

ORIGINAL ARTICLE

Comparative study of patch test using traditional method vs. prior skin abrading

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Keywords

comparative study, contact, dermatitis, methods, patch tests, strip patch test

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Summary

Background The patch test is an essential procedure for the investigation of aetiologic diagnosis of allergic contact dermatitis, although it is not yet able to fully reproduce the events of the initial site of contact with the allergen.

Objectives The aims of the present study are (i) to assess whether removal of the superficial corneous layer results in test positivity differences vs. the traditional technique, (ii) to assess the probable and/or possible and past and/or present sensitivity and relevance for each method, and (iii) to compare specific relevance of nickel sulphate for each method.

Results Concordance of positive reactions was 75.9% (66 of 87), with 21.8% (19 of 87) positivity results on the abraded side only and 2.3% (2 of 87) on the unabraded side ($P < 0.05$). Concordance of the substances with probable and/or possible and past and/or present relevance was 77.3% (58 of 75) for the abraded side and 21.3% (16 of 75) and 1.3% (1 of 75) for the unabraded side ($P < 0.05$). Analysis of isolated relevance for nickel sulphate showed 95.6% (22 of 23) concordance.

Conclusions (i) We found a greater number of positive substances on the abraded side, and when only the 2 + and 3 + reactions were considered, greater relative discordance was also observed; (ii) relevance analysis revealed a statistically significant difference between the two methods; (iii) differences in nickel sulphate test positivity and relevance for the two methods did not reach statistical significance.

Introduction

The term patch test was introduced by Cooke in 1916 and has since become the method of first choice in cases where clinical history and physical exam point to clinical suspicion of allergic contact dermatitis (ACD).¹

The present patch test technique is the product of an ongoing refinement of the method since it was first used. In the final decades of the 20th century, the studies carried out standardized the materials and methods used in patch tests.^{2–8} Concerning the allergens, it is important that they are used according to standard concentrations and vehicles and are chemically defined and pure so as to be able to trigger an allergic reaction without causing irritation.¹ Relevant substances in the battery have been standardized

internationally by different contact dermatitis research groups such as the North American Contact Dermatitis Group,^{9–11} the European Environmental Contact Dermatitis Research Group,¹⁰ and the Brazilian Contact Dermatitis Research Group.¹²

However, several pitfalls remain, such as irritant reaction, false-positive and negative results, as well as difficulties in interpreting clinical relevance of positive findings in tests.¹³

False-negative reactions can be the result of either inadequate percutaneous penetration or insufficient test concentration.¹⁴

Spier and Sixt¹⁵ showed the influence of *stratum corneum* (SC) barrier disruption on the results of patch testing in their study 'Quantitative abrasion epicutaneous test' in

1955. They found that application of 12 to 15 strips were required on the back to reduce SC by about 50%. By this they observed an increased sensitivity and constant test specificity.

The 'strip' patch test (SPT) has been used with substances that are of poor percutaneous penetration, such as drugs and aeroallergens,^{14,16,17} but there is a lack of studies that assess whether use of the strip technique leads to changes in sensitivity and specificity of the patch test compared with its standard battery form, or which is the best tape for abrading, and how many times it should be removed to best present the allergen while not provoking an irritation reaction. The amount of SC removed by tape stripping is not linearly proportional to the number of tape strips removed and varies, for example, with skin condition and adhesive characteristics. However, this acute epidermal barrier disruption is always accompanied by a transepidermal water loss (TEWL) increase,¹⁴ where Chicott *et al.*¹⁸ showed that after 10 strips, there was a small but significant increase in TEWL 1 h after stripping.

Given these data, we propose the current work to employ a 'strip' patch test using Micropore® tape, with two successive tape strips, on exactly the same skin area to be tested. The objectives of this study were as follows: (i) analyse whether removal of the superficial corneous layer of the skin leads to differences in positivity of tests compared with the traditional technique, in patients with probable ACD; (ii) assess probable and/or possible and past and/or present sensitivity and relevance for the two methods; and (iii) compare specific relevance of nickel sulphate in patients with a history of intolerance to this metal, for the two methods.

Material

A total of 65 patients were selected over a period spanning from March 2001 to November 2002, who had a clinical history and physical exam compatible with contact dermatitis and had sought treatment at the Allergy and Immunology Department of the Hospital do Servidor Público 'Francisco Morato de Oliveira', in São Paulo City, SP, Brazil. The patients answered a questionnaire to determine clinical picture, triggering factors, history for atopy, and matching of inclusion and exclusion criteria. The present study was approved by the Hospital do Servidor Público 'Francisco Morato de Oliveira' Research Ethics Committee, and prior written informed consent was given by patients or their legal guardians.

