

## Original article

# Adverse food reactions by skin contact

The skin is very much exposed to food contact, both in the occupational and nonoccupational settings. Through such an exposure, adverse reactions can occur that may be irritant or immunologic. Both such types of reactions are particularly common in children with atopic dermatitis. Immunologic reactions can be immediate (immunoglobulin E-mediated) or delayed (cell-mediated), and can be localized or systemic. The latter can be life-threatening, even following trivial exposure. Clinical and experimental data are accumulating to indicate that epicutaneous exposure to food can induce *de novo* systemic immunoglobulin E sensitization.

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In addition to ingestion, adverse reactions to food can occur through inhalation, nonoral mucous membrane contact, or skin contact (1). The latter route has been well recognized in numerous occupational settings (2). On the other hand, nonoccupational skin contact is more difficult to suspect, particularly when the clinical manifestation is not clearly a classic allergic reaction. The diagnosis can be further complicated when the allergen is not the principal food but rather a food additive or a contaminant.

### Exposure setting

Occupational exposure by skin contact can occur at numerous workplaces that deal with food (Table 1). Non-occupational or sporadic exposure primarily occurs at home or wherever a person comes in contact with food. Exposure can be direct, with the food itself, or indirect, through an article that has been contaminated with the food. Indirect, hidden, or trivial exposures can be difficult to discover.

### Manifestations

Adverse reactions to food by skin contact are manifested mostly at the site of contact, but can be generalized in the skin or in another remote organ (Table 2).

### Dermatologic manifestations

Immediate skin reactions usually occur within minutes to a few hours after exposure and can be in the form of urticaria/angioedema or dermatitis of various types. Late reactions typically present as allergic contact dermatitis.

### Contact urticaria/angioedema

Lipophilic allergens can gain access to the dermis through the hair follicles and cause an immediate-type [immunoglobulin E (IgE)-mediated] reaction manifested as urticaria ( $\pm$  angioedema), often locally but it can be generalized (3–5). The latter may be attributed to circulating allergen or to circulating mediators released at the site of contact. The medical history is often diagnostic. Serum-specific IgE antibodies are usually elevated. Skin testing by epicutaneous contact or by prick is positive when the proper allergen is used. Some foods may contain histamine or other vasoactive amines (e.g. sauerkraut, pineapple, red wine, yeast, aged cheeses, pickled herring, and contaminated tuna), or may cause direct histamine release from the mast cells without the presence of specific IgE antibodies (e.g. strawberries, tomato, pineapple, and alcohol) (6,7).

Nagano et al. (8) reported three cases of localized contact urticaria to crustaceans. Interestingly, the skin test was negative to commercial extracts but positive to fresh extracts. In one patient, the urticaria occurred on

Table 1. Settings for food skin contact

|                     |
|---------------------|
| Exposure setting    |
| A. Occupational     |
| Farms               |
| Food Industry       |
| Restaurants         |
| Grocery stores      |
| Food handling       |
| B. Non-occupational |
| Homes               |
| Schools             |
| Other               |
| Mode of contact     |
| a. Direct           |
| b. Indirect         |

Table 2. Manifestations of adverse reactions to food by skin contact

|                                   |
|-----------------------------------|
| A. Dermatologic manifestations    |
| 1. Immediate reactions            |
| Contact urticaria/angioedema      |
| Irritant contact dermatitis       |
| Phototoxic contact dermatitis     |
| Protein contact dermatitis        |
| 2. Delayed reactions              |
| Allergic contact dermatitis       |
| B. Nondermatologic manifestations |
| 1. Respiratory                    |
| 2. Systemic anaphylaxis           |

contact with the shell of the shrimp but not with its meat.

In a series of 197 children allergic to fish by ingestion, Dominguez et al. (9) reported that 29 (15%) had localized or generalized urticaria following skin contact. The age of onset by skin contact was later than by ingestion. In 17 (59%) children, the reactions occurred even after indirect contact, i.e. touching a fish-contaminated article, such as napkins, eating utensils, or the fingers of another person. One of my patients is a child who had recurrent anaphylaxis upon eating minute quantities of shrimp or fish (10). He had developed generalized urticaria by touching those foods or by being merely present in the vicinity of those foods, whether fresh or cooked.

