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Contact urticaria and protein contact dermatitis in the Finnish Register of Occupational Diseases in a period of 12 years

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Abstract

Background: Although occupational contact urticaria (CU) and protein contact dermatitis (PCD) are considered frequent among workers with exposure to proteinaceous materials, data on occupations at risk and the main causes of these occupational skin diseases are relatively limited.

Objectives: To report the causative agents and risk occupations for CU and PCD in the Finnish Register of Occupational Diseases (FROD).

Methods: We retrieved from the FROD all recognized cases of CU/PCD in the years 2005–2016.

Results: With 570 cases, CU and PCD constituted 11% of all recognized cases of occupational skin diseases in the study period. Occupations with the highest incidence of CU/PCD included bakers, chefs and cooks, farmers and farm workers, veterinarians, gardeners, and hairdressers. The most common causative agents were cow dander and flour and grain, followed by natural rubber latex (NRL) and other food. In food-related occupations, wheat and other flours were by far the most common cause of CU/PCD, with 76 cases, whereas fish and other animal-derived food caused 33 and other plant-derived food caused 23 cases.

Conclusions: Apart from the Finnish peculiarity of cow dander allergy, a striking finding was a large share of CU/PCD caused by flours in food handlers as compared to other food.

KEYWORDS

bakers, contact dermatitis, farmers, immediate allergy, incidence, occupational skin disease

1 | INTRODUCTION

Contact urticaria (CU) is defined as a wheal and flare reaction of the skin after contact with an eliciting substance, which appears immediately and usually clears within a few hours.^{1,2} Protein contact dermatitis (PCD) is a slightly controversial entity. Its mechanism is not known, but in occupational settings, it is customary to diagnose PCD when immediate allergy to a proteinaceous material is associated with eczema on the contact site. It may be accompanied by an initial wheal

reaction consistent with CU. Work-related exposure to proteinaceous materials such as food is known to carry a risk of occupational CU and occupational PCD.^{3,4} In fact, CU and PCD are rarely diagnosed outside occupational dermatology.^{5,6}

Previous literature on the epidemiology of CU and PCD is relatively limited. To provide more detailed data on occupations at risk and causative agents of CU and PCD, we analyzed data of the Finnish Register of Occupational Diseases (FROD) in a period of 12 years.

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2 | METHODS

In Finland, all employees are insured against occupational disease. The insurance companies provide data on all cases of occupational diseases to the FROD. A register entry on a case comprises data on, for example, occupation, branch of industry, and up to three causes of occupational disease and their respective diagnoses. In the FROD, cases with suspected and recognized occupational disease are recorded. Since 2005, it has been possible to distinguish the recognized cases of occupational disease in the register. We have limited the present analyses to recognized cases of CU and PCD.

For the purposes of this study, we retrieved and analyzed data on CU and PCD cases reported in FROD in years 2005–2016. In FROD, cases with CU and PCD cannot be reliably separated from each other. Consequently, we have analyzed them as one group.

Occupations are coded according to the Finnish Classification of Occupations 2010 (based on ISCO-08) since 2011. The preceding 2001 version of the national classification (based on ISCO-88) was used during 2005–2010. Statistics Finland provides conversion tables between the two classifications of occupations⁷ (in Finnish). We have previously described the problems encountered in the conversion.⁸ The conversion of some occupations (eg, chefs in this study) was impossible, and in those occupations, we decided to analyze only the latter period (2011–2016). We calculated incidences by using national labor force data of the year 2012 that we had retrieved from the web page of Statistics Finland on June 6, 2015 (no longer available on the internet).

3 | RESULTS

Skin diseases are among the most common occupational diseases in Finland. During the 12-year period 2005–2016, the FROD included a total of 5265 newly recognized cases of occupational skin disease.⁹ During this period, a total of 570 cases were filed in the FROD with a diagnosis of CU and/or PCD, which represents 11% of all recognized cases of occupational skin diseases. Among these, CU or PCD was reported as the first diagnosis in 556 cases, in 13 as the second, and in one as the third diagnosis. Occurrence of CU and PCD per year shows a decreasing trend in 2005–2016 as is illustrated by Figure 1. The incidence of CU and/or PCD in the total labor force of 2 339 904 was 2.03 per 100 000 person-years (95% confidence interval [CI] 1.87–2.20).

