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Persistence of contact allergy: a retrospective analysis

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Summary

Background. Studies have shown that not all positive patch test reactions are reproducible upon retesting, that is, persistent. Non-persistent reactions might represent initial false-positive reactions, meaning that patients might unnecessarily avoid allergens.
Objectives. To investigate the occurrence of both persistent and non-persistent patch test reactions, to explore possible explanations, and to investigate whether allergen-specific differences exist.
Methods. A retrospective analysis was performed on patients who were patch tested at least twice between 1 January 1995 and 31 October 2016, with at least one positive patch test reaction to an allergen that had been retested. Both univariable and multivariable analyses were performed to investigate the influence of several factors on persistence.
Results. Of 274 retested positive reactions in 119 patients, 183 (66.8%) reactions remained positive. The strongest predictor for non-persistence in both univariable and multivariable analyses was strength of the first patch test, with weak positive reactions being significantly less persistent. Regarding allergen groups, metals and fragrances were less persistent than other allergens.
Conclusion. Weak positive reactions have a low persistence rate, and the dermatologist should be conservative in advising the patient on avoidance of these allergens, especially if clinical relevance is uncertain.

Key words: contact allergy; patch test; persistence.

There is an ongoing debate within the contact dermatitis research community on whether contact allergy, once acquired, is persistent or can be lost. Multiple studies spanning decades have investigated the persistence of positive patch test reactions and the loss of sensitization, and still no conclusion has been reached (1–11). Diagnosing a patient with allergic contact dermatitis is based on patch testing, which is the gold standard for diagnosing contact allergy. The most common methods with which patch test reactions are evaluated are according to the criteria of the ICDRG and those of the ESCD, respectively (12). Every positive patch test reaction has to be evaluated with regard to whether it is currently relevant, that is, the patient has current exposure to the allergen at the site of the dermatitis, or of past relevance. Patients receive oral information regarding their positive patch test reactions and what to avoid, and are given written information. Studies have shown that patients' ability to remember the patch test results is mediocre at best, and that they might be inclined to avoid every allergen to which they had a positive patch test reaction, which can have a major impact on a patient's job or lifestyle (13, 14). A positive patch test reaction can therefore have substantial consequences, and it is important to know (i) the odds of a positive reaction being either a false positive or not

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clinically relevant, (ii) whether a patient with a contact allergy can become tolerant, and (iii) whether any allergen-specific differences exist. To explore the issue of non-persistent patch test reactions, we investigated patients who have been patch tested twice or more at our department.

Methods

We performed a retrospective search on our patch test database from 1 January 1995 to 31 October 2016 for patients who underwent patch testing at least twice, with at least one positive patch test reaction to an allergen that had been retested in the same concentration and the same vehicle, with no restriction on patch test series/allergen or age. If a patient had been patch tested more than twice, only the results of the last two patch tests were evaluated. All patients were tested with at least a baseline series, consisting of TRUE Test® (SmartPractice Europe, Reinbek, Germany) with additional investigator-loaded allergens (Chemotechnique, Vellinge, Sweden), tested in Van der Bend square chambers (Van der Bend, Brielle, The Netherlands). The composition of this baseline series has changed over time, having been adjusted to trends detected in epidemiological data. All patch tests were read by experienced dermatologists according to the ICDRG/ESCD criteria, with the possible outcomes being: negative, irritant, doubtful (?+), weak positive (+), strong positive (++), and extreme positive (+++). Readings were performed on day (D) 3 and D7 by one of two trained dermatologists. For the present analysis, the maximum patch test reactions of these two readings were aggregated as the patch test outcome. Furthermore, no distinction was made between doubtful and irritant reactions, and these were counted as negative when persistence of contact allergy was calculated. As a general rule, patch testing is not performed at our department in patients receiving oral immunosuppressive therapy, and a wash-out period of at least five half-lives is adhered to before patch testing is performed.

Besides patch test reactions, other variables that were analysed were: age at second patch test, sex, history of atopic dermatitis, season in which the patient was patch tested ('warm season', ranging from April to September; and 'cold season', from October to March), years elapsed between the two patch tests, and the patch test system (TRUE Test® or investigator-loaded). Persistence is reported for the 12 most frequently tested allergens and for groups of allergens as reported in Table 1.

