

A proposed relevance scoring system for positive allergic patch test reactions: practical implications and limitations

J.-M. LACHAPELLE

Unit of Dermato-allergology and Dermato-immunology, Louvain University,
30 Clos Chapelle-aux-Champs, UCL 3033, B-1200 Brussels, Belgium

A relevance scoring system for positive allergic patch test reactions is proposed. It refers to current relevance (CR) as well as past relevance (PR). The system was evaluated in adult patients between January 1 and June 30, 1996, and limited to 4 allergens: nickel sulfate, neomycin sulfate, epoxy resin and colophony. Certain methods available for increasing the accuracy of relevance were used in the present study. Practical implications and limitations of using a relevance scoring system are discussed.

Key words: patch testing; relevance scoring system; current relevance; past relevance; nickel; neomycin; epoxy resin; colophony; angry back; excited skin syndrome. © Munksgaard, 1997.

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Accurate recording of positive patch test reactions is the first difficult task facing the clinician when reading results at 2, 3 and/or 4 days. Interpretation of those positive results as true allergic reactions or false positives is even more complicated. When a positive patch test is considered to reveal a genuine contact sensitization process, there is still one more difficulty to surmount, i.e., the assessment of its relevance to the clinical situation. Relevance can be defined as the capability of an information retrieval system to select and retrieve data appropriate to a patient's need. "Evaluating the relevance of a reaction is the most difficult and intricate part of the patch test procedure, and is a challenge to both dermatologist and patient. The dermatologist's skill, experience and curiosity are crucial factors" (1). This ultimate goal is not always achieved in daily life. The aim of the present study is to propose a fairly simple relevance scoring system which could be used easily at the patch test clinic.

Relevance can be divided into current relevance (CR) and past relevance (PR). CR is related to "current" clinical symptoms (for example, occurring in the last few days or weeks) which motivated dermatologist's advice. On the other hand, PR refers to older clinical events, not directly related to the current problems. Nevertheless, there is no clear-cut line between CR and PR, since repeated but discontinuous contact with an allergen can oc-

cur in some patients, leading to a long-term sensitization process.

Relevance is related to (a) the induction of sensitization and (b) the elicitation of allergic contact dermatitis. This study is related only to b).

Method and Materials

Patch testing procedure

Patients included in this relevance study were patch tested to the allergens of the European standard series (2, 3), updated by the European Environmental and Contact Dermatitis Research Group (EECDRG). Patch tests were applied to the upper back, using Finn Chambers® on Scanpor® tape, left in place for 2 days and read at 2 and 4 days.

Positive patch test reactions

Only positive patch test reactions that were recorded as ++ or +++, as recommended by the International Contact Dermatitis Research Group (1, 4), were taken into consideration in the present study. Reactions recorded as ? + and/or + were not considered, to avoid the introduction into this preliminary study of an additional parameter, which could introduce potentially doubtful results.

Relevance scoring system

The scores (0 to 3) have been defined for current and past relevance (Table 1) as follows:

0=not traced: undetected relationship between the test result and the clinical events.

1=doubtful: Subject to cause doubt; uncertain.

2=Possible: capable of happening, existing or being true without contradictory proven facts or circumstances.

3=likely: Possessing or displaying the qualities or characteristics that make something probable.

16 combinations can therefore be considered for each individual case (Table 2).

Selection of patients

Adult patients of both sexes, aged 18–60 years, took part in the present study, which was carried out between 1 January and 30 June, 1996. Special attention was paid to the fact that, at the time of testing, the stage of dermatitis was almost or completely resolved.

Selection of allergens

4 allergens of the European standard series were selected for evaluating the interest of the relevance scoring system of positive patch test reactions:

Table 1. The relevance scoring system of positive patch test reactions

Past relevance (PR)	
PR 0	not traced
PR 1	doubtful
PR 2	possible
PR 3	likely
Current relevance (CR)	
CR 0	not traced
CR 1	doubtful
CR 2	possible
CR 3	likely

Table 2. Concomitant recording of past relevance (PR) and current relevance (CR) scores of positive patch test reactions: the 16 potential combinations

PR0 CR3	PR0 CR2
PR1 CR3	PR1 CR2
PR2 CR3	PR2 CR2
PR3 CR3	PR3 CR2
PR0 CR1	PR0 CR0
PR1 CR1	PR1 CR0
PR2 CR1	PR2 CR0
PR3 CR1	PR3 CR0