3.1 | Causes

The reported causes of CU and/or PCD are presented in Table 1. Proteins of animal origin defined as animal dander and excretions, and animal-derived foods, were reported as causes of CU and PCD in 326 cases (57% of cases with CU and/or PCD). In 265 (81%) of these, the cause was cow dander. Proteins of plant origin including flours, other plant-derived foods, grain, animal feed, and ornamental and

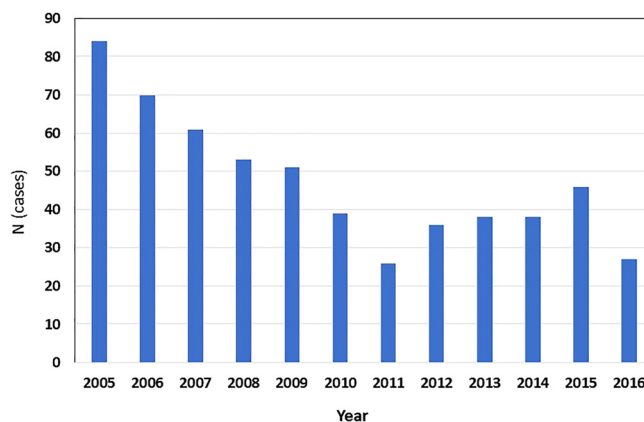


FIGURE 1 Occurrence of occupational contact urticaria and protein contact dermatitis in 2005–2016

other plants were the causes of CU and PCD in 171 cases (30% of all cases with CU and/or PCD). The most common individual causative allergen among plant proteins was wheat flour, which was the reported cause in 41 cases. However, in 20% of the cases caused by flours, the culprit grain was not defined in register data (Table 1). Natural rubber latex (NRL) proteins were the cause in 48 cases (8.4% of cases with CU and/or PCD) and thus constituted the third most common allergen group among cases with CU and/or PCD. There is a clear decrease in the amount of annually registered cases of CU and/or PCD caused by NRL (Figure 2). Chemicals were the cause of CU in 25 cases (4.4%). Among chemicals, the persulfates present in hair bleach products were the most commonly recorded cause of CU, followed by carboxylic acid anhydrides, which are used as epoxy hardeners by the electronics industry. Enzymes such as those used as flour additives were an uncommon cause of CU and/or PCD.

3.2 | Occupations at risk

Incidences of CU and/or PCD in occupations at risk and their main causes of CU and/or PCD are presented in Table 2. The occupations with the highest incidence of CU and/or PCD included bakers, pastry-cooks and confectionery makers, farmers (mixed crop and animal producers) and farm relief workers involved in cattle breeding and milk production, veterinarians, veterinary technicians and assistants, chefs and cooks, gardeners, and hairdressers. The highest number of cases of CU and/or PCD were seen in farm work (farmers, farm relief workers, dairy and livestock workers), with 287 cases (50% of all CU and/or PCD), followed by food handlers (bakers, cooks, chefs, kitchen and restaurant workers, waiters; $n = 116$), health care workers ($n = 36$), beauty sector (hairdressers and beauticians; $n = 16$), and gardeners ($n = 14$). In farm work, the most common causative agents were cow dander and flour and grain. Flours were the most important cause of CU and/or PCD in food-handling occupations. NRL was recorded as the cause in nearly all cases of CU and/or PCD in

TABLE 1 Causes of occupational contact urticaria and protein contact dermatitis in a total of 570 cases

