



## Patch testing: Facts and controversies

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**Abstract** The German dermatologist, Josef Jadassohn (1863–1936), first presented the results of his innovative patch-testing technique in 1895. The safety and efficacy of this diagnostic tool has stood the test of time and is still the gold standard for the diagnosis of allergic contact dermatitis (ACD).

Since its discovery, much effort has been put into standardization and optimization of allergens, vehicles, and concentrations of patch-test materials; in procedures of its application; and in reading and scoring of test reactions—all contributing to the development of an accurate, reliable, and safe test with a high reproducibility of its results. Even this seemingly carved-in-stone practice, which has been used for nearly 120 years, has been questioned and challenged, engendering debates, disagreements, and controversies, which show no signs of coming to an end.

Almost every step of the procedure has provoked discussions and controversies:

- Who should be patch-tested?
- What should be the criteria for referral of patients to a patch-test clinic?
- What are the criteria for including an allergen in the standard patch-test series?
- Which chambers should be used in terms of size, material, and shape?
- What is the optimal occlusion time?
- What is the optimal test-reading time?
- What is the best way of scoring patch-test reactions?
- How should the relevance of positive patch tests be classified? (This latter issue, which is the crucial and most complex and tricky phase of the process, has paradoxically not created more controversies than other apparently less problematic parts of the procedure.)

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## Patch testing: More than 100 years of use and still controversial

The German dermatologist, Josef Jadassohn (1863-1936), first presented the results of his innovative patch-testing technique in 1895. The safety and efficacy of this diagnostic tool has stood the test of time, and is still the gold standard for the diagnosis of allergic contact dermatitis (ACD).<sup>1,2</sup> Since its discovery, much effort has gone into understanding the chemical and toxicologic aspects of test allergens, in standardization and optimization of allergens, vehicles, and concentrations of patch-test materials, in procedures of its application, as well as in reading and scoring of test reactions—all contributing to the development of an accurate, reliable, and safe test with a high reproducibility of its results. What, then, is the controversy all about? **Who should be patch tested?**

In 1931, Sulzberger and Wise<sup>3</sup> supported patch testing in cases of eczema and dermatitis, as the sole means of unearthing the etiologic factors and the nature of the condition. In a later contribution, Sulzberger<sup>2</sup> stated, “The patch test has aided patients and physicians to discover the specific causes in innumerable cases of allergic eczematous contact dermatitis, and because allergic contact dermatitis is such a common disease, the patch test is one of the most useful diagnostic tools available today. The test is seemingly so simple that one wonders why it was not employed in medicine until about 1895 when Joseph Jadassohn’s publication introduced it into dermatologic practice.” In 1981, when asked what he felt were the five most important advances in clinical dermatology during the 20th century, Sulzberger said, “The increased use and usefulness of the patch test and the international standardization of test concentrations and methods” was number 1.<sup>4</sup> Those of us who are enthusiastic patch testers and are fascinated by the evaluation of patients with irritant and allergic contact dermatitis would agree.<sup>5</sup> In 1982, Colman warned that the greatest abuse of patch testing is failure to use it.<sup>6</sup> In his book, Fisher concluded that “Properly applied and correctly interpreted patch tests are, at present, the only scientific ‘proof’ of allergic contact dermatitis.”<sup>7</sup> He also cautioned that education in the technique of patch testing is as essential to physicians-in-training as is learning about most surgical procedures. “Every case of dermatitis should be regarded as a case of cell-mediated immunity until proved otherwise. The most appropriate test is the closed patch test. It is a ‘practical’ test not intended to have the quantitative precision of the fine measurements of a research procedure. The greatest hazard is omission of patch-testing procedures in the management of patients who have certain dermatoses. ... Complications from patch tests with a standard series are rare and are no excuse for the omission of this valuable test procedure.”<sup>7</sup>

The enthusiastic past and present patch testers recommend performing the test on every patient suffering from any kind of dermatitis or eczema (which often are used synonymously), as well as for many other undetermined dermatoses. According to the protagonists of the method, the more you perform it the greater the chances to help your patients and to improve their quality of life. We, respectfully,

consider that such an approach is exaggerated, impractical, and probably not in the best interests of at least some of our patients. The question of whom to test continues to provoke discussion and controversy, and the answer remains elusive.

