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Occupational protein contact dermatitis

Occupational contact dermatitis is generally caused by haptens but can also be induced by proteins causing mainly immunological contact urticaria (ICU); chronic hand eczema in the context of protein contact dermatitis (PCD). In a monocentric retrospective study, from our database, only 31 (0.41%) of patients with contact dermatitis had positive skin tests with proteins: 22 had occupational PCD, 3 had non-occupational PCD, 5 occupational ICU and 1 cook had a neutrophilic fixed food eruption (NFFE) due to fish. From these results and analysis of literature, the characteristics of PCD can be summarized as follows. It is a chronic eczematous dermatitis, possibly exacerbated by work, suggestive if associated with inflammatory perionyxix and immediate erythema with pruritis, to be investigated when the patient resumes work after a period of interruption. Prick tests with the suspected protein-containing material are essential, as patch tests have negative results. In case of multisensitisation revealed by prick tests, it is advisable to analyse IgE against recombinant allergens. A history of atopy, found in 56 to 68% of the patients, has to be checked for. Most of the cases are observed among food-handlers but PCD can also be due to non-edible plants, latex, hydrolysed proteins or animal proteins. Occupational exposure to proteins can thus lead to the development of ICU. Reflecting hypersensitivity to very low concentrations of allergens, investigating ICU therefore requires caution and prick tests should be performed with a diluted form of the causative protein-containing product. Causes are food, especially fruit peel, non-edible plants, cosmetic products, latex, animals.

Key words: protein contact dermatitis, chronic hand eczema, prick test, protein allergy, immunological contact urticaria, neutrophilic fixed food eruption

Occupational contact dermatitis is generally caused by haptens but it can also be induced by proteins causing immunological contact urticaria (ICU), chronic hand eczema in the context of protein contact dermatitis (PCD) or less common skin conditions.
We report the results of a retrospective study on occupational protein dermatitis carried out in our dermatology and allergology department and provide an update on the characteristics of occupational skin diseases induced by proteins and on the causative factors found in our study and in a review of literature.

Monocentric study on occupational protein contact dermatitis

The aim was to investigate the characteristics and prevalence of protein contact dermatitis in a French dermatology and allergology centre.
A monocentric retrospective study (from 2006 to 2014) was carried out from our computerised database (Diammallergo, Microsix, Vandoeuvre les Nancy). All patients with hand or forearm dermatitis and positive prick test reactions to proteins were included.
Results: among the 7,560 patients tested during the period of the study, 31 (0.41%) were included: 22 had occupational protein contact dermatitis (PCD) (8 males (M), 14 females (F), mean age 28 years), 3 had non-occupational PCD (mean age of the 25 patients with PCD: 31 years, 9 M, 16 F), 5 with occupational ICU (1 M, 4 F, mean age: 29 years) and 1 cook had a neutrophilic fixed food eruption (NFFE).
Characteristics of the 22 cases of occupational PCD are reported in *table 1*. Briefly, 12 occurred in cooks sensitised (sometimes multi sensitised) to fish (5 cases), shellfish (2 cases), meat (2 cases), nuts (2 cases) and, in 1 patient for each of the following ingredients: egg, reblochon cheese (in a pizza chef), buckwheat, potato and alliaceae (garlic and onion).
Six other cases occurred in other food handlers: 3 in bakers or pastry cooks (all of them sensitised to flour and, for one of them, to nuts such as almonds and hazelnuts), 1 case of sensitisation to cow's milk in a cheese producer, 1 case from cucumber in a market gardener and 1 case from buckwheat in a female grocer. The 4 other cases of occupational PCD were due to amniotic fluid in a veterinarian, hydrolyzed proteins in a hair mask in a hairdresser,

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Table 1. Characteristics of 22 cases of occupational protein contact dermatitis.

