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Environmental food exposure: what is the risk of clinical reactivity from cross-contact and what is the risk of sensitization

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Abstract

For food allergic individuals, the typical method of exposure to food proteins happens during ingestion; however, individuals may be exposed to foods in other ways. In addition to ingestion reactions, allergic patients may have reactions from cutaneous or mucosal exposures to food proteins with the classic example being a peanut allergic child touching a counter with peanut butter and then rubbing their eyes. Similar to hands, saliva can also act as a carrier for food proteins. Finally, there is a wealth of new research regarding the presence of food proteins in the environment, for example, within household floor dust. This review will focus on (1) crosscontact of food proteins and (2) environmental food protein exposures. Cross-contact occurs when one type of food comes into contact with another type of food resulting in the mixture of proteins. For food allergies, cross-contact is important when an allergen is inadvertently transferred to a food/meal that is thought to not contain that specific allergen. We will discuss the current literature

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regarding the presence of detectable food proteins in different locations, how and if these proteins are transferred or eliminated, and the clinical implications of exposures to food proteins under these different scenarios.

Keywords

Food allergy; Peanut allergy; Cross-Contact; Foods in household dust; Environment

Introduction

The prevalence of food allergies has increased greatly in recent decades with the most common offending foods being peanut, tree nuts, fish, shellfish, milk, egg, wheat, soy, and seeds.¹ When a person is allergic to a food, they develop IgE antibodies that recognize specific food proteins resulting in an allergic reaction after exposure to that protein. The typical method of exposure to food proteins happens during ingestion of foods. In addition to ingestion reactions, allergic patients may have reactions from cutaneous or mucosal exposures to food proteins with the classic example being a peanut allergic child touching a counter with peanut butter and then rubbing their eyes. Similar to hands, saliva can also act as a carrier for food proteins. Finally, there is a wealth of new research regarding the presence of food proteins in the environment, for example, within household floor dust. This review will focus on (1) cross-contact of food proteins and (2) environmental food protein exposures. We will discuss the current literature regarding the presence of detectable food proteins in different locations, how and if these proteins are transferred or eliminated, and the clinical implications of exposures to food proteins under these different scenarios.

Important Terms, Definitions, and Methods of Testing

Cross-contact occurs when one type of food comes into contact with another type of food resulting in the mixture of proteins. For food allergies, cross-contact is important when an allergen is inadvertently transferred to a food/meal that is thought to not contain that specific allergen. The amount of protein that mixes may be so small that it can't be seen or smelt. A classic example of this happens when an unwashed knife, previously used to make a peanut butter sandwich is then used to make a second sandwich not made with peanut butter. A small amount of peanut protein could be on the knife and then be unknowingly incorporated into the newly made sandwich.

Other examples of cross-contact include food proteins being transferred from hands or dishes during food preparation. Restaurant kitchens are concerning places for cross-contact given that numerous meals are prepared simultaneously in a small area. Additionally, there is the risk of cross-contact on manufacturing equipment during food product processing. Precautionary allergen labelling (PAL) is meant to protect consumers from this possible unintentional exposure. While only a small amount of protein may be transferred by cross-contact, even a minute amount may be enough protein to elicit a reaction in food allergic individuals.

The term cross-contact is a relatively new term. The previously used term that may still be incorrectly used regarding food allergies is **cross-contamination**. These two terms may be confused by individuals including those in the food service industry. Cross-contamination refers to the process of microorganisms such as bacteria or viruses being unintentionally transferred into foods during the preparation or storage.

Environmental food allergen exposure refers to residual food proteins that can be measured on floors, furniture, surfaces, or in the air. This exposure is typically not thought to result in a classic ingestion-mediated food allergy reaction, but instead can play a role during cutaneous exposure to food allergens, especially in young children and/or those with an impaired skin barrier. The majority of previous literature on this topic has focused on environmental peanut exposure.