An old rule of thumb is that the appropriate use of patch testing should yield a positive test result between 30% and 65% of the time. If one is getting more than 60% positive patch-test reactions, they are doing too few patch tests, and less than 30% positive reactions probably reflects excessive testing.<sup>5,8,9</sup> This rule falls short of meeting current needs or providing guidelines for the future, but it can serve to evaluate performance to date.

Rajagopalan et al<sup>10</sup> evaluated the cost-effectiveness of patch testing in patients suspected of having ACD in terms of their quality of life (QoL). The authors found that it was most cost-effective and reduced the cost of therapy in patients who had severe ACD. There were greater improvements in QoL in patients with recurrent/chronic ACD who were patch-tested compared with patients who were not; however, even in this study, the data showed that the approach to patch testing all, or nearly all, such patients probably reflects overuse from a QoL effectiveness standpoint, because less than 50% of patients with chronic or recurrent ACD in some dermatology practices apparently can be expected to have good prognoses without patch testing. The conclusion of this study,<sup>10</sup> that QoL benefits from patch testing, appeared to be influenced by patient-selection processes that guide treatment allocation, and that optimal effectiveness is reached at some point between 50% and 100% of use.

Another study<sup>11</sup> that addressed the question of whether the effect of patch testing on QoL depends on test results, noted that patients confirmed as having relevant positive contact allergens had significant improvement in both perceived eczema severity and Dermatology Life Quality Index at 2 months after patch testing. This improvement was not noted in patients with negative patch tests; moreover, there was no significant variation in QoL associated with the body site affected by eczema.

The benefits of patch testing in terms of morbidity, QoL, patient satisfaction, and economical/financial aspects are not altogether clear. The \$1 million question remains: Who should be patch tested? A set of criteria is needed to provide a balance between performing excessive numbers of patch testing and reaching the large numbers of individuals whose positive patch test results would direct the choice of appropriate treatment.

One very sound approach has been suggested by a contact dermatitis (CD) unit in Manchester, United Kingdom.<sup>12</sup> This clinic is unusual because it has a centralized unit to which all consultant dermatologists refer their patients and enables them to audit each consultant’s referral pattern, retrospectively. The authors analyzed data of 10 consultants over a period of 17 months, and the results showed no significant difference between those consultants in the percentage of relevant positive individuals identified as having CD. There was a very clear linear relationship between the number of individuals with relevant ACD and the number of patients

referred by each consultant. The finding of an average positive relevant allergy detection rate of 46% is in keeping with the previously cited older conclusion that the appropriate use of patch testing should yield a positive (and one assumes relevant) result between 30% and 65% of the time. The most important point of the Manchester study is that the physicians who referred the greatest numbers of patients for patch tests also identified the highest numbers of individuals with a relevant contact allergy; thus, the relationship between the numbers of referrals and the numbers of patients with a relevant positive reaction was linear. Because the consultants covered a similar spectrum of clinical load, this linear relationship indicates that they were also similar in their selection of patients for referral because there would have been a plateau effect had they referred excessive numbers of patients (ie, there would have been a lower percentage of relevant positive reactions). The authors calculated that the consultant who referred the minimum number of patients per annum had an annual referral rate of 1 per 700. They suggest that this can be a referral rate for patch testing from a predominately urban population in a developed country. Other authors have adopted this recommendation (ie, this referral rate of 1 per 700 of catchment population).<sup>13,14</sup> The Manchester authors also asked the consultants with the minimal referral numbers for their criteria for referral of patients. The responses included:

- Eczematous disorders where a contact allergy is suspected or are failing to respond to treatment as expected, especially if affected sites include the face, eye, ear, and perineum.
- Chronic hand and foot or stasis dermatitis. These authors suggest that these categories be regarded as appropriate indications for referral for patch testing. Although many experts would agree that these criteria are the minimal for recommending patch testing, some are not satisfied and would like additional criteria to be considered, such as fingertip vesicular dermatitis, chronic stasis dermatitis, CD that does not improve with avoidance of the suspected allergen or "obvious" allergen, dermatitis of unknown origin that justifies hospitalization for management or that limits a patient's ability to work or participate in the usual activities of daily living, dermatitis that recurs after treatment of systemic corticosteroids, and any contact dermatitis of unknown origin.<sup>5</sup>
- Retrospective cross-sectional analyses of North American Contact Dermatitis Group (NACDG) from 2001 to 2004<sup>15</sup> showed the value of patch testing patients with a scattered generalized distribution of dermatitis, when 49% of patients with this disease had at least one relevant positive allergen.

## Allergens in the standard patch-test series

Ideally, one might like to include all known sensitizers, but it is obviously impossible to check the several thousands

of currently known allergens. Fortunately, a small number of substances is considered to account for the majority of delayed hypersensitivity reactions. For practical reasons, most clinicians use a standard series of allergens (the "standard series") to identify the most common offending allergens in patients with ACD. The series may be augmented by patch testing with other series specifically chosen on the basis of the patient's contact and occupational history. The standard series forms the core selection of allergens used to test every patient undergoing patch testing, representing the allergens that most commonly cause ACD in the population being patch tested.

The original standard series was based on the experience of the members of the International Contact Dermatitis Research Group (ICDRG) and mirrored the findings and current situation in different parts of Europe and the United States. Such standardization is the result of years of testing large numbers of individuals, and it reflects a balance of sensitivity and specificity (ie, positive test results in the vast majority of allergic individuals and few positive findings in controls). National and international CD groups regularly evaluate the series. In general, a substance should be included in the standard battery, if it gives positive reactions in more than 1% of those tested or if, without it, a significant number of allergic reactions would be missed.<sup>16</sup>

The problem and controversy begin with the term *standard* insofar as the standard patch-test series is far from being standardized. It can be expected that any standard series will change with time, and the direction of change depends to a great extent on particular exposure circumstances in different countries, different geographical areas, climates, environments (ie, different natural occurrence of allergens, such as urushiol), different cultures, habits, behaviors, occupations, and so on. Are these variations in environment and population so large as to explain the variations of standard screening series from country to country? Could the objective variations between countries justify the fact that the NACDG contain 70 allergens, the European Standard Series 28, the Extended International Series 33, the British Contact Dermatitis Society 41, and the Swedish series 29 allergens?<sup>17</sup> The answer is clearly not. The reason for variations between the different series is far more likely to lie in the different methodologies among the research group and reflect disagreements between them. There also are variations in the concentrations of several allergens between various series,<sup>7</sup> which obviously cannot be explained by objective variations between countries but rather by different experiences and views on the part of the research groups.

## Patch-test chambers

The basic requirements for a patch-test chamber are an inert material applied to a hypoallergenic tape for providing good occlusion and fixation of the test unit to the skin. There

are currently several types of patch-test chambers from different producers, all high-quality and all fulfilling these requirements. The aluminum Finn Chamber® (Epitest, Finland) has gained popularity during recent years, and we use the IQ chambers (Chemotechnique Diagnostic, Sweden), but many other materials are also found in European clinics, such as Al-Test® (Imeco, Sweden), Leukotest® (Beiersdorf, Germany), van der Bend (van der Bend, The Netherlands), allergEaze® Patch Test Chambers (AllergEaze, UK), Hayes (HAL Allergy B.V., The Netherlands) test chambers, and others. Chambers come in different shapes (round and square) and different sizes (eg, the standard Finn chambers are 8 mm and the large ones are 12 mm). Although the large variety of chambers has no importance in terms of routine testing, it reflects the lack of consensus among dermatologists on a single optimal material.

