



Review

Occupational allergy to food-derived allergens

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Abstract: Although most cases of food allergy are related to food ingestion, occupational exposure to foods by contact or inhalation may also lead to adverse reactions, inducing contact urticaria or dermatitis, asthma, rhinitis, hypersensitivity pneumonitis, and anaphylaxis. Almost 10–25% of cases of allergic occupational asthma and rhinitis are due to food products. Animal and vegetal high-molecular weight proteins derived from aerosolized foods during food processing or handling at the workplace, as well as additives used as preservatives and antioxidants, and food contaminants, are the main causal agents. Farmers who grow and harvest crops and workers employed in food processing, storage and packing, and those involved in food preparation and transport are considered at increased risk for developing food-induced occupational asthma and rhinitis. Bakers' asthma is the most frequent type of occupational asthma all around the world. Seafood processing industry is also at higher risk for asthma and rhinitis. A proportion of cases of asthma and rhinitis in food industry is also related to latex gloves used during food processing. The diagnosis of food-related occupational asthma and rhinitis includes a careful clinical and occupational history, respiratory functional assessment and measurement of non-specific bronchial hyperresponsiveness, immunologic assessment and specific inhalation challenge. The management includes environmental interventions aimed to avoid or reduce exposure to the offending agent, pharmacologic therapy, and allergen immunotherapy when available. Only few cases of food-induced occupational anaphylaxis have been described. The management of these emergencies should follow the current guidelines on anaphylaxis. The worker should be educated in managing future possible episodes that may also occur out of the workplace, by instance after accidental ingestion of the culprit allergen, and to carry 2 pre-loaded adrenaline delivery systems and a MedicAlert bracelet.

Keywords: occupational asthma; occupational rhinitis; occupational anaphylaxis; food industry; food processing

1. Introduction

Food allergy is a growing global health issue [1]. Although most cases of food allergy are related to food ingestion, occupational exposure to foods by contact or inhalation may also lead to adverse reactions.

Food-induced respiratory reactions at the workplace include asthma, rhinitis, which may be associated to conjunctivitis [2,3,4] and hypersensitivity pneumonitis [5].

Food processing in general appears to be a major cause of the development of contact urticaria [6] and contact dermatitis. A few cases of food-induced occupational anaphylaxis (defined as anaphylaxis arising from elicitors and triggering factors attributable to a particular work environment [7]) have also been described.

The International Labour Organisation estimates that the food industry comprises about 10% of the global working population, including a broad spectrum of occupations, from farmers to food processing industry. Food-derived hazardous substances include biological agents containing high-molecular weight (HMW) (> 10 kDa) proteins derived from plant or animal sources, chemicals such as additives, and food contaminants.

This paper will review food-derived occupational asthma and rhinitis, and food-derived occupational anaphylaxis.

2. Food-Induced Occupational Asthma and Rhinitis

It is estimated that about 10–25% of adult asthma cases are related to work. Work-related asthma (WRA) encompasses two major entities, *i.e.* occupational asthma (OA), defined as a type of asthma “caused” by the workplace, and work-exacerbated asthma (WEA), *i.e.* personal asthma exacerbated at the workplace by various work-related factors (physical exercise, emotions, etc) [8].

OA is the most common type of WRA, and may be allergic, IgE or non IgE-mediated, and non-allergic, due to irritant mechanisms [8,9]. OA is associated with occupational rhinitis (OR) in up to 92% of cases, and OR may precede the onset of asthma [10]. A parallel classification of OR and OA has recently been provided [10] (Figure 1). The two conditions share same mechanisms and causal agents.

A proportion of cases of allergic OA and OR is caused by animal and vegetal HMW proteins derived from aerosolized foods during food processing or food handling at the workplace. Besides, foods may contain a variety of additives used as preservatives and antioxidants [11] and contaminants, which may also induce asthma or rhinitis [4]. A yearly updated list of occupational respiratory sensitizers including food-derived agents is available in [12].