Measurement of environmental food allergen exposure is typically done by the testing of samples obtained from (1) vacuuming settled dust, (2) wiping surfaces, or (3) collection of air. The vacuuming procedure is similar to the traditional method used to collect dust for the testing of indoor aeroallergens.² This method has been used for decades in asthma and environmental allergy studies. Typically, a standardized area of the floor, furniture, or bedding is vacuumed to evaluate for proteins in settled dust. Alternatively, hard surfaces such as countertops, tables, sinks, and utensils can be evaluated by surface wipes. Moistened fiber filter wipes are used to collect any residual food proteins on the surfaces. For the evaluation of possible aerosolized food proteins, fiber filters are inserted into air collection devices. The air sampler can then be placed in a location considered to be most appropriate to detect proteins in the air, typically in close proximity to the cooking or manipulation of foods. Regardless of the collection technique, dust is later extracted for quantification of the amount of specific protein within that sample, and quantified, usually by an enzyme-linked immunosorbent assay (ELISA) directed against the whole allergen or allergenic component of the allergen.^{3,4}

Evaluation of the Presence of Food Allergens in Different Scenarios

Peanut allergen on hands after eating peanut

After eating, parents who then hold or touch their child may transfer food allergens from their own hands to the child's skin resulting in localized reactions. Likewise, a food allergic child can transfer food allergens from environmental surfaces to their mucosal surfaces, such as their eyes. The majority of research on exposure to food allergens through hand contact has been to peanut. Brough et al. were able to detect peanut on hands, 3 hours after eating peanut, up to 1.18mg per wipe using a polyclonal ELISA against whole peanut protein.⁵ The efficacy of hand-washing was assessed by Perry et al. where they placed a large dose of peanut butter (5ml) onto the hands of participants which was then wiped/washed off with water, cleaners with bleach, sanitizing wipes, liquid soap, or a bar of soap.⁶ Soap rendered the level of peanut undetectable; however, water was less effective with 25% of participants still having detectable peanut, and hand sanitizer was the least effective with 59% of participants having residual peanut. This study led to recommendations on effective cleaning methods for hands in the Food Allergy Research and Education (FARE) website, advising to use soaps rather than alcohol based sanitizer to remove food allergens from hands: <https://>

www.foodallergy.org/lifewith-food-allergies/living-well-everyday/avoiding-cross-contact.

The use of wipes to clean and remove food proteins from hands has not yet been studied in a large scale trial. If proven successful, wipes would offer a more time-efficient way to quickly clean the hands of many children in settings such as schools.

Food allergens in saliva

Parents often report that after eating a food and kissing their child on the skin, the child will develop a local allergic reaction. French kissing can, however, result in more significant allergic reactions due to the dose of saliva received and the mucosal surfaces being exposed to the allergen. Food allergy reactions after French kissing were reported in 5% of subjects in a US study and 16% in a European study.^{7,8} The majority of research into food allergen levels in saliva has been performed for peanut. When Ara h 1 was measured in saliva samples immediately after a peanut-containing meal, levels up to 40µg/ml (enough to cause an allergic reaction) could be detected; however, 87% of subjects then had undetectable levels one hour after eating without any intervention.⁹ This one hour waiting period was more reliable at reducing levels when compared to efforts to immediately clean the mouth, such as brushing or rinsing.⁹ While this one hour waiting period is effective at reducing levels, it is not perfect and protein can be detected in saliva for hours after consumption. Using a more sensitive polyclonal ELISA against whole peanut protein, Brough et al. was able to detect peanut in saliva up to three hours after ingestion.⁵

Food allergens in the home kitchen

Given that many allergen containing foods are prepared and stored in the kitchen, it is possible that various surfaces and utensils may have cross-contact with food. In the homes of 45 infants recruited from allergy clinics, the majority of kitchen surfaces had undetectable peanut levels using a polyclonal peanut ELISA; this was related to low household peanut consumption.⁵ In homes with higher household peanut consumption, peanut protein was detected on the handles of taps and dishwashers (in ascending order of magnitudes) as well as the kitchen table and infant high-chair (at lower levels). There was high within-home correlation of peanut levels on surfaces. In another study, Brough et al. showed that peanut could be quantified (using a polyclonal ELISA against whole peanut protein) on the majority of handles of taps, fridges, dishwashers, and kitchen tables (in ascending magnitude of detection) after adult participants prepared and ate a peanut butter sandwich.¹⁰ Peanut protein levels remained elevated on kitchen table surfaces the day after original samples were taken, but was not present on other handles (probably because peanut had been removed through sampling the day before).

