

Ana GIMENEZ-ARNAU¹
Marcus MAURER²
Jesús DE LA CUADRA³
Howard MAIBACH⁴

¹ Department of Dermatology,
Hospital del Mar,
Universitat Autònoma de Barcelona,
Passeig Marítim 25-29,
08003 Barcelona,
Spain

² Department of Dermatology and Allergy,
Charité Universitätsmedizin,
Berlin,
Germany

³ Servicio de Dermatología, Hospital
General de Valencia, Spain

⁴ Department of Dermatology,
University of California,
San Francisco,
CA, USA

Reprints: A.M. Gimenez-Arnau
<22505aga@comb.cat>

Immediate contact skin reactions, an update of Contact Urticaria, Contact Urticaria Syndrome and Protein Contact Dermatitis – “A Never Ending Story”

Listening and paying attention to our patients is crucial for understanding a disease. A good example is Immediate Contact Skin Reactions (ICSR) which manifest as Contact Urticaria Syndrome (CUS), Contact Urticaria (CU) and Protein Contact Dermatitis (PCD). These entities are characterized by the immediate skin development of itchy flares, wheals, and/or dermatitis. All conditions usually appear within minutes of contact with various substances, including chemicals, animal products, antibiotics, cosmetics, and many other materials. From the clinical and diagnostic viewpoint, the patient's clinical report is critical to its description, definition and classification. Its pathogenesis still remains a challenge and our knowledge of the agents potentially responsible is slowly increasing over time, based on the descriptions of a few isolated cases. This text reviews the classic concepts, introduces new compounds responsible for these immediate skin reactions, and suggests further investigation.

Key words: contact urticaria, dermatitis, eczema, immediate contact reaction, immunology, protein contact dermatitis, syndrome, urticaria

Article accepted on 21/4/2010

Contact Urticaria Syndrome (CUS), Contact Urticaria (CoU) and Protein Contact Dermatitis (PCD) are conditions characterized by the immediate development of contact skin reactions (ICSR), mainly consisting of wheals and/or eczema.

The CUS comprises a heterogeneous group of immediate contact inflammatory reactions that usually appear within minutes after contact with eliciting substances. Systemic involvement can also be present. It was defined as a biologic entity in 1975 by Maibach and Johnson, generating increased interest in clinical medicine and biology [1]. Numerous cases have been published, providing new information concerning its etiology and clinical features. Contact Urticaria (CoU) refers to a wheal and flare reaction following external contact with a substance, usually appearing within 30 minutes and clearing completely within hours, without residual signs [2]. The term was introduced by Fisher (1973), but this phenomenon has long been recognized [3]. Urticarial lesions to nettles and hairy caterpillars were reported in the 19th century [4]. Some naturally existing urticariogens were used therapeutically as rubefacients, counter-irritants and also vesicants [5].

Hjorth and Roed-Petersen defined (1976) Protein Contact Dermatitis (PCD) as characterizing an immediate dermatitis induced after contact with proteins [6-8]. They described 33 food caterers suffering an exacerbation of itch at 10 to 30 minutes after contact with meat, fish and vegetables; this was followed by erythema and vesicles. Application of the relevant foods to the affected skin resulted in either urticaria or eczema [9]. An association

between atopy and PCD occurs in approximately 50% of affected patients [10].

Patients suffering CUS can develop CoU and/or dermatitis/eczema immediately after contact with the trigger substance (*table 1*). Wheals appear as the unique symptom in CoU and eczema can be the only symptom in PCD. Urticaria and dermatitis/eczema can be induced by the same trigger factor and can occasionally be present in the same patient.

Epidemiology and occupational relevance

The incidence of CUS is not known. Although the epidemiology of these skin reactions is inadequately documented, it has been suggested that immediate contact reactions

Table 1. Diseases involved in Contact Urticaria Syndrome

Contact Urticaria (CoU) Immediate Contact Dermatitis [chemicals or protein (PCD)] Itch, tingling or burning sensation	Stage1
Urticaria	Stage2
Bronchial asthma Rhino-conjunctivitis Orolaryngeal symptoms Gastrointestinal dysfunction	Stage3
Anaphylaxis Anaphylactoid reaction	Stage4

are common in dermatological practice [11-16]. Only sporadic cases or short series of patients are normally described; the exception is latex allergy, with a prevalence of 5-10% [17]. Nevertheless, there is convincing data about the high frequency of CUS in occupational settings [18]. Achieving precise statistical analysis is difficult because occupational health problems tend to be under-reported by employees and also by physicians. However, in Finland, where CoU has been classified as a separate occupational skin disease since 1989, the "Finnish Register of Occupational Diseases" (1990-1994) showed that CoU was the second most frequent cause (29.5%) of occupational allergic contact dermatoses, after contact allergic dermatitis (70.5%) [19, 20]. The three most commonly responsible agents reported in this register were cow dander (44.4%), natural rubber latex (23.7%) and flour, grains or feed (11.3%) [20]. A retrospective study done in a tertiary level clinic specializing in occupational dermatology in Melbourne, Australia, showed 8.3% prevalence of occupational CoU [21]. The most common sites were the hands, arms and face. Atopy was a significant risk factor for natural rubber latex allergy but also for CoU induced by foodstuffs or ammonium persulfate. The three most common occupations involved were health workers, food handlers and hairdressers.

Although CoU has occupational relevance, few occupational screening questionnaires include specific questions searching for urticaria symptoms. The long version form of the Nordic Occupational Skin Questionnaire (NOSQ-2002) includes nine questions concerning urticaria symptoms, intensity and the work activity involved [22]. A standardized method to evaluate the occupational relevance of CoU, such as that already developed for occupational contact dermatitis, Mathias' criteria [23], should be feasible.

Workers in the food industries, agriculture, farming, floriculture, health care, plastics, pharmaceutical and other laboratories, as well as hunters, veterinarians, biologists or hairdressers are among those most frequently suffering CoU or PCD. The prevalence of CoU in health care workers in Europe varies from 5 to 10%, whereas in the general population it lies between 1 and 3%.

Atopy is one of the circumstances favoring further sensitization where all protein allergens are concerned [24]. This is also true for irritant contact dermatitis, which modifies the cutaneous (skin) barrier, favors penetration, and creates inflammation, thus facilitating allergic sensitization.

Core Message

General population-based epidemiological data are limited and only occupational relevance has been seriously discussed.

Symptoms and clinical observations

CUS manifestations reflect the dose and exposure route of the responsible substance. CUS skin lesions include flare

reactions, wheals and eczema as well as symptoms such as itching, tingling or burning sensations. When CoU is present, it shows itchy wheals which are usually strictly limited to contact areas and which disappear within a few hours without residual lesions. Other sites also may be affected and generalized urticaria may be present. PCD typically affects the hands (especially the fingertips) and sometimes extends to the wrists and arms. Pruritus, erythema, wheals or angioedema are characteristic of the acute phase (a few hours) followed by vesicular lesions (a few days) whereas excoriations and finally lichenification are seen in the chronic phase. Chronic paronychia with redness and swelling of the proximal nail fold after handling food [25] and natural rubber latex [26] can also occur in PCD.

Internal organs (*e.g.*, respiratory or gastrointestinal tracts) may be involved in CUS patients, depending upon the allergen or preexisting conditions such as atopic dermatitis [27, 28]. Through contact or, in the case of a volatile allergen, rhino-conjunctivitis and asthma may accompany the skin manifestations, as occurs with bakers who are in continuous contact with flour. Abdominal pain, diarrhoea and oral allergy syndrome may develop when the allergen comes in contact with the oropharyngeal mucosa [29]. The severity of this multi-systemic disease has been reported by Von Krogh and Maibach [30].