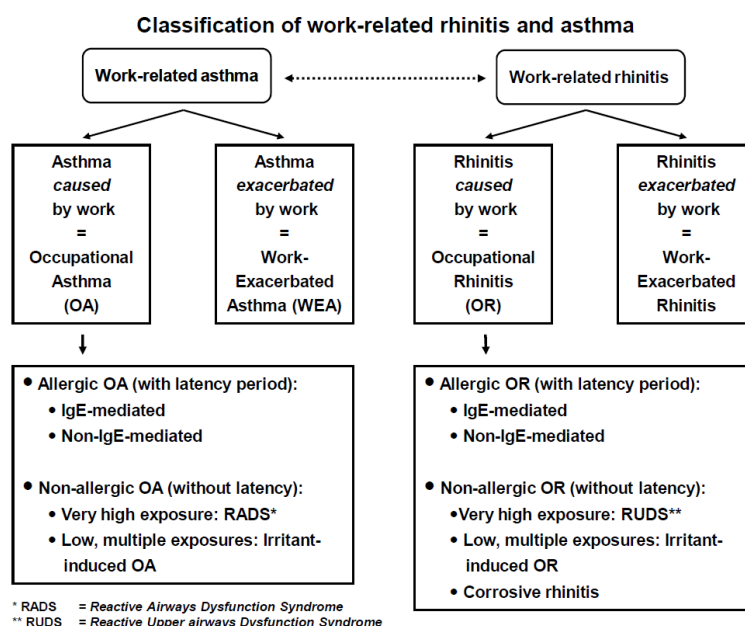


Figure 1. Classification of work-related asthma and work-related rhinitis (from Ref. 10).

Overall, 10–25% of allergic OA and OR reported to voluntary respiratory surveillance programmes are due to foods and food products [13].

The largest food-handling population is employed in the agricultural sector, and farmers who grow and harvest crops are considered at increased risk for developing food-induced OA and OR.

In food industry, workers employed in food processing, storage and packing, and those involved in food preparation (chefs and waiters) and transport are at increased risk. Cereal flour is one of the leading causes of OA and OR all around the world [14,15]. Bakers employed in small enterprises or in supermarket bakeries [16] are the workers most frequently affected, but also workers handling bakery allergens, such as confectioners, or flour millers, can develop the disease [6]. Bakers' asthma is a classical allergic IgE-mediated OA. Wheat and rye flour proteins, and the enzyme alpha-amylase used as improver are the most frequent causal allergens [14,16,17], but other enzymes [17,18,19], or contaminants such as mites or cereal pests [20,21] may be involved.

In seafood processing plants the prevalence of OA is between 2 and 36% [22]. The prevalence of OR associated with fish and seafood proteins is between 5 and 24%, although this is likely to be an underestimate [22]. OA is more commonly associated with shellfish (4–36%), which include crustaceans and molluscs, than with bony fish (2–8%).

Furthermore, the inappropriate use of latex gloves during food processing in some occupational settings, like kitchens, can also lead to the development of latex allergy and asthma [23].

2.1. Risk factors

Level of exposure and atopy are the main risk factors for the development of sensitization and OA in food industry.

An association between levels of exposure and risk of sensitisation and OA has been described in workers exposed to various allergens, such as flour, alpha-amylase, seafood [24,25,26]. In food

processing industry exposure occurs through inhalation of dust, steam, vapours, and aerosolized proteins generated during cutting, scrubbing or cleaning, cooking or boiling, or drying activities [4]. The characterization of real work exposure is a key point for prevention of allergic food-induced OA, but unfortunately air monitoring of food allergens is currently very limited [27], and a time-weighted average (TWA) Threshold Limit Value based on no observed adverse effect levels (NOAEL) has only been proposed for flour dust (0.5 mg/m^3) by ACGIH [28], but it is matter of discussion [29]. Promising new techniques able to detect various aerosolized seafood allergens at levels as low as 10 ng/m^3 have recently been developed [22], but monitoring of airborne seafood-derived allergen exposure is currently not available for routine use.

Atopy is associated with an increased risk of sensitization to seafood, green coffee beans and bakery allergens including enzymes [24,25] and with an increased risk of OA in workers exposed to flour (bakers), enzymes, and crabs, but this association has not been confirmed in other settings [24,30]. The presence of rhinitis has also been associated with an increased risk of developing OA to various food proteins [24].

2.2. Associated syndromes

Usually, workers that have developed sensitization to a food allergen at the workplace can tolerate the responsible food by ingestion, and only few cases of adverse reactions by ingestion in sensitized workers are reported in the literature [30,31]. This discrepancy may be due to localized production of specific IgE in the respiratory mucosa. Another possible explanation is that food allergens that cause OA may become denatured before they reach the alimentary tract [2].