Table 3. Past relevance (PR) and current relevance (CR) scores of positive patch test reactions to nickel sulfate ($n=50$); neomycin sulfate ($n=10$); epoxy resin ($n=8$) and colophony ($n=12$)

Nickel sulphate		Neomycin sulfate	
PR0 CR3	12/50	PR0 CR3	3/10
PR2 CR3	2/50	PR3 CR3	1/10
PR3 CR3	16/50	PE1 CR0	1/10
PR1 CR1	2/50	PR2 CR0	17/10
PR0 CR0	2/50	PR3 CR0	4/10
PR3 CR0	16/50	other combinations	0/10
other combinations	0/50		
Epoxy resin		Colophony	
PR0 CR3	3/8	PR0 CR3	3/12
PR2 CR3	1/8	PR3 CR3	1/12
PR0 CR0	1/8	PR2 CR1	2/12
PR3 CR0	3/8	PR3 CR0	6/12
other combinations	0/8	other combinations	0/12

nickel sulfate 5% pet.; neomycin sulfate 20% pet.; epoxy resin 1% pet. and colophony 20% pet. These allergens were chosen taking into account the fact that they were supposed to represent different fields of environmental exposure to allergens. Consecutive eligible positive patch test reactions were recorded (1 January–30 June 1996): 50 nickel sulfate; 10 neomycin sulfate; 8 epoxy resin; 12 colophony.

Sequential patch testing

When concomitant multiple patch test reactions were present in a patient, sequential patch testing with individual positive patch tests was performed, one by one, starting 5 days later. This approach seemed crucial in a relevance study, bearing in mind the potential trap of the "angry back" or "excited skin syndrome" (5–7). In Table 3, results of sequential patch testing were taken into account for final evaluation of relevance scoring; in other words, when a positive patch test was negative upon rechallenging, it was considered as non-reproducible, and therefore scored as negative.

Results

Results of the PR and CR scores of positive patch test reactions are presented in Table 3.

Discussion

General considerations

In this paper, we propose a simple past (PR) and current (CR) relevance scoring system applicable to positive allergic patch test reactions. In order to appreciate the potential interest of recording this parameter in patients' files, we conducted a pre-

Table 4. Methods available for increasing the accuracy of relevance scores of positive patch test reactions

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- (A) Anamnestic data: in-depth discussion with the patient, related to past and current clinical events, including previous patch testing.
- (B) Additional testing procedures.
1. With the suspected allergen(s)
 - a. Sequential patch testing
 - b. Repeated open application test (ROAT)
 - c. Use test
 2. With products brought by the patient (e.g., intermediate chemicals in the manufacturing process, end-products, etc ...) presumably containing the suspected allergen(s).
 - a. Patch testing at the appropriate concentration using the proper vehicle.
 - b. ROAT test
 - c. Use test
 - d. Repeat steps 2 a, b, c, with extracts of end-products (e.g. ultrasonic bath extracts)
- (C) Chemical analysis of the products brought by the patient.
- (D) Information collected from the manufacturer about the chemical content of products.
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liminary study during a 6-month period. Some selection criteria were chosen to provide a more precise discussion of results.

(a) Only ++ and +++ patch test reactions (reflecting presumable contact allergy) were considered; questionable (?+) and weak (+) reactions were therefore excluded. This option was taken, in order to simplify the evaluation of the relevance scoring system in this preliminary study. Indeed, we have to bear in mind that ?+ and + reactions are of difficult interpretation. Some could represent false-positive reactions, whereas many may still be allergic. If we perform tests with a dilution series when there are ++ and +++ reactions, there are + weak allergic reactions. If we increase the concentration that gives a + allergic reaction, we will find ++ allergic reactions. It would be of great interest to see if patients' + reactions give a different relevance pattern to the ++ and the +++ patients. This approach needs further studies.

(b) Only adult patients (18–60 years) were enrolled, thus providing a more homogeneous group in terms of collecting anamnestic data and patch test readings. The scoring system was limited to 4 allergens.

The term "relevance" can be defined easily on theoretical grounds, but its level of accuracy depends, in practice, upon several factors with respect to the approach taken by clinicians. Several methods for improving accuracy are detailed in Table 4. They were consistently but not exhaustively applied to this study, as discussed later on, for each individual allergen. The ultimate aim of assessing the relevance (or non-relevance) of a positive patch test reaction is to determine the intrinsic imputability of a defined allergen to a clinical event. We must bear in mind that the intrinsic imputability only relates to a possible (and not necessarily exclusive) cause-effect relationship be-

tween each positive test to an allergen and the occurrence of a given clinical event. The imputability must be determined independently for each allergen, and is not modified by the imputability of other allergens.

