

RESEARCH LETTER

Do we need more proofs for not using the same device for several subsequent skin prick tests?

Olga Nahas¹ | Gwladys Mania Byron¹ | Jean Luc Bourrain¹ | Pascal Demoly^{1,2} | Anca Mirela Chiriac^{1,2} 

¹Centre Hospitalier Universitaire de Montpellier, Département de Pneumologie et Addictologie, Hôpital Arnaud-de-Villeneuve, Université de Montpellier, Montpellier, France

²Equipe EPAR – IPLESP, Sorbonne Université, Paris, France

Correspondence

Anca Mirela Chiriac, MD, PhD, Allergy Unit, Arnaud de Villeneuve Hospital, University Hospital of Montpellier, 371, Avenue du Doyen Gaston Giraud, 34295 Montpellier Cedex 5, Montpellier, France.

Email: ancamirelachiriac@gmail.com

To the Editor,

The combination of an allergen with its specific IgE induces local mast cell degranulation and urticaria when it occurs at skin level. Skin prick tests (SPTs) represent a major tool for diagnosing IgE-mediated hypersensitivity. The positive SPT reaction occurs within a few minutes and manifests by a local and transient reaction combining oedema, erythema and pruritus.¹

Skin prick tests are simple, quick to perform, low cost and sensitive. Over the years, many different techniques and instruments have been marketed to perform SPT. Currently, there are three different registered skin tools for SPT available on the French market: Stallergenes Greer Lancet (metal), ALK Lancet (metal) and Stallerpoint® (plastic). Additionally, 23 Gauge needles can be used. Their performances have been measured and compared to those of the aforementioned registered tools.¹

When improperly performed, SPT can lead to false-positive (FP) or false-negative results. Contamination of the instrument by another allergen extract may induce FP results. Using new puncture devices for each test overcomes this problem. In fact, some physicians use a single puncture device, wiped between each test, to shorten the test procedure time and to limit total cost compared to the usage of multiple puncture devices.² Classically, the principle of SPT is “one allergen/device”. Few studies examining the advantages and disadvantages of using the same device, wiped between tests, have been published.^{3–5}

Our study was conducted in order to establish the prevalence of FP when using the same SPT tool wiped between tests, with four different devices and two wiping techniques. We further searched for the risk factors of eliciting a FP results.

Two groups of patients with allergic rhinitis and/or asthma were studied. Patients in the first group were allergic to house dust mites (*Dermatophagoides pteronyssinus*, Der p) and those in the second

to grass pollens, as demonstrated by a suggestive clinical history and positive SPT performed with standardized glycerine/phenol-based extract of *Dermatophagoides pteronyssinus* (Der p 100 IR, Stallergenes Greer®) and grass pollen mix (5 grass mix, ie, *Dactylis glomerata*, *Anthoxanthum odoratum*, *Lolium perenne*, *Poa pratensis* and *Phleum pratense*; 100 IR, Stallergenes Greer®). Patients only had SPT towards their known allergen (except for positive and negative control).

Antihistamines H1 and other drugs that might affect the interpretation of SPT were stopped at least seven days before the tests. An informed consent was obtained before testing.

Skin of forearm was cleaned with cotton wool moistened with 75% ethanol. SPTs were carried out 2 cm apart, and were 2 cm from elbow level and from the wrist. They were performed using BD Microlance TM 3 23 G needle (Becton, Dickinson and Company), Stallergenes Greer® Lancet, ALK® Lancet and Stallerpoint®. In short, the needle technique consisted in crossing the drop, bevel up, before making a slight infringement of the skin without causing bleeding. The lancet technique consisted in crossing the drop with moderate pressure while being perpendicular to the skin. Stallerpoint® consisted in applying a vertical pressure, using the technique described earlier, followed by a 90° rotation of the instrument's axis while maintaining the depression of the skin.^{2,6,7}

