

Chair and Department of Dermatology, Allergic Diseases Diagnostic Centre  
Medical University in Poznań

MAGDALENA CZARNECKA-OPERACZ, DOROTA JENEROWICZ

*The case of a very late response to a contact allergen in patch testing*

Patch tests (PT) have been introduced by Jadassohn in 1895, but only after Bloch's publication in 1924 had become generally accepted. Known as Jadassohn-Bloch tests PT became a significant element of allergological diagnostics. The essence of PT is a standardized attempt at inducing a local skin reaction as a consequence of interaction between an investigated contact allergen and lymphocytes specifically sensitized to that allergen. PT are therefore based on the type IV immunological reaction according to Gell and Coombs classification and serve as a diagnostic tool in evaluation of contact skin reactivity. TROLAB is a standard kit of 23 contact allergens (Table 1), which is well known in Europe (8).

Table 1. TROLAB – standard kit of 23 contact allergens

1	Potassium Dichromate	0.5%
2	Neomycin Sulphate	20%
3	Thiuram Mix	1%
4	Paraphenylenediamine Free Base	1%
5	Cobalt Chloride, 6H <sub>2</sub> O	1%
6	Benzocaine	5%
7	Formaldehyde (in water)	1%
8	Colophony	20%
9	Clioquinol	5%
10	Balsam of Peru	25%
11	N-isopropyl-N-phenyl Paraphenylenediamine	0.1%
12	Wool Alcohols	30%
13	Mercapto Mix	1%
14	Epoxy Resin	1%
15	Paraben Mix	16%
16	Paratertiarybutyl Phenol Formaldehyde Resin	1%
17	Frahrance Mix	8%
18	Quaternium-15	1%
19	Nickel Sulphate, 6H <sub>2</sub> O	5%
20	5-chloro-2-methyl-4-isothiazolin-3-one+ 2-methyl-4-isothiazolin-3-one (3:1)	0.01%
21	Mercaptobenzothiazole	2%
22	Sesquiterpene Lactone Mix	0.1%
23	Primin	0.01%

Analyzed allergens of appropriate concentration and base are applied – according to the Allergological Section of Polish Dermatological Society – on the skin of the interscapular or suprascapular area in Finn Chambers, attached to a hypoallergic plaster (8).

Evaluation of results should be performed after 48 hrs, then after 72 hrs and even after 96 hrs after application of allergens. Results are then presented as: erythema (+), erythema and papules (++), erythema, papules and vesicles (+++) and marked skin infiltration together with vesicles (++++). Proper diagnostics of contact allergy should be always composed of both clinical evaluation of patients and allergological testing – PT (8).

#### CASE REPORT

A 47-year-old patient attended Allergic Diseases Diagnostic Centre, presenting with numerous, disseminated inflammatory papules with intensive itch, which have been constantly reappearing for several months. Severe intensity of skin lesions was observed in the area of hypogastrium, genital organs and on the posterior surface of both thighs. Dorsal surfaces of hands were also involved in the process.

The patient was earlier treated for scabies (Novoscabin), without any clinical improvement. Initial allergological diagnostics included skin prick tests, which were negative. Results of basic laboratory investigations were within the normal range. Antiinflammatory and antipruritic treatment applied for a couple of months caused temporal improvement, however soon pruritus appeared again, without coexistence of inflammatory papules. At this point, PT with 23 allergens (TROLAB) were performed. After 48 hrs (first reading) and after 72 hrs (second reading) results were negative for all contact allergens. However, after 43 days (follow-up visit) we recorded a round, brownish macule localized within the right scapular region, clearly suggesting a positive reaction to one of the contact allergens (Fig. 1). In order to verify results of diagnostics, PT were repeated and we could prove a positive reaction (+++) with paratertiarybutyl phenol formaldehyde resin 96 hrs after application of allergens. However, after another 15 days when the patient attended again our Center, a distinct positive reaction (+++) could have been detected also with paraphenylenediamine (Fig. 2). The patient was not able to find a clear association of his skin problems with exposition to mentioned allergens. He has been working as a janitor for many years. Further treatment with antihistamine preparations allowed to control the pruritus, since no skin lesions were observed any more.