The following is one example of a controversy on test chambers. A study group of the German Contact Dermatitis Research Group (DKG)<sup>18</sup> investigated whether the size of patch-test chambers would affect allergic patch-test reactions. Patients (N = 495) were double-tested synchronously with small and large Finn Chambers containing standard preparations of fragrance mix, wool alcohols, Kathon CG, and formaldehyde. After evaluating 217 patients who had reacted with at least one allergen, the authors wrote:

For each of the 4 allergens, a significantly higher number of stronger reactions was seen with the large chambers as compared to the small ones. It is concluded that large test chambers may be useful for detection of weak sensitizations to particular contact allergens.

In another paper, appearing in the same journal<sup>19</sup> more than 1 year later, a statistical reanalysis of the results came to different conclusions:

Based on this reanalysis, the conclusions are more complex: the reaction pattern for the fragrance mix and wool wax alcohols is significantly different between small and large test chambers; however, this discrepancy arises primarily from changing weak positive reactions with small chambers to strong positive reactions with large chambers. For formaldehyde, no relationship between chamber size and patch test reaction was found in the data, while for Kathon CG, statistical evidence is borderline that more positive test reactions are yielded by large test chambers than by small ones.

Notably, one of the authors collaborated in both papers. All this serves to demonstrate that there are different opinions even on a minor factor, such as the influence of the size of the chamber, and the same applies to many other parameters, such as the influence of the amount of allergen, methods of application of test strips and fixing the chambers, test sites, the question of removal of hair and degreasing of test site, and so on.

## Occlusion time in patch testing

Although allergens had been occluded for 24 hours in the pioneering work of Josef Jadassohn and of Bruno Bloch (1878-1933) in the field of patch testing (patch testing is often quoted as the Jadassohn-Bloch technique), occlusion for 48 hours had been the standard method for decades and is still the procedure of choice today. Even this seemingly carved in stone practice has been questioned and challenged, in particular in view of the fact that a shorter occlusion period would be more comfortable for patients, especially in tropical climates, and produce less irritant and false-positive reactions. Only a few studies indicated that the two application times yielded similar results. In one multicenter study of synchronous left- versus right-sided patch tests by the German Contact Dermatitis Research Group<sup>20</sup> comprising 1,285 patients from 11 centers, 647 patients of 7 centers were exposed for 24 hours and 638 patients of 4 centers for 48 hours, and no significant differences were found between the two exposure times. In an earlier study,<sup>21</sup> out of 30 patients who were positive to 0.05% dichromate when the patch was removed after 48 hours, 29 also were positive when the patch was removed after 24 hours, yielding a very high rate of concordance.

There are many more studies that demonstrate differences in the results between the two exposure times. In one study<sup>22</sup> that compared the results of duplicate patch-test series applied to the opposite sides of the upper back on 250 consecutive patients and removed after either 24 or 48 hours of occlusion, 19% of the patients with positive results showed discordant reactions. The authors concluded that the standard 48-hour application will remain standard procedure in order to avoid significant loss of positive reactions. Several other earlier studies came to the same conclusion.<sup>23-26</sup> Interestingly, the authors of one study<sup>27</sup> that showed a 14% discordance rate believed that this rate is "a satisfactory concordance rate" and that "we could patch test patients with 1 day occlusion." We doubt whether other experts would agree that these results justify the authors' conclusion.

Finally, an interesting study by the DKG<sup>28</sup> indicated that patch tests performed with strong sensitizers and a 48-hour occlusion may cause patch-test sensitization. Paraphenylenediamine (PPD) 1% petrolatum (pet.) elicited late reactions in 1.5% of 48-hour patch tests, the majority of them probably being caused by patch-test sensitization. The authors suggested that one way to optimize PPD testing could be to reduce the exposure of PPD 1% to 24 hours.

Interestingly, a group of researchers compared 2 days of occlusion with 3 days of occlusion, with the aim of sparing the patient an additional visit. Their results confirmed their previous experience that patch testing with removal at 3 days and reading 3 hours later is a valid alternative to the standard procedure of removal after 48 hours.<sup>29</sup>

## Patch-test reading time

Although there are some disagreements and controversies about occlusion time, they are dwarfed by the ones about the optimal reading time. After decades of reading patch tests after 2 days, there is finally an overall agreement that one reading (at day 2) is insufficient. There is no consensus about the best time for an additional reading after day 2, and the optimal reading schedule has yet to be established. In the competition between day 3 and day 4 readings, day 4 seems to be winning by only a few points.<sup>30–35</sup> As for day 5, a very interesting and thorough study from Göttingen, Germany<sup>36</sup> concluded the following: for a single 2nd patch test reading after D2, D3 is the best day, and especially better than D4. If a 3rd reading is performed, it should be done at D5 to get the maximum information out of patch testing.