Eight series of six SPT were carried out for each person, during the same visit, as shown in Table A1. Skin prick tests were performed by two trained investigators. The first four series (Scenario 1) consisted of one allergen extract (Der p or five grass pollen mix) followed by five negative controls (glycerol solution). In the text, the designation *negCTRL* followed by a number stands for the position of the negative control after a SPT with an allergen extract (eg, *negCTRL1* stands for the first negative control after the SPT with the allergen extract). The same 23 G needle, Stallergenes Greer

TABLE 1 Results of SPT with different devices

	Positive SPT patients, N ^a (%)	Positive SPT, N (%)	Patients with SPT 0 mm < diameter < 3 mm, N ^b (%)	SPT with 0 mm < diameter < 3 mm, N (%)	Mean ± SD	Median (Q25-Q75)
Der p (36 patients)						
23G needle						
Allergen	35 (97.2)	142 (98.6)	1 (2.7)	2 (1.4)	5.4 ± 1.6	5.1 (4.5-6.3)
NegCTRL1	21 (58.3)	42 (29.1)	4 (11.1)	11 (7.6)	1.4 ± 1.9	0 (0-3.4)
STGR Lancet						
Allergen	35 (97.2)	143 (99.3)	1 (2.7)	1 (0.7)	5 ± 1.4	4.8 (4.2-6)
NegCTRL1	21 (58.3)	40 (27.1)	2 (5.5)	8 (5.5)	1.2 ± 1.8	0 (0-3)
ALK Lancet						
Allergen	36 (100)	144 (100)	–	–	5.3 ± 1.3	5.1 (4.5-6.1)
NegCTRL1	24 (66.6%)	46 (31.9)	3 (8.3)	14 (9.7)	1.4 ± 1.8	0 (0-3.2)
Stallerpoint						
Allergen	32 (88.8)	80 (92.3)	4 (11.1)	11 (7.6)	4.6 ± 1.8	4.6 (3.9-5.4)
NegCTRL1	18 (50)	35 (24.3)	5 (13.8)	5 (3.5)	1 ± 1.7	0 (0-2.6)
Grass mix (34 patients)						
23G needle						
Allergen	33 (97)	135 (99.2)	1 (3)	1 (0.7)	5.7 ± 1.8	5.3 (4.5-6.6)
NegCTRL1	18 (52.9)	33 (24.3)	1 (2.8)	2 (1.4)	1.1 ± 1.9	0 (0-2.6)
STGR Lancet						
Allergen	32 (94.1)	134 (98.5)	2 (5.8)	2 (1.4)	5.2 ± 1.4	5 (4.3-6.1)
NegCTRL1	22 (64.7)	47 (34.5)	6 (17.6)	14 (10.2)	1.5 ± 1.8	0 (0-3)
ALK Lancet						
Allergen	33 (97)	132 (97.1)	1 (3)	4 (2.9)	5.3 ± 1.7	5 (4.3-6.5)
NegCTRL1	22 (64.7)	40 (29.6)	4 (11.7)	11 (8.1)	1.3 ± 1.8	0 (0-3)
Stallerpoint						
Allergen	31 (91)	129 (94.8)	8.9	7	4.6 ± 1.6	4.6 (4-5.2)
NegCTRL1	19 (55.9)	30 (22.1)	7 (20.6)	13 (9.5)	1.1 ± 1.7	0 (0-2.5)

Note: False-positive results (SPT diameter ≥ 3 mm) are marked in italics. Data include results (combined) from both dry and alcohol-wiped regimens, scenarios 1 and 2. Mean and median refer to the diameter of the weal size. NegCTRL1 stands for the first negative control after a SPT with an allergen.

Abbreviations: CTRL, control; Der p, Dermatophagoides pteronyssinus; N, number; Neg, negative; SD, standard deviation; SPT, skin prick test.

^aPatients with at least one SPT ≥ 3 mm.

^bPatients with at least one SPT 0 mm < diameter < 3 mm, but with all SPT diameters < 3 mm.