Cases	Sex	Age	Test with positive results	Atopy	Cause	Profession
1	F	20	Prick t	+	Hake	Cook
2	H	23	Prick t	0	Norway lobster	Cook
3	H	50	Prick t	0	Fish (hake, cod)	Cook
4	H	24	Prick t	+	Fish (tilapia, pollock)	Cook
5	F	19	Prick t	0	Garlic, onion	Cook (kebab)
6	F	19	Prick t	+	Hazelnut, peach, apple (LTP?)	Gardener
7	F	50	Prick t	0	egg	Industrial pastry
8	F	40	Prick t	0	Fish (tuna, hake)	Cook
9	H	23	Prick t- Wearing a latex finger cot	+	Latex	Cook
10	M	38	Prick t	+	Fish (whiting, hake)	Cook
11	M	23	Prick t	+	buckwheat	Cook, creperie
12	M	32	Prick t	+	Reblochon cheese	Cook (pizzeria)
13	F	23	Prick t	+	Wheat flour	Saleswoman bakery
14	F	24	Prick t	+	Wheat flour	Saleswoman bakery
15	M	24	Prick t and specific IgE to nuts and flour	+	Hazelnut, almond no peanuts, wheat flour RAST +	Baker
16	M	25	Prick t	+	Serum milk, milk RAST +	Cheesemonger
17	F	44	Prick t	+	Cucumber leaf	Gardener
18	F	26	Prick t	+	Buckwheat and potatoes	Grocer
19	F	18	Prick t	0	hydrolyzed protein hair mask	Hairdresser
20	F	26	Prick t	0	amniotic fluid	Veterinary
21	F	30	Prick t	+	Latex	Nursery
22	F	23	Prick t	+	Flowers: tulip, lilac, lilies, baby's breath	Florist
		28	**21**	15		

prick t : prick test

some flowers in a florist (probably induced by profilins) and to latex in a nursery. We did not include 3 cases of non-occupational PCD, induced by maggots in a fisherman, cucurbitaceae (courgettes and cucumber) or latex in two women exposed to such proteins while performing household activities.

Among the 22 cases of occupational PCD, diagnosis was confirmed by positive prick test reactions in 21 cases. A cook with a negative prick test to latex showed an immediate reaction when wearing a latex finger cot with a slightly positive RAST.

Prick tests to common inhalant allergens were carried out in all patients. If at least one prick test result was positive to an inhalant allergen and if the patient had a history of atopy apart from the present skin condition, the patient was considered atopic. According to this definition, atopy was found in 15 out of 22 (68%) patients with occupational PCD, 2 out of 3 patients with non-occupational PCD and 4 out of 5 patients with ACU. Patch tests carried out with the same occupational protein (containing) products were all negative.

Patients sensitised to food did not report systemic hypersensitivity to the same food except in 3 cases. A cook with PCD secondarily developed asthma when exposed to fish stock. After developing PCD, a female cook had angioedema after eating fish. A female grocer with PCD secondarily developed rhinoconjunctivitis and angioedema after eating buckwheat. Among the 5 patients with occupational ICU, prick tests were positive to latex (3 cases), to a shampoo containing proteins or to guinea pig fur.

A case of NFFE occurred in a cook when handling fish. He had erythematous bullous plaques on his forearms. The lesions recurred on the same sites for six years and the patient was thought to be suffering from factitious disorder. Immediate and delayed readings of patch tests and prick tests performed on the scarred lesions were positive for fish and shrimp [1].

This series is the largest collection of PCD cases in France and it shows that symptoms of protein contact dermatitis are not frequent and also greatly vary, including a first case of occupational NFFE, cases of ICU but also 22 cases of PCD revealed by chronic hand eczema that had to be investigated using prick tests instead of patch tests in order to find the causative allergens.

Protein contact dermatitis

Clinical aspects

PCD may involve type I and type IV hypersensitivity reactions or may be the late phase of type I hypersensitivity.