Statistics

Persistence is given as relative frequencies together with their 95% confidence interval. The chi^2-test or Fisher's exact test was used to analyse differences between persistence proportions. Logistic regression was performed to analyse the influence of the documented independent variables on the persistence of a positive patch test reaction. Both univariable and multivariable backward regression analyses were performed. The influence of type of allergen was also included in these analyses, and allergens were grouped on the basis of chemical structure, cross-reactivity, and co-sensitization, resulting in seven groups: metals, preservatives, fragrances, rubbers, dyes/colours, topical medicaments, and corticosteroids (Table 1). Statistical analyses were performed with SPSS v.23 (IBM) and Excel 2013 (Microsoft).

Results

Overall, 119 patients (66.4% female) were included in the analysis, with 274 initial positive reactions to an allergen that was retested in a second patch test. The mean age at the first patch test was 38.9 ± 13.7 years, and that at the second patch test was 46.2 ± 14.6 years. Of the 274 positive reactions, 183 (66.8%) remained positive upon retesting, 14 (5.1%) became doubtful, 1 irritant, and 76 (27.7%) became negative (Table 2). Of these 76 initially positive reactions that became negative, 64 (84.2%) were weak positive (+) reactions, 10 (13.2%) were strong positive (++) reactions [3 to nickel sulfate, 3 to *p*-phenylenediamine (PPD), and 1 each to mercaptobenzothiazole, neomycin sulfate, cobalt chloride, and Disperse Orange 3], and 2 (2.6%) were extreme positive (+++) reactions (to zinc dimethyl dithiocarbamate 1% pet. and tixocortol 21-pivalate 0.1% pet., resp.). All 15 reactions that became either doubtful or irritant reactions upon retesting were initially weak positive (+) reactions. Conversely, of the 199 initially weak positive reactions (+), 120 (60.3%) remained positive, of the 56 initially strong positive reactions (++), 46 (82.1%) remained positive, and of the 19 initially extreme positive reactions (+++), 17 (89.5%) remained positive.

The persistence rates for the different variables that were analysed are shown in Table 3. Some of the findings are highlighted here. Of the 274 retested positive reactions, 195 were to allergens in TRUE Test®, and the remaining 79 were to investigator-loaded allergens. The persistence rates were 69.2% for TRUE Test® allergens and 60.8% for investigator-loaded allergens ($p = 0.18$). Of the 119 patients, 83 (69.7%) had (a history of) atopic dermatitis. Of the 274 retested reactions, 195 (71.2%) were in patients with past or current atopic dermatitis.

Table 1. Overview of the allergen groups used for logistic regression analysis, and the composition of each group

Allergens in group	
Metals	Cobalt chloride, mercury, nickel sulfate, and potassium dichromate
Preservatives	2-Bromo-2-nitropropane-1,3-diol, Bioban™ P1487, MCI/MI, diazolidinyl urea, dichlorophene, formaldehyde, imidiazolidinyl urea, MDBGN, *N*-methylol chloroacetamide, quaternium-15, and sodium omadine
Fragrances	FM I, FM II, *Myroxylon pereirae* (balsam of Peru), lemon grass oil (*Cymbopogon citratus/Schoenanthus*), HICC, and orange oil (*Citrus dulcis*)
Rubbers	Black rubber mix, carba mix, MBTS, dipentamethylenethiuram disulfide, mercapto mix, MBT, MOR, *N*-cyclohexyl-2-benzothiazolesulfenamide, TMTD, TMTM, and thiuram mix
Dyes/colours	4-Aminoazobenzene, Disperse Blue 124, Disperse Orange 3, PPD, and TDA
Topical medicaments	Amerchol® L 101, caine mix, Compositae mix, oleamidopropyl dimethylamine, neomycin sulfate, parthenolide, propylene glycol, quinoline mix, and sesquiterpene lactone mix
Corticosteroids	Budesonide, hydrocortisone-17-butyrate, methylprednisolone, tixocortol pivalate, and triamcinolone acetonide

FM I, fragrance mix I; FM II, fragrance mix II; HICC, hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyral™); MBT, mercaptobenzothiazole; MBTS, dibenzothiazyl disulfide; MCI/MI, methylchloroisothiazolinone/methylisothiazolinone; MDBGN, methyldibromo glutaronitrile; MOR, morpholinyl mercaptobenzothiazole; PPD, *p*-phenylenediamine; TDA, toluene-2,5-diamine; TMTD, tetramethylthiuram disulfide; TMTM, tetramethylthiuram monosulfide.

