STUDY

Symptoms and Signs Reported During Patch Testing

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Background: **In a pilot questionnaire study, there was a high frequency of subjective complaints and distant skin reactions during patch testing as reported at the day of test reading, particularly in female patients.**

Objective: **To document in a controlled study possible side-effects of a generalized nature occurring during the test procedure.**

Methods: **A questionnaire study on symptoms and signs reported at application and at reading of standard patch tests was conducted with 401 patients, with the patients serving as their own controls.**

Results: **An eczematous flare-up during patch testing was observed in 3.7% of the patients. There were plenty of different symptoms of malaise but, with one exception (itch on the back), the number of symptoms tended to be less on the day of reading than on the day of application of the tests. This held true also for itch occurring in the patients' dermatitis. There was no statistical correlation between symptoms and signs on the one hand and positive patch tests on the other.**

Conclusion: **Distant skin reactions and impairment of general health occurring during patch testing are often reported at the time of test reading. However, with the exception of itch on the back, symptoms and signs are rather less common after the application of patch tests than before.**

THE PATCH TEST TECHNIQUE for showing contact allergy has been used for a century.[1] In spite of methodological pitfalls, as well as the occurrence of false positives and false negatives, it remains the gold standard routine in the hands of experienced dermatologists. Side effects do occur but are usually local and transient.[2]

At patch test reading, patients sometimes report on distant or widespread skin reactions and even on subjective complaints and malaise of a generalized nature. Therefore, we initiated a pilot study collecting reports from several Swedish test laboratories on such possible side effects. This was later followed by a controlled study from 2 of the centres that constitutes the main part of the present article.

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Material and Methods

Pilot Study

Patch test laboratories associated with the Swedish Contact Dermatitis Group were encouraged to collect patient records on side effects of patch testing noticed at the time of reading of the tests on Day 3. The data were obtained using a standardized questionnaire regarding localized and distant cutaneous reactions as well as disturbances of general health. A total material of 43 patient records were collected in this way from 7 dermatologists.

Controlled Study

The study was based on the results obtained in 401 consecutive patients patch tested with the European standard series (with local additions) because of a suspect contact dermatitis in our 2 centers (234 from Gothenburg, 167 from Malmö). There were 266 women and girls (66%) and 135 men and boys. The tests were performed with Finn chambers (Epitest, Tuusula, Finland) on Scanpor (Norgesplaster, Vennesla, Norway), applied on the back for 48 hours, and read on day 3.

The patients were given a questionnaire immediately before testing on day 0 and the same questionnaire again immediately before test reading on Day 3, thus using the patients as their own controls. The following questions were asked:

During the last 3 days, have you

1) had a common cold or felt like you had influenza?
2) suffered itch on the back, in your dermatitis, in other skin areas, or everywhere?
3) had any of the following symptoms: fever, headache, fatigue, dizziness, insomnia, stomach problems, or other?

Based on our experience from the pilot study, the questionnaire was more specified, particularly in regard to the time of appearance and disappearance of suspected side effects. The design was discussed and made similar to a parallel study in Amsterdam, Netherlands.[3]

Statistics

Calculations in the controlled study were performed with the Mantel Haentzel test.

Results

Pilot Study

The incidence of side effects could be calculated from the Gothenburg material and was 21 out of 416 tested patients (i.e., 5%). In the entire material of 43 reports from 7 dermatologists, there were 5 reports of local reactions (irritation from adhesive), 23 of distant reactions in the skin, and 19 of subjective complaints. The 2 latter reaction types are detailed in Table 1. Among the 8 patients with a flare-up of hand eczema, 7 had positive patch test results to various standard allergens. The 2 cases with rashes implied 1 patient with a lymphocytic vasculitis and gold allergy, and 1 with urticaria and a negative patch test result.

One or more positive patch test results were observed in connection with a distant skin reaction in 16 of 23 patients (70%), in connection with subjective complaints in 7 of 19 patients (37%). Of those suffering distant skin reactions, 20 of 23 were female (87%), and of those with subjective complaints 15 of 19 were female (79%).

Controlled Study

One or more positive patch test results were observed in 216 of 401 patients (54%). The final clinical diagnosis was contact dermatitis in 38% (with positive patch test results in 73%), atopic dermatitis in 20% (with positive patch test results in 52%), and other dermatitis in 41% (with positive patch test results in 44%).

Table 1. Pilot Study: Distant Skin Reactions and Subjective Complaints Recorded in 23 and 19 Patients, Respectively, After Patch Testing

Distant skin reactions (n = 23)		*Subjective Complaints (n = 19)*	
Flare-up of hand eczema	8	Fever, shivering	8
Itch	3	Fatigue	6
Flare-up of face eczema	2	Indisposition, vomiting	6
Rash	2	Headache	4
Flare-up of leg eczema	1	Dizziness	3
Flare-up of gluteal eczema	1	Sweating	1
Flare-up of abdominal eczema	1	Fainting	1
Flare-up of otitis externa	1	Sore throat	1
Flare-up of neck eczema	1	Abdominal pain	1
Flare-up of arm eczema	1	Dyspnoe	1
Flare-up of old patch test	1		
Vesicles of oral mucosa	1		

An eczematous flare-up was registered in 15 patients, 12 of whom had a positive patch test result (80%). In the remaining, nonflaring 386 patients there were 204 with a positive patch test result (53%) (the difference was not significant). An adhesive reaction was noted in 20 patients (5%).

