

Hidden food allergens

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This review summarizes recent advances and findings in the area of 'hidden' food allergens, i.e. allergenic foods that can either contaminate other foods, or be 'disguised' as part of a food, and cause allergic reactions. Newly emerging allergenic foods of increasing importance, recently developed methods for the detection of allergenic residues, the potential allergenicity of genetically engineered foods, and some unexpected sources of food allergens are described. *Curr Opin Allergy Clin Immunol* 1:269–271.

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Introduction

It is estimated that there are 29 000 emergency room visits and approximately 150 deaths in the USA each year as a result of anaphylactic reactions to foods [1•]. Individuals with food allergies often react adversely to the ingestion of extremely low amounts of unexpected sources of allergenic foods, including trace residues of the offending food that contaminate other foods. The threshold dose needed is not precisely known and probably varies from one individual to another. Trace contamination can arise from practices in the food industry, restaurants, and in homes and schools. Food service employees and food processors alike must be very cautious about the use of shared utensils and equipment. Most of the deaths from inadvertent exposure to allergenic foods among sensitive individuals have occurred in food-service situations (restaurants, schools, homes). The lack of labeling and the lack of knowledge of food components among both wait/kitchen staff and food-allergic customers appear to be key contributing factors in cases of severe reactions to foods in food service situations. Creative recipe formulation, as a by-product of increased demand among the population for variety in the foods we eat, and the ever-increasing consumption of food prepared outside the home could assist in producing reactions to 'hidden' food allergens. Confusing labeling terms used by the food industry have been a contributing factor in some reported severe reactions. The collective term 'spices' may well mean that many different items could be present. On the other hand, the food industry has invested a significant amount of time and effort in recent years to attain better allergen control in manufacturing facilities [2].

'Hidden' ingredients in foods

A recent study of 32 cases of anaphylactic deaths caused by food [1•] showed that most reactions were caused by the inadvertent ingestion of peanut or tree nuts (over 90%), with milk and fish accounting for the others. The paper made an ardent plea for more stringent food labeling requirements, and increased education of the food-allergic individual with respect to labeling terms and how to avoid allergenic foods. The list of commonly allergenic foods remains the same: peanut, tree nuts, eggs, cows' milk, wheat, crustacea, fish, and soybean. The presence of commonly allergenic foods as a result of unlabeled inclusion as an ingredient appears to be the reason for many reported reactions in the literature caused by 'hidden' sources of allergens. 'Natural flavors' can contain a number of commonly allergenic foods [3•]. Refined, bleached, deodorized oils, although shown to

be safe for allergic individuals in oral challenge studies, have been theorized to be a source of very small amounts of protein, causing allergic sensitization in infants [4]. Less highly refined oils including cold-pressed oils may not be safe for consumption by allergic individuals, and they may not be easily identifiable in restaurant settings. Lecithins (soy and egg) and starches are unknown in their allergenicity and their presence may not always be labeled. A recent report on soy lecithin [5] showed the presence of low levels of soy allergens. The issue of allergenicity of fish gelatin remains unproved, although a recent report [6•] showed that some fish-allergic individuals possess IgE that can bind to it, indicating the potential for eliciting allergic reactions when eaten. Fish gelatin may simply be listed as 'gelatin' in ingredient listings.

Emerging food allergens

An emerging food allergen is lupine, a legume that the food industry has only started using recently for increased nutritional and functional characteristics. In France and the USA, researchers have found lupine to cause cross-reactions in peanut-allergic individuals; a French group found that lupine flour was included at a level of 10% in wheat flour without mandatory labeling [7]. In addition, lupine would probably not be recognized by peanut-allergic individuals as an ingredient to be avoided. Other recent reports of unexpected allergens include soybean flour in sausages and other legumes [8•] in various foods. In one report [9], even children's school projects have been shown to be a source of unexpected allergens.

The issue of latex particles coming off gloves used by food service workers and potentially being a threat to latex-allergic individuals continues to be debated. In addition to food service, latex gloves are often used in the food industry. One recent case history documented an allergic reaction to orange juice stirred in a double-blind fashion with a latex gloved hand [10]. In another study [11•], the direct transfer of latex protein to cheese was visualized using an immunoblot method after a gloved finger touched the cheese. In addition, the authors found that after lettuce was handled using latex gloves, it could be demonstrated that measurable amounts of latex protein were transferred to the lettuce, and that there was an exposure-dependent increase in the level [11•]. On another related note, one recent report [12] found fairly high levels of cows' milk casein as a hidden allergen in latex gloves; the authors called for discontinuing the unlabeled use of casein as a stabilizer in latex gloves.