For instance, allergic contact dermatitis to Neobacitracin® ointment could be the current clinical event; let us suppose that patch testing reveals a +++ reaction to neomycin and a ++ reaction to bacitracin: both antibiotics can be considered independently as culprits of the clinical symptoms (co-sensitization) and relevance scores are CR3 for both. If a neomycin ointment had been used by the patient in prior months, the score for neomycin should be PR3 CR3, whereas the score for bacitracin should be PR0 CR3.

Well-defined intrinsic imputability criteria for systemic drug reactions are currently used in France (8), but cannot be adapted to allergic contact reactions. In practice, the significance of both positive and negative patch test results should be made clear to the patient (9, 10). For common allergens, it is useful to have a detailed listing of "Sources and Uses" of allergens (11). This approach has been used extensively in the present study. Nevertheless, such an approach is still incomplete and may require a prolonged period of observations of exposure-exacerbation and withdrawal-remission to supplement the clinical history (12).

One point needs further discussion. PR0 and CR0 do not mean that the relevance is unlikely, but that it has not been traced by the various procedures used for detecting it. Indeed, if there is a positive allergic reaction, the patient has been sensitized to the actual substance by contact; thus relevance is present, but not traced. A good example is the following: a patient has a ++ reaction to paraphenylenediamine (PPD); a supposedly careful investigation cannot trace any potential contact

to PPD, and therefore the relevance index is PR0 CR0. Nevertheless, in this search, a simple question could have been omitted: 'Have you been patch tested previously?' If the answer is yes, a potential explanation for the ++ reaction to PPD is active sensitization to PPD induced by previous patch testing. In this case, the relevance score should be PR3 CR0.

Relevance of positive patch test reactions to nickel

The likely relevance of positive patch test reactions to nickel was considered to be very high, either CR3 (60%), or PR3 (64%). When cumulating CR3 and PR3 results, the total "likely relevance" reached 92% of cases. In the 4 cases coded either PR1 CR1 or PR0 CR0 sequential patch testing was performed. Test reactions were repeatedly positive in the 4 cases, excluding the hypothesis of an "angry back". No additional methods (as listed in Table 4) were used to increase the accuracy of relevance scores of positive allergic patch test reactions.

Relevance of positive patch test reactions to neomycin

When cumulating CR3 and PR3 results, it appears that the total "likely relevance" of positive patch test reactions to neomycin reached 80%. This high score is partly due to joint efforts by the clinician and the patient to determine the presence of neomycin in ointments prescribed some months or years earlier.

Relevance of positive patch test reactions to epoxy resin

Referring to positive patch test reactions to epoxy resin, the likely relevance was – as expected – very high (CR3: 4/8; PR3: 3/8). In only 1 case, was no relevance detected (PR0 CR0).

Among methods listed in Table 4 for increasing the accuracy of relevance scores, patch tests and ROAT tests with chemicals brought by the patient were carried out. No chemical analysis was needed, since information related to the content of the products was provided at length by the manufacturer.

Relevance of positive patch test reactions to colophony

With respect to positive patch test reactions to colophony, the likely relevance was unexpectedly high (CR3: 4/12; PR3: 7/12). As far as PR was concerned, dermatitis from adhesive tape was convinc-

ing in most cases. The available list of colophony sources and uses (11) was of great help for increasing CR accuracy in 2 cases. In case no. 1, dermatitis was most probably related to a colophony-based glue. Patch testing with an ultrasonic bath extract (13) of glue material was positive and clinical evolution of the case supported this hypothesis. Furthermore, the manufacturer indicated that colophony-based products were present in the glue. In case no. 2, fingertip dermatitis was convincingly related to newspaper handling. A newspaper extract gave a faint positive patch test; the patient was advised to use cotton gloves when he was handling newspapers and journals, and this simple measure led to complete healing of the lesions.

Chemical analysis, including HPLC, mass spectrometry and nuclear magnetic resonance, as suggested by Karlberg (14), was not performed.

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Address:

J. M. Lachapelle
Unit of Dermato-Allergology and Dermato-Immunology
Laboratory of Occupational and Environmental Dermatology
Catholic University of Louvain
30, Clos Chapelle-aux-Champs UCL 3033
B-1200 Brussels
Belgium

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