A battery comprising 30 substances (Chemotechnique Diagnostics, Malmö, Sweden) (Table 1) using Finn Chamber technique on Scanpor® tape (Epitest Ltd OY, Tuusula, Finland; Scanpor, Alphanorma AS, Norway) was used in applying tests. Abrading was carried out by means of 10-cm-wide Micropore® tape.

Inclusion criteria

- Clinical suspicion of ACD;
- Age over 10 years for both genders and all races; and
- Clinical control of disease following acute phase, for at least 2 weeks.

Exclusion criteria

- Patients with chronic debilitating diseases or immunosuppression;
- Expectant mothers;
- Sun exposure to area to be tested in the preceding 4 weeks;
- Use corticosteroids in the preceding 40 days;
- Current use of topic corticosteroids on the test placement site, or previous use less than 2 weeks prior;
- Patients with dermatographism; and
- Presence of actual or residual lesion on test site.

Method

Tests were applied in duplicate to the superior right and left regions of the dorsum for each patient, always in the same order, beginning from the position adjacent to the distal, where one, randomly chosen side was abraded (fig. 1). All applications were done by one researcher and read by another expert trained on the procedure and blind to the abraded site.

Tests were affixed according to criteria adopted by Fischer and Maibach in 1984⁴ and to basic norms of good practice for the method.^{19–21}

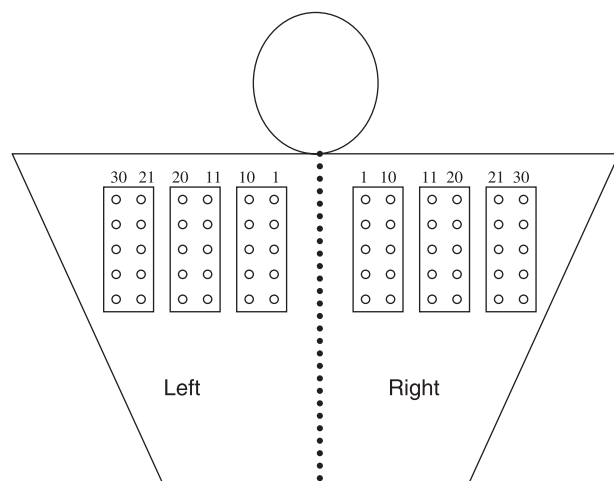


fig. 1 Method of application of the battery in duplicate, with the abraded side chosen randomly as left or right.

Table 1 Epicutaneous patch test battery used, respective concentrations, and number of patients with positive test for each substance, in decreasing order of frequency, on unabraded and abraded sides

Substance	Concentration (%)	Patients (%)	
	In petrolatum	Positive tests unabraded	Positive tests abraded
Nickel sulphate	5.0	24 (35.3%)	25 (29.4%)
Thimerosal	0.1	13 (19.1%)	16 (18.8%)
Neomycin	20.0	6 (8.8%)	6 (7.0%)
Formaldehyde	1.0 aqua	5 (7.4%)	7 (8.2%)
Cobalt Chloride	1.0	3 (4.4%)	7 (8.2%)
Carba mix (a)	3.0	2 (2.9%)	4 (4.7%)
Potassium dichromate	0.5	2 (2.9%)	3 (3.5%)
Lanolin	30.0	2 (2.9%)	1 (1.2%)
Mercapto mix (b)	2.0	2 (2.9%)	2 (2.4%)
Paraphenylenediamine	1.0	2 (2.9%)	3 (3.5%)
Fragrance mix (c)	8.0	2 (2.9%)	2 (2.4%)
Balsamo of Peru	25.0	1 (1.5%)	1 (1.2%)
Epoxy resin	1.0	1 (1.5%)	2 (2.4%)
Ethylenediamine dihydrochloride	1.0	1 (1.5%)	1 (1.2%)
<i>p</i> -tert-Butylphenol formaldehyde resin	1.0	1 (1.5%)	1 (1.2%)
Thiuram mix (d)	1.0	1 (1.5%)	2 (2.4%)
Sorbic acid	2.0	0	0
Benzocaine	5.0	0	1 (1.2%)
Butylate hydroxy-toluene	2.0	0	0
Bronopol	0.5	0	1 (1.2%)
Colophony	20.0	0	0
Chloroacetamide	0.2	0	0
Hydroquinone	1.0	0	0
Imidazolidinyl urea	2.0	0	0
Triclosan	2.0	0	0
Paraben-mix (e)	16.0	0	0
Black rubber-mix (f)	0.6	0	0
Quaternium 15	1.0	0	0
Ammonium thioglycolate	2.5 aqua	0	0
Triethanolamin	2.0	0	0
Total		68 (100%)	85 (100%)