Two studies have assessed the efficacy of removing peanut from household surfaces. After applying 5ml of peanut butter to a table, Perry et al. showed that water, cleaning products containing bleach, and alcohol-based sanitizing wipes (Lysol®) all rendered peanut undetectable (using a monoclonal peanut ELISA against Ara h 1), whereas liquid soap and a bar of soap still left detectable peanut protein in 25% of tables.⁶ Brough et al. placed a much smaller amount (0.5ml) of peanut butter on three different types of table surfaces and used a water wipe, detergent wipe, and then vigorous cleaning with detergent.⁵ A single water and detergent wipe did not remove peanut protein from these tables (using a polyclonal ELISA

against whole peanut protein), but after a vigorous detergent clean, peanut was removed from granite tables but not laminate or wooden tables, presumably due to rougher surface precluding an effective clean.^{5,11} These studies suggest that peanut was not completely removed by water, soap, and detergent, but was effectively removed by vigorous wiping with cleaning products containing bleach. The FARE website, advises using commercial cleaning agents containing bleach rather than dishwasher liquid alone to remove peanut from table surfaces: <https://www.foodallergy.org/life-with-food-allergies/living-well-evervdav/avoiding-cross-contact>.

Food allergens in food challenge unit

There are strict precautionary measures and regular cleaning procedures within food challenge units. Despite such precautions, peanut protein could be detected on bed-pillows and various surfaces within the clinical area (children's play table, toy stand, TV stand) and within the kitchen preparation area (taps, table tops, microwave) in µg/wipe levels using the peanut polyclonal ELISA.¹² The detected levels would be unlikely to be high enough for clinical reactions via the oral route.¹³

Food allergens in household dust

A wide range of food allergens have been detected in household dust including peanut,^{5,14–19} egg,^{14,20–22} cow's milk,^{14,22} and fish.^{14,20} Outside of obvious eating areas within the home, dust has been collected from bedroom areas,^{5,14,15,17–21} living rooms,^{16,20,22} and childhood play areas.^{5,17} These studies have been performed in homes in multiple countries and a detailed list of household dust studies is provided in Table 1.

The majority of these household dust studies have focused on the bedroom as a source of allergen exposure. Peanut levels in bedroom dust are strongly correlated with household peanut consumption;¹⁷ however, peanut protein is detectable in rooms where peanut is likely not being consumed or even possibly forbidden (i.e. bedroom of peanut allergic child). For example, peanut protein was present in the infant's bedsheet and play-area, even when they were not eating peanut, if other household members ate peanut.¹⁷ Sheehan et al. showed that peanut levels in the bedroom dust of school-age children with peanut allergy was lower than in the dust of children without peanut allergy, although even in children with peanut allergy the majority had detectable peanut protein levels in their bedroom dust.¹⁸ Similarly, Brough et al. also showed that a family history of peanut allergy reduced peanut levels in household dust; however, if the infant was peanut allergic, peanut levels in their bed-sheet and play-area were not reduced.¹⁷ This may be because there was no time for peanut allergen to be removed from their environment as the diagnosis was only made more recently. This also is consistent with the hypothesis that environmental peanut exposure may increase the risk of developing peanut allergy in young infants (see section below).

There are not any studies that examine the means by which food proteins, and peanut protein specifically, are spread throughout the home and into non-kitchen areas, but we have considered possible mechanisms. An obvious method would be that foods are consumed in areas of the home outside of the kitchen. Additionally, food proteins may be spread throughout the home by contact transfer on hands, clothing, or shoes. Finally, food proteins

within floor dust may be transferred with the dust around the home by passive transfer during normal activity in the home or by active transfer during cleaning of the home. These methods of transfer of protein would seem to be more likely than movement of protein via air given that while peanut proteins can become airborne, this is very short-lived and the proteins quickly settle into dust as detailed in the section below.

A study by Brough et al. has assessed methods to remove peanut protein from soft furnishings.⁵ Sofa covers were washed at 60 C without prior immediate exposure to peanut and resulted in a 98% reduction in peanut levels, whereas after immediate exposure to peanut (eating a peanut butter sandwich), washing at 60C reduced peanut levels 1000-fold. Of note, despite the significant reduction in peanut protein, there was still detectable, although very low, peanut after the wash. Similar results were found after washing pillows.