This skin condition was described for the first time in 1976 by Hjorth and Roed-Petersen [2]. The authors reported occupational contact dermatitis, mainly observed in food

handlers. They reported 10 cases with negative patch test results, mainly from fish and shellfish, but indicated that PCD might occur in veterinarians as well. The first tests carried out were open tests with the suspected food. 30 minutes after application of an open test, erythema and oedema occurred, whereas vesicular oedema developed later. Thus the authors mentioned protein immediate hypersensitivity as a cause for the occurrence of PCD. Proteins, including high molecular weight proteins, are thought to pass through the skin barrier when it is altered and thus lead to patient sensitisation. PCD is due to immediate hypersensitivity but the immediate urticarial reaction sometimes seen just after contact with the causative proteins is often missing in the patients' history. This reaction was only found in 12 out of 79 patients in the series by Brancaccio *et al*. [3]. Vester *et al*. [4] only mentioned that the immediate urticarial reaction is quite common but unfortunately no figures are provided.

Among the 27 cases (8 M, 9F) reported by Hernandez Bel *et al.* [5] - 10 cooks, 3 fish cleaners and 3 bakers - only 2 patients reported immediate pruritus just after handling food; both were returning from a long sick leave. Among the 27 cases, 15 were mainly due to PCD. In 12 cases, PCD was considered a complication of a previous skin condition. It is therefore highly important to ask patients whether pruritus – and sometimes erythema – appeared when contact with food resumed after a long sick leave or vacation. Hernandez Bel *et al*. [5] reported allergic contact dermatitis to haptens (with relevant positive patch tests) associated with PCD in 10 cases. They were mainly cases of contact dermatitis from rubber accelerators (particularly thiurams) in latex gloves. The high incidence of concomitant allergic contact dermatitis to haptens can be misleading and PCD might not be diagnosed in patients with hand eczema and relevant positive patch test results.

Whether erythema appears immediately or not, vesicles then develop rapidly and erythematous and vesicular or erythematous and squamous lesions keep developing on the following days, according to the Canadian Hand Dermatitis Management Guidelines [6]. The typical aspect is chronic hand dermatitis, mainly on the backs of the hands and fingers. Kanerva underlined the importance of paronychia with periungual oedema and erythema as a sign of PCD [7].

Chronic eczema can spread to the forearms. Other remote lesions can occur, particularly on the face, as a result of hand contact with sensitising proteins [5]. Among our patients, a cook had localised eczema on the belly, at the place where he tucked the hand towel he used when handling fish into his belt.

PCD is mainly work-related and affects the hands and forearms. However, we reported (*Journées dermatologiques* in Paris, December 2006, unpublished data) 3 cases of chronic cheilitis with erythema and dryness in 3 patients who had positive prick test results and who had been in contact with food: hazel nut and carrot in a young boy, mustard or carrot in 2 women. For the 3 of them, symptoms resolved completely after avoidance of the offending food. No concomitant contact allergy to haptens was found.

PCD: definitions and required tests

According to Vester *et al*. [4] PCD is defined as follows: patients have chronic, recurrent hand eczema that occurs in contact with proteins and have a positive prick test reaction to protein-containing material. However, for some authors, prick test results are not always positive, thus PCD is considered as chronic eczema due to immediate hypersensitivity to proteins with or without positive prick tests.

In our study, we considered that PCD was associated with either positive prick test results or the presence of specific IgE. According to this definition we therefore cannot specify the sensitivity of prick tests to investigate PCD.

In our review of literature, we arbitrarily considered as PCD skin conditions with an aspect of chronic eczema associated with an immediate hypersensitivity to protein proved by a positive skin test [8] or by the presence of specific IgE assessed *in vitro*. Thus the only essential test to investigate PCD is the prick test. Whenever possible, prick tests are carried out with commercial extracts. When none are available, in order to investigate food or other occupational protein-containing products, prick-by-prick tests are then recommended. The product has to be "pricked", for instance the food, and immediately after the forearm is pricked. As for any other prick test, following European recommendations, reading has to be done after 15 minutes, using negative (saline) and positive (histamine) controls [9]. Prick test with the protein-containing substance tested is considered positive if at 15 min the wheal diameter is at least 3 mm larger than the negative control.