Workers with prior ingestion-related food allergy that are employed in the food industry might experience allergic reactions as a result of inhaling the aerosolized food at the workplace. Besides, subjects with pollenosis and oral allergic syndrome caused by cross-reacting allergens shared by pollens and foods, or subjects with latex allergy and cross reacting allergens with fruits (*e.g.* kiwi, banana, avocado etc) might also experience symptoms when exposed to the aerosolized food at the workplace.

2.3. Diagnosis

The clinical investigation of food-induced OA is similar to other types of allergic OA [4], and include a stepwise approach encompassing clinical, physiological, immunological studies (Table 1) [32,33].

A careful clinical and occupational history is a key step, since an occupational origin should be suspected for every new-onset asthma in an adult [8,34,35]. A thorough description of current worker's job duties, processes in adjacent work areas, recent changes in work processes or materials, and workplace hygiene conditions should be obtained. Safety data sheets of the compounds to which the subject is directly and indirectly exposed should be gathered. Medical history should investigate the type of respiratory symptoms, and of associated symptoms such as nasal symptoms, and their relationship to work daily exposure (immediate, late or dual onset after starting daily work), and to presence or absence from work.

Table 1. Diagnostic workup of allergic occupational asthma to food products.

STEP	TEST
1. History suggestive for OA and exposure documentation	
2. Confirmation of bronchial asthma	Typical symptoms, spirometry, bronchodilator test, *NSBH to methacholine
3. Confirmation of work-relatedness of asthma	Serial measurements of **PEF, alone or associated to serial measurement of NSBH
4. Confirmation of sensitization and of causal role of an occupational agent	***SPT and serum °sIgE (when available), microarray, #BAT, §SIC with airway inflammation assessment (sputum and/or FeNO)

*NSBH: NonSpecific Bronchial Hyperresponsiveness, ** PEF: Peak Expiratory Flow, *** SPT: Skin prick test, °sIgE: serum specific IgE, #BAT: Basophil activation test, §SIC: Specific inhalation challenge.

History alone has a low specificity for establishing a diagnosis of OA [36], and should be confirmed objectively. Firstly, confirmation of the presence of bronchial asthma should be obtained by spirometry, bronchodilator test and/or measurement of non-specific bronchial hyperresponsiveness (NSBH) [37]. Afterwards, a first confirmation of work-relatedness of asthma may be obtained through serial measurement of peak expiratory flow (PEF) in periods at work and away from work [38]. To increase PEF sensibility and specificity serial measurements of NSBH to methacholine may be associated [35].

Demonstration of sensitization to a food-derived allergen or latex through skin prick tests (SPT) and/or measurement of serum specific IgE (sIgE) is the further step. A great limitation for these tools derives from the lack of validated extracts for several allergens, and often homemade extracts from raw materials are used. The use of engineering techniques (microarray) has allowed a better identification of the responsible allergenic proteins at a molecular level (molecular allergy diagnosis) in various foods [17]. In seafood parvalbumin appears to be the major fish allergen, while tropomyosin the major crustacean allergen [22]. In bakers' asthma, due to the great interindividual variation in IgE-binding profiles, no wheat allergen can be classified as the major allergen [17].

Identification of cross-reactive allergens may help diagnostic accuracy (*e.g.* latex cross reactive fruit allergens such as banana, kiwi and avocado; pollen cross-reactive spice/food allergens). Some experiences have been reported with the basophil activation test (BAT) [21,39], but this test is not yet for routine use.

The clinical relevance of a sensitisation to an allergen may be confirmed by specific inhalation challenge (SIC), which is considered the gold standard for diagnosis [40] and is the only method to verify hypersensitivity to non-allergic agents. SICs are complex procedures, time-consuming, require proper facilities and should be carried out in specialized centres by clinicians with expertise, also considering their potential danger of triggering asthmatic reactions [40].