Staging the severity of Contact Urticaria Syndrome

Stages 1 and 2 include cutaneous reactions only. Stage 1 involves: localized contact urticaria, immediate contact dermatitis or eczema, and symptoms such as itching, tingling or burning sensation. Stage 2 refers to the development of generalized urticaria after a local contact. Stages 3 and 4 include extracutaneous reactions or symptoms that may also occur as part of a more severe reaction. Stage 3 may include bronchial asthma, rhino-conjunctivitis, orolaryngeal symptoms or gastrointestinal dysfunctions. Finally, in stage 4, anaphylactic or anaphylactoid reactions may occur as the most severe type of CUS manifestation. Contact urticaria can be life threatening: certain substances, such as latex protein, can induce anaphylaxis and even death (*table 1*).

Core Message

Itchy flares, wheals and/or eczema can be induced by the same trigger agent (protein or chemical), presenting as urticaria and/or dermatitis in patients suffering from CUS.

Mechanisms involved in immediate skin contact reactions

Non-immunological CoU (NICoU) is the most common form of the disease. The pathogenesis of NICoU is due to the release of vasogenic mediators without the involve-

ment of immunological processes. NICOu occurs without previous sensitization. Urticariogens may act by different mechanisms. The most classic example concerns dimethyl sulphoxide (DMSO), which damages the blood vessels, making them leaky and inducing mast cell degranulation [31]. Antihistamines do not inhibit reactions to DMSO and other NICOu responsible agents, but acetylsalicylic acid and non-steroidal anti-inflammatory drugs do (both orally and topically); therefore, a role for prostaglandins has been suggested [32-34]. Release of prostaglandin D2 without concomitant histamine release has been demonstrated following topical application of sorbic acid and benzoic acid [35, 36]. Capsaicin pre-treatment (which depletes substance P) does not impair NICOu, but does inhibit the allergen prick test flare of immunologic CoU (ICoU) [37]. Non-specific tachyphylaxis of variable duration has been associated with various urticariogens [38]. Sharp hairs from animals or spines from plants penetrating the skin can deliver a cocktail of irritant chemicals or pro-inflammatory mediators causing NICOu (*figure 1*) [39]. The pathogenesis of immunological CoU (ICoU) reflects a type I hypersensitivity reaction, mediated by allergen-specific immunoglobulin E (IgE) in a previously sensitized individual [40]. Skin challenge involves allergen penetration through the epidermis, IgE binding on mast cells, its degranulation, and subsequent release of histamine and other vasoactive substances such as prostaglandins, leukotrienes and kinins (*figure 1*).

A combination of type I and type IV allergic skin reactions, the latter supported by positive delayed patch tests, has been suggested as the PCD pathogenesis [41, 42]. It has been speculated that PCD is an eczematous IgE-mediated reaction to proteins. PCD shows a similar reaction pattern to aeroallergen-induced atopic eczema or dermatitis [43].

Core Message

Protein and low molecular weight molecules can induce immediate contact skin reactions in CUS through an immunological or a non-immunological pathway.

Diagnosis of immediate skin contact reactions

Diagnosis of immediate skin contact reactions is based on full medical history and skin testing with suspected substances. *In vitro* techniques are available for only a few allergens, including latex. The simplest cutaneous provocation test for ICoU, NICOu and immediate contact dermatitis as PCD is the "open test." The suspected substance is applied and gently rubbed on slightly affected skin or on a normal-looking 3 × 3 cm area of the skin,

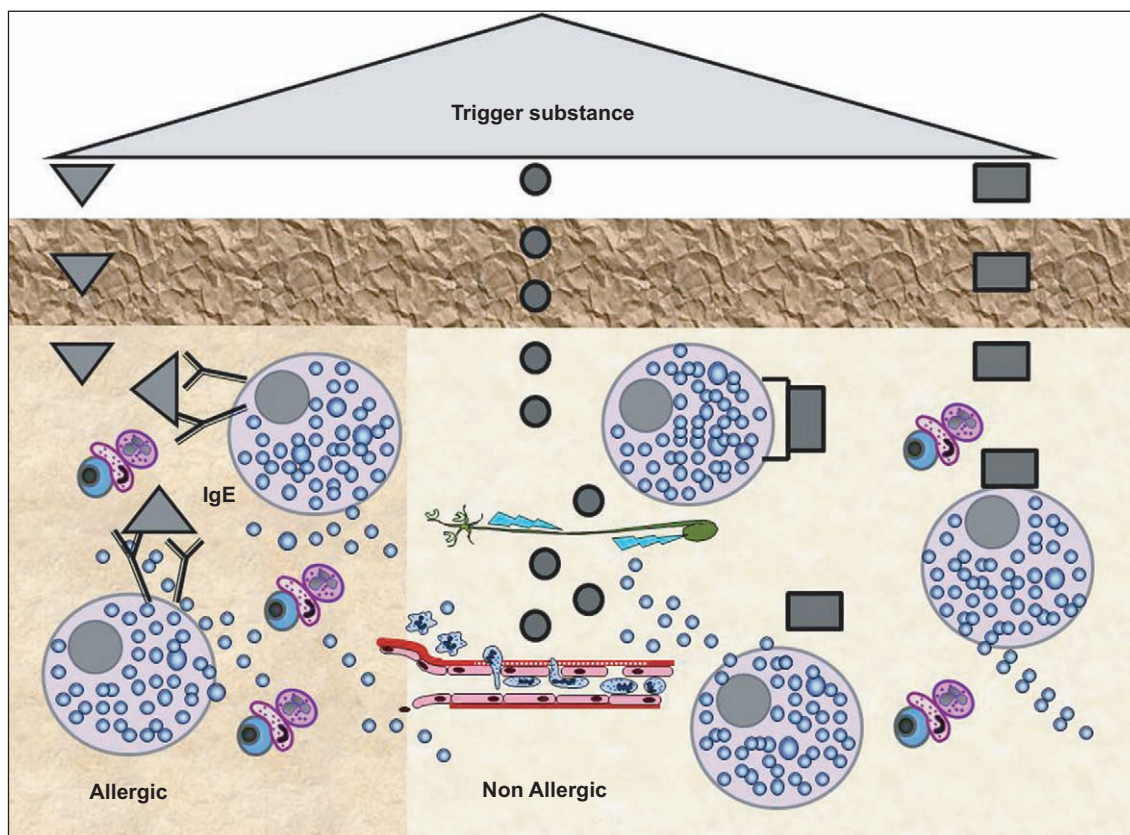


Figure 1. The trigger substance, proteins and low molecular weight molecules can induce urticaria or dermatitis through an allergic (triangle) or a non allergic pathway. Non allergic pathway include direct neural or vessels stimulation (round ball) and mast cell degranulation through specific receptors or not (square).