Mix composition: (a) diphenylguanidine 1%, dimethyl dithiocarbamate zinc 1%, dithylcarbamate zinc 1%; (b) *N*-cyclohexy-2-benzothiazole sulphonamide 0.5%, morpholinyl mercaptobenzothiazole 0.5%, dibenzothiazole disulphide 0.5%, mercaptobenzothiazole 0.5%; (c) eugenol 1%, isoeugenol 1%, geraniol 1%, cinnamic alcohol 1%, alpha-amyl cinnamic aldehyde 1%, absolute oak moss 1%, hydroxycitronellal 1%, cinnamic aldehyde 1%; (d) tetramethylthiuram monosulphide 0.25%, tetramethylthiuram disulphide 0.25%, dipentamethylenethiuram disulphide 0.25%, tetraethylthiuram disulphide 0.25%; (e) butyl, ethyl, methyl, propyl-paraben 4% cada; (f) *N*-phenyl-*N*-isopropyl-*p*-phenylenediamine 0.2%, *N*-*N*-diphenyl-*p*-phenylenediamine 0.2%, *N*-phenyl-*N*-cyclo-hexyl-*p*-phenylenediamine 0.2%.

The aim of abrading was to remove only superficial cells from the corneous layer with a standard double application of Micropore® tape, applied to one side of the patient's dorsum to cover the whole area, prior to affixing the test with substances. Tapes were applied in a cranial-caudal direction, where tape was gently pressed down by fingertips for about 2 s and removed slowly with constant force at an angle of 45° in the opposite direction twice over, where a fresh tape was used in the second application.

The tests were removed after 48 h, and the first reading taken 30 min later. The second reading was taken 96 h after the test was affixed.

The criteria used for readings were those established by the International Contact Dermatitis Research Group.²²

- (–) Negative: no reaction;
- (+ ?) Doubtful reaction: faint macular erythema only;
- (+) Weak (non-vesicular) positive reaction: erythema, infiltration, and possibly papules;
- (+ +) Strong (vesicular) positive reaction: erythema, infiltration, papules, and vesicles;
- (+ + +) Extreme positive reaction: bullous reaction; and
- (IR) Irritant reaction.

Those tests scoring as (+), (+ +), and (+ + +) were considered positive in our results assessment.

Relevance analysis

The relevance of positive tests was defined based on criteria by Fisher *et al.*¹⁹ and Saripalli *et al.*²³

- Possible relevance: the patient probably had skin exposure to a product known or suspected to contain the allergen to which he or she reacted.
- Probable relevance: the patient had known skin exposure to a product containing the allergen to which he or she reacted.
- Past relevance: the patient has previously presented contact dermatitis due to the substance positive in the test, although this not the cause of the current condition.

The definite relevance was not assessed in this study, as tests using the suspected product on an area of normal skin to elicit contact dermatitis at the site were not undertaken.

Results were analysed using GraphPad Software, *InStat guide to choosing and interpreting statistical tests*, 1998, GraphPad Software, Inc. (San Diego, CA, www.graphpad.com). The level of significance was set at 95% ($P < 0.05$), and the following models were employed: arithmetic mean and median, chi-squared test (χ^2) to assess differences between abraded and unabraded test results, and odds ratio (OR) calculation.

Results

From the 65 patients studied, 59 (90.77%) were female, and 6 (9.23%) were male. Age ranged from 11 to 75 years, with a mean age of 45.13 years, and a median of 47 years. A total of 42 patients (64.61%) were predominantly white, with 12 (18.46%) black patients, 9 (13.85%) mulattoes, and 2 (3.08%) Asian subjects.

Lesions were located mostly on the palpebrae (12.30%), face (9.2%), and arms (6.1%). Main suspected products were nail varnish, cosmetics, and hair dye in 18.5% of patients. There was a positive history of inability to use substances containing nickel in 42 patients (64.6%). A total of 39 (60%) were found not to present personal histories of atopy. Abrading was done on the left side in 33 (50.77%) patients and on the right side in 32 (49.23%).

The number of patients testing positive for at least one substance was 48 (73.84%) on the previously abraded side, and 45 (69.23%) on the unabraded side. There was predominant positivity for only one substance in 23 (47.9%) patients on the abraded side and 24 (53.3%) patients on the unabraded side.

Table 1 shows frequency of positivity for each substance on abraded and unabraded sides, in decreasing order.

On the abraded side, 85 substances were positive, with sensitivity of 83.33% and specificity of 77.27%, whereas on the unabraded, 68 substances were positive, with sensitivity of 77.27% and specificity of 71.42%. Out of the

85 positive substances on the abraded side, 21 (24.7%) were 1 + positive, 39 (45.9%) 2 +, and 25 (29.4%) 3 +. Of the 68 substances positive on the unabraded side, 20 (29.4%) scored positive 1 +, 27 (39.7%) scored 2 +, and 21 (30.9%) substances positive 3 +.