Food allergens in school dust

Outside of the home, schools have been evaluated as a source of environmental peanut protein exposure. Using a polyclonal ELISA, whole peanut protein was detectable in 100% of vacuumed floor dust samples from elementary schools in the US with similar levels in both classrooms and cafeterias.¹⁸ The levels of peanut protein in the schools were significantly higher than corresponding levels measured in students' homes. In contrast to findings for whole peanut in vacuumed dust, studies on peanut components have not shown such widespread detectability in schools. Perry et al. reported that Ara h 1 was not widely detectable by monoclonal ELISA testing of surfaces wipes collected from elementary schools.⁶ A current study evaluating the clinical impact of environmental measures to reduce aeroallergens in schools will also assess the effectiveness of these strategies to reduce peanut allergen levels in school dust.²³

Airborne food allergens

Aerosolization of food proteins can occur during the cooking or manipulation of certain foods. Examples of possible scenarios include steaming, frying, boiling, shredding, slicing, or grinding of foods. This process is more than just scents being released from foods, but can involve actual food matter, including food proteins, to become airborne during certain conditions. Once the food protein is airborne it may come into contact with a patient's mucosal surfaces including eyes, nose, and lungs. For example, some allergenic food proteins are highly water-soluble and could conceivably be extracted into steam or water vapor during cooking. In occupational environments, tropomyosin from shellfish in water vapor has been associated with sensitization in exposed workers.²⁴ It is generally recommended that allergic individuals avoid situations, such as cooking, cutting, or processing where they may come into close contact with aerosolized versions of their known allergic foods. Under specific scenarios, inhalation of aerosolized food, including fish, milk, egg, and raw meat, has been demonstrated to elicit respiratory symptoms.^{25,26}

Possible exposure to airborne peanut proteins is a common question. Several studies have demonstrated that peanut protein was not easily detected in air samples collected near peanut butter or after manipulation of peanut products including stepping on peanuts, opening bags of peanuts, and deshealing peanuts.^{5,6,27} In two studies, there was detectable airborne peanut

protein; however, this was only for a brief time and only directly above the peanuts while deshelling.^{5,27} Once the deshelling stopped, the airborne protein was no longer detectable. This indicates that the peanut dust settles and does not circulate in the air under normal conditions. Furthermore, Simonte et al. found that no children with peanut allergy experienced any symptoms when peanut butter was placed within a close distance of 12 inches to the child's face.²⁸

Food allergens in airplanes

Contact and airborne exposure to food allergens during airplane travel is commonly discussed, but infrequently studied. There are no published manuscripts evaluating the presence or absence of airborne food allergens, including peanut, on airplanes. There is one abstract presented at a meeting that found peanut in the ventilation filter of an aircraft after several hundred flights.²⁹ As noted previously, studies on land have demonstrated that peanut protein was not easily detected in air samples^{5,6,27} and that close proximity to peanut was not associated with reactions;²⁸ however, these experiments have not been conducted in airplanes at altitude where findings may or may not be different due to pressurized, recirculated air. It could be argued that food proteins should not easily circulate in the airflow because of mandated frequent air-exchange and HEPA filtration within commercial planes. Exposure to peanut or other food allergens in settled dust or on surfaces, such as seat cushions or tray tables, may be a place of unexpected food exposures on a plane. In one presented abstract, peanut-free flights had lower Ara h 2 protein measured from tray table wipes when compared to measurement of Ara h 2 from tray tables on other flights after mid-flight service with peanuts.³⁰ This supports the general recommendation that food allergic individuals clean tray tables and seat cushions prior to the start of a flight using bleach or alcohol based sanitizing wipes. It is important to carefully read cleaning product labels as certain wipes, including many baby wipes, may not contain alcohol or bleach and would be ineffective at cleaning peanut protein from surfaces.

Food allergens in restaurants

While cross-contact can happen in the home, restaurants can be particularly prone to this problem for a number of reasons including different foods being prepared in the same space, on the same counters, using the same appliances, or using the same utensils. Additionally, multiuse storage trays are prone to mixing of food and cross-contact. In a study of food allergic individuals who reported having a reaction at a restaurant, 22% of cases were reported to be the result of cross-contact from shared cooking or serving supplies.³¹ In these cases, neither the restaurant staff nor the food allergic customer was aware of the cross-contact prior to the reaction. This highlights the silent danger of cross-contact in food preparation. In a presented abstract, it was demonstrated that table surface wipes from restaurants with unshelled peanut in the eating area had higher levels of Ara h 2 as compared to table wipes from restaurants without peanuts in the eating area.³⁰ There is a lack of more advanced studies evaluating the amount of food protein in kitchen dust or other surfaces of restaurants.