Allergen group	N (cases) ^a	Main cause(s), n (cases)	Other causes, n (cases)
Animal dander and excretions	293 (51%)	Cow dander, 265 (46%)	Rat, 10 Pig, 8 Dog, 3 Mouse, 3 Single cases: Fox, cat, sheep, mink, fur dust, spider
Flour, grain and animal feed	124 (22%)	Wheat, 41 (7.2%)	Oat, 30 Barley, 27 Flour n.s., 25 Rye, 23 Buckwheat, 3
Natural rubber latex	48 (8.4%)		
Animal derived foods	33 (5.8%)	Fish, fish flour; 19 (3.3%)	Shrimp, 5 Egg, 3 Meat and entrails, 4 Milk, 1
Chemicals	25 (4.4%)	Persulfates, 13 (2.3%)	Carboxylic acid anhydrides, 6 Chloramine T (N-chloro <i>p</i> -toluene sulfonamide), 2 Hair dyes and <i>p</i> -phenylenediamine, 2 Single cases: Epoxy compounds, isocyanates, sorbic acid
Plant derived foods (flours excluded)	23 (4.0%)	Root vegetables (carrot, celery root parsnip, potato), 9 (1.6%)	Cucumber, 3 Tomato, 2 Paprika, 2 Single cases: Chili, white pepper, peppermint, pine nut, cinnamon, thyme, fruits n.s., apple, sweet potato, herbs, vegetables n.s., spices, kiwi
Ornamental plants	15 (2.6%)	Ornamental plants n.s., 6 (1.0%) <i>Ficus benjamina</i> , 5 (0.9%)	Single cases: Tulip, ivy, freesia, narcissus
Other plants	9 (1.6%)		Single cases: Hay, strawberry leaf, wood dusts, almond (cosmetic ingredient), wheat germ (cosmetic ingredient), henna, pectin, timothy, plants n.s.
Enzymes	5 (0.9%)	Enzymes n.s., 3	Single cases: Alpha-amylase, flour additives n.s., pepsin

^aA case may have several causes of CU/PCD recorded. n(cases), number of cases with the given cause recorded. n.s., not specified. Percentages of the total number of cases in parentheses.

occupations of health and dental care. In hairdressers, the most commonly recorded cause was persulfates.

In addition to the occupations shown in Table 2, there were several occupations with a single case of CU and/or PCD. Among them, there were eight cases with higher education in various natural sciences who worked for universities, universities of applied sciences, and other research units, and were therefore likely to be researchers. In most of them (six of eight), the causative agent was rat.

Occupations of 15 cases with CU and/or PCD was recorded as "unknown." In all of them, the industry was "education," mostly vocational education. These cases are likely to represent students. Their causes of CU and/or PCD included cow dander (three cases), animal-

derived foods (three cases), ammonium persulfate (two cases), NRL (two cases), flour and plant-derived foods (three cases), and rat and ornamental plants (one case of each).

4 | DISCUSSION

In the present study based on nationwide registry data, CU and PCD were analyzed as one group, since they are not reliably distinguishable in the registry. With the share of 11% of all recognized occupational skin diseases in the years 2005–2016, CU and PCD represented the third most frequent type of occupational dermatitis, after irritant and

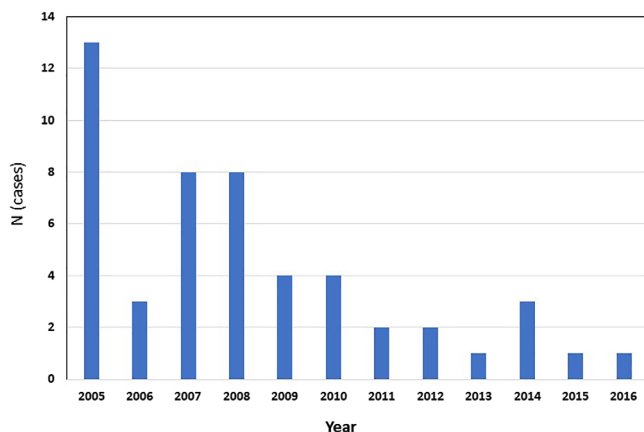


FIGURE 2 Occupational contact urticaria caused by natural rubber latex in 2005–2016

allergic contact dermatitis.⁹ Occupations with the highest incidence of CU and/or PCD included bakers, pastry cooks and confectionery makers, farmers (mixed crop and animal producers) and farm relief workers, occupations in veterinary medicine, chefs and cooks, gardeners, and hairdressers. The most common causes of CU and/or PCD were cow dander, flour and grain, NRL, and food.