If prick test results are negative, Hernandez-Bel *et al*. [5] suggest performing a rub test by applying the protein-containing substance to the area affected by PCD. We raise the issue of the value of a 15-minute exposure test to a piece of latex glove in patients with chronic eczema after wearing gloves but with only negative prick test results to latex.

Some authors suggested performing scratch-tests [8]. Whenever possible, testing for specific IgE should be carried out, for instance anti-food or anti-latex IgE. In case of multiple food sensitisation it seems relevant to investigate the presence of recombinant anti-allergen IgE which might account for cross reactions, even if such reactions have seldom been reported in cases of PCD (*table 2*).

Allergens inducing protein contact dermatitis

There are many of them and by definition they all contain proteins. The occurrence of PCD is mainly induced by occupational exposure to proteins in food professionals, farmers, animal breeders, veterinarians and healthcare professionals but non-occupational cases can occur as well, for instance after handling protein-containing food for animals or fishing maggots. There are 3 non-occupational cases of PCD in our series (food, fishing maggots).

Edible proteins

In food professionals, mainly in cooks and pastry cooks, sensitisation to a wide variety of food has been reported [7, 8].

– **Fruit and vegetables:** garlic, almond, pineapple, asparagus, aubergine, banana, carrot, peanut, camomile, celery, mushrooms, endive, cauliflower, lemon, cucumber,

Table 2. Clinical features of occupational protein contact dermatitis and recommended tests for its management.

Aspect of chronic dermatitis, possibly exacerbated by work	Suggestive but inconstant symptoms: - inflammatory perionyxis - immediate erythema with pruritis, to be investigated for example when the patient resumes work after a long period of interruption
Patch tests with protein-containing products	Negative Warning: co-sensitisation with contact allergy to haptens can be found and delay diagnosis
Prick tests	Essential with the suspected protein-containing material. If no allergen extracts available, perform a prick-by-prick test with the products the patient brought
Specific IgE	Useful if available In case of multisensitisation revealed by prick tests, it is advisable to analyse IgE against recombinant allergens
Other skin tests	Rub test, scratch test (not standardised, not evaluated)
Check for history of atopy	prick tests with inhalant allergens of the recommended European Standard Series [9]

coriander [10], watercress, chicory, fig, bean, kiwi, hazelnut, lettuce, maize, onion, potato, horseradish and tomato.
– **Spices:** curry, caraway, parsnip, paprika and parsley.
– **Meat:** beef, pork, mutton, horse [8] and liver [11].
– **Dairy products:** milk [12, 13], cheese. We report a single case of sensitisation to Reblochon cheese in a cook, a cheese he used to make cheese pizzas, and another case of milk sensitisation in a cheesemonger.
– **Flour:** prick tests were performed with the different sorts of flour handled [14], in one case prick tests were performed with the cornflour handled and specific anti-flour IgE and alpha-amylase were found [15] and in another case, sensitisation from glucoamylase was found [16].
– **Fish and shellfish** often induce PCD [17] and, based on our experience, are the most frequently found allergens in cooks.

In the Hernandez-Bel *et al*. series [5], the substances responsible for PCD were fish in 9 cases (positive prick-by-prick test results), latex (8 cases, prick testing performed with commercial extracts), potato (4 cases with positive prick-by-prick test results), chicken and flour (3 cases with positive prick-by-prick test results), alpha amylase (prick test performed with commercial extract) and aubergine (2 cases), pork, garlic, anisakis, and 3 patients were not allergic to cuttlefish but to the small fish found in its digestive tract.