Food allergens in manufacturing

Unintentional sources of allergens in packaged foods represent another potentially “hidden” risk to allergic consumers. Food manufacturers frequently used shared facilities and even shared processing equipment to make different food products. Cross-contact can occur between formulations containing commonly allergenic ingredients and other foods especially when shared equipment is used. Many food manufacturers have adopted preventive allergen controls to mitigate risks from the use of shared equipment and facilities. Food manufacturers also frequently apply voluntary PALs (e.g. “may contain”) to packaged foods made with use of shared equipment or facilities.³² The food industry has analytical tools to assess the effectiveness of their preventive allergen controls; however, because worldwide regulatory agencies have not yet accepted the concept of thresholds, food manufacturers often use effective preventive allergen controls, but still apply PAL to their packaged foods.³² Thus, some but certainly not all foods with PALs are safe for allergic consumers.³³ Unfortunately, it is impossible for the allergic consumer to determine which foods with PAL are safe. With packaged foods made using shared equipment or facilities, the biggest risk is the possibility of particulates (e.g. nut or peanut pieces) unexpectedly finding their way into other foods.

Food allergens in agriculture

Another source of unintentional allergens in packaged foods arises from agricultural comingling which occurs from shared farming fields, harvesting equipment, transportation vehicles, and grain elevators/storage facilities. The magnitude of allergic risk from agricultural comingling has not been carefully evaluated but has been shown to be low for the example of soy residues in wheat flour.³⁴ Again, particulates constitute the biggest risk with agricultural comingling. Sometimes allergen particulates can be separated from other foods, for example the screening of wheat kernels to remove soybeans.

Patients and consumers often question the risk of cross contact between peanut and tree nuts during production of these foods. The authors are not aware of any data or studies on the amount of peanut protein in tree nut products or vice versa. Agricultural comingling most typically occurs with crops that are grown or stored in close proximity. Peanuts and pecans can possibly mix during farming as both crops are grown in several southern U.S. states. Similarly, walnuts and almonds can be mixed on occasion because both are grown in California. Peanut residues would not likely be found as a result of agricultural comingling in other tree nuts beyond pecans such as walnut, almond, or cashew; however, peanut residues could occur in tree nuts as a result of cross contact in food manufacturing facilities that handle both peanuts and tree nuts.

Manufacturing companies assessment of foods for the presence of unexpected allergens

The food industry has access to a range of analytical methods to detect the presence of residues of allergenic foods in other foods or ingredients, on equipment surfaces, or in shared manufacturing facilities. ELISAs based on highly specific polyclonal or monoclonal antibodies are the most commonly employed methods.³⁵ Commercial ELISA kits are available for the detection of most of the commonly allergenic foods. The same or similar antibodies are also used to make lateral flow devices (LFDs) that can be used together with

swabs to detect qualitatively the presence of allergen residues on equipment surfaces or in rinse water.³⁶ LFDs are also commercially available for most of the commonly allergenic foods. LFDs are sufficiently rugged that they can be used within food manufacturing facilities and they can be used to validate the effectiveness of preventive allergen controls including the cleaning of shared equipment. Other methods such as PCR and mass spectrometry exist for the detection of allergen residues,³⁵ but these methods require specialized laboratories and are less widely used.

Patient assessment of foods for the presence of unexpected allergens

Currently, allergic consumers do not have access to methods for their personal use to detect allergen residues in foods; however, a handheld gluten sensor intended for consumer use was recently introduced in the U.S. Other sensing devices are known to be in development. Certainly such devices must be small, sufficiently sensitive, rugged, highly reliable, and affordable.