There were 87 positive patch test results with 1 + or more on both sides, with 75.9% concordance (66 of 87). There were 21.8% (19 of 87) of positive reactions only on the abraded side and 2.3% (2 of 87) positive reactions only on the unabraded side. Statistical analysis of discordance between the positive tests on the abraded side only and positive tests on the unabraded side only showed a significant result ($\chi^2 = 13.864$, OR = 11.875, $P < 0.05$).

Table 2 shows concordance and discordance between the two methods, analysing positive reactions of greater than or equal to 2 +. There were 67 positive patch test results, with concordance between abraded and unabraded sides in 67.2% (45 of 67). Positive reaction only on the abraded side was seen in 28.3% (19 of 67), and positive allergic reaction only on the unabraded side was seen in 4.5% (3 of 67). Statistical analysis of discordance revealed a significant result ($\chi^2 = 12.236$, OR = 8.444, $P < 0.05$).

With regard to probable and/or possible and past and/or present relevance, positive concordance was found in 58 (77.3%) substances out of the 75 positive and relevant patch test results, with positivity only on the abraded side for 16 (21.3%) substances and for just 1 (1.3%) on the unabraded side. Statistical analysis of discordance between abraded and unabraded side proved significant ($\chi^2 = 13.003$, OR = 20.068, $P < 0.05$).

Table 2 shows probable and/or possible and past and/or present relevance in those tests scoring positive with 2 + or 3 +: A total of 40 (66.7%) substances presented relevance in both patch test methods, with 17 (28.3%) positive and relevant substances on the abraded side and 3 (5.0%) on the unabraded side. Statistical analysis of discordance between abraded and unabraded side proved significant ($\chi^2 = 10.140$, OR = 7.512, $P < 0.05$).

Considering the total positive tests on both the abraded and unabraded sides, 74 (87.05%) out of the 85 positive tests with abrading were relevant, whereas 59 (86.76%) out of 68 positive tests without abrading were relevant.

Isolated concordance for nickel sulphate was 96% (24 of 25), where there was exclusive positivity on the abraded side (4%) and no exclusive positivity on the unabraded side. Relevance analysis showed 95.6% (22 of 23) concordance, where again exclusive relevance was seen only on the abraded side (4.3%), where no statistical significance was present between the two methods.

Irritation and questionable reactions appeared just as often with either method (13 times on abraded side and 16 times on unabraded sides; $P = 0.4678$).

Table 2 Comparison of tests showing concordance and discordance of abraded side and unabraded side for results with 1 + reactions or greater, 2 + reactions or greater and relevance of tests comparing abraded side and unabraded side for results with only 2 + reactions or greater

Substance	Abraded 1 + or greater	Abraded 2 + or greater	Unabraded 1 + or greater	Unabraded 2 + or greater	Abraded and unabraded 1 + or greater	Abraded and unabraded 2 + or greater	Relevant and Abraded	Relevant and Unabraded	Relevant/ Abraded and unabraded
Nickel sulphate	1	4	0	0	24	19	3	0	18
Cobalt chloride	4	3	0	0	3	3	3	0	2
Formaldehyde	2	2	0	2	5	1	2	2	1
Paraphenylenediamine	1	2	0	0	2	1	2	0	1
Thimerosal	4	2	1	1	12	10	2	1	7
Bronopol	1	1	0	0	0	0	1	0	0
Carba mix	2	1	0	0	2	1	1	0	1
Potassium dichromate	1	1	0	0	2	1	1	0	1
Epoxy resin	1	1	0	0	1	0	0	0	0
Mercapto mix	0	1	0	0	2	1	1	0	1
Thiuram mix	1	1	0	0	1	1	1	0	1
Sorbic acid	0	0	0	0	0	0	0	0	0
Balsamo of Peru	0	0	0	0	1	1	0	0	1
Benzocaine	1	0	0	0	0	0	0	0	0
Butylate hydroxyl-toluene	0	0	0	0	0	0	0	0	0
Colophony	0	0	0	0	0	0	0	0	0
Chloroacetamide	0	0	0	0	0	0	0	0	0
Ethylenediamine dihydrochloride	0	0	0	0	1	0	0	0	0
<i>p</i> -tert-Butylphenol formaldehyde resin	0	0	0	0	1	1	0	0	1
Hydroquinone	0	0	0	0	0	0	0	0	0
Imidazolidinyl urea	0	0	0	0	0	0	0	0	0
Triclosan	0	0	0	0	0	0	0	0	0
Lanolin	0	0	1	0	1	1	0	0	1
Neomicin	0	0	0	0	6	4	0	0	4
Paraben-mix	0	0	0	0	0	0	0	0	0
Fragrance mix	0	0	0	0	2	0	0	0	0
Black rubber-mix	0	0	0	0	0	0	0	0	0
Quaternium 15	0	0	0	0	0	0	0	0	0
Ammoniumthioglycolate	0	0	0	0	0	0	0	0	0
Triethanolamin	0	0	0	0	0	0	0	0	0
	19*‡ (21.8%)	19§** (28.3%)	2†‡ (2.3%)	3¶** (4.5%)	66 (75.9%)	45 (67.2%)	17††§§ (28.3%)	3‡‡§§ (5.0%)	40 (66.7%)