Lancet, ALK Lancet and Stallerpoint®, respectively, were used to perform the four series, and the device was wiped between each test with dry cotton wool few seconds after the SPT was performed. The following four series (Scenario 2) of six SPT were carried out in the same way, the first using a 23G needle, the second Stallergenes Greer Lancet, the third ALK Lancet, and the fourth Stallerpoint®. However, this time the allergen solution and negative control were used alternately.

The same two scenarios were then used with the devices wiped with cotton wool moistened in 75% ethanol between SPT.

The weals induced by the allergen extracts and 10 mg/mL histamine chlorhydrate (positive control, ALK) and the 50% glycerol solution (negative control) were recorded 15 minutes after the tests using the scotch-tape technique.² Weal size was measured as

the mean of the longest diameter and the mid-point perpendicular diameter.

A FP reaction was defined as a weal response at the site of the SPT, with an average diameter of at least 3 mm, with negative control solution SPT.

Data were expressed either as numbers and percentage (with 95% CIs) or as medians (with interquartile range). The mean was also calculated, but median was chosen because of non-normal distribution of the numerical variables. Comparisons for categorical variables were made using chi-square tests. To appreciate independent clinical risk factors linked to a FP test, a multivariate analysis was performed, enabling the calculation of odds ratios (ORs) and 95% CIs. Variables to enter the multivariate analysis were selected if the *P*-value was <0.25 in the univariate analysis.



FIGURE 1 Skin prick tests with false-positive percentage using *Dermatophagoides pteronyssinus* (Der p, A) and grass pollen mix (B) extracts. Data includes results (combined) from both dry and alcohol-wiped regimens, scenarios 1 and 2

Correlations were analysed by Spearman's rank correlation coefficient test.

Thirty-six patients sensitized to Der p (51.4%) and 34 patients sensitized to grass pollens (48.6%) were studied. There were 37 (52.8%) female patients. Dry cotton wool was used in 50 patients (71.4%), and cotton wool moistened in 75% alcohol was used in 20 patients (28.6%).

In the whole group of 70 patients, we observed no FP results with the negative control test solution, used as such.

Whatever the device used, more than half of the patients presented at least one FP negCTRL1 (Table 1). Furthermore, if weal diameter <3 mm were considered a positive result (ie, weals <3 mm are also markers of sensitization,² then a further 2.8%-20.6% of patients would have been added to false-positive results for negCTRL1. False-positive SPTs were also observed further on in Scenario 1, with negCTRL2 and up to negCTRL5 sites, as shown in Figure 1.

The prevalence of FP negCTRL1 for a given device depended on the investigator performing SPT, the allergen extract, the use of dry or moistened cotton wool and also the sex of the patient. Table 2 presents these variations (univariate analysis), related to each device, separately. After adjustment on each of the variables considered for each device (multivariate analysis), the investigator performing SPT was a risk factor independently associated with the FP result for the 23G needle; the use of moistened cotton wool was protective against FP results compared to dry cotton wool for the Stallerpoint® (OR = 0.51, 95% CI 0.28-0.95) and the Stallerpoint® (OR = 0.34, 95% CI 0.16-0.74). Male patients were more likely to have FP negCTRL1 than female patients, with Stallerpoint® (OR = 2.41, 95% CI 1.34-4.33).

A sensitivity analysis was performed, considering the SPT with a diameter of <3 mm as potential FP (they were considered as negative tests in the above analysis). The results were similar, with variations between devices and no unique risk factor clearly associated with a FP result (data not shown).

When correlations between two subsequent SPT (ie a pair of SPT including a SPT to an allergen and negCTRL1, or negCTRL x and negCTRL x + 1) were analysed, they were mostly positive and weak to moderate ($p < .5$) for all four devices. However, these correlations were inconsistent and did not concern every pair of subsequent SPT.

