Clinical Reviews in Allergy and Immunology
© Copyright 2006 by Humana Press Inc.
All rights of any nature whatsoever reserved.
1080-0549/06/39–46/$30.00
ISSN (Online) 1559-0267

Occupational Contact Urticaria

Jean Luc Bourrain

Allergologie-Photobiologie, Dermatologie-DPM, CHU de Grenoble, Grenoble Cedex 9, France.
E-mail: JLBourrain@chu-grenoble.fr.

Abstract

Among contact dermatosis, irritant contact dermatitis and allergic eczema are by far the most frequent. Nevertheless, concerning occupational dermatosis, contact urticaria should be not neglected. Allergy to natural rubber latex is well-known; however, many other substances found in catering jobs and in jobs involving close contact with animals or vegetables can cause allergies. Discrete forms are not rare and should be remembered during questioning of the patient, as well as during a clinical examination. Accordingly, a physician should perform the appropriate cutaneous tests—particularly prick tests—and the relevance of these tests then needs to be assessed.

Index Entries

Allergy; contact urticaria; dermatosis; occupational; skin; urticaria.

Introduction

Contact urticaria is probably one of the most frequent pathologies. During the course of a lifetime, most people will have felt the burning sting of a nettle on their skin at least once. In professional exposures, contact urticaria through allergy to natural rubber latex is also a very frequent pathology, although it is much less frequent than occupational eczemas, which account for more than 90% of occupational dermatitis.

Definition

Contact urticaria is a cutaneous syndrome defined by the appearance of a pruriginous wheal-and-flare within minutes of contact with the responsible substance; this wheal-and-flare then vanishes quickly when the contact has

Table 1
Staging System of Contact Urticaria Syndrome Proposed by Maibach

	Contact urticaria
Stage 1	Localized urticaria
Stage 2	Generalized urticaria
Stage 3	Urticaria and extracutaneous reactions (bronchial asthma, rhinitis, conjunctivitis, angiooedema, gastrointestinal symptoms, etc.)
Stage 4	Anaphylactoid or anaphylactic shock

Adapted from ref. *1*.

ceased. Nonetheless, clinical forms are frequent, and this pathology is characterized by diversity in its mechanisms or its atypical aspects. Depending on interindividual variability, etiology, and, especially, the intensity and the length of the contact, it can evolve into a simple pruritus or a pruritical erythematosous macule (Table 1). Delayed forms, in which the lesions appear within hours of contact, have also been reported *(1,2)*.

Physiopathology

Contact urticaria is traditionally divided into two groups: immunological and nonimmunological mechanisms. Immunological urticaria usually results from sensitizations by immunogobulin (Ig)E, with the exception of rare cases in which the IgG or specific IgM responsible for activation of complement have been incriminated. Therefore, contact urticaria is an anaphylactic localized reaction caused by an histamine release by mastocytes and basophils that are mediated by IgE and specific allergens *(1,3,4)*. Occasionally, symptoms are not limited to the skin: IgE and mastocytes can also be present in other organs. The urticaria can then be associated with rhinitis, conjunctivitis, asthma, or even shock. However, some substances can essentially trigger a nonimmunological mechanism and can be, in certain cases, a source of genuine allergies. Nonetheless, the causative mechanism often remains unknown or associated (e.g., pine processionary caterpillar) *(5,6)*. Nonimmunological urticaria are the most frequent; they occur at first contact, even without any prior sensitization. Theoretically, nonimmunological urticaria are triggered in all subjects who come into cutaneous contact with the substance at issue.

That may be true for some molecules found in sea animals, insects, and vegetables, such as nettles, but others (cinnamaldehyde, benzoic acid, sorbic acid, sodium benzoate, myroxylon pereirae) generate a much weaker reactivity, although the reactivity is much higher than in allergies. This finding bears witness to a certain interindividual susceptibility that also determines the intensity of the response. In the majority of cases, the lesions appear within 45 min after application and disappear in 2 h *(3,7)*. Although the mechanism is usually a nonspecific histamine release, other mediators—with or without related mastocytes—are sometimes responsible (prostaglandins, leukotrienes, substance P) and might originate in skin nerves or vessels. Therefore, concerning benzoic acid, cinnamic acid, cinnamaldehyde, and methylnicotinate, the lesions are inhibited not by antihistamines but by nonsteroidal anti-inflammatory drugs *(4)*.