– **Mushrooms:** two cases of occupational PCD from shiitake mushroom were reported by Aalto-Korte *et al*. [18]. There was no immediate reaction, prick tests performed with fresh mushroom were slightly positive but in one case an open test using dry shiitake was clearly positive. The presence of specific IgE antibodies to shiitake was found using the immunospot method.

In our series we also found PCD induced by egg or buckwheat.

Animal protein not meant to be eaten

Apart from work-related food handling or leisure activities, exposure to animal proteins has been reported to induce PCD:

– Amniotic fluid, blood, serum, organs, placenta, saliva and mesentery in veterinarians,
– Stomach: 22% in 144 slaughterhouse workers in contact with animals
– Cow dander (the best test is thought to be a prick test with a mixture of cow dander and skin scrapings) [19, 20] or pig dander [21].
– Mammals, amphibians, fish
– Shellfish fed to aquarium fish,
– Parasites: anisakis [5]
– Worms and maggots in fishermen [22, 23] as we also observed in one case.

Protein from non-edible plants

These can induce PCD as has been reported with latex (2 cases in our series) or ficus [7]. Flowering plants such as chrysanthemum or Spathiphyllium [24] can also induce PCD. We observed a case of multi-sensitisation to flowers, possibly caused by profilin sensitisation with multiple positive prick-by-prick tests performed with flowering plants.
Laukkanen *et al*. [25] reported lactase-induced occupational PCD in a pharmacist with immediate pruritus and dermatitis of the hands and uncovered areas associated with rhinoconjunctivitis. Prick-test and open test gave positive results and lactase-specific IgE antibodies were found.
Corn starch glove powder, with no sensitisation from latex but with positive prick test results with corn starch, was thought to have induced a case of PCD [26].
Moreover, we report a case of PCD probably induced by hydrolysed proteins in a hair mask with a positive prick test with the commercial product.

Disability caused by PCD

In their study, Vester *et al*. [4] showed the very negative impact of PCD on the future of workers in the food industry compared to other occupational skin diseases in this field. Among 175 food-handlers who had occupational hand dermatitis, the prevalence of PCD was high as 50 cases (28.6%) were found and all 50 patients with PCD, experienced work-related consequences of their skin conditions.

Compared to the 123 patients with hand contact dermatitis due to other conditions (B group) in 100% of patients with PCD, the cause of symptoms was work-related (*vs*. 93%) 31/50 had to change jobs (60% *vs*. 43%) and 7 patients had to retire (10% *vs*. 6%, p = 0.02). Sick leave >3 weeks was more frequent in workers with PCD (10/16, 62.5% *vs*. 30% in the B group, p = 0.02) and patients with PCD more frequently consulted a physician (55%) than patients in the B group (31.5%, p = 0.004).
Improvement of the skin condition was found after a job change in 27/31 (87% *vs*. 82%), in the B group, 3 workers reported exacerbation of the disease after job change but none in the PCD group. Thus PCD has more severe consequences than other skin conditions and leads to more frequent medical consultations, longer sick leaves and more job changes.

