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Occupational Urticaria

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INTRODUCTION

Many exposures in the workplace that can result in occupational asthma can also cause a variety of dermatological problems. These include irritant contact dermatitis, allergic contact dermatitis (Type IV delayed hypersensitivity), and urticaria (Type I immunologic and nonimmunologic). Urticaria will be discussed here because of its more direct association with occupational asthma, in terms of both clinical coexistence and mechanistic similarities.

Urticaria is defined as the transient appearance of elevated, erythematous pruritic wheals or serpiginous exanthem, usually surrounded by an area of erythema. In addition, areas of macular erythema or erythematous papules may also be present. These skin lesions appear and peak in minutes to hours after the etiological exposure and individual lesions usually disappear within 24 hours. Urticarial lesions usually involve the trunk and extremities, although they can involve any epidermal or mucosal surface. Large wheal formation, where the edema extends from the dermis into the subcutaneous tissue, is referred to as angioedema. This condition is more commonly seen in the more distensible tissues, such as the eyelids, lips, ear lobes, external genitalia, and mucous membranes.

Urticarial wheals result from local subcutaneous and intradermal leakage of plasma filtrate from postcapillary venules. The erythema and surrounding swelling result from locally increased blood flow. Biopsy specimens of urticarial lesions may exhibit only subtle microscopic changes. There may be evident subcutaneous or dermal edema, an increase in the number of mast cells, and a modest perivascular lymphocytic infiltrate, perhaps intermingled with cosinophils. Electron microscopy reveals mast cell and eosinophilic degranulation (1).

CLASSIFICATIONS OF URTICARIA

Urticarial lesions can be classified in one or more of the following categories based upon characteristic features:

1. Duration or chronicity—acute or chronic.

2. Clinical distribution of the lesions or the extra-dermal manifestations—localized, generalized, or systemic associated with rhinitis, conjunctivitis, asthma, or anaphylaxis.
3. Etiology—idiopathic or cause-specific.
4. Route of exposure—direct contact, inhalation, or ingestion.
5. Mechanism—nonimmunological, immunological, or idiopathic.

Acute urticaria ranges from a single episode of urticaria to recurrences lasting less than 6 weeks. Common causes of acute urticaria include insect bites or stings and food or drug allergies. Chronic urticaria occurs daily (or almost daily) over a period longer than 6 weeks. Food, drugs, and infections can also be causes of chronic urticaria. However, in the chronic form, the exact causative agents may never be identified. The majority of cases of urticaria remain idiopathic.

Occupational urticaria is a general etiological classification of urticaria. It is urticaria that is presumed or proven to be caused by exposure to one or more substances or physical agents in the workplace. Beyond this definitional idiosyncracy, occupational urticaria may fall into any of the other classifications of urticaria. It may be acute or chronic, may be localized, generalized, or associated with systemic manifestations, such as asthma. In occupational settings, direct contact with substances, and possibly inhalation may be the more common routes of exposure inducing urticaria. The pathological mechanisms may be nonimmunological, immunological, or of uncertain etiology.

EPIDEMIOLOGY

Limitations of Epidemiological Data

It can be difficult to obtain accurate epidemiological data for occupational and non-occupational urticaria, and all sources have their limitations. First of all, though a case definition is a prerequisite for the gathering of epidemiological data, there is no standard case definition in the literature to define occupational urticaria, and there is no standard approach to prove the presumed occupational-relatedness of the urticaria. Cases may be defined using a variety of criteria. These include the following: the self-reporting of current or past episodes of urticaria in the workplace; histories of urticaria associated with a specific occupational exposure or work activity; objective signs of urticaria on clinical examination in the workplace, sometimes associated with the use of the alleged etiologic substance; evidence of specific IgE to suspect occupational antigens (e.g., radioallergosorbent test (RAST) assays or skin prick testing). A case definition used in a study or a data source may be based upon one or more of these criteria. Therefore, because the epidemiological case definition for occupational urticaria varies from one data source to another, it is difficult to compare different sources of information and different findings.

The accuracy of the diagnosis of occupational urticaria is related to the skill level, experience, and knowledge of the medical professional. The diagnosis is based on the medical and exposure history, physical findings, and in vitro or in vivo testing. The lack of a standard case definition and the difficulty of diagnosis lead to potential misclassification of occupational urticaria, which can result in either over- or underestimation of disease frequency. In allergic contact urticarial syndromes, the lack of standardized occupational test allergens also contributes to the problem of vague case definitions.

Much of the literature of urticaria in the workplace is filled with anecdotal case reports and limited observations. This usually results in information about a single worker or a relatively small number of workers. Many of the cases in the literature are based upon clinical presentations, a determination that the urticaria is based upon a "probable" occupational exposure, and a "probable" allergic or nonallergic mechanism. Further attempts to prove etiology or mechanisms may be lacking or inadequate. Although the literature is filled with cases of occupational urticaria, tabulating these cases cannot be considered a basis for epidemiological assessment (2).

Because of the problems with case definition and diagnosis, the limited number of subjects, and the difficulty in proving etiologies and mechanisms, the epidemiology of occupational urticaria remains obscure. There are other problems in assessing the epidemiology of occupational urticaria and other occupational skin diseases (3):

1. Occupational urticaria is not a reportable disease (except in states that require reporting of all occupational diseases). This makes health department data sources useless for monitoring occupational urticaria.
2. Occupational urticaria is not a disease that commonly leads to mortality or hospitalization; thus, death certificates or hospital records are not potential data sources.
3. Occupational urticaria is a disease seen and treated (though not always specifically diagnosed) by medical professionals in multiple specialties, especially primary care practitioners, making review of physician-based data sources inefficient.
4. Occupational urticaria may be a disease that often goes untreated and undiagnosed; thus, many cases may never be documented in any data source.
5. Once a diagnosis of occupational urticaria is made, a case does not necessarily elicit a public health response.
6. Individuals with occupational urticaria who seek medical care may be a unique subset of those with the condition. Through this self-selection bias, the information obtained may not reflect the epidemiology of the disease in the general population.
7. Unique exposures may occur in different populations and different industries, making the epidemiology of occupational urticaria in one population or workforce not necessarily generalizable to other populations.
8. The evaluation of past exposures causing occupational urticaria may be exceedingly difficult, often relying on historical information and patient recollection, which are subject to recall and information bias.
9. Cross-sectional studies of working populations, a common epidemiological study design, are subject to survivor bias. Those with severe occupational urticaria may leave the workforce, leaving only those who are not affected or less affected to be included in the studies.
10. An occupational urticaria case, especially if treated by a company's own occupational health personnel, may not involve lost wages or any costs to the worker. Thus, there would be no workers' compensation claim, reducing the utility of this already limited data source.

Descriptive Epidemiology of Occupational Urticaria

Accurate data on the general prevalence of urticaria are not available, although it is estimated that in a lifetime 5%–23% of the U.S. population may have had an episode of acute urticaria (4). Of 1011 consecutive patients seen in a dermatology practice, 26% gave a history of at least one urticarial episode (5). Data from the National Ambulatory Medical

Care Survey, a national probability sample survey of nonfederal office-based physicians in the United States, showed that from January 1989 to December 1990 over 25 million visits (4% of the total 698 million visits) were made to dermatologists. Urticaria was listed as the seventeenth most common principal diagnosis, accounting for 240,000 visits (1% of the total visits to dermatologists) (6). Unfortunately, similar data are not available for patient visits to allergists and immunologists.

International data are also limited. Of 4600 patients seen in a Spanish dermatology clinic and referred for patch testing from 1973 to 1977, 3.5% were given a final diagnosis of urticaria (7). A questionnaire study of 4492 respondents from a population of randomly selected Norwegians showed that 9% reported at least one episode of urticaria (8).

National occupational disease and illness data are available from the U.S. Bureau of Labor Statistics (BLS), but once again data specific for occupational urticaria are limited. The BLS conducts annual surveys of approximately 250,000 employers, selected to represent most private industries in the United States (9). The survey results are then projected to estimate the number and incidence rates of occupational injuries and illnesses in the American working population. BLS data are limited because they exclude several groups, including self-employed individuals, small farms, and government agencies; they depend on misinterpretable definitions of reportable occupational injuries and illnesses; they rely to a large extent on employees reporting conditions to the employer; and they do not provide information on the etiology of the disease.