In our series of patients with severe food allergies by skin contact (11), an infant had facial angioedema after rubbing his face with his hand that was contaminated with peanut butter from another child's hand. Another infant developed generalized urticaria after his brother ate peanut butter and touched his bare leg. In some instances, the indirect exposure through skin contact can be difficult to detect. In a report on two peanut-sensitive school children (12), a few episodes of facial urticaria/angioedema occurred when playing basketball. No recurrences were noted once the ball was washed before the game and the other players washed their hands if they ate peanut butter.

Kissing is being increasingly recognized as a common method of indirect contact (skin or oral mucosa) with food allergens. This was noted in some of our milk-sensitive infants (11) as well as in reports by other authors. In a series of 379 subjects with self-reported food allergy, 20 (5.3%) reported reactions by kissing (13). The implicated foods were mostly peanuts and tree nuts. Four subjects continued to react though their partners had their teeth brushed.

#### Irritant contact dermatitis

Irritant contact dermatitis is the most common adverse reaction to foods, particularly among food handlers (14–16). The most common irritant foods are spices, garlic, onion, citrus fruits, potato, pineapple and carrot. It usually develops after chronic exposure, particularly in areas of wet skin. It primarily affects the hands, but can be limited to the finger tips. It appears as erythematous scaly eruptions that may be difficult to differentiate from chronic allergic contact dermatitis.

#### Phototoxic contact dermatitis

Food-induced phototoxic cutaneous reactions are typically caused by exposure to sunlight of the skin areas that had contact with the food. The most commonly implicated foods are celery, lime, lemon, parsley, parsnip, fig and spices. These foods contain furocoumarines, specifically bergamot (5-methoxypsoralen), that upon exposure to UVA induce a local reaction (16). The eruption is primarily erythematous and can be associated with vesicles or bullae. It appears after 1–2 days and subsides in a few to several days leaving a hyperpigmentation that may last for a few weeks. The occurrence of this type of reaction is increasing in individuals who apply perfumes and cosmetics that incorporate bergamot-containing spices (17).

#### Protein contact dermatitis

The term protein contact dermatitis was proposed in 1976 by Hjorth and Roed-Petersen (18) in referring to a particular form of contact dermatitis (not urticaria) that developed rapidly (within 30 min) in food handlers after contact with the offending food protein. The most commonly implicated foods are raw seafood, and less commonly meats, vegetables, fruits and spices (5,16,19,20).

The affected skin area is eczematous, with erythema and vesiculation. Although the clinical picture and biopsy findings are consistent with eczema, patch testing is negative.

These patients are often atopic and show positive skin prick test or specific IgE antibodies to the offending food. The underlying mechanism of this reaction is perhaps a combination of immediate (type I) and delayed (type IV) hypersensitivity reactions, possibly together with an irritant component (5,16). Some authors believe that

IgE antibodies bound to cutaneous Langerhans cells possibly mediate protein contact dermatitis (21,22).

#### Allergic contact dermatitis

When a contactant sensitizes T cells, re-exposure to the same allergen initiates a cell-mediated (type IV) reaction. A localized eczematous rash develops within 6–48 h and abates within several days. Typically, the patch test is positive but not the skin prick test or the serum-specific IgE.

The most commonly involved foods are vegetables, fruits and spices (5,16). Garlic and onion seem to be the most common (14,23,24), followed by other foods, such as citrus fruits, artichoke, asparagus, broccoli, cauliflower, celery, chicory, endive, lettuce and mango (25–28).

The major allergens in garlic are diallylsulfide and to a lesser extent allylpropyldisulfide and allicin (29,30). There is no significant cross-reactivity between garlic and onion (23) but patients sensitized to onion may react to tulip and hyacinth flowers (31). The allergen in mustard is allylisothiocyanate which is also found in horseradish, cabbage, broccoli, cauliflower, watercress, kale and brussels sprouts (32). The sensitizing allergen can be an exogenous substance added as a preservative (e.g. benzoic acid and sorbic acid), a flavoring agent (e.g. vanillin, cinnamic aldehyde, and Balsam of Peru), or an antioxidant (e.g. butylated hydroxyanisole and butylated hydroxytoluene) (5).