Epidemiology

One must immediately disregard nonimmunological occupational urticaria triggered by common substances found in ants, nettles, and other vegetables or animals *(8,9)*. Those are extremely frequent and are usually not very serious and are unreported. Another notable situation is that of allergy to natural rubber latex *(10–12)*. The prevalence of this sensitization varies from 5 to 10% in health care workers in Europe (sometimes more in certain American studies), whereas in the general population, the prevalence lies between 1 and 3%. Other professionals, including hairdressers,

maintenance workers, and glove or doll manufacturers, now experience risk with a similar prevalence. Certain circumstances favor the occurrence of such an allergy and double the risk. Atopy is the first factor to be accounted for because it causes further sensitization where all protein allergens are concerned. This is also true for irritant contact dermatitis, which modifies the cutaneous barrier, favors cutaneous penetration, and creates a cutaneous inflammation, thus making allergic sensitization easier *(13)*. This problem is critical in professional pathologies. Irritant contact dermatitis is particularly frequent among health care workers and hairdressers. Prevention and treatment constitute important steps in the medical care of these populations. Conversely, in the case of nonallergic urticaria, atopy does not appear to be a predisposing factor *(1,2)*.

Concerning the other causative substances, the statistical data are less definite, partly because of the fact that this pathology is assessed simultaenously with the protein contact dermatitis.

Therefore, bakers appear to be the most affected (0.14% of exposed subjects), followed by other food professionals (0.057–0.072%), those in contact with animals or vegetables, and finally health care professionals *(8)*.

Etiologies

The causative substances correspond to the earlier mentioned occupations—for example, the protein of cows (which constitutes the first cause of occupational contact urticaria in Finland), natural rubber latex, flours, other food, plants (ficus, yucca), lycopodium, detergent protease, and so forth *(14–21)*. One must also mention other proteins (egg) and modified proteins (wheat, soy) that are added to shampoos (e.g., Crotein Q) and are responsible for contact urticaria among hairdressers *(22)*.

The words referring to these allergens—dander allergy or latex allergy—are often inaccurate and ambiguous, causing misinterpretation and misunderstanding. It is more accurate to say that such sensitizations are related to proteins that are present in animals or plants. Allergy to natural rubber latex is actually a sensitization to *Hevea brasiliensis* proteins. The word latex refers to different materials, some of which do not contain any *H. brasiliensis*, making it more difficult for patients to follow the eviction advice.

To provide an exhaustive list of the proteins that present a risk of allergy may not be possible; rather, let us say that exposures to plant proteins and especially to animal proteins present risk, which increases as the cutaneous contacts grow frequent and are repeated *(23)*. Nonprotein substances are few but very diverse and can include paraphenylenediamine, ethylhexylacrylate, hexahydrophtalic anhydride, potassium and ammonium persulfate, epoxy resins, iridium salts, abietic acid, and furfuryl aldehyde (Table 2; refs. *24–45*).

The hairs of pine and oak processionary caterpillars can cause nonimmunological and immunological contact urticaria among foresters and nurserymen. They are often associated with rhinitis, conjunctivitis, or asthma and, occasionally, eczema *(6)*.

Particular Cases

Physical Contact Urticaria or With Physical Participation

Some physical urticaria are triggered by the direct contact of the physical agent with the skin (e.g., heat, cold, light [solar urticaria], water [aquagenic urticaria], or mechanical contacts [dermographism, delayed pressure urticaria, and vibratory angioedema]). Sometimes, the physical agent does not act alone but activates a chemical substance, making it allergenic or active. This is true of photo-induced contact urticaria with benzophenones, chlorpromazine, methamine hippurate, or formaldehyde and one case of electrical triggering during iontophoresis with mexiletine *(46–48)*.