In 1993, BLS estimated 60,200 cases of occupational skin diseases or disorders in the U.S. workforce (9). Further information is available on the 12,613 cases which involved days away from work. Of this subgroup, 142 (1.1%) were diagnosed with urticaria/hives. The median time away from work for workers with urticaria was 5 days. These 142 workers included 81 from the services industry, 39 from manufacturing, 9 from transportation and public utilities, and 13 not classified. It must be emphasized that because of BLS survey limitations, it has been estimated that the number of actual occupational skin diseases may be on the order of 10 to 50 times higher than reported by the BLS (10). Only limited clinically-based epidemiological information on occupational urticaria is available in the United States. Of 250 consecutive dermatology patients who had filed workers' disability compensation benefits, 8 (3.2%) were found to have urticaria and/or dematographism (11). However, in this study none were deemed to be work-related dermatoses.

In contrast, more specific occupational data are available in Finland. Between 1990 and 1994, occupational contact urticaria was responsible for 29.5% of all reported occupational dermatoses (12). Of the 815 cases of occupational contact urticaria, 70% were in women. Table 1 lists the most common causes which include cow dander (44%); natural rubber latex (24%); flour, grains, and feed (11%); foodstuffs (3%); industrial enzymes (2%); and decorative plants (2%). Interestingly, cow protein allergens also represented the most common cause of occupational asthma in Finland (13). Other, less common causes included roots, spices, pork, vegetables, storage mites, ethylhexyl acrylate, onions, egg, fish, fish meal, poultry, chicken, and other birds. Table 2 lists the occupations with the highest number of cases per 100,000 workers, which included bakers (140 cases per 100,000 employed persons), processed-food preparers, dental assistants, veterinarians, animal attendants, farmers, chefs and cooks, dairy workers, horticultural supervisors, laboratory technicians, physicians, butchers, laboratory assistants, dentists, and nurses.

In general, risk factors for contact urticaria and contact anaphylaxis (e.g., natural rubber latex glove proteins) include a history of atopy, a compromise to the barrier function of intact skin (such as eczema, abrasions, ulcers), and in some cases, occupation (14).

Table 1 Ranking List of the Causes of Occupational Contact Urticaria and Protein Contact Dermatitis During 1990–1994 (815 cases) According to the Finnish Register of Occupational Diseases

Ranking/cause	No. of cases	%	Men/women
1. Cow dander	362	44.4	132/230
2. Natural rubber latex	193	23.7	22/171
3. Flour, grains and feed	92	11.3	ng
4. Handling of foodstuffs	25	3.1	9/16
5. Enzymes	14	1.7	ng
Cellulase	8		
Alfa-amylase	2		
Other enzymes	4		
6. Decorative plants	13	1.6	1/12
7. Roots	10	1.2	2/8
8. Spices	9	1.1	1/8
9. Pork	8	1.0	4/4
10. Vegetables	8	1.0	ng
11. Storage mites	6	0.7	5/1
12. Ethylhexyl acrylate	5	0.6	0/5
13. Onions	4	0.5	1/3
14. Egg	4	0.5	1/3
15. Fish, fish meal	3	0.4	0/3
16. Poultry, chicken, other birds	3	0.4	1/3
Total	815	100	148/567

ng: not given.
Source: Ref. 12.

Epidemiology of Natural Rubber Latex Allergy

Urticaria is an important manifestation of natural rubber latex allergy. Although many studies have been published on natural rubber latex allergy, the prevalence and incidence are still unknown. Still, some occupational epidemiological details are available. Health care workers are the occupational group with the highest risk for developing immediate hypersensitivity reactions to natural rubber latex. A survey of hospital workers showed that 2.9% of 512 employees had positive latex skin prick tests (15,16). Positive reactions were seen in 7.4% of the surgeons and 5.6% of the surgical nurses. Questionnaire data showed that 2% of operating and dental personnel reported localized contact urticaria (17) and 4% of U.S. Army dentists reported symptoms of probable latex allergy (18). Recent studies in dental students and staff revealed that 14% of 203 students and staff reported pruritus and 3% reported urticaria within minutes of exposure to latex gloves; 10% of 131 who underwent skin prick tests had a positive response to natural rubber latex (19).

A cross-sectional study of 741 registered nurses in a large U.S. metropolitan hospital showed that 8.9% were positive for antilatex IgE antibodies (20). The prevalence ranged from 6.4% for operating room nurses to 13.6% for labor and delivery nurses. In this study, the factors that were most closely associated with the presence of antilatex IgE included nonwhite race, self-reported allergy to penicillin, pruritus, conjunctivitis, localized urticaria on latex exposure, history consistent with atopy, and allergies to avocado or ragweed.

Table 2 Ranking List of Occupations with Occupational Contact Urticaria in Finland During 1990–1994 (n = 815) per 100,000 Employed Workers*

Ranking/occupation	No. per 100,000 workers (total no.)
1. Bakers	140.5
2. Preparers of processed food	101.8
3. Dental assistants	95.5
4. Veterinary surgeons	72.5
5. Domestic animal attendants	69.1
6. Farmers, silviculturalists	57.7
7. Chefs, cooks, cold buffet managers	38.5
8. Dairy workers	37.9
9. Horticultural supervisors	37.8
10. Laboratory technicians, radiographers	35.6
11. Physicians	33.0
12. Butchers and sausage makers	28.9
13. Laboratory assistants	24.6
14. Dentists	23.4
15. Nurses	21.2
16. Waiters in cafes and snack bars, etc.	15.1
17. Kitchen assistants, restaurant workers, etc.	13.6
18. Hairdressers, beauticians, bath attendants, etc.	11.8
19. Housekeeping managers, snack bar managers, etc.	11.5
20. Packers	11.2
21. Horticultural workers	10.7
22. Assistant nurses, hospital attendants	10.2
23. Industrial sewers, etc.	9.1
24. Cleaners, etc.	6.7
25. Electrical and teletechnical equipment assemblers	6.6
26. Homemakers, home helps (municipal)	6.2
27. Technical nursing assistants	4.2
28. Machine and engine mechanics, etc.	3.9
29. Shop assistants, shop cashiers	2.1
Total	3.7

*Occupations with at least three cases of occupational urticaria were included.
Source: Ref. 12.

Another cross-sectional study of 1351 Canadian hospital workers showed a prevalence of positive latex skin prick tests of 12.1% (21). The highest prevalence was found in laboratory workers (16.9%) and nurses and physicians (13.3%). The latex skin prick–positive workers reported work-related symptoms, including urticaria, more often than latex skin test–negative workers; 11.3% of latex skin test–positive workers reported urticaria, compared to 2.5% of latex skin test–negative workers (adjusted odds ratio 6.3; confidence interval 3.2–12.5).

Natural rubber latex allergy may be seen in other occupations as well. In a Finnish clinic, 144 adult patients (66 health care workers and 78 from other occupations) were diagnosed with natural rubber latex allergy over a 10-year period. In 88% of the 66 health

care workers, but in only 24% of the other workers, was the sensitization determined to be work-related (22). The other affected occupations included kitchen workers, cleaners, workers in a rubber band plant, textile workers, farmers' wives, a papermill worker, a gardener, a food worker, a dairy worker, a secretary, and a private caretaker. In a survey of latex allergy in a surgical glove manufacturing plant, seven of 68 workers (10%) stated that they had hives at work, and seven of 64 workers who had skin testing had positive reactions to latex (23). In a study of 418 greenhouse workers who used latex gloves, 18% reported immediate symptoms associated with wearing gloves, and 5% had positive skin prick tests (24).