Table 2. Reaction pattern of the second patch test stratified by strength of the original patch test

		Patch test 2						
		Negative	+	++	+++	Doubtful	Irritant	Total
Patch test 1	+	64	70	48	2	14	1	199
	++	10	16	23	7	0	0	56
	+++	2	1	7	9	0	0	19
Total		76	87	78	18	14	1	274

The persistence rate of positive patch test reactions in atopic dermatitis patients was 64.6%, as compared with 72.2% in patients without (a history of) atopic dermatitis ($p = 0.26$). The influence of time elapsed between the two patch tests was also assessed, and three groups of patients were compared: retest within 3 years, retest between 3 and 8 years, and retest after >8 years. Persistence rates for these three groups were, respectively, 64.4%, 73.3%, and 61.5% ($p = 0.20$). Moreover, seasonal influence on persistence was examined. The highest persistence rate was found in patients who were tested both times in a warm season (71.9%), and the second highest was found in patients tested both times in a cold season (67.5%). Patients who were tested in a different season had lower persistence rates: 64.5% for warm to cold, and 63.9% for cold to warm. The influence on persistence of the season during which patch testing took place was, however, not significant ($p = 0.77$).

To assess whether there was variation between allergens, persistence was calculated for individual allergens and for grouped allergens (Tables 3 and 4). Corticosteroids had the lowest persistence rate (44.4%; n = 9), and preservatives had the highest persistence rate (78.0%, n = 41). Fragrances also had a relatively low persistence rate (53.6%; n = 28). The persistence rate for individual allergens ranged from 0.0% to 100.0%, although this was mostly a consequence of many allergens having been retested only once. However, large variation was seen in the top 12 most frequently retested allergens (Table 4), ranging from 35.3% for cobalt (n = 17) to 100.0% for potassium dichromate (n = 11), also indicating strong variation within allergen groups (in this case, metals).

In the univariable logistic regression analysis, only the strength of the first patch test reaction reached significance, confirming that strong (++) and extreme (+++) positive patch test reactions have higher persistence rates than weak (+) positive patch test reactions, with odds ratios (ORs) of, respectively, 3.03 and 5.60. A multivariable model was built with all variables included, with backwards elimination, resulting in model 1 (Table 5). In this model, the strongest significant positive predictor for persistence of a positive patch test reaction remained strength of the patch test reaction (++ reaction, OR 3.09; +++ reaction, OR 6.55). Atopic dermatitis, metals and the investigator-loaded patch test technique were negative predictors, with ORs of, respectively, 0.6, 0.55, and 0.53 (significant). Because we were interested in the predictive power of specific allergen groups, a second model was built with the same technique but excluding strength of the patch test reaction, as this might overpower the

Table 3. Persistence for all analysed variables

Factor		Total (N)	Persistent reactions	
			n (%)	95%CI (%)
Total		274	183 (66.8)	60.9–72.3
Sex	Male	69	45 (65.2)	52.8–76.3
	Female	205	138 (67.3)	60.4–73.7
Age at second patch test (years)	<40	95	59 (62.1)	51.6–71.9
	≥40	179	124 (69.3)	62.0–75.9
TRUE Test® versus chamber-loaded	TRUE Test®	195	135 (69.2)	62.2–75.6
	Chamber-loaded	79	48 (60.8)	49.1–71.6
Atopic dermatitis	Non-atopic	79	57 (72.2)	60.9–81.7
	Atopic	195	126 (64.6)	57.5–71.3
Strength of the first patch test reaction	+	199	120 (60.3)	53.1–67.2
	++	56	46 (82.1)	69.6–91.1
	+++	19	17 (89.5)	66.9–98.7
Metals	Other allergens	201	138 (68.7)	61.8–75.0
	Metals	73	45 (61.6)	49.5–72.8
Preservatives	Other allergens	233	151 (64.8)	58.3–70.9
	Preservatives	41	32 (78.0)	62.4–89.4
Fragrances	Other allergens	246	168 (68.3)	62.1–74.1
	Fragrance	28	15 (53.6)	33.9–72.5
Rubbers	Other allergens	230	149 (64.8)	58.2–70.9
	Rubbers	44	34 (77.3)	62.2–88.5
Dyes	Other allergens	241	161 (66.8)	60.5–72.7
	Dyes	33	22 (66.7)	48.2–82.0
Topicals	Other allergens	252	169 (67.1)	60.9–72.8
	Topicals	22	14 (63.6)	40.7–82.8
Corticosteroids	Other allergens	265	179 (67.5)	61.5–73.1
	Corticosteroids	9	4 (44.4)	13.7–78.8
Time between patch tests	Retest within 3 years	82	53 (64.6)	53.3–74.9
	Restest >3 years up to 8 years	101	74 (73.3)	63.5–81.6
	Retest >8 years	91	56 (61.5)	50.8–71.6
Season	Warm to warm	57	41 (71.9)	58.5–83.0
	Cold to cold	83	56 (67.5)	56.3–77.4
	Warm to cold	62	40 (64.5)	51.3–76.3
	Cold to warm	72	46 (63.9)	51.7–74.9