Using the same SPT device wiped between tests is appealing, since it might seem to reduce costs and time dedicated to SPT performance. In a previous study of ours, we had already showed 12.5%-67.5% FP results when using the same needle or lancet (wiped with dry cotton wool) for multiple SPT with house dust mite or grass pollen allergen extracts.⁴ Kupczyk et al³ used a similar methodology and found that a lancet wiped in cotton moistened with 75% alcohol still gave 57% FP results when all reactions (whatever the diameter) were considered and 37.1% when a 3-mm cut-off was considered. A correlation was found between the size of the FP reaction and the one to the allergen applied before the negative control. On the contrary, Semik-Orzech et al⁵ found that one injection needle rinsed in alcohol for multiple SPT seemed to have similar quality to the technique using injection needle changed between each SPT.

In this study, we further analysed the risk factors of eliciting a FP result, by increasing the number of patients (seventy patients were tested), by using four different devices for SPT, by performing SPT by two investigators and by combining the dry cotton wool technique and the one using 75% alcohol. We found that whatever the device

TABLE 2 Characteristics of the false-positive negCTRL1

SPT device Risk factor	Total SPT, N	FP SPT negCTRL1, N (%)	P*	Adjusted OR (95% CI)	P
23G needle					
Investigator					
Number 1	160	68 (24.3)	<0.0001	1	
Number 2	120	7 (2.5)		0.15 (0.05-0.4)	0.0006
Cotton wool					
Dry	200	72 (36)	<0.0001	1	
Moistened in + 75% alcohol	80	3 (3.7)		0.35 (0.06-1.6)	0.18
Stallergenes Greer Lancet					
Allergen extract					
Der p	144	40 (27.8)	0.22	1	
Grass pollens	136	47 (34.5)		1.40 (0.83-2.35)	0.19
Cotton wool					
Dry	200	70 (35)	0.02	1	
Moistened in + 75% alcohol	80	17 (21.2)		0.51 (0.28-0.95)	0.03
Sex					
Female	148	38 (25.7)	0.03	1	
Male	132	49 (37.1)		1.64 (0.98-2.75)	0.06
ALK Lancet					
Cotton wool					
Dry	200	68 (34.1)	0.05	1	
Moistened in + 75% alcohol	80	18 (22.5)		<u>0.57 (0.31-1.05)</u>	<u>0.07</u>
Sex					
Female	148	40 (27)	0.14	1	
Male	132	46 (35.1)		1.40 (0.84-2.35)	0.19
Stallerpoint					
Cotton wool					
Dry	200	56 (20)	0.002	1	
Moistened in + 75% alcohol	80	9 (11.2)		0.34 (0.16-0.74)	0.0067
Sex					
Female	148	23 (15.5)	0.001	1	
Male	132	42 (31.8)		2.41 (1.34-4.33)	0.003

Note: Results marked in *italics/bold/underline* are considered statistically significant ($P < 0.05$).

Abbreviations: FP, false positive; N, number; negCTRL1, first negative control following an allergen; SPT, skin prick test.

*Chi-square test (only variables with $P < 0.25$ in univariate analysis, further introduced in the multivariate model, are listed).

used, more than half of the patients had at least one FP, which is an unacceptable rate. False-positive results concerned not only negCTRL1, but also the following negCTRL, up to the 5th negCTRL after a positive SPT to an allergen extract. Moreover, if all reactions at negCTRL sites were considered (irrespective of the diameter), this percentage is even higher. Indeed, 1-2 mm SPT results can in some circumstances be considered as a marker of immunological response.² It can be easily accepted that in a clinical setting, when only allergen extracts are tested one after another, even small increases in SPT (<3 mm) related to the previous positive SPT might change the interpretation of SPT when a single device wiped between tests is used.

Performance and interpretation of SPT are highly dependent on the technique, comprising both investigator and device-related factors. Using different devices and two investigators allowed us to adjust the risk factors of eliciting a FP test on indispensable variables. We found no consistent risk factor associated with a FP result.