Epidemiology of Occupational Urticaria in Specific Occupations

The prevalence of occupational skin diseases within specific occupations is based upon the exposures inherent within those occupations. Cross-sectional studies of workers in a specific occupation or workplace may allow for an estimation of skin disease within that occupation or workplace. However, there are few studies of specific occupations where occupational urticaria is a measured endpoint. In a study of 801 car mechanics, 120 (15%) reported hand eczema and five (0.6%) had a history of contact urticaria; scratch tests were all negative (25). In 5,641 laboratory animal handlers, 1304 (23.1%) reported one or more allergic symptoms related to the animals (26). Of this symptomatic group 45.6% had skin symptoms and 16% reported contact urticaria. Various combinations of symptoms were noted—19.3% had nasal or eye and skin symptoms, and 11.6% had nasal or eye, respiratory, and skin symptoms. A study of laboratory workers handling rats showed that of 323 workers surveyed, 31% reported at least one work-related symptom with 22% reporting eye and nose symptoms, followed by skin (15%), and chest symptoms (10%) (27). In another study of biology laboratory workers, 27 (11.3%) of those who had frequent exposure to animals had reactions, of whom 15 had various skin reactions, including urticaria; 21 had positive prick tests to animal dander (28). A study of 101 laboratory technicians showed that 14 cases of contact urticaria were caused by rat, seven by mouse, four by guinea pig, and two by cat exposure (29).

Case studies alone do not allow an estimation of occupational prevalence but may describe potential high-risk occupations based upon exposures to specific allergens or urticants. In one study of nine veterinary surgeons, all nine exhibited specific IgE against cow hair and dander; seven were symptomatic (30). A study of 50 food handlers/caterers with possible immediate protein contact dermatitis showed that nine (18%) had positive prick tests, most commonly to fish (31). Another study of 33 food handlers with a similar skin condition showed that 10 had positive scratch tests to explain their dermatitis, with the major allergens being fish and shellfish (32).

CONTACT URTICARIA

Contact urticaria is defined as urticaria that occurs after direct skin contact with a substance. Table 3 lists some of the many substances that can cause contact urticaria in occupational settings. Extensive lists are available in several sources, and new etiological agents are continually being described (33,38).

There are four types of contact urticaria: (1) *nonallergic* (nonimmunological; primary urticariogenic agents); (2) *allergic* (immunological); (3) *combined allergic and nonallergic*; and (4) *combined allergic eczematous and urticarial* (35). Some contactants affect normal

Table 3 Selected Causes of Occupational Contact Urticaria

Agent	Nonimmunological	Immunological
Animals	Caterpillars	Animal products, e.g., placenta, saliva
	Jellyfish	
	Moths	
Foods	Cayene pepper	Cheese, egg, milk
	Fish	Kiwi, mango
	Mustard	Maize
	Thyme	Peanut butter, sesame food, sunflower seed
		Beef, chicken, lamb, liver, turkey
		Seafood (e.g., fish, prowns, shrimp)
		Bean
Fragrances and flavorings	Balsam of Peru	Balsam of Peru
	Cassia (cinnamon oil)	Menthol
	Cinnamic acid	Vanillin
	Cinnamic aldehyde	
	Alcohols	
Medications	Benzocaine	Antibiotics
	Camphor	Ampicillin
	Capsaicin	Bacitracin
	Dimethyl sulfoxide	Cephalosporins
	Friar's balsam	Gentamycin
	Tincture of benzoin	Idochlorhydroxyquine
		Neomycin
		Penicillin
		Rifamycin
		Streptomycin
		Virginiamycin
		Benzocaine
		Phenothiazines
		Chlorpromazine
		Levomepromazine
		Promethazine
Plants	Nettles	Plant products
	Seaweed	Cornstarch (?)
		Henna
		Latex rubber
		Teak
		Tulip
Preservatives and disinfectants	Benzoic acid	Benzoic acid
	Chlorocresol	Chlorhexidine
	Formaldehyde	Chlorocresol
	Sodium benzoate	Benzyl alcohol
	Sorbic acid	Formaldehyde
		Gentian violet
		Sodium hypochlorite
Miscellaneous	Histamine	Carbonless copy paper
	Sulfur	Formaldehyde resin
	Turpentine	Paraphenylenedimine
		Seminal fluid

Source: Ref. 38.

skin while others require eczematized or fissured skin to produce urticaria (37,39). Small molecules may penetrate intact skin while large proteinaceous molecules may require disruption of the epidermal barrier.

There may be a variety of skin manifestations associated with contact urticaria. Because of the potential of this varied morphology, terms such as "immediate contact reactions" are also used to describe what may be different skin manifestations of urticaria (36). Contact urticaria may comprise a spectrum of manifestations "that flows continuously from wheals to erythema to pruritus" (40). Pruritus, tingling, or burning accompanied by erythema is the weakest type of immediate contact reaction. A local wheal and flare is the prototypical reaction of contact urticaria, while generalized urticaria after a local contact is considered a rare phenomenon. Symptoms in other organ systems, such as asthma, rhinitis, conjunctivitis, orolaryngeal effects, and gastrointestinal and cardiovascular symptoms, can occur (36). The term "contact urticaria syndrome" is used to describe both local and systemic immediate reactions caused by contact uticarial agents (41,42). The contact urticaria syndrome was initially divided into the following four stages:

1. Stage 1—localized urticaria at the point of contact
2. Stage 2—contact urticaria and angioedema
3. Stage 3—contact urticaria and asthma
4. Stage 4—contact urticaria and anaphylaxis (42)

Another variety of immediate reaction is termed "protein contact dermatitis." This condition had been initially described in food handlers exposed to certain food proteins (especially fish and shellfish), who developed immediate (10–30 min after exposure) pruritus and erythema, and sometimes vesicle formation (32). Other causes of protein contact dermatitis include animal proteins, enzymes, fruits, grains, plants, spices, and vegetables (43). In most cases a delayed skin reaction with patch tests is negative but scratch tests are positive.

Concomitant type I (urticarial) and type IV (allergic contact dermatitis) skin reactions have been increasingly reported. Some of the contactants that can produce both an immediate and delayed reaction include acrylic acid, benzocaine, carrot, chlorhexidine, chlorocresol, chrysanthemum, cinnamic aldehyde, epoxy resin, garlic, latex, lettuce, nickel sulfate, potato, soybean, and textile dyes (37).

In terms of pathomechanisms, contact urticaria may be caused by nonimmunological, immunological, or undetermined mechanisms. In instances where the mechanism of urticaria is undefined, both unknown nonimmunological and immunological mechanisms could be operative. Examples include urticaria due to ammonium persulfate (used as an oxidizing hair bleach) (44,45), formaldehyde, and some physical agents (2).

Nonimmunological Contact Urticaria

Nonimmunological (nonallergic) contact urticaria occurs without previous sensitization. The mechanisms of nonimmunological urticaria remain unclear. It can result from a direct influence on dermal blood vessel walls or a non-antibody–mediated release of vasoactive substances such as histamine, prostaglandins, leukotrienes, platelet-activating factor, and cytokines (35,46,47). Indirect provocation of mast-cell degranulation by complement activation or neutral reflex vasodilation can occur. Multiple stimuli can cause the nonimmunological degranulation of mast cells within the subcutaneous tissues and dermis. This causes the release of preformed mediators (e.g., histamine), which cause vasodilation and

increase capillary permeability. Also, cellular regulatory factors secreted by lymphocytes, neutrophils, eosinophils, platelets, and macrophages, such as C-C chemokines (e.g., MCP-1, MCP-3), possess histamine-releasing factor (HRF) that can activate exocytosis of histamine from mast cells or basophils (48).

Nonimmunological contact urticaria needs to be distinguished from irritant reactions, although this may be difficult at times. Strong irritants, such as hydrochloric acid, formaldehyde, and phenol, can cause immediate urticaria formation. However, this reaction does not disappear within 24 hr but is followed by erythema, scaling, or crusting (49). Some substances may be both primary irritants and contact urticants.

Nonimmunological contact urticaria may be the most common form of occupational contact urticaria and is usually not associated with systemic symptoms (37). However, in one case, severe systemic immediate allergic reactions have been reported after occupational exposure to benzoic-acid–containing materials (35). A variety of agents have been shown to cause a nonimmunological contact urticaria. These include: acetic acid, ethyl and butyl alcohol, balsam of Peru, benzoic acid, butyric acid, caterpillar hair, cinnamic acid, cinnamic aldehyde, cobalt chloride, diethyl fumarate, dimethyl sulfoxide (DMSO), formaldehyde, insect stings, methyl nicotinate, moths, sodium benzoate, and sorbic acid (35,37). Exposures to these substances may occur in occupational settings, one example being contact urticaria due to airborne sodium benzoate in a pharmaceutical manufacturing plant (50). Some of the physical urticarias may also be classified as nonimmunological urticarias.

