to be replicated in other populations. Links between food allergies and several human leukocyte antigen (HLA) genotypes have also been found, with significant associations reported between *HLA class II DR β-1 (HLA-DRB1)*, *DQ β-1* and *DP β-1* gene polymorphisms and peanut allergies as well as between the *HLA-DRB1*07* allele and apple allergies.¹⁷ The recent increase in the prevalence of allergic disease has been attributed to either an increase in exposure to allergens among genetically predisposed individuals or via a heritable epigenetic mechanism from events that occurred while the baby was *in utero*.¹⁸ This is an exciting area for further research.

The coexistence of various allergic symptoms in the same individual cannot be explained by chance. One concept that explains this is the previously described allergic march hypothesis, which suggests a progression of symptoms from eczema and food allergies to asthma and allergic rhinitis; the later presentation of allergic rhinitis in relation to food allergies supports this concept.² Using Bayesian machine learning methods

on two large cohorts, Belgrave *et al.* suggested that this is only one of several mechanisms and concluded that heterogeneous patterns exist, with different manifestations sometimes existing independently.¹⁹ A few studies have suggested that patients with food allergies have an increased risk of developing respiratory allergies; however, these studies were relatively small and relied primarily on self-reported data.^{7,20} Of the major food allergens, peanut, milk and egg allergies significantly predispose individuals to the development of both allergic rhinitis and asthma. Additionally, patients with multiple food allergies are at increased risk of developing allergic rhinitis and asthma as compared to patients with a single food allergy.²¹ Further research on the causal relationship between food allergies and allergic rhinitis may shed more light on this topic.

Allergic Rhinitis and Food Allergies in Children

Children may be affected by different or co-existing allergic and atopic manifestations. Although allergic rhinitis affects about a third of the population, the greatest frequency of the condition is found in children and adolescents.²² The coexistence of primary food allergies and allergic rhinitis in children has been studied in a few cohort studies. In a prospective longitudinal birth cohort study in Sweden, Goksör *et al.* concluded that 40% of children with food allergies in infancy had allergic rhinitis by the time they were eight years old.²³ The onset of the food allergy was found to precede the onset of allergic rhinitis, with 47% of the children initially developing the food allergies within one year of birth while only 7.9% of children with allergic rhinitis developed the condition before two years of age; the mean age of onset of the food allergies was one year and two months, which was much earlier than the mean age at diagnosis of the allergic rhinitis at four years and nine months.²³ Although an early food allergy appears to be the strongest predictor of subsequent allergic disease, allergic march is only one of several postulated causal mechanisms.

The increased prevalence of allergic rhinitis in older children may be explained by their increased sensitisation to airborne allergens once they reach school age. In a retrospective cohort study of paediatric patients with established food allergies, Hill *et al.* found that 35% went on to develop allergic rhinitis.²¹ Additionally, the food allergens most likely to cause allergic rhinitis were peanuts, milk and eggs (odds ratios: 2.59, 1.46 and 1.8, respectively).²² In a study of French schoolchildren, Pénard-Morand *et al.* concluded that self-reported food allergies, food sensitisation and skin prick-tested

food allergies were all significantly positively associated with allergic rhinitis; moreover, these associations persisted even when the food allergy did not result in any respiratory symptoms ($P < 0.001$).²⁴

Allergic Rhinitis and Food Allergies in Adults

True food allergies occur at a rate of 0.1–1% in adults.^{25,26} Al-Rabia suggested that the peak prevalence was between 21–40 years of age, after which it decreased.²⁷ However, the available literature regarding adult allergies is limited in comparison to that of paediatric allergies. Among adults, the prevalence of food allergies varies according to culture and population. In a retrospective analysis of *in vitro* enzyme-linked immunosorbent assay results, Sahin-Yilmaz *et al.* found that the most common food allergens associated with allergic rhinitis among adults in the USA were peanuts (23.4%) and shrimp (22.2%), whereas allergies to milk (13.2%) were much less frequent.²⁸ This seems to indicate that while children tend to outgrow most common food allergies, others like peanut and crustacean allergies persist into adulthood. Among the allergens tested, peanuts had a 100% specificity and 100% positive predictive value in diagnosing food allergies with low sensitivity (26.7%) and a negative predictive value (48.8%).²⁸

Kumar *et al.* identified positive skin prick tests to one or more foods among 29.3% of Indian adult and adolescents with asthma and allergic rhinitis.²⁹ In contrast, rice (6.2%) and black gram *legumes* (5.9%) were the most common allergens, while peanuts and soybean allergens were less frequent (2–3%).²⁹ Moreover, citrus fruits and chocolate have been reported to be the primary food allergens in the Mediterranean region and Russia, while nuts, apples, pears and kiwifruit allergens are most common in Denmark and Sweden.³⁰ Additional research is therefore needed to identify the prevalence of specific allergens in other populations.

Conclusion

The development of allergic disease is complex and not well understood. Various manifestations can coexist based on individual susceptibility and exposure to different environmental factors. Early food allergies appear to be the strongest predictor of subsequent allergic disease. In terms of natural history, allergic march is a credible theory, particularly as allergic rhinitis usually presents later than food allergies. However, additional studies are needed to understand the relation between food allergies and allergic rhinitis. Exciting areas for future research include the role of genetics and epi-

genetics, the identification of specific food allergens that cause allergic rhinitis and the prevalence of various allergens in different regions of the world.

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