Patients who have allergic contact dermatitis are at risk of developing 'systemic allergic contact-type dermatitis' if they ingest the offending allergen in sufficient quantities. The eruption may be limited to the previously involved sites or it may become generalized. It appears several hours to a couple of days after ingestion and subsides within several days (16,33).

This type of reaction has been related to the ingestion of garlic, onion, certain herbs, quinine tonic water and certain spices (33). It has occurred from cashew nutshell oil which cross-reacts with the oleoresin in mango peel, ginkgo, poison ivy and poison oak (34,35). It has been caused also by food preservatives (e.g. parabens and Balsam of Peru) (33) and emulsifiers (e.g. gums and propylene glycol) (36). Cross-reactivity exists between Balsam of Peru and cinnamon, clove, orange peel, vanilla and eugenol (37). Although skin contact with nickel-containing foods has not been reported to initiate sensitization, patients who are already sensitized to nickel may develop systemic eruption after the ingestion of foods that contain nickel (33,38,39).

#### Non-dermatologic manifestations

Respiratory reactions, whether allergic or irritative, are much more likely to occur through inhalation than by skin contact. In the series reported by Dominguez et al. (9), of 29 children who reacted to fish on skin contact, one child had wheezing in addition to urticaria. Bronchospasm

secondary to food allergy by skin contact is more likely to occur as a part of multiple system involvement, i.e. systemic anaphylaxis. Systemic reactions to food by skin contact are more common in children with atopic dermatitis (40,41) or when food is applied to inflamed skin. There are two case reports (42,43) of milk-sensitive infants who developed systemic anaphylaxis following the application to an inflamed skin diaper area of an ointment that contained just 5% calcium caseinate. Interestingly, caseinate was among the 11 ingredients listed on the label of the outer paper box but not among the contents listed on the ointment tube itself. Peanut-allergic patients should be cautioned against dermatologic preparations that contain peanut oil unless the latter is of a 'refined' quality (44). One of our milk-sensitive infants, while bathing in the bathtub, developed acute urticaria and upper respiratory symptoms after a few drops of cow's milk were accidentally spilled in the bath water by a younger brother (11).

#### Causative allergens in food

In occupational cases, the offending food depends on the occupational setting (2,14,18,23,26,28). In sporadic cases, particularly in children with atopic dermatitis, the most commonly involved foods are egg, milk, fish and peanut butter (9,11,40,41). It is worth noting however, that when an adverse reaction develops following skin contact with food, the specific causative agent may not be the principal food itself. With the increasing consumption of commercially prepared foods, one has to suspect additives and potential contaminants (Table 3). Several thousand substances are used as additives in various countries. A very large number of them is widely used in the food industry for various purposes (16,45,46). In the United States, approximately 3000 additives are on file with the Food and Drug Administration; 1755 of which are regulated (47). In addition to the difficulty in obtaining such substances, they may not be listed on the food label. Furthermore, skin testing and *in vitro* tests are of very limited diagnostic reliability, except for patch testing for allergic contact dermatitis. Contaminants of foods can complicate the process of identifying the offending agent. They can be extrinsic or naturally occurring (39,48).

#### IgE sensitization by skin contact

Whereas skin contact is known to be the primary route for cell-mediated sensitization, its role in inducing *de novo* IgE sensitization is not clear. Lantner et al. (49) reported the case of systemic anaphylaxis in a 60-year-old woman after eating a psyllium-containing cereal for the first time. Her only previous exposure to psyllium was through dispensing as a nurse a psyllium-containing laxative 4 years earlier, without any symptoms. She showed a positive-skin prick test to psyllium. Her basophils