Atopic and nonatopic individuals are at equal risk for nonimmunological contact urticaria. Even with well-documented chemical urticants, such as benzoic acid, cinnamic acid, and methyl nicotinate, there is wide interindividual variation in response (51). In addition, there is regional body site variation in the response to chemical urticants (52).

Immunological Contact Urticaria

Immunological (allergic) contact urticaria occurs in individuals previously sensitized to the offending substance. The sensitization route may be through the skin or through extracutaneous organs such as the respiratory and gastrointestinal tracts (2). Confirmation of an allergic basis for contact urticaria is achieved by demonstration of specific IgE to a causative antigen either by demonstrating serum specific IgE (e.g., via a RAST assay) or by skin prick testing. In the past, immediate hypersensitivity was demonstrated by the passive transfer of allergic serum to naive skin where wheal and flare responses could be elicited by injection of allergen (Prausnitz-Küstner reaction); at that time, the transferrable allergic factor was referred to as "reagin" which is now known to be IgE.

A variety of stimuli can cause mast cell activation and release of mediators. These include specific IgE molecules which are bound to mast cell membrane via high affinity receptors for IgE. The cross linking of these IgE receptors by the interaction of the IgE antibody and its antigen initiates cell activation and subsequent degranulation. Other mechanisms that can effect histamine release in occupational urticaria are unproven. They include the activation of the complement cascade and generation of anaphylotoxins (C3a, C4a, C5a) which activate mast cells via specific complement receptors. A variety of peptides may activate mast cells including bradykinin and substance P. As mentioned, C-C chemokines secreted by mononuclear cells and neutrophils can induce histamine release.

As a rule, usually a low proportion of exposed individuals are affected by allergic contact urticaria, and it is likely that it is more common among atopic individuals. It is

also likely that most cases are mediated by IgE since non-specific elevation of IgE is frequently reported. In many cases, specific IgE has also been documented (37). In other cases, specific IgG and perhaps IgM may be responsible by activating the classical complement system (37).

Based upon reviews of epidemiological studies, exposures, and patterns seen in case reported, several occupations may be at higher-risk for the development of allergic contact urticaria. These include the following:

1. food handlers, cooks, caterers, and bakers;
2. general health care workers (53), dental professionals (54), and pharmaceutical industry workers (55);
3. animal handlers such as laboratory workers or veterinarians; and
4. gardeners, florists, woodworkers, and agricultural workers.

For food handlers, cooks, caterers, and bakers the following foods have been reported to produce allergic contact urticaria: apples, bean, beer, caraway seed, carrot, egg, endive, fish, garlic, kiwi fruit, lettuce, meat (beef, chicken, lamb, liver, pork, and turkey), milk, peach, potato, rice, shellfish, spices, and strawberries (35,37). Bakers can develop contact urticaria and other systemic symptoms after exposure to cereal flours, buckwheat flour, and additive flour enzymes such as alpha-amylase (from *Aspergillus oryzae* or *Bacillus subtilis*) (37,56,57). A unique food-related contact urticaria in nontraditional "food handlers" has been described in hairdressers using egg shampoos (58).

In health care, dental, and pharmaceutical environments, handling or producing a variety of medications or chemical disinfectants can put workers at risk. Exposures that can cause allergic contact urticaria include aminothiazole, bacitracin, benzocaine gel, cephalosporins, chloramine (a sterilizer, disinfectant, and chemical reagent), chloramphenical, chlorhexidine (an antiseptic), chlorocresol (a disinfectant), ethylene oxide, gentamicin, neomycin, nitrogen mustard, penicillin, pentamidine isethionate, phenothiazines, rifamycin, and streptomycin (35,37,59). In most circumstances skin patch or prick tests were used to confirm the diagnoses. Specific IgE has not been demonstrated for most of these exposures.

The initial 1979 case report of natural rubber latex allergy occurred in a woman using gloves for hand protection during housework (60). The next reported case occurred in a nurse using surgical gloves (61). Since then, natural rubber latex has been found to be an important cause of allergic contact urticaria, asthma, and anaphylaxis in health care professionals. The most frequently reported manifestation is contact urticaria, followed by rhinoconjunctivitis (62). Atopic individuals and individuals with hand eczema seem to be at higher risk for natural rubber latex allergy.

Allergic contact urticaria has been found to be caused by animal hair (rat and guinea pig exposure in laboratory workers), dander, insects (such as cockroaches and locusts), animal placenta, saliva, seminal fluid, and serum (35). Slaughterhouse workers can develop contact urticaria to animal blood (63). Contact urticaria can be seen in veterinarians after exposure to cow's hairs and placenta, horse dander, and pig's bristles (37).

Certain woods and plants can cause allergic contact urticaria. These include the larch, limba, obeche (African maple), and teak woods (35,64) and plants such as chrysanthemum, *Ficus benjamina* (weeping fig), lilies, *Limonium tataricum, Phoenix canariensis* (canary palm), *Spathiphyllum walisii* (spathe flower), tulips and fungi (shiitake mushrooms) (65–71). High-risk occupations include agricultural workers, carpenters, florists, gardeners, and woodworkers. Caterpillar hair, insect stings, and moths can also cause an allergic contact urticaria in outdoor workers (35). In one investigation, of 46 farm workers with allergic

symptoms, 17 had an allergic contact urticaria and respiratory complains and 29 had respiratory complaints resulting from contact with *Tetranychus urticae* (red spider mite) (72). Agricultural workers may also be exposed to fertilizers and pesticides, some of which can cause allergic contact urticaria.

A variety of industrial chemicals can cause allergic contact urticaria, including: acrylic monomers (plastics), aliphatic polyamines (epoxy resins), alkyl-phenol novolac resin (found in carbonless copy paper), ammonia, castor bean pomace (fertilizers), diethyltoluamide (DEET), formaldehyde (used in clothing, leather, fumigation, and resins), lindane (a parasiticide), paraphenylenediamine, phenylmercuric priopionate (an antibacterial fabric softener), plastic additives (such as butylhydroxytoluene and oleylamide), reactive dyes, sodium sulfide (used in photographs, dyes, and tanning), sulfur dioxide, vinyl pyrilidine, xylene and other solvents (35,37). Allergic contact urticaria can occur with exposure to a variety of metal salts, including iridium, nickel, platinum, and rhodium (35,73). Also, silk, wool, and nylon, which may be found in work clothing, are rare causes of allergic contact urticaria (74).

Some causes of allergic contact urticaria are well documented with in vivo and in vitro testing. An example of one of the more completely documented causes of occupational contact urticaria and asthma are the acid anhydrides, which include phthalic anhydride (PA), tetrahydrochlorophthalic anhydride (TCPA), and trimellitic anhydride (TMA). The anhydrides are used as crosslinking agents or hardeners in epoxy resins, which are used in paints, plastics, and for encapsulation of electronic components. Immediate allergy has been verified by an open test with undiluted PA, a scratch chamber test using 1% PA, prick tests, specific IgE determinations, RAST inhibition studies, and chamber provocation tests (75). Exposure to airborne acid anhydrides has been documented as causing sensitization in some workers (76).

AIRBORNE EXPOSURE URTICARIA

Contact urticaria caused by airborne exposures is an unusual condition as most agents that can cause contact urticaria are not volatile and do not easily vaporize. But in some cases airborne aerosols, dusts, fumes, mists, or vapors have been shown to cause contact urticaria (77). Examples of agents that can cause airborne contact urticaria include acrylic acid, ammonia, formaldehyde, garlic, naphtha, natural rubber latex (protein alone or protein-cornstarch powder combination), phthalic anhydrides, sodium benzoate, soybean, 1,1,1-trichloroethane, and xylene (15,50,76,78–81).