Clinical Impact of Exposure to Food Allergens in the Environment

The majority of studies assessing the impact of environmental food allergen exposure on the development of food sensitization and allergy have focused on peanut exposure and allergy. One Spanish study found that household consumption of almond was associated with almond sensitization, and they also found this for peanut, but not walnut.³⁷

Clinical studies on association between environmental peanut exposure, peanut sensitization, and allergy

There is an increasing body of evidence suggesting sensitization via the skin as a route for developing peanut allergy.^{38,39} In order for sensitization to occur via the skin, there must be peanut allergen in the environment. Household peanut consumption as an indirect marker of environmental peanut exposure has been shown to be associated with peanut allergy during infancy.⁴⁰ Fox et al. demonstrated that total household peanut consumption was significantly higher in houses of peanut allergic children (18.8 grams per week) than in houses of egg allergic children without peanut allergy (1.9 g/week) and in houses of non-atopic children without peanut allergy (6.9 g/week).⁴⁰

Subsequently, the role of directly measured environmental peanut exposure on the development of peanut allergy was assessed in children with a disrupted skin barrier defined by filaggrin loss of function mutations. In the birth cohort Manchester Asthma and Allergy Study (MAAS), a dose-response relationship was demonstrated between early environmental peanut protein exposure in the home and peanut sensitization and peanut allergy in children with filaggrin loss-of-function mutations.⁴¹ For every natural log (*ln*) unit increase in house dust peanut protein exposure during infancy, these children had a five-fold increased odds of peanut sensitization (OR 5.2, 95% CI: 2.1–13.1, $p<0.001$) and a three-fold increase odds in developing challenge-proven peanut allergy (OR 3.2, 95% CI: 1.1–9.8, $p=0.04$).⁴¹ Thus the more concentrated the exposure to peanut levels in dust during early life the higher the risk of subsequent peanut sensitization and peanut allergy. Data from the ALSPAC study also demonstrated that infants who were exposed to topical peanut oil (in the

form of *Arachis* oil) were at an increased risk of peanut allergy but only if they also had eczema.⁴² In the high risk CoFAR2 study, peanut levels in dust during infancy were associated with peanut sensitization.¹⁶ Furthermore, a history of eczema modified the impact of environmental peanut exposure on peanut sensitization and peanut allergy. For children with a history of eczema, each log₂ increase in peanut-dust levels more than doubled the odds of peanut allergy by 2.34 (OR 2.34, 95% CI: 1.31–4.18, $p < 0.01$).¹⁶ A schematic of the association between exposure to peanut allergens in household dust and the associated clinical outcomes is illustrated in Figure 1.

Introduction of the dual allergen exposure hypothesis

The dual-allergen exposure hypothesis proposes that early oral exposure to food protein induces tolerance, whereas early cutaneous exposure to environmental food allergen results in food sensitization and allergy development.⁴³ Randomized controlled trials such as the Learning Early About Peanut (LEAP) and Enquiring About Tolerance (EAT) studies both support the concept of inducing tolerance by early oral exposure.^{44,45} It is thought that peanut allergy results from an imbalance or improper timing of the two different routes of exposure, particularly in atopic individuals.³⁸ This hypothesis is supported by evidence that high levels of early oral exposure to peanut in infants abrogated the risk from high household peanut consumption in the study by Fox et al.⁴⁰ Likewise, in the EAT study, peanut levels in the infants' bed-dust were associated with challenge proven peanut allergy by age 36 months, but only in participants randomized to the standard introduction group (where peanut was introduced from 6 months versus 3 months in the early introduction group). Thus, in children randomized to the later introduction group, environmental peanut exposure conferred an even greater risk of developing peanut allergy, in keeping with the concept of the dual allergen exposure hypothesis.

Unanswered Question and Future Research

The evidence for clinical implications of environmental peanut exposure during infancy is strong and clinically important; however, it is uncertain if similar findings would result from environmental exposures to other foods, as peanut has been shown to have inherent adjuvant properties capable of activating innate and adaptive immune systems.⁴⁶ Future similar studies in other foods are needed. Additionally, the location of food protein exposures outside the home has not been thoroughly studied. Research in restaurants could focus on developing and assessing best practices to reduce cross-contact or unintentional exposures. Another location in need of research is the commercial airline industry. Lessons learned in the home environment may or may not be transferred to a crowded and enclosed airplane cabin travelling at a high altitude where numerous passengers share the exact same seat over the course of a day. Future research and development could focus on reliable and easy to use products for patients and consumers to reduce their risk of unintentional exposure. An example would be simple testing kits to allow for testing of foods for the presence of unexpected food proteins resulting from cross-contact or another error during processing or preparation. If reliable, this testing kit would be ideally useful for food allergic individuals when eating at a restaurant, although this may still not protect against particulate allergens in food. Additionally, easy to use and safe products could be designed to effectively remove or