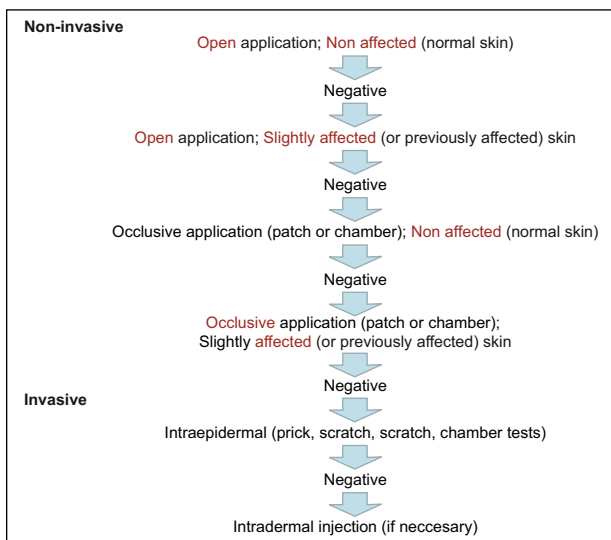


Figure 2. Protocol for the diagnosis of immediate skin contact reactions.

either on the upper back or the extensor side of the upper arm. Often it is desirable to apply contact urticants to skin sites suggested by the patient's history. A positive result is an edema and/or erythema typical of CoU, or tiny intraepidermal spongiotic vesicles typical of acute eczema. An immunological and non-immunological contact reaction usually appears within 15-20 minutes. ICoU can also show a delayed onset, although this is rare. When the open test results are negative, "prick testing" of suspected allergens is often the method of choice for immediate contact reactions. "Scratch test" and "chamber scratch test" (contact with a small aluminium chamber for 15 minutes) are less standardized than the prick test, but are useful when a non-standard allergen must be studied. For both prick and scratch tests, histamine hydrochloride serves as the positive control and aqueous sodium hydroxide as negative reference (*figure 2*). When organs other than cutaneous ones are involved, it is important to begin ICoU testing with much diluted allergen concentrations and to use serial dilutions to minimize allergen exposure. When testing with poorly or non-standardized substances, control tests should be assessed on at least 20 people to avoid false positive interpretations. Non-steroidal anti-inflammatory drugs and antihistamines should be avoided because of the risk of false negative results. Following the recommended protocol is important for minimizing the occurrence of hazardous extracutaneous reactions. Life-threatening reactions have been documented during skin tests; therefore, caution is advised, especially when testing certain occupational substances. Skin tests should be performed only if resuscitation equipment and trained personnel are readily available [44, 45].

Core Message

Diagnostic tools reproduce the immediate skin contact reaction. Although positive, such diagnostic tools do not always help to explain the pathogenic mechanism involved.

Agents responsible for immediate contact skin symptoms

Proteins (molecular weight 10,000 to several hundred thousands) and also chemicals (molecular weights below 1,000) are involved. It is estimated that more than 85,000 chemicals are currently in use [46]. Low molecular weight molecules normally act as haptens; they become antigens through covalent linkages with proteins or macromolecules because of nucleophil reactivity. Nevertheless, nickel or palladium (for example) can react non-covalently. IgE antibodies have been demonstrated in sensitized workers reactive to platinum and nickel-serum albumin complexes [47, 48].

Stinging nettle wheals induced from *Urtica dioica* define NICOu (*figure 3*). Other responsible agents are preservatives, fragrances and flavorings in cosmetics, toiletries, topical medications or foodstuffs. Benzoic and sorbic acid can elicit NICOu at concentrations in use in salad dressing, as demonstrated in 18 of 20 school children in a published study [49, 50]. Household, industrial, insecticide and laboratory chemicals can induce NICOu.

Plant or animal proteins, chemicals such as drugs and preservatives, or more diverse substances such as metals and industrial chemicals can induce ICoU. Raw fruits and vegetables such as apples, carrots and tomatoes are a common cause of ICoU in daily life (*figure 4*). Natural rubber latex allergy drew global interest at the end of the 20th century. Latex sensitization risk factors include atopy and prolonged exposure via damaged epidermis *e.g.*, glove wearers with hand eczema. Both hypo- and hyperpigmentation can be a permanent outcome (*figure 5*).

A few substances elicit mixed features of NICOu and ICoU through an unestablished mechanism. Something other than IgE is involved in ammonium persulfate induced CoU, where specific IgG and IgM activate the complement cascade through the classical pathway [51-53]. Immediate reactions to formaldehyde cannot be mediated by IgE [54]. Although an *in vitro* test of carbonless copy paper was not conclusive, the open test with it showed immediate positive CoU and respiratory symp-



Figure 3. Stinging nettles wheals induced from *Urtica dioica* define NICOu.



Figure 4. Positive prick-by-prick test of fresh fruits and vegetables in a fruit vendor suffering occupational CoU and PCD demonstrated melon, banana, potato and pear reactions, although she tolerated ingestion of fruits and vegetables.



Figure 5. Hand palms with hypo- and hyperpigmentation as a consequence of persistent CoU and chronic eczema induced by occupational exposure to natural rubber in a condom factory. Latex prick test and RAST test were both positive.

toms. A prostaglandin role was suspected because thromboxane B₂ and prostaglandin PGF₂ increased in one of these patients [55].

Animal products, plants and plant derivatives, foods, fragrances, cosmetics, flavorings, medications, preservatives, disinfectants, enzymes, metals and miscellanea of different substances can be responsible for non-occupational CUS (tables 2-7).

Core Message

Agents responsible for immediate contact skin reactions can be classified by molecular weight, mechanism of action, occupational relevance or, most easily, by common use in our daily lives.

Table 2. Animals, plants and derivatives (natural products) responsible for immediate contact reaction

Animals and their derivatives	Plants and derivatives
Amniotic fluid ^{*I}	Algae ^I
Anisakis simplex	Aloe (Morrow)
Blood ^{*I}	Birch ^I
Brucella abortus ^I	Bougainvillea
Calf [*]	Camolile [*]
Cow [*]	Camomilla
Caterpillars ^{NI}	Cannabis sativa [*]
Cephalopodos (Loligo vulgaris) [*]	Chrysanthemum ^{*I}
Chironomus ^I	Cinchona [*]
Cockroaches ^{*I}	Coral ^{NI}
Corals ^{NI}	Corn powder
Dander ^{*I}	Cotoneaster
Dogs; milk, seminal fluid	Crateagus (hawthorn) ^I
	Elm tree
Gut (pig) ^{I,*}	Eruca sativa ^I
Guinea pig ^{*I}	Eucalyptus ^I
Hair (rat-mice) ^{*I}	Ficus benjamina ^I
Horse	Gerbera [*]
Human hair	Grevillea juniperina ^{NI,I,?}
Jellyfish ^{I,NI}	Hakea suaveolens
Liver (mouse) ^{*I,?}	Larch
Locust Tee ^{*I}	Lichens
Lumbrineris impatients	Lilies ^{*I}
Mites ^{*I}	Lime (Tilia)
Moths ^{NI}	Limonium tartaricum ^{I,*}
Nereis diversicolor	Mahogany [*]
Pig [*]	Mulberry
Pearl oysters [*]	Obeche ^{*I}
Placenta (cow) ^{*I}	Phaseolus multiflorus
Saliva ^I	Poppy flowers ^I
Sarcophaga carnaria	Sea anemona ^{NI}
Rat [*]	Semecarpus anacardium
Roe deer	Sunflower seeds ^I
Seminal fluid ^I	Teak ^I
Serum (amphibian) ^{*I}	Tobacco ^{I,*}
Silk ^I	Tropical woods ^{*,I,?}
Spider mite ^{*I}	Tulips ^{*I}
Urine (mice, rat) ^{*I}	Verbena ^{*I}
Worms [*]	
	Plants derivatives
	Abietic acid
	Colophony ^{*I}
	Cornstrach ^{*I}
	Latex rubber ^{*I}
	Turpentine ^{NI}

^{*}Occupational, ^I: immunologic, ^{NI}: nonimmunologic.