Link between atopy and protein contact dermatitis

Among our patients, 15/22 (68%) with occupational PCD and 68% of the 25 patients with PCD had a history of atopy with at least a positive prick test to an inhalant allergen. Such high numbers are close to the ones found by Vester *et al*. [4] who found 56% of food-handlers with occupational PCD suffered from atopy. In the literature, the frequency of atopic dermatitis in workers with skin conditions is 57-60.5% in bakers, 46.5-48% in cooks and 39% in butchers [27].
Thus PCD develops in patients with a history of atopy and it seems to be occurring in workers frequently and repeatedly exposed to protein. The occurrence of PCD could be facilitated by micro-trauma to the skin as it might lead to the penetration of large proteins through the skin. Such skin exposure to proteins might cause IgE-mediated immediate sensitisation as revealed by prick tests or by the presence of circulating protein specific IgE. Sensitisation causes immediate mild allergic skin reactions, which might cause the development of the late phase of the skin reaction from protein-containing allergens as it is described in atopic dermatitis. To our knowledge, no sequential analysis of the type of T cells infiltrating the area where PCD occurred has been carried out in the hours or days following contact with the protein-containing allergen.
Such seriously affected patients do not develop secondary contact urticaria. They rarely suffer from systemic food allergy when they eat the proteins inducing PCD, however, we reported 3 patients in whom such was the case. In our patients with PCD from fish, one cook secondarily developed asthma when exposed to fish stock whereas the other cook developed angioedema after eating fish. A female grocer with PCD from buckwheat and potato developed rhinoconjunctivitis and angioedema after eating buckwheat.
Over the past years, the study of cross-reactivity between inhalant allergens and food has been carried out by searching for recombinant anti-allergen IgE. Unfortunately, there are no series of patients in whom recombinant allergens inducing PCD have been analysed. Such analysis might be recommended in the future in order to specify if some patients, such as the multi-sensitised cooks previously mentioned, have recombinant anti-allergen IgE which might account for a large number of positive prick test results or if such patients have multiple co-sensitisations. Besides, it could be relevant to specify, in case of a history of allergy from inhalant allergens, if cross reactivity between food and inhalant allergens is found in these patients.
In most patients PCD does not seem to be chemically related to pre-existing sensitisation to inhalant allergens. Skin sensitisation is the first symptom, it can then be complicated by systemic allergic reactions from food but in most cases consumption of the food in question is well tolerated. The link with sensitisation to inhalant allergens is thought to be the history of atopy. *Table 1* summarises the characteristics of PCD and recommends tests to manage patients suffering from PCD.

Immunological occupational contact urticaria from proteins

There are two types of contact urticaria: non-immunological or chemical urticaria and immunological urticaria [28, 29]. Non-immunological contact urticaria is investigated with open tests or patch tests read at 20 and 60 min. It is induced by animals such as arthropods, coral, food such as mustard, pepper, balsamic derivatives, some drugs, plants, benzoic acid or formaldehyde. Immunological contact urticaria induced by anti-protein IgE can also be found.
Occupational exposure to proteins can thus lead to the development of ICU. ICU often reflects hypersensitivity to very low concentrations of allergens. Investigating ICU therefore requires caution and should be done in hospital. Prick tests should be performed with a diluted form of the causative protein-containing product.
Among the 5 patients with occupational ICU, prick tests were positive to latex (3 cases), to the proteins in a shampoo and to guinea pig. Other causative agents have been reported in literature: food (fruit, vegetables, spices and plants), dairy products, animal skin and dander, other animal biological fluids, fish, seafood and shellfish, larvae, grains and enzymes [28].

Allergens causing ICU

Food

A very large number of food products have been reported as causes of ICU [28]. Globalisation has influenced ways of cooking and thus protein sources that were so far traditionally unknown in some countries now have to be investigated.
Two cases of CU in Asian housewives living in Europe who made chapatti or nan (unleavened flatbread sometimes made with barley flour) were reported with positive prick test results to chapatti flour [30]. A case of occupational contact urticaria with multisensitisation from fish was reported in a sushi maker [31]. Serum-specific IgE antibodies against two major fish allergens (parvalbumine and collagen) were detected.
Recently, studies on recombinant allergens have led to better knowledge of allergens involved in food-induced ICU.

Peach contact urticaria is caused by sensitisation from late transfer proteins (LTP) specific IgE: Pru p3, an LTP with a concentration 2.5 higher in peach peel than in peach pulp [32]. Patients experience reactions with peach peel but little or no reaction when in contact with the pulp. Peach contains other allergens such as Pru p1 (a Bet v1 analogue, an allergen in betulaceae pollen, responsible for food contact allergy and oral allergy syndrome from peach) and a profilin, Pru p4. Patients sensitised to Pru p1 or Pru p4 do not develop contact urticaria. Among 57 Spanish children sensitised to peach peel, 90% tolerated eating peeled peach [32]. This syndrome, which associates ICU with potential conjunctivitis and palpebral and/or lip angioedema, can cause occupational contact urticaria in market gardeners.