Table 3. Allergens in foods that may cause reactions by skin contact

|                                                                                              |                                                                                                                                                                                          |
|----------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>A. Foods</b>                                                                              |                                                                                                                                                                                          |
| Raw or processed vegetables, fruits, herbs, meats (beef, pork, lamb, seafood, fish, poultry) |                                                                                                                                                                                          |
| <b>B. Additives (common examples)</b>                                                        |                                                                                                                                                                                          |
| 1. Spices:                                                                                   | bay leaves, cayenne pepper, cinnamon, clove, laurel, nutmeg, vanilla                                                                                                                     |
| 2. Preservatives                                                                             | benzoates, nitrites, nitrates, parabens, salicylates, sorbic acid                                                                                                                        |
| 3. Antioxidants:                                                                             | butylated hydroxyanisole, butylated hydroxytoluene, citric acid, ethylene diamine, propyl gallate, sulfiting agents, tetraacetic acid, tocopherols,                                      |
| 4. Stabilizers:                                                                              | gums, waxes, carrageenan                                                                                                                                                                 |
| 5. Emulsifiers:                                                                              | lecithin, propylene glycol                                                                                                                                                               |
| 6. Dyes:                                                                                     | a. azo dyes: allura red amaranth, ponceau, tartrazine, sunset yellow<br>b. non-azo dyes: annatto, brilliant blue, erythrosine, indigotine<br>c. natural dyes: carmine, saffrons, tumeric |
| <b>C. Contaminants</b>                                                                       |                                                                                                                                                                                          |
| 1. Exogenous:                                                                                | fertilizers, fungicides, insecticides, herbicides, lead, mercury                                                                                                                         |
| 2. Naturally occurring:                                                                      | histamine, serotonin, tyramine, nickel                                                                                                                                                   |

released increased histamine upon exposure to psyllium, a response that was suppressed after desensitization of cells with anti-IgE. Such clinical evidence of IgE sensitization by skin contact has been supported by experimental studies in mice.

Spergel et al. (50) demonstrated that the application of ovalbumin to the shaved skin of mice induced a rise in serum total IgE and ovalbumin-specific IgE, localized allergic dermatitis, and airway hyper-responsiveness

to a single ovalbumin aerosolization. In a more recent similar study, Hsieh et al. (51) reported that mice which had been epicutaneously sensitized with ovalbumin showed a substantial rise in specific IgE and some rise in specific IgG1 antibodies. They also developed anaphylaxis and increased plasma histamine following intragastric challenge with ovalbumin. Jejunal as well as lung biopsies taken 6 h post-challenge showed inflammatory reactions. Also the spleen cells cultured with ovalbumin showed an increase in interleukin-5 production but not interferon- $\gamma$ . Their findings indicate that epicutaneous sensitization can induce T helper type 2 systemic sensitizations.

## Conclusion

Skin contact with food is very common in a wide variety of occupational and nonoccupational settings. Such an exposure can cause irritant or immunologic reactions. The latter can be of the immediate IgE-mediated or of the cell-mediated types. They particularly occur in children with atopic dermatitis and can be localized or systemic. The latter can be life-threatening, even from trivial exposures. Furthermore, there is evidence to indicate that skin contact with food can induce *de novo* systemic sensitization.

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## References

- BAHNA SL. Unusual presentations of food allergy. *Ann Allergy Asthma Immunol* 2001;**86**:414–420.
- ARESERY M, CARTIER A., WILD L., LEHRER SB. Occupational reactions to food allergens. In: METCALF, DD, SAMPSON, HA, SIMON, RA, editors. *Food Allergy: Adverse Reactions to Foods and Food Additives*, 2nd edn. Cambridge MA: Blackwell Scientific, 2003:270–298.
- LAHTI A, MAIBACH HI. Immediate contact reactions: contact urticaria syndrome. *Semin Dermatol* 1987;**6**:313–320.
- AMIN S, TANGLERTSAMPAN C, MAIBACH HI. Contact urticaria syndrome. *Am J Contact Dermatitis* 1997;**8**:15–19.
- WUTHRICH B. Food-induced cutaneous adverse reactions. *Allergy* 1998;**53**:131–135.
- MONERET-VAUTRIN DA. False food allergies: non-specific reactions to food-stuffs. In: LESSOF MA, editor. *Clinical Reactions to Food*. New York: John-Wiley, 1983:135–154.
- BURDICK AE, MATHIAS CGT. The contact urticaria syndrome. *Dermatol Clin* 1985;**3**:71–84.
- NAGANO T, KANAO K, SUGAI T. Allergic contact urticaria caused by raw prawns and shrimps: three cases. *J Allergy Clin Immunol* 1984;**74**:489–493.
- DOMINGUEZ C, OJEDA I, CRESPO JF, PASCUAL C, OJEDA A, MARTIN-ESTEBAN M. Allergic reactions following skin contact with fish. *Allergy Asthma Proc* 1996;**17**:83–87.
- BAHNA SL. Exquisite food allergy without eating. *Allergy* 1994;**49**:129–130.
- TAN BM, SHER MR, GOOD RA, BAHNA SL. Severe food allergies by skin contact. *Ann Allergy Asthma Immunol* 2001;**86**:583–586.
- TKACHYK SJ. Basketball urticaria/angioedema. *Can J Allergy Clin Immunol* 2000;**5**:6–7.
- HALLETT R, HAAPANEN L, TEUBER SS. Food allergies and kissing (Letter). *N Engl J Med* 2002;**346**:1833.
- ADAMS RM. Dermatitis in food service workers. *Allergy Proc* 1990;**11**:123–124.
- CAMARASA JG. Foods. In: GUIN, J, editor. *Practical Contact Dermatitis, a Handbook for the Practitioner*. New York: McGraw-Hill, Inc., 1995:519–537.
- CHAN EF, MOWAD C. Contact dermatitis to foods and spices. *Am J Cont Dermatol* 1998;**9**:71–79.