The subjective complaints in connection with patch testing are presented in Table 2. It will be seen that, in general, the number of symptoms reported is higher on day 0 than on day 3. However, there is 1 conspicuous exception, itch on the back. Table 2 also shows that this itch usually started at application day and remained at least until reading.

In regard to the patients' dermatitis (i.e., the reason for consulting) a new itch present on day 3 or 4 that was absent on day 0 was reported in 21 patients (14 with positive test results [67%]); the reverse development (i.e., a disappearing itch) occurred in 75 patients (46 with positive test results [59%]). The number of patients with no itch in the dermatitis on day 0, or on day 3 or 4, was 223 (114 with positive test results [51%]), and the number of patients with itch on both occasions was 82 (42 with positive test results [51%]).

Table 2. Subjective Complaints at Patch Testing

	Day 0	*Day 3*
Itch	198	272
On back	13	196
In dermatitis	157	103
In other areas	16	14
Influenza	72	48
Fever	4	6
Headache	60	28
Fatigue	49	38
Dizziness	21	14
Insomnia	19	9
Stomach problems	27	17
Itch on back		
Started day 0		90
Started day 1		70
Started day 2		22
Disappeared day 0		5
Disappeared day 1		46
Remained day 3		130

NOTE. Symptoms reported on day 0 and day 3. Itch on back specified in regard to time sequence.

The symptoms present on day 0 but absent on day 3 and vice versa are presented in Table 3. The table shows that the incidence of all complaints except fever (which were very few) decreased from day 0 to day 3. One or more positive patch test results seemed to occur more often in patients acquiring a symptom than in those losing it; However, these differences were not statistically significant when all symptoms (except itch) were compared as a group. Flare-up reactions were not particularly observed in any of the patient groups.

Table 3. Number of Patients With Symptoms On Day of Test Application But Not On Day of Test Reading and Vice Versa

	d0 pos, d3 neg	*d0 neg, d3 pos*	*Pos Test*	*Flare-up*
Influenza	39		22 = 56%	2
		15	11 = 73%	2
Fever	2			
		4		
Headache	44		22 = 50%	
		12	8 = 67%	2
Fatigue	28		15 = 54%	1
		17	12 = 71%	1
Dizziness	16		3 = 19%	2
		9	5 = 56%	1
Insomnia	17		8 = 47%	1
		7	5 = 71%	1
Stomach problems	17		10 = 59%	0
		7	3 = 43%	1

NOTE. Also shown are number of patients with one or more positive patch tests ("Pos test") and that with eczematous flare-up in each group ("Flare-up").

Discussion

The pilot study was initiated by our clinical impression that various skin reactions, as well as symptoms of a general character, were not unusual among patients undergoing patch testing. Therefore, it was not surprising to find such signs and symptoms in some 5% of our tested patients. The most frequent were eczematous flare-up reactions, particularly of hand eczema, and rashes and transient fever (Table 1). All this reminds one of clinical reactions occurring in patients with contact allergy exposed to a circulating contact allergen,[4,5] which in our study should have to be elicited by percutaneous resorption. In that case, one might have expected a positive correlation between clinical reactions and a positive patch test, but this occurred in only 70%.

We considered a controlled study was warranted, but no ideal control group was found. Eczema patients not selected for patch testing were not deemed comparable, and sham testing was discarded for ethical reasons. The decision to use the patients as their own controls might be criticized. However, we believe that, from the patients' point of view, it was natural to expect an increase of signs of symptoms because of the procedure, but the opposite was rather the case.

In the controlled study, a large number of subjective complaints was recorded just before applying the patch tests, but the majority had disappeared at the time of test reading (Table 2). The same change from day 0 to day 3 was observed in the two materials from Gothenburg and Malmö. If only those patients are taken into account whose symptoms appeared or disappeared, respectively, between day 0 and day 3 (Table 3), there is an indication of "cure" during, or because of, the test procedure. However, there was no statistical difference to ascertain such an effect.

As expected, itch on the back (where the patches had been applied) was a common complaint. It was learned from the study that the itch usually started on the day of test application; however, in many cases, it started on the following day (Table 2). In most patients, the back itch was prolonged and present at the time of reading.

Clinical impressions of distant skin reactions and subjective symptoms of a general character occurring during patch testing were supported by a pilot study. To exclude the possibility of random findings, a controlled study was carried out that could not corroborate our primary suspicions. Probably, pilot studies in general should never be definite.

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