eliminate unwanted food proteins from kitchen surfaces, dishes, and utensils. Finally, more research is needed in the area of the dual allergen exposure hypothesis including the appropriate timing of different allergenic foods and the benefit of early introduction in infants at low-risk in addition to those at high-risk. The summation of all these future research efforts could lead to a reduction in the prevalence of food allergies and/or a reduction in the incidence of food allergy reactions.

Conclusions

There has been much learned about environmental food exposures in recent years, for example, the clinical implications of household environmental peanut exposure during infancy. Future research should focus on expanding this field of knowledge to include more detailed studies, the evaluation of foods other than peanut, other exposure locations, and the evaluation of how these might related to clinical outcomes.

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CME EXAM

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MS# & Article title: 18–00350, Environmental Food Exposure: What is the risk of clinical reactivity from cross-contact and what is the risk of sensitization

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Learning Objectives:

1. To accurately use terminology, such as “cross-contact” and “contamination,” to describe different ways that consumers can be exposed to unexpected proteins in foods.
2. To describe how food allergens can be measured on surfaces and floors in locations such as kitchens, bedrooms, schools, and airplanes.
3. To discuss the impact of efforts to clean surfaces to eliminate unintended exposures to food proteins.
4. To discuss recent findings from clinical studies demonstrating the association between cutaneous exposures to food proteins in the environment and atopic outcomes.

Questions:

1. A young child with known peanut allergy has an allergic reaction immediately after eating his usually tolerated sandwich of only ham and cheese. It was later discovered that his sandwich was cut with an unwashed knife that had just previously been used to make a peanut butter sandwich. What is the proper term for such an occurrence where food proteins are inadvertently transferred during food preparation resulting in an increased risk for food allergic individuals?

- A. Cross-contamination
- B. Cross-contact
- C. Cross-reactive
- D. Cross-sensitization

Answer: B

Explanation: Cross-contact is the proper term to describe the process of one type of food coming into contact with another type of food resulting in the mixture of food proteins and increasing the risk of an inadvertent food exposure. Cross-contact can happen during food preparation or manufacturing. The previously used term that still may sometimes be incorrectly used is cross-contamination. Cross-contamination refers to the inadvertent transfer of microorganisms such as bacteria or viruses.

2. The amount of peanut protein in vacuumed dust samples from infants' bedrooms has been shown to be strongly correlated with which of the following?

- A. The amount of total household peanut consumption
- B. The number of people living in the home
- C. The age of the infant
- D. The variety of foods contained in the home

Answer: A

Explanation: In a study of dust samples collected from homes of infants, there was a positive correlation between peanut protein levels in the infant's bed and reported household peanut consumption in recent months. In fact, household peanut consumption was the most important variable associated with peanut protein levels in both the infant's bedding and the infant's play area.

Reference:

Brough HA, Santos AF, Makinson K, et al. Peanut protein in household dust is related to household peanut consumption and is biologically active. *J Allergy Clin Immunol* 2013;132:630–8.

3. The majority of studies assessing the relationship between environmental food allergen exposure and associated health outcomes have focused on which of the following foods?

- A. Milk
- B. Egg
- C. Peanut
- D. Wheat

Answer: C

Explanation: To date, most of the research in this field has focused on peanut exposure in household dust and associated clinical outcomes (peanut sensitization and peanut allergy). It is uncertain if similar findings would result from environmental exposures to other foods.

4. Exposure to higher levels of peanut in environmental dust during infancy has been associated with an increased risk of the development of peanut sensitization and peanut allergy particularly in children with which of the following conditions?

- A. Rhinitis
- B. Wheezing
- C. Gastroesophageal reflux
- D. Eczema and/or filaggrin mutations

Answer: D

Explanation: In a 2015 study, it was demonstrated that there was an exposure-response relationship between peanut protein levels in household dust and peanut sensitization and likely peanut allergy. This effect was augmented in children with a history of atopic dermatitis and augmented even further in children with a history of severe atopic dermatitis. Prior to these findings, a 2014 study found that early-life environmental peanut exposure was associated with an increased risk of peanut sensitization and allergy in children who carry a filaggrin mutation.