* $\chi^2 = 48.669$ (Yates correction), $P < 0.05$, OR = 0.08890. † $\chi^2 = 95.811$ (Yates correction), $P < 0.05$, OR = 0.007487. ‡ $\chi^2 = 13.864$ (Yates correction), $P < 0.05$, OR = 11.875. § $\chi^2 = 18.694$ (Yates correction), $P < 0.05$, OR = 0.1935. ¶ $\chi^2 = 54.567$ (Yates correction), $P < 0.05$, OR = 0.02292. ** $\chi^2 = 12.236$ (Yates correction), $P < 0.05$, OR = 8.444. †† $\chi^2 = 16.174$ (Yates correction), $P < 0.05$, OR = 0.1977. ‡‡ $\chi^2 = 46.971$ (Yates correction), $P < 0.05$, OR = 0.02632. §§ $\chi^2 = 10.140$ (Yates correction), $P < 0.05$, OR = 7.512.

Discussion

The patch test is a key instrument for the aetiological diagnosis of ACD, being considered the gold standard.²⁴ Accurate detection of all relevant allergens is essential for effective prevention and proper guidance of the patient. The main challenge is ascertaining whether the positive substance in the test is directly linked to the current cause of the ACD. There are a number of pitfalls to be considered, including false-negative and false-positive reactions and doubts in interpreting clinical relevance.

A 77% sensitivity and 71% specificity is deemed good for a biological assay²⁵ in patients with suspected contact dermatitis, and factors influencing these rates depend on a thoroughly taken clinical history allowing selection of allergens to be tested as well as on use of standardized tests, correct technique, and experience of the physician in interpreting results.²⁶

The present study found sensitivity and specificity levels that were in line with the literature for unabraded tests (77.3%/71.42%). However, values in tests employing prior abrading proved higher (83.3%/77.27%).

In terms of percentage of patients testing positive for at least one substance, our values of 73.8% for the abraded side and 69.2% for the unabraded were higher than the positivity found by other authors, which range from 38% to 66.5% (mean, 50.7%).^{12,26–29} Nevertheless, the latest study by the North American Contact Dermatitis Group, carried out between 2001 and 2002, obtained a positivity value of 69%, resembling that of the present study.³⁰

Regarding the number of substances with positivity per patient in our study, we can note that there was predominantly a single positive substance (47.9% and 53.3%, respectively) for both abraded and unabraded sides, where these results are in agreement with the study of Brash *et al.*²⁷

The present work yielded a rate of 75.9% concordance for positive substances, between abraded and unabraded sides. Concerning discordance, significant differences between the two groups ($P < 0.05$) were evident in only two tests (2.3%); those of lanolin and thimerosal that tested positive exclusively on the unabraded side, along with 19 positive tests (21.8%) on the abraded side only, distributed as follows: four tests for cobalt chloride and thimerosal, two tests for carba mix and formaldehyde, and one test for benzocaine, bronopol, potassium dichromate, epoxy resin, paraphenylenediamine, nickel sulphate, and thiuram mix.

In the light of observations by Fisher and Rystedt³¹ with regard to epicutaneous tests, showing that 2+ are relevant 80% to 90% of the time, and 3+ are relevant 95% to 100% of the time, and that reactions with papules and vesicles are more characteristic of true allergies,¹⁹ we

deemed it fitting to assess only tests with 2+ or 3+ of positivity (Table 2), thereby increasing the accuracy of the method. We verified a decrease in concordant positive reactions to 67.2% along with a relative increase in percentage of positive reactions to 28.3% on the abraded side and to 4.5% on the unabraded side.

Upon comparing our results with the literature,^{19,27} we observed high levels of positivity when considering our results of 2+ and 3+, both on the abraded (75.3%) and unabraded (70.6%) sides. We believe this occurred due to our rigorous screening for inclusion of patients, where a clinical history highly suggestive of ACD was required for enrolment.

Our evaluations of studies that applied duplicate epicutaneous tests on the left and right sides of patients, using similar methods and accurate technique, and that were carried out using a standard patch test battery,^{32–34} revealed reproducibility ranging from 96% to 98%; thus, we could not expect 100% concordance, but something approaching this. In 1989, Lachapelle achieved discordance of 4.2%,³⁵ whereas Schiess *et al.* reported 5% in 2004.³³

Analysis of the results of the present study in this context revealed reproducibility of 75.9% of substances between the abraded and unabraded side. The discordance of 21.8%, however, most likely stems from the fact that one side was abraded, implying a higher number of positive substances reaching statistical significance. This difference becomes greater if only tests with more than 1+ are considered, when discordance then increases to 32.8%.