Table 2
Nonprotein Molecules Responsible for Contact Urticaria

Substances	Type (with reserves)
Abietic acid	I
Acetic acid	NI
Acetylsalicylic acid	I
Aescin	
Albendazole	
Aluminum	
Aminophenazone	I
Amyl alcohol	NI
Bacitracin	I
Balsam of Friar	NI
Basic blue 99	
Benzaldehyde	NI
Benzocaine	I, NI
Benzoic acid	NI
Benzonitrile	
Benzophenone	I
Benzoyl peroxide	I
Benzylic alcohol	I
Butyl alcohol	NI
Butylhydroxytoluene	I
Butyric acid	NI
Capsaicin	NI
Cephalosporins	I
Chloramine T	I
Chlorhexidine	I
Chlorocresol	NI
Chloroform	NI
Chlorpromazine	I
Cinnamaldehyde	NI
Cinnamic acid	NI
Cisplatin	
Cobalt chloride	NI
Colophony	I
Copper	I
Cyclopentolate hydrochloride	
Di(2-ethylhexyl) phthalate (DOP)	I
Diethyl fumarate	NI
Diethyltoluamide	I
Diglycidyl ether of bisphenol A (DGEBA) epoxy resin	I
Diphenylmethane-4,4-diisocyanate (MDI)	
Ethyl alcohol	NI
Etofenamate	I
Formaldehyde	I, NI
Fragrances	I, NI
Fumaric acid	
Gentamycin	I
Geraniol	
Hexahydrophthalic anhydride	
Iodine	N, I
Iridium salts	I

(continued)

Table 2 (Continued)

Substances	Type (with reserves)
Isopropyl alcohol	NI
Levomepromazine	I
Lindane	I
Maleic anhydride	
Menthol	I, NI
Methylhexahydrophthalic anhydride	I
Methyltetrahydrophthalic anhydride	I
Methylmetacrylate	I
Myroxylon pereirae (balsam of Peru)	I, NI
Naphthylacetic acid	I
Nickel	I
Neomycin	I
Nicotinic acid	NI
Nylon	I
Oleic acid	I
O-phenylphenate	I
Penicillins	I
Pentamidine isethionate	
Persulfates	I, NI
Phenoxyethanol	
Phenylmercuric acetate	I
Phosphorus sesquisulphide	
Platinum salts	I
Polyethylene	I
Polyfunctional aziridine hardener	I
Promethazine	I
Propylene glycol	
Pyrazolone	I
Pyridine carboxaldehyde	
Rifamycin	I
Silicone rubber	
Sodium benzoate	NI
Sodium fluoride	
Sorbic acid	NI
Sorbitan sesquioleate	
Tar	NI
Triphenyl phosphite	
Wool alcohol	I
Xylene	I

Delayed and Prolonged Contact Urticaria

Czanecki *(49)* reported the case of a contact urticaria resulting from elm, which was delayed and lasted a maximum of 48 h, disappearing after 6 d. Its histology was that of urticaria and not of eczema. Other specific publications have described cases of prolonged urticaria caused by vaseline or castor oil *(50)*.

Contact Urticaria, Protein Contact Dermatitis, and Allergic Contact Dermatitis

Immediate allergic manifestations, such as urticaria, and delayed manifestations, such as allergic contact dermatitis or protein contact dermatitis, are not exclusive and, in some cases, appear associated. The patient experi-

ences urticaria within the first hours after contact and develops eczematosous lesions on the following days. The conditions of exposure are important because eczematosous lesions do not necessarily appear during the epicutaneous tests. Conversely, a wheal-and-flare that may not have been initially noticed by the patient because it is mild and fleeting may sometimes be revealed during the tests *(47,51)*.