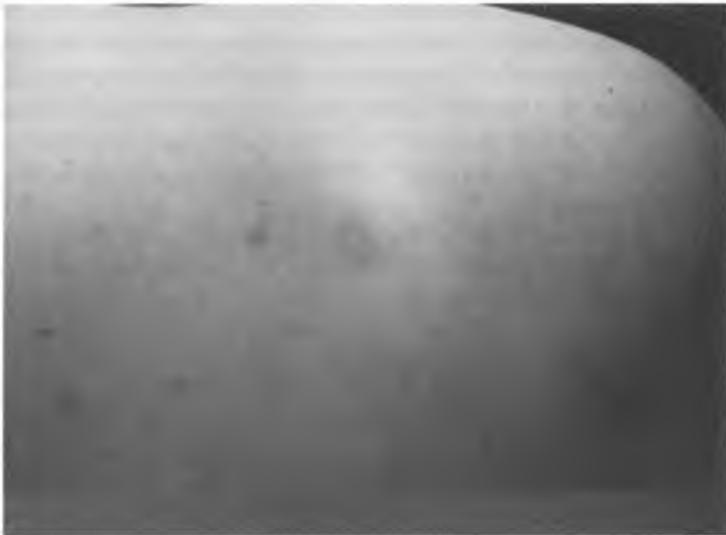


Fig. 1. Follow-up visit 43 days after application of allergens: round, brownish macule localized within the right scapular region suggesting a positive reaction to a contact allergen



Fig. 2. Positive reaction (+++) to paraphenylenediamine, detected over two weeks after application of allergens

## DISCUSSION

Contact dermatitis is an eczematous reaction, resulting from interaction of extrinsic substances with the skin. Allergic contact dermatitis is a delayed hypersensitivity reaction that clinically results in dermatitis. After sensitization, potential for reaction persists and the dermatitis will develop if the re-exposure to the allergen occurs.

Allergic contact dermatitis is a relatively common clinical problem. According to Braun-Falco et al. (1), allergic contact dermatitis accounts for 5–15% of all inflammatory skin disorders they deal with. The incidence of allergic contact dermatitis in general population has been estimated between 1–10%. In South Sweden, hand dermatitis accounts for 2% of examined population. It has been proven, that contact dermatitis is the cause of 4–7% of dermatological consultations and 1–3% of the population is allergic to cosmetic components (3). Allergic contact dermatitis seems to be equally common in men and women, although hand dermatitis appears more commonly in women. Clinically, contact dermatitis presents as erythema, swelling and vesicles in an acute stage, while in chronic reaction lichenification, scaling and fissuring are observed. Pruritus or burning sensation are also significant symptoms of contact dermatitis (1).

In the case described above, the patient did not present typical symptoms of contact dermatitis, but disseminated inflammatory papules, followed by isolated, persistent and generalized pruritus. However, it was necessary to consider contact allergy in etiopathogenesis of his clinical problem.

Results of PT performed in the case of our patient indicated very late reactions to certain allergens and possible necessity of additional readings. Additional late readings are accepted generally for such allergens as corticosteroids (additional reading on day 7 after application of allergens). This is due to anti-inflammatory pharmacological features of corticosteroids which are masking contact allergy. Another allergen is neomycin, characterized by poor skin penetration and possibility of reservoir formation in horny layer of epithelium, from where an allergen can be released for a long period of time (7). For the remaining allergens, two readings are mandatory (after 48 and 72 hrs after application) and additional readings are still discussed. MacFarlane et al. (9) confirmed positive responses to contact allergens after day 4 from the application of tests in 7.2% of patients. Geier et al. (5) emphasized the need of an

additional reading on day 5. Jonker (7) found additional days 6 and 7 reading as very valuable (additional positive reactions with nickel sulphate, neomycin sulphate, tixocortol-21-pivalate, butylphenol formaldehyde resin and Cl+Me isothiazolizone in 8.2% of patients). On the other hand, Saino et al. (10) confirmed positive reactions after day 3 only in 3% of the examined patients and therefore evaluated additional readings as time-consuming to introduce them to the routine diagnostic approach.

According to some authors, one of the factors possibly influencing PT results may be the sex of patients – men possibly react slower than women to patch testing. (5). Another factor may be the type of an allergen itself. Geier et al. (5) characterize certain allergens as “slow”, causing very late reactions far more often than others like: neomycin, cobalt salts and paraphenylenediamine. With fragrance mix and balsam of Peru opposite time relations are noted.