Airborne dermatoses are usually caused by direct skin contact with a substance. In some instances skin diseases may appear after inhalation of a substance (82). Inhaled agents, however, are considered rare causes of urticaria. Case reports have described generalized urticaria and metal fume fever-like symptoms in welders exposed to zinc oxide and polyurethane (83–84). Other occupational exposures that have been reported to induce inhalant urticaria include aminothiazide, ammonia, animal danders, castor bean dust and pomace, coffee bean dust, formaldehyde, lindane, mold spores, complex platinum salts, pollens, and sulfur dioxide (85–88). In many circumstances the exact etiology, route of exposure, and mechanism remain unproven (84). A precise distinction between an inhalational exposure and an epidermal exposure to airborne aerosols, dusts, fumes, mists, or vapors is seldom made in these reports.

PHYSICAL URTICARIAS

Urticarias that result from non-chemical exposures are commonly classified as "physical urticarias." Up to 17% of chronic urticarias may be attributable to physical causes (89). These include mechanical urticarias (caused by trauma, pressure, friction, and fibration) and urticaria resulting from local exposure to physical agents (such as cold, heat, and solar radiation) and water (90,91). The physical urticarias can also be classified mechanistically as immunological, nonimmunological, and uncertain. An allergic mechanism is supported for certain forms of the physical urticarias (e.g., dermatographism) by demonstration that the urticarial response can be passively transferred to a naïve donor (i.e., the Prausnitz-Küstner reaction) (92).

Causes of trauma-induced urticaria include mechanical irritants, for example fiberglass fragments that puncture the skin (93). Pressure urticaria, compromising less than 1% of all urticarias, occurs as deep, indurated, tender hives, usually on the buttocks, feet, or palms, that occur 3–12 hr after application of pressure. These lesions, which may occur after manual labor, walking, climbing stairs, and using hand tools, may persist for up to 48 hr and can be accompanied by fever, chills, and arthralgias (90). A nonimmunological mechanism seems most likely (94). Although rare, pressure urticaria can be very disabling. This condition may be associated with chronic idiopathic urticaria and dermatographism. Dermatographism, the most common form of physical urticaria (seen in 2–5% of the population), results in a linear wheal and flare at the site of firm stroking or friction. The very rare vibratory urticaria may be acquired or familial (autosomal dominant inheritance) and can occur after occupational exposure to vibration, as in metal grinding or jackhammer operation (95,96).

Cold urticaria occurs as an acquired form, an inherited form, and a secondary form associated with serum abnormalities (cryoglobulinemia, cold agglutinins, cryofibrinogens, and cold hemolysins) (97). Urticarial lesions develop during rewarming after direct cold contact or immersion and may be associated with bronchospasm, flushing, hypotension, and syncope. A positive Prausnitz-Küstner reaction shows that acquired cold urticaria, which compromises 1–3% of all urticarias, may be IgE mediated (91,97). Examples of occupational exposures causing cold urticaria include contact sprays, cold lithography solutions, and cold environments (98–100).

Localized heat urticaria is a very rare entity in which pruritic lesions occur quickly after localized heat contact. These lesions can be associated with nausea, diarrhea, abdominal pain, headache, and dizziness. Urticaria caused by heat is likely to be nonimmunological (97). Cholinergic urticaria, which may comprise 5–7% of all urticarias, is marked by a sensation of warmth followed by the appearance of small (1–3 mm) pruritic wheals (91). This condition, which can be accompanied by systemic symptoms, develops after increases in core body temperature and is induced by heat, exercise, or emotion (97). One report documented occupational exposures causing cholinergic uticaria in U.S. Air Force personnel (101). Cholinergic urticaria is mediated by cholinergic substances liberated from stimulated peripheral nerves (102). The rare exercise-induced anaphylactic syndrome needs to be distinguished from cholinergic urticaria. Some individuals develop symptoms only during exercise (or strenuous work) following the eating of certain foods, and the condition is not related to core body temperature (91).

Solar urticaria, seen in less than 1% of persons with urticaria, occurs after exposure to a variety of wavelengths of light and occurs only on exposed skin surfaces. Solar urticaria may be associated with other photosensitive disorders such as systemic lupus

erythematosus and porphyria cutanea tarda (103). Solar urticaria can be associated with systemic symptoms as well; the mechanism is uncertain.

Aquagenic urticaria is a very rare disorder associated with water contact at any temperature and is not associated with any systemic symptoms. It is typically marked by punctate, perifollicular hives. There is some evidence that a water-soluble epidermal antigen permeates the skin after contact with water and activates mast cells, although the mechanism remains uncertain (91).

DIAGNOSIS OF WORK-RELATED URTICARIA

Although a reliable clinical diagnosis of urticaria may usually be established on the basis of clinical examination alone, reliable attribution of causation to an occupational exposure is generally difficult. In part, this difficulty is inherent to the investigation of urticaria in general. No cause can be identified in at least 70% of cases of chronic urticaria (94). As urticaria is common, cases will inevitably occur within the working population. In the absence of an obvious explanation, some workers and physicians will ultimately attribute the cause of the urticaria to an exposure in the workplace. While patient observation and insight may offer valuable clues to any medical investigation, the etiology of a case of urticaria may remain in question unless objective criteria can be established to support an occupational relationship.

Although no general consensus yet exists, a review of the best-documented cases of occupational urticaria cited in this review and elsewhere (104) suggests that the following seven criteria are most useful:

1. The clinical diagnosis of urticaria has been documented by medical examination. The pathognomonic lesion of urticaria is the wheal—a circumscribed, pruritic, raised, pink to erythematous, effervescent swelling of the superficial dermis, without any changes (such as scaling) in the overlying epidermis. The wheal usually lasts only a few hours, rarely more than 24 hr. The appearance of new wheals, coupled with the relatively rapid disappearance of older wheals, may give rise to the patient's perception that the rash is "moving around the body." There are no particular characteristics of wheals caused by occupational exposures that allow them to be distinguished from urticaria due to other causes (including idiopathic).

Urticaria may sometimes be confused with other acute erythematous cutaneous eruptions, such as morbilliform rashes caused by drugs or viruses, erythema multiforme, or even acute contact dermatitis. These latter conditions are more persistent and individual lesions last longer than 24 hr. A skin biopsy is not usually helpful or necessary to confirm a diagnosis of urticaria, but may sometimes be useful to exclude these other dermatological conditions (including urticarial vasculitis) when uncertainty exists. Objective medical documentation is essential since patients' self-reported histories of hives can be unreliable. Similarly, pruritus alone is not objective proof of urticaria unless wheals can be observed.

2. Exposure has occurred in the workplace to an agent that has already been documented as a potential cause of urticaria, based on published medical or toxicological studies. Published studies must be critically evaluated. Upon careful scrutiny, rigorous or convincing proof is often lacking; skin tests allegedly supporting a causal relationship may not have adequate standardization or controls, and the etiological relationship to many purported causes of occupational urticaria, such as formaldehyde, seems to be based upon subjective historical data, such as "hives occur only when working; do not occur when not working."

3. The temporal relationship between exposure and onset of symptoms should be consistent with the diagnosis of urticaria, an immediate hypersensitivity reaction. Under ordinary circumstances, hives should develop at least within 30–60 min of exposure to the putative causal agent in the workplace. However, no general consensus yet exists concerning the time lag between initial exposure and first occurrence of urticaria; symptoms may not develop for weeks, months, or even years after first exposure or date of hire.

4. Associated medical symptoms and the anatomical localization of urticaria must be consistent with the clinical route of exposure to the alleged causal agent. If the skin is the primary route of exposure, the skin should urticate first and foremost on anatomical areas (e.g., the hands and arms) where the causal substance has directly contacted the skin. Although hives may remain localized to the primary areas of direct contact (contact urticaria), generalized urticaria may develop if sufficient percutaneous absorption occurs. In the latter case, the appearance of hives elsewhere on the body surface should follow, not precede, the appearance of hives at the site of primary skin contact. If the primary route of exposure is airborne, urticaria is often associated with additional medical symptoms consistent with rhinitis, conjunctivitis, or asthma. These symptoms should precede, rather than follow, the onset of hives. Medical documentation of these associated symptoms is valuable, since self-reported symptoms are unreliable and difficult to distinguish from minor irritation caused by noxious vapors. In rare instances of alleged contamination of food from workplace exposures, the gastrointestinal tract will be the primary route of exposure. In this case, hives should be associated with nausea and abdominal cramping. Lip and oropharyngeal swelling may also occur as a result of direct contact with the mucous membranes of the mouth.