According to the underlying mechanism, CU may be classified into immunological or allergic CU (ICU) and nonimmunological CU (NICU). ICU occurs in previously sensitized individuals and is a type I hypersensitivity reaction mediated by allergen-specific immunoglobulin E (IgE)¹⁰ and may be complicated with mucosal and systemic symptoms. The mechanism of NICU is not completely understood, but it is a nonimmunologic immediate reaction that occurs without prior sensitization and limits itself to the skin.¹ In CU, concomitant airway diseases caused by the same allergen is common.¹¹ PCD is an allergic skin reaction induced by proteins of plant or animal origin, which clinically is a recurrent, itchy, sometimes vesicular eczema on the contact site of the causative agent.¹² The immunological mechanisms of PCD remain to be fully elucidated. It is considered mainly to be caused by type I allergy, although also a combination of types I and IV hypersensitivities has been suggested.¹³ In practice, PCD is largely a clinical diagnosis, as a diagnostic test is lacking. Open application only very rarely produces vesicles that are an indisputable sign of eczema. At Finnish Institute of Occupational Health (FIOH), we have assumed that the minute papules that are commonly seen in open application tests are small wheals and not eczematous papules. Patients we diagnose with PCD often have had a clear wheal reaction consistent with CU in open application test. On the other hand, in most patients, there is no way to reliably differentiate PCD from irritant contact dermatitis caused by the same culprit material and other concomitant irritant factors.

Owing to the lack of generally accepted diagnostic criteria for CU and PCD, there may be differences in the diagnostic procedures used in different countries. In addition, the methods of surveying and collecting data on occupational diseases are variable. Consequently, it is challenging to compare the results of studies on the frequency and

causes of CU and PCD. Previous literature on the incidence of CU and PCD based on labor force numbers is sparse. From the British THOR network based on voluntary reporting by physicians, the annual incidence rate of occupational CU was reported to be 3.1/100 000 as reported by dermatologists, and 12.6 as reported by occupational physicians.¹⁴ In a review of the literature before 2010, occupational CU accounted for 1 to 8% of all occupational skin diseases.¹⁵ In Australia, in a clinic specializing in occupational dermatitis, 9.9% of patients with occupational skin disease had CU in 1993–2004.¹⁶ Similar to our present results, the share of reported cases of CU and PCD was 11.2% of all cases of occupational skin disease in Finland according to previous FROD data in 2002.¹⁷ Workers involved in handling of food are a known risk group of CU and PCD.^{18,19} In a Danish study, 22% of patients with occupational food-related skin diseases had PCD and 2.4% had CU.³ The frequency of CU or PCD in the general population is unknown. Based on German patient cohorts, the frequency of CU has been estimated to be <0.4%.⁶

Previously reported causes of CU and PCD include a variety of proteinaceous substances such as plant- and animal-derived foodstuffs, NRL, enzymes, and in cases of CU, some chemicals.^{4,18,20–23} In our data, the most common causative agent was cow dander, which was recorded as a cause in 46% of cases with CU and/or PCD. Cow dander has for long been the most frequent cause of occupational CU in Finland.^{24,25} PCD caused by cow dander has been reported previously.^{26,27} It is also a well-known cause of occupational asthma and allergic rhinoconjunctivitis in farmers.^{28–30}