The study by Bourke *et al.*³² analysed past and present relevance as well as reproducibility, although its main target was false negatives, given that they lead to failure in the diagnosis of ACD and unnecessary continued suffering for a patient. According to their results, discordant reaction with clinical relevance occurred in less than 2% of cases. Comparison of these results with our study shows that the degree of relevance for discordance on the unabraded side (1.3%) is in agreement with the results found by Bourke, in that they remain within those expected for non-reproducibility of the test, although the same cannot be said for the abraded side which had 21.3% of relevant discordant substances. This finding may be explained by the higher test sensitivity associated with abrading compared with the present patch test technique.

On evaluation of probable and/or possible and past and/or present relevance for positive substances, we continue to have a similar degree of concordance (77.3%) to that obtained from analysis of positive substances only. Nevertheless, when only tests scoring 2+ or 3+ are considered (Table 2), there is a decrease in the rate of concordant and relevant reactions to 66.7%.

The total relevance presented in our study in relation to the abraded side of 87.0% (74/85), and to the unabraded side of 86.7% (59/68), is in line with data from the North American Contact Dermatology Group,²⁸ which obtained 87% present or past relevance in 1688 positive patch test patients.

Nickel sulphate analyses revealed that of the 42 patients with a history of intolerance to this metal, only 23 (54.7%) showed positivity on the abraded side and 22 (52.3%) on the unabraded side. From among 20 patients with a negative history, 19 (95%) presented negative tests on both sides. Our results proved discretely higher than those found in the literature, showing that 46% of patients with a positive history of intolerance to metal use had patch tests that were negative for nickel sulphate,⁹ whereas Cronin found 38% positivity to nickel sulphate through patch tests in patients with no history of reaction to this substance.³⁶

Although no statistically significant difference in positivity between both sides to nickel sulphate was observed, when we compared the reactions with 2+ and 3+, a decrease in concordance was seen (24–19). We believe that tape stripping increases the penetration of the allergen, allowing more accurate tests in the abraded side, although we were unable to increase concordance of results with the positivity of the clinical history. This leads us to believe that some substances depend on many factors in order to penetrate the SC and produce allergic sensitivity, and that the patch tests are not yet able to fully reproduce the events that occurred at the initial site of contact with the allergen.

In the literature, data on clinical relevance for nickel varies widely from 10% to 85%.³⁷ In our study, the values for relevance were 92% on the abraded side and 91.6% on the unabraded side, similar to the 85% level reported by the North American Contact Dermatitis Group.

Given the lack of studies using the same design adopted by us, where abrading was done by means of adhesive tape prior to affixing the test, we encountered difficulties in assessing the reproducibility of our results. The authors believe, however, that the present study will draw the attention of other Contact Dermatitis research centres to the importance of validating this technique.

ACD depends on the penetration of the allergen through the epidermal barrier. The percutaneous penetration of the same allergen may differ between patients for many reasons such as skin colour, age, friction, skin maceration, or small skin traumas.^{14,19} False-negative reactions on patch tests can be due to many reasons, for example, inadequate percutaneous penetration, insufficient test concentration, or insufficient reproduction by the test of the conditions that produced the dermatitis, such as friction and the presence of damaged SC.¹⁹

The tape stripping technique has been used for the determination of chemical penetration at different depths in the skin by using adhesive tape to remove target cells and to examine the morphological details of corneocytes. It may be used to clarify a persisting clinical suspicion of a contact allergy in case of a negative patch test, to more effectively test substances with poor percutaneous penetration, and to create contact conditions more adequate for exposure.^{14,38–40}

The amount of SC removed by tape varies, for example, with skin condition and the tape adhesive characteristics,¹⁴ and there are no studies standardizing the type of tape to be used. We decided on the Micropore® tape because it is hypoallergenic and easily found for use by physicians in Brazil.

Spier and Six¹⁵ were the first to utilize the 'strip' patch test as a modification of the traditional patch test, but the literature does not reveal any guidelines for SPT procedure. Dickel *et al.* performed a multicentre study towards a standardization of the SPT. For the tape used (3M Blenderm surgical tape), they determined in their pilot study the specific correction factor 11/26 with whom they multiplied the individual number of strips necessary to reach the stratum lucidum (described with at least three small glistening spots) to get finally the individual number of strips for the SPT.¹⁴

Morhenn *et al.*⁴¹ also used tape to strip skin cell layers. The aim of the cited study, however, was to differentiate ACD and irritant contact dermatitis reactions using a relatively non-invasive technique by measuring mRNA levels. The author applied and removed the adhesive tape 23 times, and one of the relevant conclusions for our study was that removal of superficial layers of the skin with an adhesive tape does not affect cytokine production by the skin in the first hours, and also that inflammatory cells do not migrate from circulation to the dermis or epidermis. For the first 10 tape strips, the main material found is non-nucleated SC.