New compounds are constantly described. An immediate positive patch test and prick test demonstrated lidocaine involvement in the simultaneous presence of CoU and allergic contact dermatitis in the same patient [56, 57]. Ketoprofen, a well-known cause of photocontact dermatitis, photosensitivity and urticaria, has recently been described as responsible for CoU [58]. Fragrances and

Table 3. Foods and food additives responsible for immediate contact reaction

Meat^I	Vegetables^I	Fruits^I	Flavoring and fragrances
Beef*	Asparagus*. ^I	Almond*	Balsam of Peru ^{I,Nl}
Calf*. ^I	Beans*	Apple*	Benzaldehyde*. ^{Nl}
Chicken*	Cabbage*. ^I	Apricot	Benzoic acid
Codfish	Carrots*	Apricot stone*	Cinnamon oil
Ham (T. putrescentiae)	Castor bean*. ^I	Banana	Cinnamic acid ^{Nl}
Lamb	Celery*	Kiwi	Cinnamic aldehyde ^{Nl,*}
Liver	Chamomilla	Litchi	Menthol ^{Nl}
Pork*	Chicori	Lemon*	Vanillin ^{Nl}
Sausage	Chives	Lemon peel*	
Turkey	Coffee been (green)*. ^I	Lime*	Condiments and species
	Cucumber pickle*. ^{I?}	Mango	Cayenne pepper ^{Nl}
	Dill ^I	Nuts ^I	Caraway*
Fish*.^{I,Nl}	Endive*. ^I	Orange	Coriander
Cod*	Fungi	Peach	Curry*
Crab	Garlic*. ^I	Peanuts	Paprika (capsicum annum)*. ^I
Frog*. ^I	Lettuce*. ^I	Peanut butter	Thyme ^{Nl}
Herring*	Lime*	Plum	
Lobster*	Mentha* [90]	Strawberry*	
Lupin	Mushrooms*. ^I	Watermelon*	Colouring agents
Oysters*	Mustard*. ^I		Amaranth
Plaice*	Onion*. ^I	Seeds^I	Allura red
Pork*	Parsley*	Sesame seeds	Cochineal red
Raw fish*	Parsnip*	Sunflower seeds	Ponceau
Seafood ^I	Potato*		Sunset Yellow
Shrimp*	Rice	Grains^I	Tartrazine
	Rocket	Buckwheat*	
	Runner bean ^{Nl}	Flour*	
Other animal products	Rutabaga (Swede)	Maize*	
Cheese*	Salami casing molds*. ^I	Malt	
Eggs*	Soybean*	Rice*	
Honey	Stock (Matthiola incana)	Wheat*	
Milk*	Tomato*. ^{Nl,I}	Wheat bran	
	Winged bean*. ^I		

*Occupational, I: immunologic, Nl: nonimmunologic.

cosmetics have been demonstrated as causes of anaphylaxis and photocontact urticaria [59-63]. Excipients and preservatives have been identified as responsible for NiCoU, ICoU, urticaria, or anaphylaxis [64-70]. Azo dyes used as food additives, such as tartrazine, amaranth, sunset yellow, ponceau 4R, cochineal red and recently allura red, induce ICoU [71]. Plants, vegetables or foods that have been described as causes of CoU, angioedema, urticaria or anaphylaxis include dill, [72] runner beans (*Phaseolus coccineus*), [73] rice, [74] *Matricaria chamomilla*, [75] chicory [76], chapatti flour [77], anchovy fillet mustard sauce [78], codfish [79] or lupin [80]. Specific IgE to dill, aniseed, cumin and carrot was reported in one patient, as shown by ELISA and prick testing. Immediate reactions to mustard are not frequent, but an occupational CoU from mustard has been reported in fish-finger and fillet production workers. One of them, a 19-year-old man with a previous history of fish allergy, suffered urticaria and dry cough 20 min after his cousin, a fisherman, walked out of his store and greeted him by placing his hands firmly on his bare upper arms. During

open patch testing over intact skin, he developed anaphylaxis and local reaction. Concerning animal allergens, a 21-year-old, atopic, male hunter reported localized urticaria and systemic symptoms after contact with the raw meat and hair of roe deer, although cooked venison was well tolerated. Finally urticaria with angioedema and mucosal reaction has been described from exposure to maggots of the flesh fly *Sarcophaga carnaria* used by an amateur fisherman [81]. The route of sensitization, whether respiratory, cutaneous or by ingestion, remains uncertain [82]. Sporadic reports of the causes of occupational CUS have included animal products, foods, fragrances and flavorings, medications, metals, plant products, preservatives and disinfectants, enzymes and miscellanea of other substances (figure 6). Baker's asthma has been a well-known occupational disease since 1700 [83]. Niels Hjorth stated that most baker's dermatitis was an immediate-type hypersensitivity [84]. Herxheimer described 20% of bakers' apprentices who developed sensitization did so within five years [85, 86]. Many IgE-mediated allergenic proteins have been identified in

Table 4. Fragrances and Cosmetics responsible for immediate contact reaction

Hair care products
Ammonium persulphate*
Basic blue 99 (amino ketone dye) [60] ^I
Henna*, ^I
Panthenol [61]
Protein hydrolysate*
Paraphenylenediamine*, ^I
Emulsifiers
Cetyl alcohol
Polysorbate ^{I?}
Sorbitan monolaurate ^{I?}
Sorbitan monostearate ^{I?}
Sorbitan sesquiolate ^{I?}
Stearyl alcohol
Fragrances
α -amyl cinnamic aldehyde ^{NI}
Anysil alcohol ^{NI}
Balsam of Peru*, ^{NI,I?} [62]
Cassia oil ^{NI}
Cinnamic aldehyde ^{NI} [59]
Cinnamic alcohol ^{NI}
Cinnamic acid ^{NI}
Coumarin ^{NI}
Eugenol ^{NI}
Geraniol ^{NI}
Hydroxycitronellal ^{NI}
Other substances
Allantoin ^{I?}
Aloe gel ^{I?}
Benzophenone ^{I,NI} [63]
Chamomile extract ^{I?}
Lecithin ^{I?}
Melissa extract ^{I?}
Pyrrolidone carboxylate ^{NI}
Propylene glycol ^{NI}
Resorcinol ^{NI}
Wool alcohol ^I

*Occupational; I: immunologic; NI: nonimmunologic.

wheat flour, especially in the water-soluble albumin and globulin fractions [87]. There is extensive cross-reactivity between cereals. Enzymes (e.g., α -amylase, cellulase, glucoamylase or proteases) and flour additives increasingly used to improve baked products and accelerate the baking process have also been proven to be sensitizing. One of the most studied occupational CoU urticaria inducers is *Hevea brasiliensis* or natural rubber latex, with an occupational prevalence of 3-16%. Nutter described the first case in 1979 [88]. This IgE-mediated CoU is especially relevant in health care workers, as well as in other professions. A decreased prevalence has been observed due to preventive measures [89]. Latex has largely been replaced by other materials, such as neoprene or nitrile rubber [90].