Allergenicity of genetically engineered foods

In the process of genetically engineering foods, proteins from one source can be expressed in another food, so it is

theoretically possible to transfer an allergen into a transgenic food product. Foods produced through agricultural biotechnology such as corn and soybeans are already in the marketplace. Agricultural biotechnology offers the promise to produce crops with improved agronomic characteristics (insect resistance, herbicide tolerance, disease resistance, climatic tolerance) and enhanced consumer benefits (better taste and texture, longer shelf life, more nutritious). Certainly, the products of agricultural biotechnology should be subjected to a careful and complete safety assessment before commercialization. As the genetic modification results in the introduction of new proteins into the transgenic crop, the potential allergenicity of the newly introduced proteins must be assessed. Although most allergens are proteins, only a few of the many proteins found in foods are allergenic under the usual conditions of exposure. The potential allergenicity of the introduced proteins can be evaluated by assessing the source of the gene, the sequence homology of the novel protein to known allergens (not only food), the expression level of the novel protein in the transgenic crop, the functional classification of the novel protein, the reactivity of the novel protein with IgE from the serum of individuals with known allergies to the source of the transferred genetic material, and various physicochemical properties of the newly introduced protein such as heat stability and digestive stability. Few transgenic crops will involve the transfer of genes from known allergenic sources. The biotechnology industry uses a decision scheme encompassing all of the aforementioned factors to assess the allergenicity of potential new crops. The original scheme was published in 1996 [13], but no improvements have so far been published, although there are efforts in this regard currently underway around the world. The scheme provides assurance that the risk of food allergens being transferred through biotechnology is extremely small.

Detection methods for allergenic residues

Several new methods based on enzyme-linked immunosorbent assay methodology have been developed in recent years for the detection of allergenic residues in foods that are not supposed to contain them. These tests have the most application in the food industry, for checking that raw ingredients and processing equipment are free of allergens. Methods for peanut have been described in the past, but in the past few years methods for hazelnut [14,15], egg [16•], sesame [17], and almond [18•] have been developed. In some studies [14,15,18•], several packaged food products were found to contain undeclared tree nut residues at levels that could be potentially hazardous to allergic individuals, whereas another study of 13 non-egg products [16•] produced no detectable egg residues. These specific and sensitive tools will enable the food industry to protect the food-

allergic consumer more efficiently, and in addition, provide a tool for the allergist to investigate cases of possible 'hidden' allergens in foods.

Conclusion

Life-threatening and fatal reactions to foods continue to occur. The global nature of the food market now brings variety to our plates, but will continue to bring us new allergenic threats as we eat foods that have never been a part of our diets before. The majority of these new foods appear to be rarely occurring allergens, and the list of commonly allergenic foods remains the same: peanut, tree nuts, eggs, cows' milk, wheat, crustacea, fish, and soybean. The food industry has made extensive changes in the way manufacturing is carried out worldwide, with control of allergens in mind, and in the past few years, immunochemical tools to assist in their risk assessment have been forthcoming, allowing for greater protection of the food-allergic consumer and more complete and accurate labeling of foods. However, there exists a need for more of these types of assays, as we lack these important tools for some of the most commonly allergic foods (e.g. crustacea, fish, soybean). Certain labeling practices still remain confusing, and there are initiatives in some countries to make ingredient listings more easily understood or more complete. In addition, we will be consuming more biotechnology derived foods in the future. The risks of food allergens being transferred through biotechnology are extremely small, and there are safety assessment schemes in place to allow an adequate assessment of the allergenic risk. There is still a great need for the education of food service workers and the allergic consumer on the practices of the food service industry with regard to 'hidden' allergens, as this is the area in which many severe and fatal reactions are occurring. On the clinical research side, there is a need for more research on the threshold levels for allergenic foods, to begin to determine the distribution of dose-response among the food-allergic population and enable us to carry out science-based risk assessment. Advances in the area of vaccines or other therapies for food allergies would allow for a reduction in the risk to food-allergic patients from 'hidden' allergens. Advances using genetic engineering techniques to downregulate or remove allergens from foods could result in the creation of reduced-allergenicity foods that cause less severe reactions.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

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