The authors explained: Considering the history of 100 years of patch testing, one might ask why an additional patch test reading at D5 has not been recommended up to now. The answer might be: with a reading at D5, the procedure of patch testing has a total duration of 6 days, so one cannot avoid doing at least 1 patch test reading on Saturday or Sunday (if the application of the patches does not take place at 1 of these days).

The issue of reading after 5 days is even more controversial. According to Mayo Clinic experience,<sup>37</sup> late patch-test readings (day 7 or beyond) were useful when interpreting reactions to metals and topical antibiotics, but they were not useful in the diagnosis of reactions to other allergens, including topical corticosteroids that are known to give late reactions. Reactions to certain preservative and fragrance allergens dissipated after the day 5 reading, so that the authors concluded that reactions are optimally read at days 3 and 5, with an additional reading recommended on day 7. Researchers from a Department of Occupational Dermatology of a University Hospital in Amsterdam<sup>38</sup> concluded that an extra reading on days 6 or 7 (in addition to days 2 and 3) “is very useful as it gives additional information in 8.2% of patch-tested patients.”

Interesting conclusions and views are drawn by the DKG.<sup>28</sup> According to that group, Patch test reactions, which *de novo* become positive at D7 or even later are regarded as late reactions. Some allergens, e.g., neomycin or corticosteroids are known to be ‘late reactors;’ however, late reactions may also indicate sensitization caused by the patch test (patch test sensitization, active sensitization), or reflect a particular (individual) reaction pattern (slow responders).

Those authors performed a prospective multicenter study in order to obtain data on late patch-test reactions in consecutively tested patients. The authors observed late patch-test reactions to PPD in 1.5% and to epoxy resins in 0.3% of the patients. Only 2 of 21 patients with a late patch-test reaction (10%) to PPD had a history of PPD exposure. This was significant compared with patients with a history of PPD exposure among those reacting on day 3. The final conclusion was that “In the majority of patients the late reactions to PPD in

all likelihood were caused by patch test sensitization.” We would like to add that, it does not matter if the positive tests are a result of sensitization or of a late reaction in an allergic individual because they indicate a present allergy and therefore the usefulness of reading on day 7.

In conclusion, the issue of when to read a patch is far from being settled, and the debate shows no sign of coming to an end. Each investigator’s choice of practice, the patterns of allergens identified, geography, and criteria for entry into a patch-test clinic differ as widely as the days on which readings are taken. Although delay in reading proved valuable and yielded a consensus approval, there is still a wide variety of time schedules within the 3- to 7-day range, and no sign of agreement on an optimal reading schedule.

## Scoring patch-test reactions

The most common and most agreed on method of recording and evaluating patch test reactions is the one proposed in 1970 by the ICDRG.<sup>39,40</sup> These recommendations (summarized in Table 1) are followed worldwide and are cited in most scientific reports. It is a subjective method, based on inspection and palpation of the test area, and one that depends on the observer’s eye, skill, knowledge, experience, as well as on local convention and tradition. As such, interindividual differences in scoring and interpretations are to be expected. Indeed, interindividual, discordances and variations in reading and scoring have been documented<sup>41,42</sup>; however, these are within reasonable and acceptable limits.