New occupational CUS inducers involve health/scientific and cleaning personnel, and the cosmetics, foods, chemi-

Table 5. Drugs responsible for immediate contact reaction

Acetylsalicylic acid
Aescin ^{I?}
Aminophenazone
Ampicilin ^I
Amoxicilin*
Bacitracin ^I
Benzocaine
Benzoyl peroxide ^I
Capsaicin ^{NI}
Carboxymethylcellulose sodium ^I
Chloroform ^{NI}
Cephalosporins*, ^I
Cisplatin*, ^I
Chloramphenicol ^I
Chlorpromazine
Dinitrochlorobenzene
Diphenylcyclopropenone ^I
Dimethylsulfoxide ^{NI}
Donezepil
Gentamycin ^I
Guanidinium salts*
Iodochlorhydroxyquin ^I
Ketoprofen
Lidocaine
Levopromazine*
Lindane ^I
Mechlorethamine ^I
Methamizole*
Mezlocillin*, ^I
Neomycin ^I
Nicotinic acid esters ^{NI}
Penicillin*, ^I
Pentamidine isethionate ^{I,*}
Phenothiazides ^I
Pilocarpine
Propylphenazone
Promethazine
Pyrazolones ^I
Rifamycin ^I
Steroids
Streptomycin ^{I,*}
Tar extracts ^{NI}
Tincture of benzoin ^{NI}
Uranium salts*
Virginiamycin ^I

*Occupational; I: immunologic; NI nonimmunologic.

cal, rubber, plastics and automobile industries. Among chefs and food workers, polyethylene gloves, [91] heat-sensitive raw fish [92] and Pennyroyal (*Mentha pulegium*) [93] are most likely to induce CoU. A sandwich shop proprietor and a supermarket checker suffered CoU from parmesan cheese [94]. *Tyrophagus putrescentiae* mites in cured ham was responsible for erythematous and desquamative contact lesions in a 24-year-old woman supermarket checker, although ham ingestion was well tolerated [95]. New CoU cases have been reported as due to amox-

Table 6. Preservatives responsible for immediate contact reaction

Acetic acid
Aescin polysulfate [65]
Alcohols ^{I,NI}
– Amyl
– Ethyl
– Butyl
– Isopropyl
– Benzyl ^{I,NI}
Ammonia ^I
Benzoic acid ^{NI,I?}
Benzyl alcohol [70]
Bronoprol ^{NI}
Butylated hydroxytoluene ^{I?}
Camphor ^{NI}
Chloramine ^I
Chlorhexidine ^I
Chlorine
Chlorocresol ^{*,I,NI}
Formaldehyde ^{*,NI,I} [69]
Gentian violet ^I
Imidazolidinyl urea ^{NI}
Kathon CG ^{NI}
Mercurochrome ^I
α-Phenylphenate ^I
P-chlorocresol [68]
Parabens ^{I?}
2-phenoxyethanol [66, 67]
Phenylmercuric acetate ^{*,I}
Phenyl mercuric propionate ^I
Polyethileneglycol [64]
Sodium benzoate ^{*,NI}
Sodium hypochlorite ^I
Sorbic acid ^{NI}

**Occupational; I: immunologic; NI: nonimmunologic.*

icillin [96] and corn powder glove [97] in nurses; to dog's milk [98] and Bull terrier seminal fluid [99] in veterinarians; to guanidinium/uranium salts with systemic involvement in a research scientist [100]; with rhinitis and cephalgia to Cannabis sativa in a Forensic Science Service technician [100-102]; to didecyl dimethyl ammonium chloride in a cleaning employee [103]; to beauty masks with chamomile and lime in a beautician [104], to bacillus-subtilis detergent protease in a chemical enzyme factory employee [105]; to benzonitrile in the rubber industry [106]; to triphenyl phosphate in a plastic polymer worker [107]; to di(2-ethyhexyl)phthalate (DOP) in an automobile tyre worker's clothes [108] and to donezepil in a nurse [109].

Core Message

New cases of immediate reactions from occupational skin contact reflect social changes related to new occupations.

Table 7. Miscellaneous chemicals and metals responsible for immediate contact reaction

Acetyl acetone ^I
Acid anhydrides ^{*,I}
Acrylic acid ^{I?}
Acrylic monomers ^{*,I}
Aliphatic polyamide ^{*,I}
P-aminodiphenylamine ^{*,I}
Aminothiazole
Aziridine ^{*,I}
Benzonitrile [*]
Butylhydroxytoluol
Calcium hypochloride
Carbamates ^{*,I}
Carbonless copy paper ^{*,I}
Chlorotalonil ^{*,I}
Citraconin anhydride
Denatonium benzoate ^{*,I?}
Di(2-ethyhexyl)phthalate [*]
Dicyanidamide
Diethylfumarate
Diethyltoluamine ^I
Dimethyl ammonium chloride [*]
Didecyl dimethyl ammonium chloride
Dicycidyl ether of bisphenol A ^{*,I}
Formaldehyde resin ^{*,I}
Fumaric acid
Guanidinium salts [*]
Methyl ethyl ketone ^I
Monoamylamine ^I
Naphtha ^{*,NI}
Naphthylacetic acid
Nitrile [*]
Nylon ^I
Oleamide
Phosphorus sesquisulfide
Polypropylene [*]
Potassium ferricyanide
Sodium fluoride
Sodium silicate
Sodium sulfide
Sulfur ^{NI}
Triphenyl phosphate [*]
Trichloroethanol
Uranium salts [*]
Vinyl pyridine [*]
Xylene [*]
Zinc diethyldithiocarbamate [*]
Metals
Aluminium
Chromium ^{*,I}
Cobalt ^{*,I}
Cooper
Gold
Iridium ^{*,I}
Mercury ^{I?}

(continued)

Table 7 (continued)

Nickel ^{*,I}
Palladium
Platinum salts ^{*,I}
Rhodium [*]
Ruthenium
Tin
Zinc

^{*}Occupational; ^I: immunologic NI : nonimmunologic.

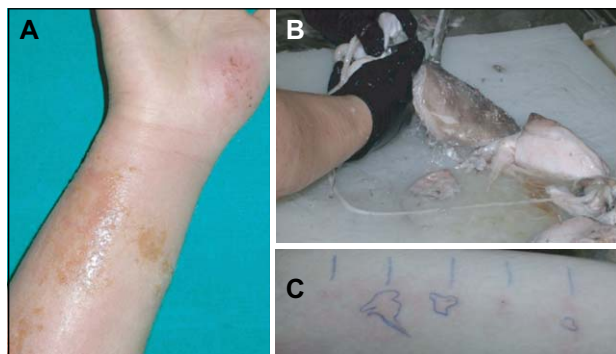


Figure 6. Cuttlefish-induced occupational protein-contact dermatitis. **A)** Eczema present in both arms during working periods. **B)** The worker cleaning cuttlefish. **C)** This reaction was reproduced in the patient using prick-by-prick test with fresh cuttlefish.

Management

CUS clinical symptoms are determined by the route, duration and extent of exposure, the inherent sensitizing properties of the allergen, and an individual's genetic and/or acquired susceptibility. Treating the cause is the most desirable course of action. Discovering the responsible agent is necessary to identify correct avoidance of the eliciting trigger [110]. In addition, treatments that inhibit the release and effect of mast cell mediators and possibly other inflammatory mediators can ameliorate or suppress symptoms. Considering their good safety profile, second generation antihistamines must be considered the preferred first-line symptomatic treatment for urticaria. Before considering alternative treatment, higher doses of antihistamines should be used. When dermatitis is present, topical immunomodulation can be conducted using topical steroids and/or calcineurin inhibitors. Severe cases of CUS require a short course of oral steroids or even treatment in an emergency unit.