5. Urticaria should occur only in the workplace and should completely resolve on weekends, vacations, layoffs, or termination of employment. As urticaria is a common disorder in general, care should be taken to distinguish urticaria that may be aggravated by nonspecific workplace conditions that elevate skin temperature (such as hot environments and heavy physical exercise) from hives caused by an exposure that occurs only at work.

6. Nonoccupational causes of urticaria should be excluded. Unfortunately, since no specific cause is objectively documented in the majority of cases of chronic urticaria, a natural temptation exists to blame idiopathic cases on any temporal association, e.g. workplace exposures, although the scientific proof is seldom more than "guilt by association."

7. Medical testing should support a causal relationship between urticaria and a workplace exposure. The following tests may be employed in the investigation of contact or systemic urticaria suspected to be caused by an occupational exposure. In all cases where skin tests are performed, the patient should be off conventional antihistamine therapy for at least 72 hr and long-acting antihistamine therapy for at least 2 weeks. If asthma or anaphylactic symptoms have been associated with urticaria, cardiopulmonary resuscitation equipment should be readily available.

Open or closed patch test this is the primary test utilized for the diagnosis of contact urticaria and is the preferred test for the evaluation of systemic urticaria thought to be caused by skin exposure, as it most closely approximates the conditions under which exposure is actually occurring in the workplace. In the open patch test, the suspected etiological agent is placed directly on the skin "as is" and the test site observed up to 60 mins for erythema or a wheal-and-flare reaction. In the closed patch test, the suspected causal agent is placed on a standard commercial patch test device (e.g., Finn Chamber on Scanpor Tape) and occluded against the skin for 15–30 min. The device is then removed

and the test site observed for a reaction for an additional 30 min (total of 60 min). The preferred test site is the ventral forearm, upper outer arm, or upper back. In cases where occupational cutaneous exposure has been occurring on eczematous skin exclusively (e.g., natural rubber latex gloves over eczememateous hand dermatitis), these tests may be cautiously repeated over the eczematous skin (e.g., cutting a finger off a latex glove and placing it over an affected finger). No standardization of test concentrations exists, and ideally the interpretation of a test as "positive" should be supported by at least 20 negative controls. In some instances, published case reports supported by negative controls may serve as "literature" controls.

With *prick or scratch tests* the skin is either pricked with a 26-gauge needle or blood lancet, or scratched (approximate 7–8-mm-length scratch) with a 20-gauge needle. If the suspected causal agent is a liquid, a drop should be placed on the skin first and the skin pricked or scratched through the liquid. If the suspected causal agent is a solid, the skin should be pricked or scratched first, and then the solid placed over it after first moistening it with water. A variation called the scratch-chamber test has been developed and is particularly useful for solids such as food substances. With this procedure, the test substance is placed into a standard patch test device (e.g., Finn Chamber on Scanpor Tape) and then taped to the skin over a 7–8-mm-length scratch and observed for response. These invasive tests may be necessary if the primary route of exposure is airborne, as mucous membranes are generally more permeable to absorption than the general skin surface and false-negative patch tests (open or closed) may occur as the result of inadequate percutaneous penetration of the test substance. Unfortunately, many industrial chemicals may be nonspecifically irritating to the skin when tested in this fashion. No prick or scratch test standardization exists for most industrial test substances in terms of vehicle or concentration, and the onus is on the investigator to test a sufficient number of control subjects, using positive histamine and negative saline controls as well as the test substance(s), which may turn a clinical evaluation into a time-consuming research project. Ideally, controls should include other subjects with chronic urticaria unrelated to workplace chemical exposure. The mean wheal diameter (i.e., longest diameter + perpendicular diameter divided by 2) should be measured for any positive reaction. Kanerva et al. (105) have recommended a test reaction grading system as follows: 1+ = reaction diameter less than 1/2 diameter of a histamine control, but at least 2 mm greater than the diameter of a saline control; 2+ = reaction diameter greater than 1/2 diameter but less than the full diameter of a histamine control; 3+ = reaction diameter greater than or equal to, but less than twice, a histamine control; 4+ = reaction diameter equal to or greater than twice a histamine control. A weak test reaction of 1+ intensity can be considered significant if other aspects of the evaluation overwhelmingly support this conclusion.

Intradermal tests should not ordinarily be performed unless standardized materials already exist (e.g., wheat antigen for evaluation of baker's asthma associated with hives). The lack of standardization for the majority of workplace allergens makes this test almost impossible to interpret reliably. Furthermore, the majority of workplace chemicals are likely to be highly irritating to tissue when injected intradermally, even in diluted aqueous vehicles, and some may be corrosive.

RAST materials are not commercially available for most workplace chemicals, with few exceptions (natural rubber latex protein, diisocyanates, acid anhydrides). Where available, the RAST can be an extremely helpful diagnostic aid, especially if generalized urticaria exists. However, the test may be negative unless there is a sufficient amount of circulating specific IgE antibody to the suspected allergen. The RAST is generally considered quite specific but not as sensitive as a properly performed and standardized skin test for the diagnosis of immediate hypersensitivity.

Miscellaneous blood tests such as increased total serum IgE levels and peripheral blood eosinophilia are sometimes suggestive of a true allergic reaction, but none are specific for any causal agent.

Skin biopsies are seldom helpful in establishing a diagnosis of urticaria, which is usually made on clinical grounds alone, unless a diagnosis of urticarial vasculitis is suspected. A biopsy is never helpful for establishing a specific etiological cause.

TREATMENT

In all cases of occupational urticaria where a specific causal agent can be identified, the treatment of obvious choice is avoidance of the offending agent. In some cases, a nonallergenic substance may simply be substituted, and the affected worker kept in the same job (e.g., substitution of nitrile gloves for natural rubber latex gloves for workers allergic to latex protein). In other cases, the affected worker will have to be removed from that part of the work environment where exposure has been occurring, even if it ultimately means changing jobs. However, medical recommendations to leave employment should not be made lightly and should be supported by adequate objective medical findings, including tests that specifically identify the causal agent.

Since the overwhelming majority of cases of urticaria occurring among workers will not be due to any occupational exposures, treatment may be instituted according to the same therapeutic principles to manage any other case of chronic urticaria. First-generation antihistamines that block H_1 receptors (e.g., diphenhydramine, hydroxyzine) should be employed initially, but they frequently cause sedation; this may present a safety issue for certain occupations (e.g., heavy-equipment operators). When sedation occurs or presents a safety concern, nonsedating, second-generation antihistamines (cetirizine, astemizole, loratadine, fexofenadine) may be employed. When H_1 histamine blockers alone are not sufficient, they may be combined with H_2 blockers (e.g., cimetidine, ranitidine, famotidine) or doxepin, a tricyclic antidepressant with potent H_1 and H_2 blocking activity. Doxepin is extremely sedating and should be used cautiously, if at all, when safety concerns arise on the job. Oral corticosteroid therapy may be employed for severe cases of chronic urticaria, especially those associated with angioedema, which are unresponsive to the above measures.

REFERENCES

1. Lever WF, Schaumburg-Lever G. Histopathology of the Skin, 7th ed. Philadelphia: Lippincott, 1990:152–153.
2. Harvell J, Bason M, Maibach H. Contact urticaria and its mechanisms. Food Chem Toxicol 1994; 32:103–112.
3. Lushniak BD. The epidemiology of occupational contact dermatitis. Dermatol Clin 1995; 13: 671–680.
4. Greaves MW. Chronic urticaria. N Engl J Med 1995; 332:1767–1771.
5. Elpern DJ. The syndrome of immediate reactivities (contact urticaria syndrome)—an historical study from a dermatology practice. Hawaii Med J 1985; 44:426–440.
6. Nelson C. Office visits to dermatologists: National Ambulatory Medical Care Survey, United States 1989–90. Vital and Health Statistics of the Centers for Disease Control and Prevention/ National Center for Health Statistics 1994; no. 240:1–12.