It is remarkable that despite all the limitations of this subjective recording method, it has been adapted by most clinics and experts, with relatively few disagreements and debates and only minor suggested modifications.<sup>42,43</sup> Also, the repeated proposals to use instruments for readings have been rejected, and they are considered as being impractical for most of the patch-test clinics; nonetheless, there are some debates and discussions on this issue as well, mainly about the importance and relevance of doubtful or weak reactions. This question has not yet been put to rest. It is amazing and at the same time amusing to see how most of the articles dealing with this problem (for which we must admit there are no easy solutions) try to circumvent or ignore it. The title of

**Table 1** Recommended recording and evaluation of patch-test reactions

| Score | Reaction intensity        | Manifestation                                             |
|-------|---------------------------|-----------------------------------------------------------|
| ?+    | Doubtful reaction         | Faint erythema only                                       |
| +     | Weak positive reaction    | Erythema, infiltration, possibly papules                  |
| ++    | Strong positive reaction  | Erythema, infiltration, papules, vesicles                 |
| +++   | Extreme positive reaction | Intense erythema and infiltration and coalescing vesicles |

one such study,<sup>44</sup> “Should macular erythema reactions be counted as positive allergic patch-test reactions?” gives the reader the impression that somebody is finally going to take the bull by the horns and get straight to the point. Indeed, the objective of the study as stated by the authors was “to investigate the prevalence and relevance of reactions graded as macular erythema at the Mayo Clinic.” In the introduction, the authors mention that “A positive allergic patch test reaction is ‘generally interpreted to be’ a reaction manifested by erythematous papules, vesicles, or a spreading reaction with crust and ulcerations. This definition of an allergic patch-test reaction, however, does not explicitly recognize macular erythema, which is the grade between the grade for a negative reaction and the grade for erythema, infiltration, and possibly papules.

The NACDG may grade a reaction as questionable (macular erythema), but it may also interpret that questionable reaction as allergic, although this is not documented in the reports from NACDG.” These lines express a tendency, by not other than the NACDG “not explicitly include macular erythema reactions in the definition of a positive allergic patch-test reaction.” Instead of finally receiving a convincing clear-cut answer to the dilemma, the reader gets a yet another evasive statement and a conclusion of what we had already known: that “macular erythema reactions should not be categorically deemed negative” and that “Patch-test reactions rated as macular erythema are common and may be of clinical relevance. For the purposes of patient education, they should not be disregarded.” In other words, these authors emphasize what should not be done, that these reactions should not be disregarded. We want to make it crystal clear that we have absolutely no intention to detract from the value of this large and extremely well-designed study; on the contrary. We applaud the caution and fastidiousness of the authors and the modesty of their conclusions and recommendations. The inconclusive nature of their findings reflects the complexity of the problem and the fact that a solution has yet to be found.

Similar views are expressed in other papers. “It is advisable to discuss the relevance of these ?+ [weak] reactions with the patient and to inform the patient that sometimes reactions become stronger later on. If so, they should be seen again.”<sup>38</sup> Another study concludes,<sup>45</sup> “Based on the patients’ assessments of relevance, allergens with doubtful late reactions were considered relevant almost as frequently as were allergens with + late readings.” In the latter study, however, patients who had a doubtful reaction on the first reading were excluded from the study. Similarly, another study<sup>46</sup> evaluated the relevance of positive patch-test reactions to fragrance mix (FM) and compared them with the strength of the reaction. The relevance of reactions to FM increased with the strength of the reactions. Those authors concluded, “the validity of the FM patch test procedure varies with the strength of the test reaction.” To our question about how to interpret doubtful reactions, the authors recommended “retesting with FM and its ingredients” to

raise the level of relevance. Once again, there is no one clear-cut answer as to the value of weak reactions.