Conclusion

ICSR present pathogenic, epidemiological and diagnostic challenges. General population-based epidemiological studies are still missing and occupational relevance has been seriously considered in only a few countries. Skin clinical manifestations of ICSR can be expressed as urticaria and/or dermatitis. Both symptoms can be developed

by the same patient and can be induced by the same compound simultaneously. This fact opens the door for new insights into immune system pathomechanisms. Substances responsible for immediate contact skin reactions can be classified by molecular weight, mechanism of action, occupational relevance or their common use in our daily life. Cosmetics, plants, vegetables and foods continue to be the most common agents responsible for new cases of immediate contact skin reactions. However, detailed chemical and biological study is required to determine the how and why, the epidermal interactions and behavior that provide immunological signals. It will be useful to replace *in vivo* tests by effective *in vitro* testing for diagnostic purposes. At present, some *in vitro* tests are available for certain immunologic CoU. Avoiding the trigger factor seems to be the best treatment. After symptoms control, a global approach is required to treat immediate contact skin reactions. This includes appropriate diagnosis and the development of preventive measures. Further research is underway and will help us better understand and prevent the disease. ■

Acknowledgments. The authors appreciate the revision of English grammar and style by Elaine Lilly, PhD, of *Writer's First Aid*. Conflicts of interests: Marcus Maurer is or recently was a Speaker and/or Advisor for Almirall Hermal, Bayer Schering Pharma, Biofrontera, Essex Pharma, Genentech, JADO Technologies, Jerini, Merckle Recordati, Novartis, Sanofi Aventis, Schering-Plough, Leo, MSD, Merck, Shire, Symbiopharm, UCB, and Uriach.

References

1. Maibach HI, Johnson HL. Contact urticaria syndrome: contact urticaria to diethyltoluamide (immediate type hypersensitivity). *Arch Dermatol* 1975; 111: 726-30.
2. Wakelin SH. Contact Urticaria. *Clin Exp Dermatol* 2001; 26: 132-6.
3. Fisher AA. *Contact Dermatitis*. Philadelphia: Lea & Febiger, 1973.
4. Lesser E. *Lehrbuch der Haut-und Geschlechtskrankheiten für Studierende und Ärzte (in German)*. Leipzig: Verlag von FCW Vogel, 1894.
5. Burdick AE, Mathias T. The contact urticaria syndrome. *Dermatol Clin* 1985; 3: 71-84.
6. Maibach HI. Immediate hypersensitivity in hand dermatitis: role of food contact dermatitis. *Arch Dermatol* 1976; 112: 1289-91.
7. Hannuksela M. Atopic contact dermatitis. *Contact Dermatitis* 1980; 6: 30.
8. Veien NK, Hattel T, Justesen O, Norholm A. Dietary restrictions in the treatment of adult patients with eczema. *Contact Dermatitis* 1987; 17: 223-8.
9. Hjorth N, Roed-Petersen J. Occupational protein contact dermatitis in food handlers. *Contact Dermatitis* 1976; 2: 28-42.
10. Doutre M-S. Occupational contact urticaria and protein contact dermatitis. *Eur J Dermatol* 2005; 15: 419-24.
11. Elpern DJ. The syndrome of immediate reactivities (contact urticaria syndrome). An historical study from a dermatology practice. I. Age, sex, race and putative substances. *Hawaii Med J* 1985; 44: 426-39.
12. Rudzki E, Rebanel P. Occupational contact urticaria from penicillin. *Contact Dermatitis* 1985; 13: 192.
13. Nilsson E. Contact sensitivity and urticaria in "wet" work. *Contact Dermatitis* 1985; 13: 321-8.