Diagnosis

Cutaneous exploration must be performed through tests that are read "immediately"—that is, between 15 and 60 min after application of the product. Some authors may recommend a progressive method that starts with an open-test on sound skin and then on the affected part, followed by a patch test (again on sound and affected skin), and, if necessary, a prick test and a scratch test or intradermal reaction test; however, this practice is hardly feasible in daily practice. Therefore, the choice of the test must depend on the suspected product and the symptoms. The more serious the symptoms, the more careful and progressive the method must be, using diluted preparations tested in growing concentration. It is also necessary to account for the capacity of the substance that is suspected to have penetrated the skin; a prick test allows immediate penetration. Most professional products are not available for ready tests on skin. Therefore, it is necessary to use them as they are and to be very careful when performing and interpreting tests. Concerning protein allergens, extracts at our disposal allow for testing under good conditions of safety and in reliability, with the exception of a case involving fruits and vegetables, for which prick and prick tests with native products often show a higher sensibility. However, physicians must proceed more carefully with the skin tests when using native products because the risk of anaphylactic reaction is higher, and they should also make use of the available bibliography or tests on healthy subjects in the absence of false-positive results by nonspecific histamine-release. Among biological tests, the revelation of IgE by radioallergosorbent test allows confirmation of an anaphylactic sensitization, but in the case of contact urticaria to nonprotein molecules, tests are available for a limited number of allergens. Cellular tests, like the cellular allergen stimulation test, could become more widely used in the future, but they are currently awaiting approval for numerous substances.

Prevention

Because they are frequent and bear serious consequences both in professional and private life, allergic sensitizations responsible for contact urticaria deserve a sustained primary and secondary prevention *(52)*. The effectiveness of prevention in the case of allergy to natural rubber latex (*H. brasiliensis*) encourages its development and systematic application in occupations at risk *(53,54)*. It requires a narrow collaboration between the different patients, their employers, and the physicians—particularly the occupational physicians in the countries where those are present. Prevention is based on the limitation of direct cutaneous contacts at risk—that is, contacts with products containing proteins (plant, animal). Because the skin is the first protective barrier, it is necessary to favor its hygiene and preventive measures aimed at irritant contact dermatitis. A mechanical protection by gloves fitting in size and material composition is recommended when possible. Concerning natural rubber latex gloves, a reduction in the quantity of proteins contained and a suppression of corn starch powder have proved effective in both primary and secondary prevention *(53)*.

Conclusion

If contact urticaria related to *H. brasiliensis* allergy appears to be reasonably well-treated

despite the frequent confusion with other forms of contact dermatitis, in many other cases, the discrete form of the symptoms, or the preponderance of delayed symptoms where protein contact dermatitis are particularly concerned, lead to misinterpretation. However, it is necessary to remember them and to perform an appropriate allergological exploration, especially in the case of a professionally exposed individual *(55)*.