Based on these data, we can infer that the two tape strips removed only the superficial layer of the SC, without affecting the physiopathologic mechanism of ACD, evidenced by the fact that the irritant and questionable reactions occurred in the abraded and unabraded testes in about equal numbers.

Conclusions

There was a statistically significant difference regarding the number of positive substances on the abraded side only, and if only 2+ reactions or greater were considered, with the increase of the accuracy of the test. We found a greater relative discordance between abraded and unabraded sides.

Analysis of probable and/or possible and past and/or present relevance showed statistically significant differences between abraded and unabraded sides, where this repeated when only 2 + reactions or greater were considered.

The sensitivity and specificity were concordant in both methods and attained a level considered in the literature to be very good for a clinical assay, although sensitivity and specificity were higher on the abraded side of patients in our study.

No statistically significant difference was seen for the two methods in terms of positivity and relevance of the test in isolated analysis of nickel sulphate.

It is possible that SPT for the application of allergens, particularly those which do not efficiently penetrate the SC, may become a useful variant of patch testing in the future, although further studies will be necessary to validate and standardize this technique.

References

- Devos AS, Van Der Valk PGM. Epicutaneous patch testing. *Eur J Dermatol* 2002; **12**: 506–514.
- Fischer T, Maibach H. Finn chamber patch test technique. *Contact Dermatitis* 1984; **11**: 137–140.
- Suneja T, Belsito DV. Comparative study of Finn Chambers and T.R.U.E. test methodologies in detecting the relevant allergens inducing contact dermatitis. *J Am Acad Dermatol* 2001; **45**: 836–839.
- Löffler H, Freyschmidt-Paul P, Effendy I, Maibach HI. Pitfalls of irritant patch testing using different test chamber sizes. *Am J Contact Dermat* 2001; **12**: 28–32.
- Magnusson B, Blohm SG, Fregert S et al. Routine patch testing II. *Acta Derm Venereol* 1966; **46**: 153–158.
- Manuskiatti W, Maibach HI. 1- versus 2- and 3-day diagnostic patch testing. *Contact Dermatitis* 1996; **35**: 197–200.
- Fischer T, Kihlman I. Patch testing technique. *J Am Acad Dermatol* 1989; **21**: 830–832.
- Moffitt DL, Sharp LA, Sansom JE. Audit of Finn Chamber patch test preparation. *Contact Dermatitis* 2002; **47**: 334–336.
- Belsito DV. The diagnostic evaluation, treatment, and prevention of allergic contact dermatitis in the new millennium. *J Allergy Clin Immunol* 2000; **105**: 409–420.
- Mydlarski PR, Katz AM, Mamelak AJ, Sauder DM. Contact dermatitis. In: Adkinson NF, Yunginger J, Busse W et al. eds. *Middleton's Allergy Principles & Practice*, 6th edn. Mosby, Philadelphia, 2003: 1581–1597.
- Marks JG Jr, Belsito DV, DeLeo VA et al. North American Contact Dermatitis Group patch-test results, 1998 to 2000. *Am J Contact Dermat* 2003; **14**: 59–62.
- Grupo Brasileiro de Estudo em Dermatite de Contato. (GBEDC). Estudo multicêntrico para a elaboração de uma bateria-padrão brasileira de teste de contato. *An Bras Dermatol* 2000; **75**: 147–156.
- Diepgen TL, Coenraads PJ. Sensitivity, specificity and positive predictive value of patch testing: the more you test, the more you get? ESCD Working Party on Epidemiology. *Contact Dermatitis* 2000; **42**: 315–317.
- Dickel H, Bruckner TM, Erdmann SM et al. The 'strip' patch test: results of a multicentre study towards a standardization. *Arch Dermatol Res* 2004; **296**: 212–219.
- Spier HW, Sixt I. Untersuchungen über die Abhängigkeit des Ausfalles der Ekzem-Läppchenproben von der Hornschichtdicke. Quantitativer Abriß-Epikutantest. *Hautarzt* 1955; **6**: 152–159.
- van Voorst Vader PC, Lier JG, Woest TE, Coenraads PJ, Nater JP. Patch tests with house mite antigens in atopic dermatitis patients: methodological problems. *Acta Derm Venereol* 1991; **71**: 301–305.
- Heinemann C, Schliemann-Willers S, Kelterer D et al. The atopy patch test – reproducibility and comparison of different evaluation methods. *Allergy* 2002; **57**: 641–645.
- Chilcott RP, Dalton CH, Emmanuel AJ, Allen CE, Bradley ST. Transepidermal water loss does not correlate with skin barrier function in vitro. *J Invest Dermatol* 2002; **118**: 871–875.
- Rietschel RL, Fowler Jr JF, eds. *Fischer's Contact Dermatitis*, 5th edn. Lippincott Williams & Wilkins, Philadelphia, 2001: 607–608.
- Drake LA, Dorner W, Goltz RW et al. Guidelines of care for contact dermatitis. Committee on Guidelines of Care. *J Am Acad Dermatol* 1995; **32**: 109–113.
- Bourke J, Coulson I, English J; British Association of Dermatologists. Guidelines for care of contact dermatitis. *Br J Dermatol* 2001; **145**: 877–885.
- Wilkinson DS, Fregert S, Magnusson B et al. Terminology of contact dermatitis. *Acta Derm Venereol* 1970; **50**: 287–292.
- Saripalli YV, Achen F, Belsito DV. The detection of clinically relevant contact allergens using a standard screening tray of twenty-three allergens. *J Am Acad Dermatol* 2003; **49**: 65–69.
- Valk PGMV, Devos SA, Coenraads PJ. Evidence-based diagnosis in patch testing. *Contact Dermatitis* 2003; **48**: 121–125.
- Nethercott JR. The positive predictive accuracy of patch tests. *Immun Allergy Clin Am* 1989; **9**: 549–553.
- Goulden V, Wilkinson SM. Evaluation of a contact allergy clinic. *Clin Exp Dermatol* 2000; **25**: 67–70.
- Brasch JB, Uter W, Geier J, Schnuch A; German Contact Dermatitis Research Group and the Information Network of Departments of Dermatology in Germany. Associated positive patch test reactions to standard contact allergens. *Am J Contact Dermat* 2001; **12**: 197–202.
- Marks JG, Belsito DV, DeLeo VA et al. North American Contact Dermatitis Group patch test results for the detection of delayed-type hypersensitivity to topical allergens. *J Am Acad Dermatol* 1998; **38**: 911–918.
- Cohen DE, Brancaccio R, Andersen D, Belsito DV. Utility of a standard allergen series alone in the evaluation of allergic

