

Review Article

Is contact allergy in man lifelong?

An overview of patch test follow-ups

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In contradistinction from certain strains of mice, contact allergy in man is hypothesized to be either lifelong or at least to last for years. We examined follow-up studies on contact allergy, as evaluated by patch testing, attempting to quantify its natural history. The allergens include colophonium, gold sodium thiosulfate, nickel, and cobalt. At present, due to technical limitations, we cannot state in quantitative terms whether contact allergy in man is lifelong and whether its clinical manifestations change. Thus, we list some criteria for future studies which may help resolve the above question.

Key words: contact allergy; follow-up study; eczema; patch testing. © Munksgaard, 2001.

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Contact allergy in man is considered to be either lifelong or at least to last for years (1). We examined follow-up studies on contact allergy, as evaluated by patch testing, attempting to quantify its natural history. In addition to utilizing Medline and the Science Citation Index (1960 to 2000), we concentrated our efforts on the following: *Contact Dermatitis*, *Dermatosen*, *American Journal of Contact Dermatitis*, *Archives of Dermatology*, *Journal of the American Academy of Dermatology*, and *American Journal of Clinical Dermatology*.

Colophonium

Färm et al. retested 83 patients after 9–13 years in whom contact allergy to colophonium had been diagnosed (2). 16 participants (19%) were negative to colophonium and in 7 the reaction was doubtful. We are uncertain of the biological significance of the doubtful reactions, because test substances from another supplier were used. In addition, since colophonium is not particularly known to cause irritant patch test reactions (3), the doubtful reactions may in fact have represented contact allergy. The composition of this complex natural product may also have varied over the decade.

Gold Sodium Thiosulfate

Bruze et al. (3, 4) examined the development and course of test reactions to gold sodium thiosulfate. This patch-test response has a rate of approximately 10% when added to the standard series. Over 2 months, 10 patients were retested epicutaneously (e.c.) and intracutaneously (i.c.) with dilution series. All 10 patients (100%) had a positive test reaction of some form during the retest. During the entire study, 26 positive e.c. reactions were diagnosed. Within the 1st week, 17 (65%) were recorded; in 10 days, another 9 reactions (35%) appeared. The patients with the latter reactions also had positive test reactions within the 1st week. After 2 months, 9 reactions remained. Out of 30 i.c. tests, 25 became positive within 1 week.

Though the authors did not provide information on the rapidity of the initial patch test to diagnose allergy, they did suggest that active sensitization can occur, leading to a more rapid response on retesting. To diagnose contact allergy to gold sodium thiosulfate, readings at 3 days might be supplemented by readings at 1 and 3 weeks (4). All the patients remained positive for contact allergy to gold sodium thiosulfate from the point of their initial diagnosis to the time of this study.

Nickel

Schubert et al. (5) restudied 104 nickel-positive patients 3 years later; 13 (12.5%) were then negative. Christensen (6) examined the prognosis in nickel allergy and hand eczema in 2 similar patch-test studies performed 6 years apart. 52 of 54 (96.2%) patients remained positive.

Hindsen et al. (7) tested 30 women allergic to nickel on 4 occasions. No patient showed the same patch test reactivity on all 4 occasions, and the highest individual difference noticed was 250× for the 4 test occasions. Furthermore, 2 patients had negative test reactions on at least 1 test.

Cobalt

Rystedt (8) studied cobalt (Table 1). During a 5-year period, 286 of 4034 (7.1%) standard-series tested eczema patients reacted. 50 (1.2%) showed isolated cobalt reactions (i.e., without simultaneous reaction to chromium and/or nickel). 3 of the 50 (6%) who had originally shown isolated reactions to cobalt, failed to react to cobalt on subsequent standard testing and were therefore excluded from the group to be tested with a serial dilution test (SDT). A follow-up study of 36 of these patients included an SDT: 15 of the 36 patients (42%) had negative reactions in the SDT.

Discussion

In evaluating these results, other factors that may influence patch testing must be considered. There is individual variation in patch-test reactivity due to factors such as hormones, drugs, and ultraviolet radiation (9, 10, 12, 13, 17–20). For example, there can be changes in transepidermal water loss and

cutaneous blood flow during the menstrual cycle (9, 10). On the back and forearm, transepidermal water loss (TEWL) is significantly higher on the day of minimal estrogen/progesterone secretion as compared to the day of maximal estrogen secretion. There is also a higher baseline blood flow on the day of maximal progesterone secretion compared to the day of maximal estrogen secretion. 1 group found the skin response to challenge with sodium lauryl sulfate to be significantly stronger at day 1 than at days 9 through 11 in the menstrual cycle (10). Since patch testing is at least a 4-day procedure, it is conceivable that more transient hormonal peaks than the aforementioned could also have an impact on its results.

There are regional variations of patch-test response in nickel-sensitive patients (11). Routine patch test results can also be seasonally influenced through ultraviolet radiation (UVB) (12). Elicitation of positive patch tests may lead to an increased skin reactivity towards the same allergen when the patients are re-tested weeks later (13). Studies were performed on the reproducibility of contact allergy and a highly reproducible response was found, but we are concerned about the low number of patients studied and the fact there was only 1 retest (14). As well, 1 longitudinal study of contact sensitivity in patients with atopic dermatitis found changed reactivity patterns (15). In doubtful cases of contact allergy to metals, intradermal testing can be utilized (16). At present, due to technical limitations noted here, we cannot state in quantitative terms whether contact allergy in man is lifelong or whether its patch test and clinical manifestations change. Taken together, in spite of a century of diagnostic patch testing, we are unable to state with reasonable certainty the length of delayed hypersensitized immunologic reactivity.

Table 1. Summary of follow-up studies involving contact allergy indicating remission of allergy as evaluated by patch testing

Allergen	Colophonium	Nickel	Nickel	Cobalt
frequency of positive patch test reactions to allergen among patients	3–7%	6–7% of patients	6–7% of patients	7.1%
duration	9–13 years	3 years	6 years later	5 years
# patients in follow-up study	83	104	63	36
# patients showing loss of reactivity	16(19%) negative, 7 doubtful patch test result	13(12.5%) negative, 68 free from nickel dermatitis, 16 with a very mild eczema or dyshidrosis	30% were healed, but patch testing revealed a negative patch test in only 2 of 54 (3.8%) patients previously positive; patients with pompholyx-type eczema had worst prognosis; atopy made prognosis worse.	15(42%) negative reactions in the SDT (serial dilution test); however, 11 of those demonstrated weak reactions in the previous standard test
ref.	(2)	(5)	(6)	(8)

Criteria for Future Studies

The following observations should provide data that might aid in the interpretation of future studies.

- Simple retest at the 1st positive to rule out excited skin syndrome.
- Serial dilutions at both time periods to provide more quantitative data.
- Utilize same test site (i.e., upper versus lower back), patch chamber, patch application, tape, pure rather than complex allergen (i.e., nickel versus Myroxyton Pereirae resin).
- Consider provocative use test (PUT/repeated) open application test (ROAT) to provide additional clinically relevant data.
- Observations on the clinical course.

In principle, serial dilutions and PUT are probably the most valuable in assessing clinical relevance. Serial dilutions (1) give one an estimate of relative potency and (2) the lower the concentration a subject reacts to, the less likely the result will be a false positive due to irritation.

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