References

1. Amin, S. and Tanflertsampan, C. (1997), *Am J Contact Dermatitis* **8,** 15–19.
2. Trémeau-Martinage, C. and Giordano-Labadie, F. (1995), *Rev Fr Allergol* **35,** 44–49.
3. Fisher, A. A. (1986), *Contact Dermatitis*, Philadelphia: Lea and Febiger, pp. 686–709.
4. Rycroft, R. J. G. and Menné, T. (1992), *Textbook of Contact Dermatitis*, Berlin: Springer-Verlag, pp.62–71.
5. Wakelin, S. H. (2001), *Clin Exp Dermatol* **26,** 132–136.
6. Vega, J. and Vega, J. M. (2004), *Contact Dermatitis* **50,** 60–64.
7. Bourrain, J. L. (1999), *Progrès en Dermato-Allergologie*, Paris: John Libbey Eurotext, pp. 19–26.
8. Kanerva, L. and Toikkanen, J. (1996), *Contact Dermatitis* **5,** 229–233.
9. Valsecchi, R. and Leghissa, P. (2003), *Contact Dermatitis* **49,** 1667,1668.
10. Jolanki, R. and Estlander, T. (1999), *Contact Dermatitis* **40,** 329–331.
11. Valks, R. and Conde-Salazar, L (2004), *Contact Dermatitis* **50,** 222–224.
12. Alanko, K and Susitaival, P. (2004), *Contact Dermatitis* **50,** 77–82.
13. Vervloet, D. (1997), *Rev Fr Allergol* **37,** 1180–1183.
14. Bourrain, J. L. (2001), *Ann Dermatol Venereol* **128,** 1363–1366.
15. Bourrain, J. L. (2001), *Les Urticaires de la Clinique à la Thèrapeutique*, Paris: John Libbey Eurotext, pp. 139–143.
16. Barbaud, A. (2001), *Ann Dermatol Venereol* **128,** 1161–1165.
17. Kanerva, L. and Estlander, T. (2001), *Allergy* **56,** 1008–1011.
18. Estlander, T. and Jolanki, R. (2001), *Contact Dermatitis* **44,** 213–217.
19. Kanerva, L. and Vanhanen, M. (2001), *Contact Dermatitis* **45,** 49–51.
20. Kiistala, R. and Mäkinen-Kiljunen, S. (1999), *Allergy* **54,** 635–639.
21. Rask-Andersen, A. and Boman, J. (2000), *Allergy* **55,** 836–841.
22. Niinimaki, A. and Niinimaki, M. (1998), *Allergy* **53,** 1078–1082.
23. Lovell, C. R. (1993), *Plants and the Skin*, Oxford: Blackwell Scientific, pp. 29–41.
24. Maibach, H. L. and Johnson, H. L. (1975), *Arch Dermatol* **11,** 726–730.
25. Belsito, D. V. (1993), *Contact Dermatitis* **29,** 158.
26. Camarasa, J. G. and Serra-Baldrich, E. (1993), *Contact Dermatitis* **28,** 294.
27. Chiba, Y. and Takahashi, S. (1999), *Contact Dermatitis* **41,** 234.
28. El Sayed, F. and Manzur, F. (1995), *Contact Dermatitis* **32,** 361.
29. Escribano, M. M. and Munoz-Bellido, F. J. (1997), *Contact Dermatitis* **37,** 233.
30. Hardy, M. and Maibach, H. I. (1995), *Contact Dermatitis* **32,** 360.
31. Jagtman, B. A. (1996), *Contact Dermatitis* **35,** 52.
32. Kanerva, L. and Alanko, K. (2000), *Contact Dermatitis* **42,** 170–172.
33. Kanerva, L. and Alanko, K. (1997), *Contact Dermatitis* **37,** 180–181.
34. Kanerva, L. and Alanko, K. (1999), *Contact Dermatitis* **41,** 339–341.
35. Kanerva, L. and Estlander, T. (1995), *Contact Dermatitis* **33,** 304–309.
36. Kanerva, L. and Grenquist-Norden, B. (1999), *Contact Dermatitis* **41,** 50–51.
37. Kanerva, L. and Hyry, H. (1997), *Contact Dermatitis* **36,** 34–38.
38. Munoz-Bellido, F. J. And Beltran, A. (2000), *Allergy* **55,** 198–199.
39. Sasseville, D. (1998), *Contact Dermatitis* **38,** 57–58.
40. Schena, D. and Barba, A. (1996), *Contact Dermatitis* **34,** 220,221.
41. Shaw, D. W. (1999), *Am. J. Contact Dermatitis* **10,** 228–232.
42. Torresani, C. and Caprari, E. (1993), *Contact Dermatitis* **29,** 282,283.
43. Weiss, R. R. and Mowad, C. (1998), *Am J Contact Dermatitis* **9,** 125–127.
44. Bergman, A. and Svedberg, U. (1995), *Contact Dermatitis* **32**, 14–17.
45. Pasche-Koo, F. and French, L. (1998), *Allergy* **53,** 904,905.
46. Miranda-Romero, A. and Navarro, L. (1998), *Contact Dermatitis* **38,** 558,559.
47. Bourrain, J. L. and Amblard, P. (2003), *Contact Dermatitis* **48,** 45,46.
48. Yamazaki, S. and Katayama, I. (1994), *Br J Dermatol* **130,** 538–540.
49. Czarnecki, D. and Nixon, R. (1993), *Contact Dermatitis* **28,** 196,197.

50. Grin, R. and Maibach, H. I. (1999), *Contact Dermatitis* **40,** 110.
51. Katsarou, A. and Armenaka, M. (1999), *Contact Dermatitis* **41,** 276–279.
52. Bernstein, D. I. and Karnani, R. (2003), *Ann Allergy Asthma Immunol* **90,** 209–213.
53. Allmers, H. and Schmengler, J. (2004), *J Allergy Clin Immunol* **114,** 347–351.
54. Nettis, E. and Colanardi, M. C. (2004), *Allergy* **59,** 718–723.
55. Holness, D. L. and Mace, S. R. (2001), *Am J Contact Dermatitis* **12,** 88–92.