- contact dermatitis: a retrospective study of 732 patients. *J Am Acad Dermatol* 1997; **36**: 914–918.
- 30 Pratt MB, Belsito DV, DeLeo VA *et al.* North American Contact Dermatitis Group patch-test results, 2001–2002 study period. *Dermatitis* 2004; **15**: 176–183.
 - 31 Fischer T, Rystedt I. False-positive, follicular and irritant patch test reactions to metal salts. *Contact Dermatitis* 1985; **12**: 93–98.
 - 32 Bourke JF, Batta K, Prais L, Abdullah A, Foulds IS. The reproducibility of patch tests. *Br J Dermatol* 1999; **140**: 102–105.
 - 33 Schiessi C, Wolber C, Strohal R. Reproducibility of patch tests: comparison of identical test allergens from different commercial sources. *Contact Dermatitis* 2004; **50**: 27–30.
 - 34 Lindelof B. A left versus right side comparative study of Finn Chamber patch tests in 220 consecutive patients. *Contact Dermatitis* 1990; **22**: 288–289.
 - 35 Lachapelle JM. A left versus right comparative study of Epiquick patch test results in 100 patients. *Contact Dermatitis* 1989; **20**: 51–56.
 - 36 Cronin E. Patch testing with nickel. *Contact Dermatitis* 1975; **1**: 56–57.
 - 37 Bruze M, Condé-Salazar L, Goossens A, Kanerva L, White IR. Thoughts on sensitizers in a standard patch test series. The European Society of Contact Dermatitis. *Contact Dermatitis* 1999; **41**: 241–250.
 - 38 van der Molen RG, Spies F, van't Noordende JM, Boelsma E, Mommaas AM, Koerten HK. Tape stripping of human stratum corneum yields cell layers that originate from various depths because of furrows in the skin. *Arch Dermatol Res* 1997; **289**: 514–518.
 - 39 Jacobi U, Weigmann HJ, Ulrich J, Sterry W, Lademann J. Estimation of the relative stratum corneum amount removed by tape stripping. *Skin Res Technol* 2005; **11**: 91–96.
 - 40 Chao YCE, Nylander-French LA. Determination of keratin protein in a tape-stripped skin sample from jet fuel exposed skin. *Ann Occup Hyg* 2004; **48**: 65–73.
 - 41 Morhenn VB, Chang EY, Rheins LA. A noninvasive method for quantifying and distinguishing inflammatory skin reactions. *J Am Acad Dermatol* 1999; **41**: 687–692.