influence of allergen groups on persistence. This resulted in a model with three significant negative predictors for persistence: the investigator-loaded technique (OR 0.5), metals (OR 0.48), and fragrances (OR 0.40).

Discussion

A retrospective analysis of our contact allergy database showed that, when positive patch test reactions were later retested, 66.8% remained positive, meaning that >30% became negative. This is in line with previous literature (4, 5, 7, 8). As expected, the large majority (almost 85%) of these non-persistent reactions were initially weak positive (+). One might argue that many or most of these had been false positives, as many allergens also have an irritant potential, even though the concentration in which allergens are tested is such that the risk of an irritant reaction should be minimal. Other possibilities must be considered; the patient could have become tolerant, or the threshold for elicitation could have changed. One study by Katsarou et al. investigated differences in T cell subsets expressed in persistent reactions as compared with diminished or lost reactions, and found that, in persistent reactions, a proliferation of $CD45RO^+$/memory cells was seen, whereas in non-persistent reactions $CD45RA^+$/suppressor-inducer cell proliferation was observed (15). These results support the theory that certain patients can be become tolerant.

Another explanation for a non-persistent positive patch test reaction could be that the skin was momentarily more (or less) reactive. One known example of this is the excited skin syndrome or angry back (16, 17); however, when this is observed in our department, we report these reactions as negative. Experimental studies have also shown that the area of skin around

Table 4. Top 12 allergens most frequently retested

	Total	Persistent reactions	
		n (%)	95%CI (%)
Nickel sulfate 200 μg/cm^2	44	27 (61.4)	45.5–75.6
Cobalt chloride 20 μg/cm^2	17	6 (35.3)	14.2–61.7
Fragrance mix I 430 μg/cm^2	14	9 (64.3)	35.1–87.2
p-Phenylenediamine μg/cm^2	13	9 (69.2)	38.6–90.9
Quaternium-15 100 μg/cm^2	12	11 (91.7)	61.5–99.8
Potassium dichromate 23 μg/cm^2	11	11 (100.0)	71.5–100.0
Carba mix 250 μg/cm^2	10	8 (80.0)	44.4–97.5
Colophonium 850 μg/cm^2	9	7 (77.8)	40.0–97.1
Mercaptobenzothiazole 75 μg/cm^2	9	5 (55.6)	21.2–86.3
Myroxylon pereirae (balsam of Peru) 800 μg/cm^2	8	5 (62.5)	24.5–91.5
Formaldehyde 180 μg/cm^2	8	7 (87.5)	47.3–99.7
Thiuram mix 25 μg/cm^2	8	7 (87.5)	47.3–99.7

a strong or extreme positive reaction has higher reactivity, possibly explaining false-positive reactions (18). Neither the amount of positive reactions that a patient had during a patch test nor the proximity of reactions to other strong/extreme positive reactions were taken into account in the current analysis.

There are known factors that can explain variation in individual skin reactivity during patch testing, for example hormones and ultraviolet radiation (19–22). Although there have been conflicting reports, in general it is believed that the immune response of the skin diminishes with ageing (23). Our data, however, show that the persistence rate is higher in patients aged ≥40 years at the second patch test than in patients aged <40 years (69.3% versus 62.1%). This might result from chance, as patients aged ≥40 years are over-represented. Age at second patch test was not significant in the univariable regression analysis. The effect of age might be overshadowed by the fact that the most likely reason for retesting is persistent dermatitis, suggesting that senescence of the immune system is not evident in these patients.