17. VAN DEN AKKER THW, VAN TOORENENBEREN AW, VAN JOOST TH. Contact allergy to spices. *Contact Dermatitis* 1990;**22**:267–272.
18. HJORTH N, ROED-PETERSEN J. Occupational protein contact dermatitis in food handlers. *Contact Dermatitis* 1976;**2**:28–42.
19. JANSSENS V, MORREN M, DOOMS-GOOSSENS A, DEGREEF H. Protein contact dermatitis: myth or reality? *Br J Dermatol* 1995;**132**:106.
20. ILIEV D, WUTHRICH B. Occupational protein contact dermatitis with type I allergy to different kinds of meat and vegetables. *Int Arch Occup Environ Health* 1998;**71**:289–292.
21. BRUIJNZEEL-KOOMEN C, VAN WICHEN DF, TOONSTRA J, BERRENS L, BRUYNZEEL PL. The presence of IgE molecules on epidermal Langerhans cells in patients with atopic dermatitis. *Arch Dermatol Res* 1986;**278**:199–205.
22. TOSTI A, FANTI PA, GUERRA L, PIANCASTELLI E, POGGI S, PILERI S. Morphological and immunohistological study of immediate contact dermatitis of the hands due to foods. *Contact Dermatitis* 1990;**22**:81–85.
23. VAN KETEL WG, DEHAAN P. Occupational eczema from garlic and onion. *Contact Dermatitis* 1978;**4**:53–54.
24. MCFADDEN J, WHITE DR, RYCROFT RJG. Allergic contact dermatitis from garlic. *Contact Dermatitis* 1992;**27**:333–334.
25. VAN KETEL WG. A cauliflower allergy. *Contact Dermatitis* 1975;**1**:324–325.
26. KROOK G. Occupational dermatitis from *Lactuca sativa* (lettuce) and *Cichorium* (endive). Simultaneous occurrence of immediate and delayed allergy as a cause of contact dermatitis. *Contact Dermatitis* 1977;**3**:27–36.
27. HAUSEN BM, WOLF C. 1,2,3-Trithiane-5-carboxylic acid, a first contact allergen from *Asparagus officinalis* (Liliaceae). *Am J Contact Dermatitis* 1996;**7**:41–46.
28. SANCHEZ-GUERRERO IM, ESCUDERO AI. Occupational contact dermatitis to broccoli. *Allergy* 1998;**53**:621–622.
29. PAPAGEORGIOU C, CORBET JP, MENEZES-BRANDAO F, PECEGUEIRO M, BENEZRA C. Allergic contact dermatitis to garlic (*Allium sativum*): identification of allergens. *Arch Dermatol Res* 1983;**275**:229–234.
30. LEMBO G, BALATO N, PATRUNO C, AURICCHIO L, AYALA F. Allergic contact dermatitis due to garlic. *Contact Dermatitis* 1991;**25**:330–331.
31. BURKS JW. Classic aspects of onion and garlic dermatitis in housewives. *An Allergy* 1954;**12**:592.
32. GAUL IE. Contact dermatitis from synthetic oil of mustard. *Arch Dermatol* 1964;**90**:158–159.
33. VEIEN NK. Ingested food in systemic allergic contact dermatitis. *Clinics Dermatol* 1997;**15**:547–555.
34. MARKS JG JR, DEMELFI T, MCCARTHY MA, WITTE EJ, CASTAGNOLI N, EPSTEIN WL, ABER RC. Dermatitis from cashew nuts. *J Am Acad Dermatol* 1984;**10**:627–631.