In the series of 14 cases of ICU from melon of Gandolfo-Cano *et al*. [33], only 4 patients only had ICU and no other symptoms. In the other 10 cases, ICU was associated with other immediate hypersensitivity symptoms (oral allergy syndrome in 9 cases, conjunctivitis in 2 cases, palpebral angioedema in 2 cases and lip angioedema in 2 cases). In all cases, skin prick-by-prick test to melon peel was positive. Sensitisation with positive prick test to melon or serum-specific IgE to melon pulp was found in 3/3 cases and to Pru p3 in 13/14 cases or to pollen (12/14 cases). ICU to melon is often associated with good tolerance of peeled melon ingestion.

An asthmatic patient sensitised to several types of pollen developed urticaria of the hands after handling lychee; several years later he developed food allergy after eating lychee. Prick-by-prick test with lychee was positive (10 control subjects) and a high serum IgE level was detected [34].

ICU occurred in one case after handling raw potato, with a positive prick-by-prick result but no *in vitro* tests were performed [35].

A very disabling case of ICU was reported in a female supermarket produce manager. ICU affected the hands and arms then later she had widespread urticaria with bronchospasm, gastrointestinal discomfort and hypotension when she ate fruit or vegetables [36]. Prick test reactions revealed multisensitisation to solanaceae and alliacea. Open tests and patch tests gave negative results. Unfortunately, no detection of specific IgE to recombinant allergens was carried out.

Non-edible plants

Occupational contact urticaria to cannabis was reported in a worker of a firm who harvested cannabis for therapeutic use [37]. In this patient with primary sensitisation to pollens, prick-by-prick test with cannabis Sativa leaf yielded positive results whereas patch tests gave negative results. *In vitro*, serum IgE were found with two protein-binding bands of 12 and 14 kDa. The allergen of cannabis sativa (can s 3) is supposed to belong to the Lipid Transfer Protein (LTP) family. In this Spanish patient there was no cross-reactivity between cannabis allergen and Pru p3 (peach LTP).

Cosmetic products

Handling cosmetics or shampoos containing hydrolysed wheat proteins (HWP) can induce ICU. We observed a case of ICU to an enhancing shampoo in a female hairdresser. Few occupational cases have been reported but a review of literature finds cases of ICU in cosmetic users. It might be supposed that the handling of such products by beauty professionals or workers in the cosmetic industry might increase the risk of developing ICU. The following examples underline the variety of proteins involved in the occurrence of ICU.

Among the 9 cases reported by Laurière *et al*. [38], all patients had positive prick test results with the suspected cosmetic products, 7/7 patients had IgE to at least 3 gluten hydrolysates and all patients had IgE to at least one extract of hydrolysed wheat proteins (HWP). A case of occupational contact urticaria from HWP contained in a shampoo was reported in a female hairdresser [39]. This case was similar to the one we observed with enhancing shampoo. High-molecular weight HWP might have more sensitising properties.

In cosmetic products, other proteins can induce ICU. A woman who had experienced several episodes of fish allergy developed ICU after she applied a face cream containing codfish-derived elastin [40]. Immunoblot analysis of the patient's serum detected IgE antibodies that reacted with proteins of 10,000 to 20,000 kDa, corresponding to codfish elastin. A case of contact urticaria to oats contained in an emollient cream has been reported [41].

Latex

Latex-induced contact urticaria has become less frequent since the quality of latex dipping processes has improved and led to finished products containing no or very few sensitising proteins. ICU can still be found and has to be investigated by prick tests with standard extracts and measurement of serum IgE. 8/17 (47%) sensitised workers had positive IgE results [42]. Among 17 health care workers sensitised to latex, 10 (59%) had positive test results to inhalant allergens and 11 (65%) to food extracts [42].