7. Romaguera C, Grimalt F. Statistical and comparative study of 4600 patients tested in Barcelona (1973–1977). Contact Dermatitis 1980; 6:309–315.
8. Bakke P, Gulsvik A, Eide GE. Hay fever, eczema and urticaria in southwest Norway. Allergy 1990; 45:515–522.
9. Bureau of Labor Statistics (BLS). Occupational Injuries and Illnesses in the United States. US Department of Labor, BLS, published annually since 1972; data for 1993 published August 1996 in Bulletin 2478.
10. National Institute for Occupational Safety and Health (NIOSH). National Occupational Survey—Pilot study for development of an occupational disease surveillance method. Rockville, MD: US Department of Health, Education, and Welfare, 1975; HEW Publication (NIOSH) 75–162.
11. Plotnick H. Analysis of 250 consecutively evaluated cases of workers' disability claims for dermatitis. Arch Dermatol 1990; 160:782–786.
12. Kanerva L, Toikkanen J, Jolanki R, Estlander T. Statistical data on occupational contact urticaria. Contact Dermatitis 1996; 35:229–233.
13. Kanerva L, Vaheri E. Occupational rhinitis in Finland. Int Arch Occup Environ Health 1993; 32:150–155.
14. Skinner SL, Fowler JF. Contact anaphylaxis: a review. Am J Contact Dermatitis 1995; 6: 133–142.
15. Hamann CP. Natural rubber latex sensitivity in review. Am J Contact Dermatitis 1993; 4: 4–21.
16. Turjanmaa K. Incidence of immediate allergy to latex gloves in hospital personnel. Contact Dermatitis 1987; 17:270–275.
17. Wrangsjo K, Osterman K, van Hage-Hamsten M. Glove-related skin symptoms among operating theatre and dental care unit personnel. Contact Dermatitis 1994; 30:102–107.
18. Berky ZT, Luciano WJ, James WD. Latex glove allergy, a survey of the US Army Dental Corps. JAMA 1992; 268:2695–2696.
19. Tarlo SM, Sussman GL, Holness DL. Latex sensitivity in dental students and staff—a cross-sectional study. J Allergy Clin Immunol 1997; 99:396–401.
20. Grzybowski M, Ownby DR, Peyser PA, Johnson CC, Schork MA. The prevalence of anti-latex IgE antibodies among registered nurses. J Allergy Clin Immunol 1996; 98:535–544.
21. Liss GM, Sussman GL, Deal K, Brown S, Cividino M, Siu S, Beezhold DH, Smith G, Swanson MC, Yunginger J, Douglas A, Holness DK, Lebert P, Keith P, Wasserman S, Turjanmaa K. Latex allergy: epidemiological study of 1351 hospital workers. Occup Environ Med 1997; 54:335–342.
22. Turjanmaa K. Update on occupational natural rubber latex allergy. Dermatol Clin 1994; 12: 561–567.
23. Tarlo SM, Wong L, Roos J, Booth N. Occupational asthma caused by latex in a surgical glove manufacturing plant. J Allergy Clin Immunol 1990; 85:626–631.
24. Carillo T, Blanco C, Quiralte J, Castillo R, Cuevas M, Rodriguez de Castro F. Prevalence of latex allergy among greenhouse workers. J Allergy Clin Immunol 1995; 96:699–701.
25. Meding B, Barregard L, Marcus K. Hand eczema in car mechanics. Contact Dermatitis 1994; 30:129–134.
26. Aoyama K, Ueda A, Manda F, Matsushita T, Ueda T, Yamauchi C. Allergy to laboratory animals: an epidemiological study. Br J Ind Med 1992; 49:41–47.
27. Cullinan P, Lowson D, Nieuwenhuijsen MJ, Gordon S, Tee RD, Venables KM, McDonald JC, Newman-Raylow AJ. Work-related symptoms, sensitization and estimated exposure in workers not previously exposed to laboratory rats. Occup Environ Med 1994; 51:589–592.
28. Lincoln TA, Bolton NE, Garret AS. Occupational allergy to animal dander and sera. J Occup Med 1974; 16:465–469.
29. Agrup G, Sjostedt L. Contact urticaria in laboratory technicians. Acta Derm Venereol (Stockh) 1985; 65:114–115.
30. Prahl P, Roed-Petersen J. Type I allergy from cows in veterinary surgeons. Contact Dermatitis 1979; 5:33–38.

31. Cronin E. Dermatitis of the hands in caterers. Contact Dermatitis 1987; 17:265–269.
32. Hjorth N, Roed-Petersen J. Occupational protein contact dermatitis in food handlers. Contact Dermatitis 1976; 2:28–42.
33. Lahti A, Maibach HI. Immediate contact reactions: Immunol Allergy Clin North Am 1989; 9:463–478.
34. Lahti A, Maibach HI. Immediate contact reactions: contact urticaria and the contact urticaria syndrome. In: Marzulli FN, Maibach HI, eds. Dermatotoxicology. New York: Hemisphere, 1991:473–495.
35. Fisher AA. Contact urticaria due to occupational exposures. In: Adams RM, ed. Occupational Skin Disease. Philadelphia: W.B. Saunders, 1990:113–126.
36. Lahti A. Immediate contact reactions. In: Rycroft RJG, Menne T, Frosch PJ, eds. Textbook of Contact Dermatitis. Berlin: Springer-Verlag; 1992:62–74.
37. Reitschel RL, Fowler JF. Contact urticaria. In: Reitschel RL, Fowler JF. Fisher's Contact Dermatitis. 4th ed. Baltimore: Williams & Wilkins, 1995:778–807.
38. Hogan DJ, Tanglertsampan C. The less common occupational dermatosis. Occup Med: State of the Art Reviews 1992; 7:385–401.
39. Andersen KE, Maibach HI. Multiple application delayed onset contact urticaria: possible relation to certain unusual formalin and textile reactions. Contact Dermatitis 1984; 10:227–234.
40. Kligman AM. The spectrum of contact urticaria—wheals, erythema, and pruritus. Dermatol Clin 1990; 8:57–60.
41. Tanglertsampan C, Maibach HI. Contact urticaria. In: Hogan DJ, ed. Occupational Skin Disorders. New York: Igaku-Shoin, 1994:81–88.
42. Maibach HI, Johnson HL. Contact urticaria syndrome. Arch Dermatol 1975; 111:726–730.
43. Janssens V, Morren M, Dooms-Goosens A, Degreef H. Protein contact dermatitis: myth or reality? Br J Dermatol 1995; 132:1–6.
44. Calnan CD, Shuster S. Reactions to ammonium persulfate. Arch Dermatol 1963; 88:812–815.
45. Fisher AA, Dooms-Goosen A. Persulfate hair bleach reactions. Arch Dermatol 1976; 112: 1407–1409.
46. Marks JG, DeLeo VA. Contact urticaria. In: Marks JG, DeLeo VA, eds. Contact and Occupational Dermatology. St Louis: Mosby–Year Book, 1992:309–318.
47. Beltrani VS. Urticaria and angioedema. Dermatol Clin 1996; 14:171–198.
48. Kaplan AP, Kuna P, Reddigari SR. Chemokines and the allergic response. Exp Dermatol 1995; 4:260–265.
49. Lahti A, Maibach HI. Immediate contact reactions. Immunol Allergy Clin North Am 1989; 9:463–478.
50. Nethercott JR, Lawrence MJ, Roy AM, Gibson BL. Airborne contact urticaria due to sodium benzoate in a pharmaceutical manufacturing plant. J Occup Med 1984; 26:734–736.
51. Basketter DA, Wihelm KP. Studies on non-immune immediate contact reactions in an unselected population. Contact Dermatitis 1996; 35:237–240.
52. Shriner DL, Maibach HI. Regional variation of nonimmunologic contact urticaria—functional map of the human face. Skin Pharmacol 1996; 9:312–321.
53. Cohen SR. Skin disease in health care workers. Occup Med: State of the Art Reviews 1987; 2:565–580.
54. Kanerva L, Estlander T, Jolanki R. Occupational skin allergy in the dental profession. Dermatol Clin 1994; 12:517–531.
55. Sherertz EF. Occupational skin diseases in the pharmaceutical industry. Dermatol Clin 1994; 12:533–536.
56. Valdivieso R, Moneo I, Pola J, Munoz T, Zapata C, Hinojosa M. Losada E. Occupational asthma and contact urticaria caused by buckwheat flour. Ann of Allergy 1989; 63:149–152.
57. Morren MA, Janssens V, Dooms-Goosens A, Van Hoeyveld E, Cornelis A, De Wolf-Peeters C, Heremans A. Alpha-amylase, a flour additive: an important cause of protein contact dermatitis in bakers. J Amer Acad Dermatol 1993; 29:723–728.