35. HAMILTON TK, ZUG KA. Systemic contact dermatitis to raw cashew nuts in a pesto sauce. *Am J Contact Dermatitis*.
36. HANNUKSELA M, FORSTROM L. Reactions to peroral propylene glycol. *Contact Dermatitis* 1978;**4**:41–45.
37. FISHER AA, MITCHELL JC. *Toxicodendron* plants and spices. In: REITSCHER, RL, FOWLER, JF, editors. *Fisher's Contact Dermatitis*. Baltimore: Williams & Wilkins, 1995:461–525.
38. NIELSEN GD, JEPSEN LV, JORGENSEN PJ, GRANDJEAN P, BRANDRUP F. Nickel-sensitive patients with vesicular hand eczema: oral challenge with a diet naturally high in nickel. *Br J Dermatol* 1990;**122**:299–308.
39. PURELLO D'AMBROSIO F, BAGNATO GF, GUARNERI B et al. The role of nickel in foods exacerbating nickel contact dermatitis. *Allergy* 1998;**53**:143–145.
40. ORANJE AP, AARSEN RS, MULDER PG, LIEFAARD G. Immediate contact reactions to cow's milk and egg in atopic children. *Acta Derm Venereol (Stockh)* 1991;**71**:263–266.
41. ORANJE AP, AARSEN RS, MULDER PG, VAN TOORENENBERGEN AW, LIEFAARD G, DIEGES PH. Food immediate-contact hypersensitivity (FICH) and elimination diet in young children with atopic dermatitis. *Acta Derm Venereol (Stockh)* 1992;**176**:41–44.
42. LECKS HI. Anaphylaxis from milk protein in diaper ointment. *JAMA* 1980;**244**:1560.
43. JARMOC LM, PRIMACK WA. Anaphylaxis to cutaneous exposure to milk protein in a diaper rash ointment. *Clin Pediatr* 1987;**26**:154–155.
44. YUNGINGER JW, CALOBRISI SD. Investigation of the allergenicity of a refined peanut oil-containing topical dermatologic agent in persons who are sensitive to peanuts. *Cutis* 2001;**68**:153–155.
45. SAULSON D, SAULSON E. *A Pocket Guide to Food Additives*. Huntington Beach, CA: VPS Publishing, 1991.
46. DAVID JJ. *Food and Food Additive Intolerance in Childhood*. Cambridge, MA: Blackwell Scientific Publications, 1983:177–221.
47. US FOOD AND DRUG ADMINISTRATION. *Everything Added to Food in the United States*. Boca Raton, FL: CRC Press, 1993.
48. TAYLOR SL. Food toxicology. In: METCALFE, DD, SAMPSON, HA, SIMON, RA, editors. *Food Allergy: Adverse Reactions to Foods and Food Additives*, 2nd edn. Cambridge MA: Blackwell Scientific, 1997:485–497.
49. LANTNER RR, ESPIRITU BR, ZUMERCHIK P, TOBIN MC. Anaphylaxis following ingestion of a psyllium-containing cereal. *JAMA* 1990;**264**:2534–2536.
50. SPERGEL JM, MIZOGUCHI E, BREWER JP, MARTIN TR, BHAN AK, GEHA RS. Epicutaneous sensitization with protein antigen induces localized allergic dermatitis and hyperresponsiveness to methacholine after single exposure to aerosolized antigen in mice. *J Clin Invest* 1998;**101**:1614–1622.
51. HSIEH KY, TSAI CC, WU CH, LIN RH. Epicutaneous exposure to protein antigen and food allergy. *Clin Exp Allergy* 2003;**33**:1067–1075.