14. Veien NK, Hattel T, Justesen O, Norholm A. Dietary restrictions in the treatment of adult patients with eczema. *Contact Dermatitis* 1987; 17: 223-8.
15. Turjanmaa K. Incidence of immediate allergy to latex gloves in hospital personnel. *Contact Dermatitis* 1987; 17: 270-5.
16. Weissenbach T, Wutrich B, Weihe WH. Allergies to laboratory animals. An epidemiological, allergological study in persons exposed to laboratory animals. *Schweiz Med Wochenschr* 1988; 118: 930-8.
17. Doutre MS. Occupational contact urticaria and protein contact dermatitis. *Eur J Dermatol* 2005; 15: 419-24.
18. Kanerva L, Jolanki R, Toikkanen J. Frequencies of occupational allergic diseases and gender differences in Finland. *Int Arch Occup Environ Health* 1994; 66: 111-6.
19. Kanerva L, Toikkanen J, Jolanki R, Estlander T. Statistical data on occupational contact urticaria. *Contact Dermatitis* 1996; 35: 229-33.
20. Kanerva L, Jolanki R, Toikkanen J, Estlander T. Statistics on occupational contact urticaria. In: Smita A, Lahti A, Maibach HI, eds. *Contact urticaria syndrome*. Boca Raton: CRC Press, 1997: 57-69.
21. Williams JD, Lee AY, Matheson MC, Frowen KE, Noonan AM, Nixon RL. Occupational contact urticaria: Australian data. *Br J Dermatol* 2008; 159: 125-31.
22. Susitaival P, Flyvholm MA, Meding B, et al. Nordic Occupational Skin questionnaire (NOSQ-2002): a new tool for surveying occupational skin diseases and exposure. *Contact Dermatitis* 2003; 49: 70-6.
23. Mathias CG. Contact dermatitis and workers' compensation: criteria for establishing occupational causation and aggravation. *J Am Acad Dermatol* 1989; 20: 842-8.
24. Bourrain JL. Occupational Contact Urticaria. *Clin Rev Allergy Immunol* 2006; 30: 39-46.
25. Tosti A, Guerra L, Morelli R, Bardazzi F, Fanti R. Role of foods in the pathogenesis of chronic paronychia. *J Am Acad Dermatol* 1992; 27: 706-10.
26. Kanerva L. Occupational protein contact dermatitis and paronychia from natural rubber latex. *J Eur Acad Dermatol Venereol* 2000; 14: 504-6.
27. Crisi G, Belsito D. Contact urticaria from latex in a patient with immediate hypersensitivity to banana, avocado and peach. *Contact Dermatitis* 1993; 28: 247-8.
28. Jeannot-Peter N, Piletta-Zanin PA, Hauser C. Facial dermatitis, contact urticaria, rhinoconjunctivitis, and asthma induced by potato. *Am J Contact Dermat* 1999; 10: 40-2.
29. Morren M, Janssens V, Dooms-Goossens A, et al. alpha-Amylase, a flour additive: an important cause of protein contact dermatitis in bakers. *J Am Acad Dermatol* 1993; 29: 723-8.
30. Von Krogh G, Maibach HI. The contact urticaria syndrome. An update review. *J Am Acad Dermatol* 1981; 5: 328-42.
31. Kligman AM. Dimethyl sulphoxide I and II. *JAMA* 1965; 193: 796-804, 923-8.
32. Lahti A, Oikarinen A, Viinikka L, Ylikorkala O, Hannuksela M. Prostaglandins in contact urticaria induced by benzoic acid. *Acta Dermatol Venereol (Stockh)* 1983; 63: 425-7.
33. Lahti A, Vaananen A, Kokkonen E-L, Hannuksela M. Acetylsalicylic acid inhibits non-immunologic contact urticaria. *Contact Dermatitis* 1987; 16: 133-5.
34. Johansson J, Lahti A. Topical non-steroidal anti-inflammatory drugs inhibit non-immunological immediate contact reactions. *Contact Dermatitis* 1988; 19: 161-5.
35. Morrow JD, Minton TA, Awad JA, Roberts LJ. Release of markedly increased quantities of prostaglandin D2 from the skin in vivo in humans following the application of sorbic acid. *Arch Dermatol* 1994; 130: 1408-12.
36. Downard CD, Roberts LJ, Morrow JD. Topical benzoic acid induces the increased synthesis of prostaglandin D2 in humans skin in vivo. *Clin Pharmacol Ther* 1995; 74: 441-5.
37. Lundblad L, Lundberg JM, Anggard A, Zetterstrom O. Capsaicin sensitive nerves and the cutaneous allergy reaction in man. Possible involvement of sensory neuropeptides in the flare reaction. *Allergy* 1987; 42: 20-5.
38. Lahti A, Maibach HI. Long refractory period after application of one nonimmunologic contact urticaria agents to the guinea pig ear. *J Am Acad Dermatol* 1985; 13: 585-9.
39. Lovell CR. Urticaria due to plants. In: Lovell CR, ed. *Plants and the Skin*. Oxford: Blackwell Academic Ltd., 1993: 29-41.
40. Amaro C, Goossens A. Immunological occupational contact urticaria and contact dermatitis from proteins: a review. *Contact Dermatitis* 2008; 58: 67-75.
41. Kanerva L, Estlander T. Immediate and delayed skin allergy from cow dander. *Am J Contact Dermat* 1997; 8: 167-9.
42. Conde-Salazar L, Gonzalez MA, Guimaraens D. Type I and Type IV sensitization to *Anisakis simplex* in 2 patients with hand eczema. *Contact Dermatitis* 2002; 46: 361.
43. Saloga J, Knop J. Does sensitization through skin occur? Allergy Review Series V: The skin as target for IgE-mediated allergic reactions. *Allergy* 2000; 55: 905-9.
44. Hausteiner UF. Anaphylactic shock and contact urticaria after patch test with professional allergens. *Allergie Immunol* 1976; 22: 349-52.
45. Maucher OM. Anaphylaktische Reaktionen beim Epicutantest. *Hautarzt* 1972; 23: 139-40.
46. Tupasela O, Kanerva L. Skin tests and specific IgE determinations in the diagnostics of Contact urticaria caused by low-molecular-weight chemicals. In: Smita A, Arto L, Howard IM, eds. *Contact Urticaria Syndrome*. CRC Press, 1997: 33-44.
47. Cromwell O, Pepys J, Parish WE, Hughes EG. Specific IgE antibodies to platinum salts in sensitized workers. *Clin Allergy* 1979; 9: 109.
48. Estlander T, Kanerva L, Tupasela O, Heskinen H, Jolanki R. Immediate and delayed allergy to nickel with contact urticaria, rhinitis, asthma and contact dermatitis. *Clin Exp Allergy* 1993; 23: 306.
49. Lahti A. Non-immunologic contact urticaria. *Acta Derm Venereol* 1980; 60 (Suppl.): 3-49 (Stockh).
50. Clemmensen O, Hjorth N. Perioral contact urticaria from sorbic acid and benzoic acid in a salad dressing. *Contact Dermatitis* 1982; 8: 1-6.
51. Kligman AM. The spectrum of contact urticaria: wheals, erythema and pruritus. *Dermatol Clin* 1990; 8: 57-60.
52. Babilas P, Landthaler M, Szeimies RM. Anaphylactic reaction following hair bleaching. *Hautarzt* 2005; 56: 1152-5.
53. Barbaud A. Urticaires de contact. *Ann Dermatol Venereol* 2002; 128: 1161-5.
54. Von Krogh G, Maibach HI. Contact Urticaria. In: Adam RM, ed. *Occupational skin disease*. New York: Grune & Stratton, 1983: 58-69.
55. Hannuksela M. Mechanisms in contact urticaria. *Clin Dermatol* 1997; 15: 619-22.
56. Jovanovic M, Karadaglic D, Brkic S. Contact urticaria and allergic contact dermatitis to lidocaine in a patient sensitive to benzocaine and propolis. *Contact Dermatitis* 2006; 54: 124-6.
57. Waton J, Boulanger A, Trechot PH, Schumtz JL, Barbaud A. Contact urticaria from Emla cream. *Contact Dermatitis* 2004; 51: 284-7.
58. Suzuki T, Kawada A, Yashimoto Y, Isogai R, Aragane Y, Tezuka T. Contact urticaria to ketoprofen. *Contact Dermatitis* 2003; 48: 284-5.
59. Diva VC, Statham BN. Contact urticaria from cinnamal leading to anaphylaxis. *Contact Dermatitis* 2003; 48: 119.
60. Jagtman BA. Urticaria and contact urticaria due to basic blue 99 in a hair dye. *Contact Dermatitis* 1996; 35: 52.
61. Schallock PC, Storrs FJ, Morrison L. Contact urticaria from panthenol in a hair conditioner. *Contact Dermatitis* 2000; 43: 223.
62. Cancian M, Fortina AB, Peserico A. Contact urticaria syndrome from constituents of balsam of Peru and fragrance mix in a patient with chronic urticaria. *Contact Dermatitis* 1999; 41: 3000.
63. Bourrain JL, Amblard P, Béani JC. Contact urticaria photoinduced by benzophenones. *Contact Dermatitis* 2003; 48: 45-6.
64. Co-Minh HB, Demoly P, Guillot B, Raison-Peyron N. Anaphylactic shock after oral intake and contact urticaria due to polyethylene glycols. *Contact Dermatitis* 2007; 62: 92-3.
65. Escibano M, Muñoz-Bellido FJ, Velazquez E, et al. Contact urticaria due to aescin. *Contact Dermatitis* 1997; 37: 233-53.
66. Birnie AJ, English JS. 2-phenoxyethanol-induced contact urticaria. *Contact Dermatitis* 2006; 54: 349.
67. Hernández B, Ortiz-Frutos FJ, García M, Palencia S, García MC, Iglesias L. Contact urticaria from 2-phenoxyethanol. *Contact Dermatitis* 2002; 47: 44-54.
68. Walker SL, Chalmers RJG, Beck MH. Contact urticaria due to p-chloro-m-cresol. *Contact Dermatitis* 2004; 51: 936-7.
69. Torresani C, Periti I, Beski L. Contact urticaria syndrome from formaldehyde with multiple physical urticarias. *Contact Dermatitis* 1996; 35: 174-5.
70. Guin JD, Goodman J. Contact urticaria from benzyl alcohol presenting as intolerance to saline soaks. *Contact Dermatitis* 2001; 45: 182-3.
71. Baron SE, Moss C. Contact urticaria to play dough: a possible sign of dietary allergy. *Contact Dermatitis* 2004; 51: 927-52.
72. Monteseirín J, Pérez-Formoso JL, Hernández M, Sánchez-Hernández MC, Camacho MJ, Bonilla I, Chaparro A, Conde J. Contact urticaria from dill. *Contact Dermatitis* 2003; 48: 275.
73. Narayan S, Sanson JE. Contact urticaria from runner bean (*Phaseolus coccineus*). *Contact Dermatitis* 2002; 47: 243.