Another issue that has engendered considerable discussion is how to interpret pustular and follicular patch-test reactions. Currently, it is generally accepted that they are irritant in nature not allergic, but there are only few studies to support this view. Two studies on 853 hard metal workers with serial dilutions of tungstate<sup>47</sup> and other metals (nickel, chromium, and cobalt)<sup>48</sup> concluded that “follicular reactions are probably nonallergic, originating from the nature of the patch test material together with constitutional factors.” Their conclusions are based mainly on the results of retesting with another vehicle and serial dilutions, as well as on the fact that no relevance could be found for such reactions. As the authors themselves stated “weak allergy cannot be completely ruled out.” There also are experimental animal studies aimed at producing follicular or pustular reactions. In one of them,<sup>49</sup> eight chemicals were put under large occlusive chambers (12 mm diameter) with petrolatum as the vehicle. Of the eight chemicals studied, sodium lauryl sulfate and HgCl<sub>2</sub> gave reproducible pustulation and clear dose-response curves. Other materials gave less reproducible results when the concentration was raised or when the skin barrier had been damaged. Those authors concluded that their findings support the hypothesis that this pustulation is an expression of irritancy. In an earlier experiment,<sup>50</sup> the application of a 5% nickel sulfate patch test to a scratch on the rabbit’s abdomen resulted in a double row of intraepidermal pustules. Those authors observed that the induced pustules were very similar to the pustules that occur with the pustular patch test. The fact that sterile pustules can be induced on the skin by local application of substances known as pustulogens has been known for decades.<sup>51</sup> On the other hand, the assumption that follicular reaction usually indicates an irritant reaction has been challenged. In one study<sup>52</sup> designed to test this hypothesis, eight patients with known contact allergy to either colophony or quarternium-15 allergic and irritant patch test reactions were recruited, and 4-mm punch biopsies were taken after 6 to 8 hours and assessed blindly by two pathologists. All biopsies from the allergic patch tests were characterized by follicular spongiosis, whereas biopsies from the irritant patch tests showed no recognizable changes except for a slight follicular spongiosis in only one patient. Our own experience (admittedly subjective and non-evidence-based) is that a considerable number of follicular patch-test results indicate true relevant allergy, and that they often become positive in later testing.

In conclusion, although there is relative consensus on the issue of reading and scoring patch tests, it is still not altogether free of controversy.

## Patch-test relevance

In one of his provocative publications, Albert Kligman (1916-2010)<sup>53</sup> stated that “No area of inquiry is more

controversial than the question of relevance when the patch test reveals a true allergic response. The commanding question has to be ‘What does this mean for the patient?’ Is avoidance necessary or feasible?’ In the same paper, he states “I stand by the comments I made in 1983: ‘Anyone can do a patch test. Few do it well. Fewer still can properly interpret patch tests’. I heartily endorse the position of the European Society of Contact Dermatitis that to ‘determine the clinical relevance of a positive patch test depends upon a blend of knowledge and experience known as clinical judgment.’” In other words, interpreting patch tests and determining the relevance of a positive reaction is the crucial phase of the procedure while also being the most complex and tricky part of it. One would expect, therefore, that this crucial part of patch testing would stimulate a heated debate. Paradoxically, this is not the case, and there are no more controversies about determining relevance than other apparently less problematic parts of the procedure. The currently used classification of clinical relevance of the positive patch-test reactions are as follows<sup>7,54</sup>:

1. Relevance to present dermatitis
  - a. Primary cause
  - b. Aggravating factor
2. Relevance to a preceding bout of dermatitis
  - a. Primary cause
  - b. Aggravating factor
3. Not relevant
4. Unknown or “unexplained positive”

Our group proposed an alternative classification<sup>55,56</sup>:

1. Relevance to present dermatitis.
2. Relevance to a present allergy other than the presenting dermatitis.
3. Not relevant.
4. Unknown or “unexplained positive.”

Why a new classification? We believe that the current classification does not cover several common scenarios and situations. For example, everyday questions such as “How should I define a positive true reaction to fragrance (of which the patient has long been aware) in a patient tested for a hand dermatitis with a positive relevant allergy to nickel?” or “How should I define a positive reaction to nickel when the patient actually has a postauricular dermatitis due to fragrance allergy?” In other words, many patients who are tested for dermatitis also have known allergies to other allergens, but having avoided the sensitizers before examination, they are free of this dermatitis, and so their allergy is not the cause of the dermatitis for which they were tested. Categorizing their reaction to known allergens as having “past” relevance seems to us as being inappropriate and misleading because all they have to do is re-expose themselves to the sensitizing agent and the relevance

would quickly revert to “present.” It follows, therefore, that an alternative possibility is needed in the current division of the various types of clinical relevance, namely, “relevance to an existing allergy other than the presenting dermatitis.”

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