The persistence rate in patients with atopic dermatitis was lower than that in patients without (a history of) atopic dermatitis. Atopic dermatitis was also included in the first multivariable regression model, but it was not significant. It is interesting to note that atopic dermatitis was no longer included in the second model, in which strength of the first patch test reaction was not entered, suggesting that patients with (a history) of atopic dermatitis have more stronger patch test reactions that are not persistent than patients without atopic dermatitis. Of the 12 initially strong/extreme positive (++/+++) reactions that became negative, 11 were in patients with atopic dermatitis (data not shown). It has been suggested that strong inflammatory activity of atopic dermatitis can decrease the elicitation response in patch testing, leading to a higher chance of false-negative reactions (24).

Persistence of a patch test reaction can also depend on the patch test technique used. A previous retrospective study focusing solely on patients tested with TRUE Test® found a persistence of 66%, which is similar to our results, in which 69.2% of positive TRUE Test® reactions were persistent, as compared with 60.8% of investigator-loaded reactions (7). Reactions to investigator-loaded allergens were significantly less persistent in the first multivariable regression model than reactions to TRUE Test® allergens, meaning that this difference was independent of the strength of patch test reaction. Gollhausen et al. investigated the reproducibility of TRUE Test® as compared with allergens tested in Finn Chambers®, and found that, in Finn Chambers®, reproducibility was half that in TRUE Test® (25). Ale and Maibach tested 491 patients with TRUE Test® on both sides of the back, and found a concordance of 95% (26). This is most likely a direct consequence of the fact that TRUE Test® is more standardized, whereas the investigator-loaded technique depends on the investigator, and the amount of vehicle containing allergen applied to each chamber might vary, except when a micropipette is used for aqueous solutions.

It has been suggested by previous studies that the chance of an irritant or doubtful reaction increases in cold and dry weather conditions, therefore increasing the risk of a false-positive reading (27, 28). This is more likely for allergens that are also marginally irritant, for example formaldehyde, for which the most evidence exists of increased odds of questionable and irritant reactions in cold/dry weather (28, 29). Other allergens for which this effect might exist are methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) and PPD (29). The effect of weather conditions on patch test outcome might be stronger for hydrophilic allergens tested in aq. as the vehicle, as is the case for formaldehyde and MCI/MI (29). In our results, no influence of season on persistence was seen, and the persistence rates for formaldehyde, MCI/MI and PPD were all relatively high for cold to warm (81.8%, n = 9/11) and relatively low for warm to cold (62.5%, n = 5/8), which is in contrast to what one would expect on the basis of previous studies (28, 29). One possible explanation might be that formaldehyde and MCI/MI were tested in a povidone gel instead of aq. A more likely explanation is that, for all three allergens, only a few of the reactions were initially tested in a cold season and subsequently retested in the summer. It must also be considered that weather conditions in central Europe vary, and that the dichotomous distribution of 'cold' and

Table 5. Univariable and multivariable log-binomial regression analysis with persistence as outcome

Factor		Univariable analysis OR (95%CI)	Multivariable analysis	
			Model 1[a] OR (95%CI)	Model 2[b] OR (95%CI)
Sex	Female	1.00	–	–
	Male	0.91 (0.51–1.62)	–	–
Age at second patch test (years)	<40	1.00	–	–
	≥40	1.38 (0.82–2.32)	–	–
TRUE Test® versus chamber-loaded	TRUE Test®	1.00	1.00	1.00
	Chamber-loaded	0.69 (0.40–1.19)	**0.53 (0.28–0.98)**	**0.50 (0.27–0.93)**
AD	No AD	1.00	1.00	–
	AD	0.71 (0.40–1.25)	0. 60 (0.33–1.09)	–
Strength of first patch test reaction	+	1.00	1.00	–
	++	**3.03 (1.44–6.35)**	**3.09 (1.46–6.55)**	–
	+++	**5.60 (1.26–24.89)**	**6.55 (1.44–29.79)**	–
Metals	Other	1.00	1.00	1.00
	Metals	0.73 (0.42–1.28)	0.55 (0.29–1.04)	**0.48 (0.25–0.92)**
Preservatives	Other	1.00	–	–
	Preservatives	1.93 (0.88–4.24)	–	–
Fragrances	Other	1.00	–	1.00
	Fragrances	0.54 (0.24–1.18)	–	**0.40 (0.17–0.92)**
Rubber	Other	1.00	–	–
	Rubber	1.85 (0.87–3.93)	–	–
Dyes	Other	1.00	–	–
	Dyes	0.99 (0.46–2.15)	–	–
Topicals	Other	1.00	–	–
	Topicals	0.86 (0.35–2.13)	–	–
Corticosteroids	Other	1.00	–	–
	Corticosteroids	0.38 (0.10–1.47)	–	–
Time between patch tests (years)	<3	1.00	–	–
	3–8	1.50 (0.80–2.82)	–	–
	>8	0.88 (0.47–1.63)	–	–
Season	Warm to warm	1.00	–	–
	Warm to cold	0.71 (0.33–1.54)	–	–
	Cold to warm	0.69 (0.33–1.46)	–	–
	Cold to cold	0.81 (0.39–1.69)	–	–