Grain, in the form of flour, cultivated grain, or animal feed, was the second most important cause of CU and PCD in our data. Flour was the most frequent cause in bakers and other food-handling occupations, and a frequent cause in occupations involved in cattle breeding. Immediate allergy to flour is among the most frequent causes of occupational respiratory diseases, and bakers are a known risk group of occupational asthma and rhinitis.^{31–34} In contrast to our results, in a study from Denmark on professional food handlers with hand dermatitis, flour was not so prominent among the skin prick test-positive allergens.³ Instead, vegetables and fruits were the most commonly positive allergen groups. The reason for this difference might be that in the Danish study, the flours were tested as commercial extracts, whereas in Finland, the flours have since the early 1990s been skin-prick tested “as is,” moistened with a small amount of water, with prick-to-prick technique. This was based on findings that fresh foods are more effective in the skin-prick test than commercial food extracts.³⁵ More recently, a concern has been raised on the variable and sometimes low antigen content of commercial skin-prick test extracts for several important occupational allergens including wheat flour and cow dander.^{36,37}

Occupational type 1 allergy to NRL was a major concern in health care workers in the 1990s. In the 2000s, a decline in new cases of occupational CU caused by NRL has been observed.^{38,39} This decline in incidence has been attributed to a ban on powdered NRL gloves in the health care sector and limitation of leachable NRL protein in gloves. In our data, NRL was the cause in nearly all cases of occupational CU and/or occupational PCD in health and dental care. In this

TABLE 2 Occupations at risk of occupational contact urticaria or protein contact dermatitis

Occupation	Occupational code (earlier occupational code)	N cases	Incidence per 10 000 person years (95% CI)	Most common cause(s) of CU/PCD (n cases) ^a
Food-related				
Bakers, pastry-cooks, and confectionery makers	7512 (7412)	31	10.54 (7.29–14.78)	Flour (26)
Chefs ^b	3434, 6 years	3	2.61 (0.66–7.11)	Flour (3)
Cooks	51201 (5122)	49	1.84 (1.38–2.41)	Flour (27), fish (14)
Food and related products machine operators	8160 (827)	14	0.78 (0.44–1.27)	Flour and grain (8)
Kitchen helpers	9412 (91323)	9	0.41 (0.20–0.72)	Flour (7)
Restaurant services supervisors and shift managers	51202 (51211)	7	0.29 (0.13–0.58)	Flour (3)
Waiters, waitresses, and bartenders	5131, 5246, 9411, 5132 (5123)	3	0.08 (0.02–0.22)	Wheat (2), food n.s. (1)
Farming and animal care				
Mixed crop and animal producers	6130 (6130)	223	8.62 (7.54–9.81)	Cow dander (196), flour and grain (34)
Farm relief workers	61214 (6123)	60	8.61 (6.57–11.08)	Cow dander (50), flour and grain (3)
Veterinary technicians and assistants	3240 (3227)	3	5.68 (1.46–15.46)	Cow dander (3)
Veterinarians	2250 (2223)	5	3.18 (1.17–7.06)	Cow dander (3), dog (1), entrails (1)
Dairy and livestock workers	61212 (6122)	4	1.77 (0.56–4.28)	Cow dander (2), grain (2)
Health care				
Life science technicians	3141 (3211)	3	0.73 (0.19–1.98)	Rat (2)
Dental assistants	53291 (51325)	4	0.64 (0.20–1.55)	NRL (4)
Dentists	2261 (2222)	3	0.60 (0.15–1.63)	NRL (3)
Medical and pathology laboratory technicians	3212 (32314)	3	0.44 (0.11–1.19)	NRL (2)
Nursing and midwifery associate professionals	322 (32311, 32312, 3232)	10	0.13 (0.06–0.23)	NRL (10)
Health care assistants	5321 (513, 51321, 51322, 51324, 51326)	12	0.12 (0.07–0.21)	NRL (9), Chloramine T (1), isocyanates n.s. (1)
Medical doctors	221 (2221)	2	0.09 (0.01–0.29)	NRL (1), rat (1)
Industrial				
Plastic products machine operators	8142 (8232)	2	0.28 (0.05–0.93)	NRL (1)
Electrical and electronic equipment assemblers	8212 (8282, 8283)	2	0.26 (0.04–0.87)	Carboxylic acid anhydrides (2)
Electrical mechanics and fitters	7412 (7241)	2	0.16 (0.03–0.53)	Carboxylic acid anhydrides (2)
Miscellaneous				
Gardeners, horticultural, and nursery growers	6113 (6112)	14	1.63 (0.93–2.67)	<i>Ficus benjamina</i> (5)
Hairdressers	5141 (51411)	15	0.91 (0.53–1.47)	Persulfates (11)
Cleaners	91121, 91122, 91129 (91322)	4	0.06 (0.02–0.15)	NRL (3), Chloramine T (1)
Heavy truck and lorry drivers	8332 (8324)	2	0.04 (0.01–0.13)	Pig (1), molds n.s. (1)