About a dozen latex allergens have been identified. In health care workers, Hev b 5 and 6 are the most common allergens but Hev b 2, 4, 7 and 13 can also be found in health care workers and are therefore relevant allergens [43]. IgE against Hev b 1 and 3 are the main allergens in patients with spina bifida. Some allergens are involved in cross-reactivity syndromes between latex and fruit. Hev b 5, shows homology with the kiwi acid protein. Hev b 6.02 shows homology with the chitinases from fruits such as banana, avocado and chestnut. Hev b 7 shows homology with patanin, thus explaining the cross-reactivity between latex and solanaceae. Hev b 8 is latex profilin and accounts for cross-reactivity with kiwi and avocado but also non-relevant prick tests to latex in patients with pollen sensitisation to profilins in plants.

It is therefore essential to know whether patients with suspected latex-induced ICU suffer from pollen allergy, to analyse the relevance of positive prick test results to latex, to record the presence of associated food allergy and to perform prick tests with food likely to induce cross-reactivity using allergen extracts but also fresh food. It is recommended to analyse specific IgE against recombinant allergens in order to provide better advice on associ-

ated food allergy. Although the incidence of latex-induced ICU has decreased markedly, this condition should not be neglected.

Animals

Cases of occupational ICU induced by animals (fur, skin, biological fluids) have been described in veterinarians or animal care workers [28, 44], particularly sensitisation to giraffe hair in a female zookeeper [45]. Prick tests were positive, serum IgE antibodies to giraffe hair were found and the basophil activation test revealed expression of CD63 in the 19-year-old female zookeeper but all tests were negative in controls.

Pine processionary caterpillars (*Thaumetopoea pityocampa*) induce non-immunological contact urtcaria but ICU or anaphylaxis can also occur [46-48]. Prick tests with larva extracts and specific IgE were found positive in some patients. IgE directed against a 15kDa allergen called Tha p 1 [48] were found in 9/11 sensitised patients. This allergen is not recognised by patients with immediate hypersensitivity to elm caterpillar. In Spain, in forestry workers, urticaria of exposed body areas or angioedema is likely to be ICU when occurring from October to December when pine-cones are collected or in mid-summer.

Neutrophilic fixed food eruption

We reported the only case of NFFE with a fixed eruption on the forearms which recurred when handling seafood, avocado and fish [1]. The lesions were similar to fixed pigmented erythema sometimes with central bullae and left a discrete scar. The diagnosis of factitious disorder was even discussed in this patient. Even if all tests on the back gave negative results, prick tests and patch tests on site were positive. Prick-by-prick tests turned positive over an hour after they were carried out and delayed eczema-like lesions developed. Skin biopsy at 24 hours found a dense polynuclear neutrophil infiltrate which led to the suggested name NFFE. Secondarily, the patient developed asthma when exposed to fish stock. Thus NFFE is a skin condition always recurring at the same site, sometimes with bullae and for which contact and then ingestion of the food protein leads to local recurrence with a dense polynuclear neutrophil infiltrate. Prick tests and patch tests with proteins must be carried out on the site of the lesions and read at 30 mins, at 1h but also at 24hrs.

Conclusion

Although occupational protein contact dermatitis is not frequent, the diagnosis must be considered when confronted with varied clinical aspects such as chronic contact dermatitis of the hands, ICU or oval recurrent bullae of a NFFE. Prick tests or prick-by-prick tests with protein-containing substances brought by the patient should be carried out.

In most cases of food protein allergy, ingestion of the incriminated food is usually well tolerated by sensitised workers with PCD and even by workers with ICU. However, whatever the type of symptoms, occupational contact dermatitis from fish protein is often associated either with food allergy or asthma from fish stock. ■

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