AD, atopic dermatitis; OR, odds raio.
Bold values indicate significant effects ($p < 0.05$).
[a]Model 1; multivariable regression analysis with all variables entered, and then backward elimination according to Wald.
[b]Model 2; multivariable regression analysis with all variables entered except for strength of first patch test reaction, and then backward elimination according to Wald.

'warm' seasons is a very crude and possibly inaccurate approximation of actual weather conditions (28).

This is, to our best knowledge, the first time that separate allergen groups have been compared with respect to the persistence of positive patch test reactions. In the second multivariable regression model, excluding strength of the first patch test reaction, metals and fragrances were significantly less persistent than other allergens. For metals, this effect appears to be mostly determined by nickel (persistence rate of 61.4%), as this gave the majority (60.3%) of all metal reactions. In previous studies, the persistence rate of nickel allergy ranged from 54% to 87% (1, 5, 30, 31). Cobalt had a very low persistence rate (35.3%), which is lower than seen in previous reports, in which the persistence rate was also on the low side, ranging from 47% to 57% (15, 31). Potassium dichromate, on the other hand, had a 100% persistence rate (n = 11), as compared with a previously reported persistence rate of 63–79%(15, 32). An easy explanation for the low persistence rate of cobalt would be the high proportion of weak positive reactions (15/17): however, 7 of the 11 retested reactions to potassium dichromate were also weak positive (data not shown). There is no obvious explanation for why metals would have a low persistence rate as compared with other allergens. A possible explanation could be tolerization through oral exposure, which

has been observed in both experimental animal studies and retrospectively in humans, especially for nickel (33, 34). One caveat, however, was that oral exposure had to take place prior to cutaneous exposure, although it could still be possible that oral exposure (at an appropriate dose) after cutaneous exposure might result in suppression of contact allergy (35).

The persistence rate of fragrances was mostly determined by fragrance mix (FM) I and *Myroxylon pereirae* (balsam of Peru), which have the highest sensitization prevalence in Europe of all fragrance markers (36). The persistence rate of FM I (64.3%) was similar to that in a previous report, that is, 62% (7). The low persistence rate of fragrances as a group might be merely an artefact resulting from the small sample size.

As a retrospective database study, the current study had some inherent limitations. In order to achieve an as large as possible sample size, we enforced no limitation with regard to which allergen was retested, which led to a heterogeneous sample consisting of a wide range of allergens. To assess whether there was any variability in persistence rates between allergen groups, they were pooled together. However, even larger sample sizes are required for any statements to be made on differences in persistence rates between allergens. Another limitation was that, for most patch test readings, data on the relevance of a patch test reaction were lacking. This could help to differentiate false-positive reactions from true-positive reactions.

In conclusion, our study once again confirms that the persistence of a patch test reaction is not 100%, and that non-persistence is particularly an issue for weak positive reactions. It is therefore important to be conservative in advising a patient in the case of a weak positive reaction, especially if the clinical relevance of the reaction is uncertain, as future avoidance of the specific allergen might be unnecessary. A repeated open application test might help to assess clinical relevance. Differences in the results of two consecutive patch tests in a patient might be explained by changing reactivity of a patient's skin, owing to both internal factors (atopic dermatitis activity and age) and external factors (meteorological conditions and ultraviolet radiation). Differences in persistence rates between specific allergens and allergen groups appear to exist, but further investigation is required.

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