74. Yamakawa Y, Ohsuna H, Aihara M, Tsubaki K, Ikezawa Z. Contact urticaria from rice. *Contact Dermatitis* 2001; 44: 91-3.
75. Foti C, Nettis E, Panebianco R, Cassano N, Diaferio A, Porzia Pia D. Contact urticaria from *Matricaria chamomilla*. *Contact Dermatitis* 2000; 42: 360-1.
76. Willi R, Pfab F, Huss-Marp J, et al. Contact anaphylaxis and protein contact dermatitis in a cook handling chicory leaves. Contact dermatitis in a cook handling chicory leaves. *Contact Dermatitis* 2009; 60: 226-7.
77. Davies E, Orton D. Contact urticaria and protein contact dermatitis to chapatti flour. *Contact Dermatitis* 2009; 60: 113-4.
78. Le Coz CJ, Ball C. Contact urticaria syndrome from mustard in anchovy fillet mustard sauce. *Contact Dermatitis* 2000; 42: 114-5.
79. Kalogeromitros D, Armenaka M, Katsarou A. Contact urticaria and systemic anaphylaxis from codfish. *Contact Dermatitis* 1999; 41: 170.
80. Gutierrez D, Conde A, duran S, Delgado J, Guardia P, Martinez R, Garcia-Cubillana A, Gonzalez J, Conde J. Contact urticaria from lupin. *Contact Dermatitis* 1997; 36: 311.
81. Valsecchi R, Santini M, Leghissa P. Contact urticaria and asthma from *Sarcophaga carnaria*. *Contact Dermatitis* 2009; 61: 186-7.
82. Geyer E, Kränke B, Derhaschnig J, Aberer W. Contact urticaria from roe deer meat and hair. *Contact Dermatitis* 1998; 39: 34.
83. Bonnevie P. Occupational allergy in bakery. In: European Academy of allergy (ed) Occupational allergy. CC Thomas, Springfield, Illinois, pp 161-168
84. Hjorth N. Occupational dermatitis in the catering industry. *Br J Dermatol* 1981; 105: 37.
85. Herxheimer H. Skin sensitivity to flour in baker's apprentices. *Lancet* 1967; 1: 83-4.
86. Herxheimer H. The skin sensitivity to flour of baker's apprentices: a final report of long term investigation. *Acta Allergol* 1967; 28: 42-9.
87. Sutton R, Skerritt JH, Baldo BA, Wrigley CW. The diversity of allergens involved in bakers' asthma. *Clin Allergy* 1984; 14: 93-107.
88. Nutter AF. Contact urticaria to rubber. *Br J Dermatol* 1979; 101: 597-8.
89. Crippa M, Balbiani L, Baruffini A, et al. MAaggio GM, Marcer G, Micheloni GP, Montomoli L, Moscato G, Previdi M, Sartorelli P, Sossai D, Spatari G, Zanetti C. Consensus Document. Update on latex exposure and use of gloves in Italian health care settings. *Med Lav* 2008; 99: 387-99.
90. Brehler R, Sedlmayr S. Contact urticaria due to rubber chemicals? *Contact Dermatitis* 1997; 37: 125-7.
91. Sugiura K, Sugiura M, Shiraki R, et al. Contact urticaria to polyethylene gloves. *Contact Dermatitis* 2002; 46: 262-6.
92. Porcel S, León F, Cumplido J, Cuevas M, Guimaraens D, Conde-Salazar L. Contact urticaria caused by heat-sensitive raw fish allergens. *Contact Dermatitis* 2001; 45: 139-42.
93. Pérez-Calderon R, Gonzalo-Garijo A, Bartolomé-Zavala B, Lamilla-Yerga A, Moreno-Gastón I. Occupational contact urticaria due to pennyroyal (*Mentha pulegium*). *Contact Dermatitis* 2007; 57: 285-6.
94. Williams JD, Moyle M, Nixon RL. Occupational contact urticaria from Parmesan cheese. *Contact Dermatitis* 2007; 56: 113-4.
95. Quiñones Estevez MD. Occupational contact urticaria-dermatitis by *Tyrophagus putrescentiae*. *Contact Dermatitis* 2006; 55: 308-9.
96. Conde-salazar L, Guimaraens D, Gonzalez MA, Mancebo E. Occupational allergic contact urticaria from amoxicillin. *Contact Dermatitis* 2001; 45: 109.
97. Liu W, Nixon RL. Corn contact urticaria in a nurse. *Australas J Dermatol* 2007; 48: 130-1.
98. Foti C, Antelmi A, Mistrello G, Guarneri F, Filotico R. Occupational contact urticaria and rhino-conjunctivitis from dog's milk in a veterinarian. *Contact Dermatitis* 2007; 56: 169-71.
99. Krakowiak A, Kowalczyk M, Palczyński C. Occupational contact urticaria and rhinoconjunctivitis in a veterinarian from bull terrier's seminal fluid. *Contact Dermatitis* 2005; 51: 34.
100. Yung A, Papworth-Smith J, Wilkinson SM. Occupational contact urticaria from solid-phase peptide synthesis coupling agents HATU and HBTU. *Contact Dermatitis* 2003; 49: 108-9.
101. Williams C, Thompson J, Wilkinson M. Work-related contact urticaria to *Cannabis sativa*. *Contact Dermatitis* 2008; 58: 62-3.
102. Majmudar V, Azam NAM, Finch T. Contact urticaria to *Cannabis Sativa*. *Contact Dermatitis* 2006; 54: 127.
103. Houtappel M, Buijzeel-Koomen CAFM, Röckmann H. Immediate-type allergy by occupational exposure to didecyl dimethyl ammonium chloride. *Contact Dermatitis* 2008; 59: 111-6.
104. Rudzki E, rapiejko P, Rebandel P. Occupational contact dermatitis, with asthma and rhinitis, from camomile in a cosmetician also with contact urticaria from both camomile and lime flowers. *Contact Dermatitis* 2003; 49: 162.
105. Kanerva L, Vanhanen M. Occupational allergic contact urticaria and rhinoconjunctivitis from a detergent protease. *Contact urticaria* 2001; 45: 49-51
106. Lin-Feng L, Sujan SA, Li QX. Contact urticaria syndrome from occupational benzonitrile exposure. *Contact Dermatitis* 2004; 50: 377-8.
107. Torresani C, Zendri E, Vescovi V, De Panfilis G. Contact urticaria syndrome from occupational triphenyl phosphite exposure. *Contact Dermatitis* 2003; 48: 237-8.
108. Sugiura K, Sugiura M, Hayakawa R, Shamoto M, Sasaki K. A case of contact urticaria syndrome due to di(2-ethylhexyl)phthalate (DOP) in work clothes. *Contact Dermatitis* 2002; 46: 13-6.
109. Galvez Lozano JM, Alcantara M, Saenz de San Pedro B, Quiralte J, Caba I. Occupational contact urticaria caused by donezepil. *Contact Dermatitis* 2009; 61: 176.
110. Zuberbier T, Asero R, Bindslev-Jensen C, et al. EAACI/GA₂LEN/EDF guideline: management of urticaria. *Allergy* 2009; 64: 1427-43.

Recommended text books

Smita A, Artho L, Howard IM. *Contact Urticaria Syndrome*. Boca Raton. New York: CRC Press, 1997.

Latex intolerance. In: Chowdhury MMU, Maibach HI, eds. *Basic Science, epidemiology and Clinical Management*. New York: CRC Press Boca Raton, 2005.