1. Brough HA, Liu AH, Sicherer S, et al. Atopic dermatitis increases the effect of exposure to peanut antigen in dust on peanut sensitization and likely peanut allergy. *J Allergy Clin Immunol* 2015;135:164–70.

2. Brough HA, Simpson A, Makinson K, et al. Peanut allergy: effect of environmental peanut exposure in children with filaggrin loss-of-function mutations. *J Allergy Clin Immunol* 2014;134:867–75 e1.

5. Which of the following statements is the basic premise of the dual allergen exposure hypothesis?

A. Early cutaneous exposure to food allergens in the environment induces tolerance, whereas early oral exposure to foods is associated with sensitization and the development of allergy.

B. Early oral exposure to foods induces tolerance, whereas early cutaneous exposure to food allergens in the environment is associated with sensitization and the development of allergy.

C. Early exposure to food proteins by either the oral or cutaneous route induces tolerance to those foods.

D. The timing of either cutaneous or oral food exposures is not associated with the development of food allergy.

Answer: B

Explanation: As noted in response to question #4 above, early exposure to environmental food proteins in children with an impaired skin barrier has been associated with the development of food allergy. In contrast, recent studies have demonstrated that early oral introduction of foods have been associated with tolerance and reduced rates of developing food allergy. These two factors comprise the dual allergen exposure hypothesis.

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Figure 1:
Peanut Allergen in Household Dust and the Associations with the Development of Peanut Allergy

Table 1:**Studies on the Presence of Food Allergens 472 in Household Dust**

<u>Study</u>	<u>Country</u>	<u>Food</u>	<u>Location in Home</u>	<u>Findings</u>
Brough HA et al.⁵ (2013)	UK	Peanut	Bedroom Childhood Play Area	<ul style="list-style-type: none"> Majority of samples from parents' bedrooms, infants' bedrooms, and parents play areas had detectable peanut There was high within-home correlation across rooms
Bertelsen RJ et al.¹⁴ (2014)	Norway	Peanut Egg Cow's Milk Fish	Bedroom	<ul style="list-style-type: none"> Detection in mattress dust samples: fish allergen (46%), peanut (41%), milk (39%), egg (22%) Smaller home and closer proximity to kitchen were associated with detectable allergens in the bedroom
Brough HA et al.¹⁵ (2018)	Sweden	Peanut	Bedroom	<ul style="list-style-type: none"> Higher levels of peanut allergen in maternal bed dust postnatally was associated with peanut sensitization later in life for the infant
Brough HA et al.¹⁶ (2015)	USA	Peanut	Living Room	<ul style="list-style-type: none"> Higher levels of peanut allergen in living room dust was associated with peanut sensitization and likely peanut allergy This association was augmented in children with atopic dermatitis
Brough HA et al.¹⁷ (2013)	UK	Peanut	Bedroom Childhood Play Area	<ul style="list-style-type: none"> There was a positive correlation between household peanut consumption and peanut allergen levels in dust from infants' sleep and play areas
Sheehan WJ et al.¹⁸ (2017)	USA	Peanut	Bedroom	<ul style="list-style-type: none"> Peanut allergen was detectable in 97% of bedroom dust samples Levels were lower, but still detectable, in bedrooms of children with peanut allergy
Trendelenburg V et al.¹⁹ (2013)	Germany	Peanut	Bedroom Eating Area	<ul style="list-style-type: none"> Majority of houses had detectable peanut in eating area or bedroom Levels were associated with peanut consumption
Dotterud LK et al.²⁰ (1997)	Norway	Egg Fish	Bedroom Living Room	<ul style="list-style-type: none"> All living room samples were detectable for codfish allergen
Trendelenburg V et al.²¹ (2018)	Germany	Egg	Bedroom Eating Area	<ul style="list-style-type: none"> Egg was detectable in dust from eating area and bed of all houses Levels were significantly increased 48 hours after egg consumption
Wittman AM et al.²² (1995)	Netherlands	Egg Cow's Milk	Living Room	<ul style="list-style-type: none"> Egg and milk proteins were detectable in the majority of dust samples