Besides, concerns related to the interpretation of SPT, the risk of self-pricking (ie accidentally pricking oneself after having pricked the patient) by using the same device even when it is deeply cleaned must be taken into account.

This study shows that using the same device (whether 23G needle, metal or plastic lancets) for performing several subsequent SPT

is associated with FP results. Considering the importance of SPT, such uncertainty is not acceptable and we ought to carry on utilizing different devices for each test.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CONFLICT OF INTEREST

Pascal Demoly is a consultant and a speaker for Stallergenes Greer, ALK, Circassia, Allergopharma, Pierre Fabre Medicaments and Chiesi and a speaker for Merck, AstraZeneca, Menarini and GlaxoSmithKline. Jean-Luc Bourrain is a speaker for ALK.

ORCID

Anca Mirela Chiriac  <https://orcid.org/0000-0002-1558-1966>

REFERENCES

1. Bousquet J, Heinzerling L, Bachert C, et al. Practical guide to skin prick tests in allergy to aeroallergens. *Allergy*. 2012;67:18-24.
2. Chiriac AM, Bousquet J, Demoly P. In vivo methods for the study and diagnosis of allergy. In: Burks AW, Holgate ST, O'Hehir RE, et al., eds. *Allergy, Principles and Practice, Chapter 67*, 9th ed. New York, NY: Mosby Co; 2019:1-14.e1.
3. Kupczyk M, Kuprys I, Gorski P, Kuna P. Not one lancet for multiple SPT. *Allergy*. 2001;56:256-257.
4. Piette V, Bourret E, Bousquet J, Demoly P. Prick tests to aeroallergens: is it possible simply to wipe the device between tests? *Allergy*. 2002;57(10):940-942.
5. Semik-Orzech A, Barczyk A, Pierzchała W. The comparison of reactions in skin prick test performed with the standardized lancet and the injection needle. *Pol Merkur Lekarski*. 2008;24:495-501.
6. Carr WW, Martin B, Howard RS, Cox L, Borish L, the Immunotherapy Committee of the American Academy of Allergy, Asthma and Immunology. Comparison of test devices for skin testing. *J Allergy Clin Immunol*. 2005;116:341-346.
7. Masse MS, Granger Vallee A, Chiriac A, et al. Comparison of five techniques of skin prick tests used routinely in Europe. *Allergy*. 2011;66:1415-1419.

How to cite this article: Nahas O, Mania Byron G, Bourrain JL, Demoly P, Chiriac AM. Do we need more proofs for not using the same device for several subsequent skin prick tests? *Clin Exp Allergy*. 2019;49:1374-1378. <https://doi.org/10.1111/cea.13458>

APPENDIX 1

TABLE A1 Description of the order of skin prick test with the two Scenarios

	Scenario 1				Scenario 2			
	23G Needle	StallergenesGreer Lancet	ALK Lancet	Stallerpoint®	23G Needle	StallergenesGreer Lancet	ALK Lancet	Stallerpoint®
1	Allergen	Allergen	Allergen	Allergen	Allergen	Allergen	Allergen	Allergen
2	negCTRL1	negCTRL1	negCTRL1	negCTRL1	negCTRL1	negCTRL1	negCTRL1	negCTRL1
3	negCTRL2	negCTRL2	negCTRL2	negCTRL2	Allergen	Allergen	Allergen	Allergen
4	negCTRL3	negCTRL3	negCTRL3	negCTRL3	negCTRL1	negCTRL1	negCTRL1	negCTRL1
5	negCTRL4	negCTRL4	negCTRL4	negCTRL4	Allergen	Allergen	Allergen	Allergen
6	negCTRL5	negCTRL5	negCTRL5	negCTRL5	negCTRL1	negCTRL1	negCTRL1	negCTRL1

Note: neg CTRL, followed by a number, stands for the position of the negative control after a skin prick test with an allergen extract.