2.4. Management

The management of food-derived OA includes timely pharmacologic therapy and environmental interventions aimed to avoid or reduce exposure to the offending agent to increase the

probability of recovery [4]. Interventions should be carried out as early as possible after onset of symptoms to prevent permanent asthma, therefore an early diagnosis is mandatory for a favourable outcome of the disease [34]. Cessation of exposure is the best option, but when the causative agent cannot be completely avoided, reduction of exposure may be considered as an alternative [41]. Strategies to reducing exposure to the causal agent are specific to each occupation, and in food industry may include modification of food processing, mechanization or automation, use of modified materials, better organization of work, improvement of workplace conditions, improving ventilation, use of protective devices [15,30]. In individuals with IgE-mediated food-induced OA specific allergen immunotherapy [SIT] might be a useful management option when validated extracts are available [34]. A short- and a long-lasting beneficial effect of SIT with wheat flour in reducing symptoms while keeping the patient at work has been shown in bakers' asthma [15,42], but at present SIT is not for routine use for bakers' asthma due to the lack of commercial validated extracts. A better identification on a molecular basis of allergens involved in flour and in other IgE-mediated food-derived OA might help in preparing new extracts suitable for immunotherapy. In selected cases of bakers' asthma, the monoclonal antibody omalizumab has been effective in reducing symptoms [43,44].

The optimal management of OA should include a follow-up programme, with periodic assessment of symptoms and lung function, and close collaboration between health care providers and patients, to provide education and skills on the disease. Education of workers on work practices able to reduce exposure and on therapy may help for a favourable outcome, and should be implemented in high-risk occupation.

3. Food-Induced Occupational Anaphylaxis

Anaphylaxis is a clinical emergency, defined as a 'severe', life-threatening systemic hypersensitivity reaction, characterized by being rapid in onset with potentially life-threatening airway, breathing, or circulatory problems. Usually, but not always, it is associated with skin and mucosal changes [45]. Foods, drugs, and stinging insects, all acknowledged also as occupational sensitizers, are key triggers. Hence, anaphylaxis occurring after exposure to food allergens at the workplace can be considered as occupational anaphylaxis (OcAn) [7]. The route of occupational exposure is by inhalation and skin contact. Similar to non-occupational allergy, the mechanisms underlying the anaphylactic reactions to workplace food-derived allergens are more usually IgE-mediated, but can be due to non-IgE allergic mechanism, or may even be non-allergic [7].

Only few cases of food-induced OcAn have been reported in the literature. Most regard subjects who had developed sensitization to a food allergen at the workplace, by inhalation and/or skin contact, but experienced systemic anaphylactic reactions outside the work environment, after ingestion of the relevant food [46–49]. A case of protein contact dermatitis with associated anaphylactic reactions occurring after direct contact and/or airborne exposure to chicory at the workplace has been described in a cook [50]. In workers employed in food industry the possibility of a non-occupational (*e.g.* domestic) exposure by ingestion, inhalation or skin contact to the same food allergens responsible for workplace reactions should always be considered and taken into account for prevention.

3.1. Diagnosis

Symptoms and signs of anaphylaxis [51], and the evidence of the causative role of a specific food sensitizer, whose exposure at the workplace can be demonstrated, are the two key points for the diagnosis of OcAn [7]. SPT and serum sIgE are suggested, when an IgE-mediated reaction is suspected. Component-resolved diagnosis, when available, may be useful in differentiating primary sensitizers from cross-reactive allergens [52]. Challenge test should be proposed only in selected cases, because of its potential danger for the patient.

3.2. Management and prevention

Emergency management of food-induced occupational anaphylactic reactions should follow current guidelines [7,51,53]. In particular, adrenaline should be administered immediately and emergency services should be called. Meanwhile, available emergency measures to maintain the airway and provide cardiopulmonary resuscitation should be delivered.

Primary prevention comprises avoiding, or at least reducing, exposure to sensitizing foods, by personal protective equipment (gloves and masks), and improved ventilation. Secondary prevention focuses on early recognition of warning signs of an allergic response. Tertiary prevention, after diagnosis is confirmed and the culprit agent identified, consists in immediate removal from further exposure, along with patient's education in managing future possible episodes that may also occur out of the workplace, by instance after accidental ingestion of the culprit allergen. Particularly, the subject should be advised to carry 2 pre-loaded adrenaline delivery systems with appropriate instructions for use and a MedicAlert bracelet stating "anaphylaxis, carries EpiPen" (or equivalent) [7].

4. Conclusion

Exposure to food allergens at the workplace may lead to cutaneous, respiratory and systemic reaction. A timely and stepwise approach is mandatory in subjects with suggestive symptoms, to plan the most appropriate management strategy including pharmacologic and environmental interventions.

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Conflict of Interest

All authors declare that they have no conflict of interest in this paper.

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