Occupational codes are according to the Finnish classification of occupations 2010 (in use since year 2011). Earlier occupational codes are according to the previous version of the national classification. Incidences calculated based on Finnish labor force in year 2012 according to Statistics Finland.

Abbreviations: CI, confidence interval; n.s., not specified; NRL, natural rubber latex.

^aA case may have several causes of CU/PCD recorded.

^bFor chefs, only data from years 2011–2016 is included because this occupation does not appear in the previous classification of occupations in use until year 2011; see Methods.

sector, the largest number of cases were seen in “nursing and midwifery associate professionals” and “health care assistants,” whereas the dental assistants and dentists had the highest incidence. In addition, individual cases caused by NRL occurred in a variety of other occupations, which might reflect the fact that natural rubber gloves are widely used in various work tasks.

The present study provides data from a nationwide register of occupational diseases, the FROD. In Finland, all employees are statutorily insured against occupational disease, and the insurance companies involved are obliged to provide data on suspected and recognized cases of occupational diseases to the FROD.⁹ Based on this, we assume that the present data reflect the incidence of CU and PCD in the Finnish working population more accurately than data based on voluntary reporting might do. As a limitation of the FROD data, insurance against occupational disease is mandatory for employees but voluntary to entrepreneurs and self-employed persons. Therefore, the occupational diseases of entrepreneurs without insurance will not be notified to the insurance companies, and consequently are not registered in the FROD. Another important limitation is that from the registry data, it is not possible to review the diagnostic methods used in each case. It therefore is not possible to evaluate the accuracy of the diagnoses and causes. However, all recognized cases of occupational diseases filed in the FROD have been evaluated by an insurance company that has had access to the relevant medical data. In the FROD, the individual information is not sufficiently detailed in all cases to permit a reliable distinction of cases with CU, PCD or both, which is a limitation. The consequences of CU and PCD for the patient's ability to work are different. CU is often a mild condition, and easily preventable with personal protective equipment, whereas PCD as an eczematous disease with tendency to reoccur may necessitate treatment and sick-leave, and might compromise the patient's ability to continue in a work with exposure to the causative agent.⁴⁰

In conclusion, CU and PCD comprise approximately 11% of all occupational skin diseases in Finland. Occupations with a high incidence include bakers, cooks, chefs, and other food-handling occupations; farmers, farm workers and other occupations with exposure to cattle; gardeners, and hairdressers. Main causes of CU and PCD in Finnish workers are animal dander, grain, NRL, and plant- and animal-derived foods. It is noteworthy that among food-related occupations, wheat and other flours constitute by far the largest causative group of CU/PCD, with a 2- to 3-fold number of cases as compared with those caused by other foods.

AUTHOR CONTRIBUTIONS

Maria Pesonen: Conceptualization; data curation; investigation; visualization; writing-original draft. **Kirsi Koskela:** Data curation; formal analysis; writing-review and editing. **Kristiina Aalto-Korte:** Conceptualization; data curation; formal analysis; methodology; project administration; writing-review and editing.

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How to cite this article: Pesonen M, Koskela K, Aalto-Korte K. Contact urticaria and protein contact dermatitis in the Finnish Register of Occupational Diseases in a period of 12 years. *Contact Dermatitis*. 2020;83:1–7. <https://doi.org/10.1111/cod.13547>