58. Temesvari E, Varkonyi V. Contact urticaria provoked by egg. Contact Dermatitis 1980; 6: 143–144.
59. Belsito DV. Contact urticaria from pentamidine isethionate. Contact Dermatitis 1993; 29:158.
60. Nutter AF. Contact urticaria to ruber. Br J Dermatol 1979; 101:597–598.
61. Forstrom L. Contact urticaria from latex surgical gloves. Contact Dermatitis 1980; 6:33–34.
62. Turjanmaa K. Alenius H. Makinen-Kiljunen S, Reunala T, Palusuo T. Natural ruber latex allergy. Allergy 1996; 51:593–602.
63. Goransson K. Occupational contact urticaria to fresh cow and pig blood in slaughtermen. Contact Dermatitis 1981; 7:281–282.
64. Hinojosa M, Subiza J, Moneo I, Puyana J, Diez ML, Fernandez-Rivas M. Contact urticaria caused by Obeche wood (*Triplochiton scleroxylon*). Report of eight patients. Ann of Allergy 1990; 64:476–479.
65. Blanco C, Carillo T, Quiralte J, Pascual C, Martin Estaban M, Castillo R. Occupational rhinoconjunctivitis and bronchial asthma due to *Phoenix canariensis* pollen allergy. Allergy 1995; 50:277–280.
66. Quirce S, Garcia-Figueroa B, Alaguibel JM, Muro MD, Tabar AI. Occupational asthma and contact urticaria from dried flowers of *Limonium tartaricum*. Allergy 1993; 48:285–290.
67. Kanera L. Makinen-Kiljunen S, Kiistala R, Granlund H. Occupational allergy caused by the spathe flower (*Spathiphyllum walisii*), Allergy 1995; 50:174–178.
68. Tanaka T, Moriwaki SI, Horio T. Occupational dermatitis with simultaneous immediate and delayed allergy to chrysanthemum. Contact Dermatitis 1987; 16:152–154.
69. Tarvainen K, Salonen JP, Kanerva L, Estlander T, Keskinen H, Rantenen T. Allergy and toxicodermia from shiitake mushrooms. J Am Acad Dermatol 1991; 24:64–66.
70. Lahti A. Contact urticaria and respiratory symptoms from tulips and lilies. Contact Dermatitis 1986; 14:317–319.
71. Axelsson IGK, Johansson SGO, Zetterstrom O. Occupational allergy to weeping fig in plant keepers. Allergy 1987; 42:161–167.
72. Astarita C, Di Martino P, Scala G, Franzese A, Sproviero S. Contact allergy: another occupational risk to *Tetranychus urticae*. J Allergy Clin Immunol 1996; 98:732–738.
73. Bergman A, Svedberg U, Nilsson E. Contact urticaria with anaphylactic reactions caused by occupational exposure to irridium salt. Contact Dermatitis 1995; 32:14–17.
74. Dooms-Goosens A, Duron C, Loncke J, Degreef H. Contact urticaria due to nylon. Contact Dermatitis 1986; 14:63.
75. Kanerva L, Hyry R, Jolanki R, Hytonen M. Estlander T. Delayed and immediate allergy caused by methylhexahydrophthalic anhydride. Contact Dermatitis 1997; 36:34–38.
76. Tarvainen K, Jolanki R, Estlander T, Tupasela O, Pfaffli P, Kanerva L. Immunologic contact urticaria due to airborne methylhexahydrophthalic and methyltetrahydrophthalic anhydrides. Contact Dermatitis 1995; 32:204–209.
77. Dooms-Goosens A, Deleu H. Airborne contact dermatitis: an update. Contact Dermatitis 1991; 25:211–217.
78. Lindskov R. Contact urticaria to formaldehyde. Contact Dermatitis 1982; 8:333–334.
79. Fowler JF. Contact urticaria to 1,1,1-Trichoroethane. Amer J. Contact Dermatitis 1991; 2: 239.
80. Goncalo M, Chiera L. Goncalo S. Immediate and delayed hypersensitivity to garlic and soybean. Amer J Contact Dermatitis 1992; 3:102–104.
81. Palmer KT, Rycroft RJG. Occupational airborne contact urticaria due to xylene. Contact Dermatitis 1993; 28:44.
82. Bjorkner BE. Industrial airborne dermatoses. Dermatol Clin 1994; 12:501–509.
83. Farrell FJ. Angioedema and urticaria as acute and late phase reactions to zinc fume exposure, with associated metal fume fever-like symptoms. Am J Ind Med 1987; 12:331–337.
84. Kanerva L, Estlander T, Jolanki R, Lahteenmaki MT, Keskinen H. Occupational urticaria from welding polyurethane. J Am Acad Dermatol 1991; 24:825–826.
85. Kanerva L, Estlander T, Jolanki R. Long-lasting contact urticaria from castor bean. J Amer Acad Dermatol 1990; 23:351–355.

86. Mathias CGT. Occupational dermatoses. J Am Acad Dermatol 1988; 19:1107–1114.
87. Key MM. Some unusual allergic reactions in industry. Arch Dermatol 1961; 83:3–6.
88. Morris GE. Urticaria following exposure to ammonia fumes. Arch Ind Health 1956; 13:480.
89. Champion RH, Roberts SOB, Carpenter RG, Roger JH. Urticaria and angioedema: a review of 554 patients. Br J Dermatol 1969; 81:588–595.
90. Black AK. Mechanical trauma and urticaria. Am J Ind Med 1985; 8:297–303.
91. Caslae TB, Sampson HA, Hanifin J, Kaplan AP, Kulczycki A, Lawrence ID, Lemanske RF, Levine MI, Lillie MA. Guide to physical urticarias. J Allergy Clin Immunol 1988; 5:758–763.
92. Soter NA. Physical urticaria/angioedema. Semin Dermatol 1987; 6:302–312.
93. Farkas J. Fiberglass dermatitis in employees of a project-office in a new building. Contact Dermatitis 1983; 9:79.
94. Soter NA. Urticaria and angioedema. In: Fitzpatrick TB, Eisen AZ, Wolff K, Freedberg IM, Austen KF, eds. Dermatology in General Medicine. New York: McGraw-Hill, 1993:1483–1493.
95. Wener MH, Metzger WJ, Simon RA. Occupationally acquired vibratory angioedema with secondary carpal tunnel syndrome. Ann Intern Med 1983; 98:44–46.
96. Cohen SR, Bilinski DL, McNutt NS. Vibration syndrome: cutaneous and systemic manifestations in a jackhammer operator. Arch Dermatol 1985; 12:1544–1547.
97. Page EH, Shear NH. Temperature-dependent skin disorders. J Amer Acad Dermatol 1988; 18:1003–1119.
98. Bjorkner B. Occupational cold urticaria from contact spray. Contact Dermatitis 1981; 7: 338–339.
99. Fitzgerald DA, Heagerty AHM, English JSC. Cold urticaria as an occupational dermatosis. Contact Dermatitis 1995; 32:238.
100. Miller SD, Pritchard D, Crowley JP. Blood histamine levels following graded cold challenge in atypical acquired cold urticaria. Ann of Allergy 1992; 68:27–29.
101. Whinnery JE, Anderson GK. Environmentally induced cholinergic urticaria and anaphylaxis. Avia Space Environ Med 1983; 54:551–553.
102. Hirschmann JV, Lawlor F, English JSC, Louback JB, Winkelmann RK, Greaves MW. Cholinergic urticaria. Arch Dermatol 1987; 123:462–467.
103. Jorizzo JL, Smith EB. The physical urticarias. Arch Dermatol 1982; 118:194–201.
104. Amin A, Lahti A, Maibach HI, eds. Contact Urticaria Syndrome. Boca Raton, FL: CRC Press, 1997.
105. Kanerva L, Estlander E, Jolanki R. Skin testing for immediate hypersensitivity in occupational allergology. In: Menna T, Maibach HI, eds. Exogenous Dermatoses: Environmental Dermatitis. Boca Raton, FL: CRC Press, 1990.

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