In the case of our patient PT results were positive with two important contact allergens: paratertiarybutyl phenol formaldehyde resin and paraphenylenediamine. Paratertiarybutyl phenol formaldehyde resin is a product of condensation of paratertiary butylphenol and formaldehyde. It is mainly used as glue in various fields: automobile industry, plywood, prostheses, glass wool and also in the production of shoes, other leather products and rubber articles. A positive reaction to this substance may be due to the resin itself or to one of the source fractions.

Paraphenylenediamine (PPD) is a very strong contact allergen. It is used in dyes for hair, fur, leather, printer's ink, fax machines, photographic products and lithography. According to literature, PPD belongs to the group of contact allergens, which may actively sensitize the patient by the epicutaneous application. Therefore, in the opinion of some authors PPD as a strong sensitizer should be removed from the standard series and used only when strongly indicated (4, 6).

In the case described above, we were not able to exclude the possibility of an active sensitization of the patient, although according to Cronin (2), this phenomenon mostly occurs after 10–14 days from application and in case of our patient it took a longer period of time.

PT are considered to be a reliable and helpful element of allergological diagnostics. It also has to be emphasized that the problem of a very late response to an investigated contact allergen is still a matter of debate, and an exact pathomechanism of this phenomenon together with all the causing factors have not yet been entirely characterized.

From the practical standpoint, patients diagnosed for contact allergy should be instructed to attend for the control visit immediately after the appearance of a very late response in the area of epicutaneous allergen application. It will definitely facilitate diagnostic procedure and correct interpretation of the results with no necessity to repeat PT.

## REFERENCES

1. Braun-Falco O. et. al.: *Dermatology*. Springer, 457, Berlin 2000.
2. Cronin E.: *Contact Dermatitis*. Churchill Livingstone, Edinburgh, 15, 1980.
3. Czarnecka-Operacz M.: Komentarz do pracy: J. Bourke et al. Kontaktowe zapalenie skóry – wytyczne postępowania. *Dermatologica*, 2, 5, 2002.
4. Devos S. et. al.: The risk of active sensitization to PPD. *Contact Dermatitis*, 44, 273, 2001.
5. Geier J. et. al.: Patch test reactions at D4, D5 and D6. *Contact Dermatitis*, 40, 119, 1999.
6. Gliński W., Rudzki E.: *Alergologia dla lekarzy dermatologów*. 184, Lublin 2002.
7. Jonker D., Bruynzeel D.: The outcome of an additional patch-test reading on days 6 or 7. *Contact Dermatitis*, 42, 330, 2000.
8. Kruszewski J. et. al.: Standardy w alergologii, cz. I – testy skórne. The UCB Institute of Allergy, 22, 2003.

9. Macfarlane A. et. al.: Delayed patch test reactions at days 7 and 9. *Contact Dermatitis*, 20, 127, 1989.
10. Saino M. et. al.: Reading patch tests on day 7. *Contact Dermatitis*, 32, 312, 1995.

#### SUMMARY

Patch tests (PT) are a significant element of allergological diagnostics. PT are based on the type IV immunological reaction according to Gell and Combs classification and serve as a diagnostic tool in evaluation of contact skin reactivity. In the Allergic Diseases Diagnostic Centre, Medical University in Poznań, contact allergy is diagnosed by using TROLAB – a standard kit of 23 contact allergens. The allergens are applied on the skin of the interscapular or suprascapular area in Finn Chambers, attached to a hypoallergic plaster. Evaluation of PT results is performed after 48, 72 and even after 96 hrs after application of allergens. The paper describes a case of a very late response to one of contact allergens – paraphenylenediamine (the reaction was observed 15 days after application of patch tests). The precise pathomechanism of this phenomenon, as well as all factors inducing skin reactivity still remain unexplained. Correct instruction of the patient in case of appearance of a very late response to contact allergen will facilitate the diagnostic procedure and will enable correct interpretation of results.

#### Przypadek bardzo późnej reakcji na alergen kontaktowy w naskórkowych testach płatkowych

Naskórkowe testy płatkowe stanowią ważny element diagnostyki alergologicznej. Badanie to opiera się na typie IV reakcji nadwrażliwości według Gella i Coombsa i służy do oceny kontaktowej reaktywności skóry. W Ośrodku Diagnostyki Chorób Alergicznych AM w Poznaniu alergię kontaktową diagnozujemy przy zastosowaniu zestawu 23 alergenów standardowych – TROLAB. Odczytu wyniku naskórkowych testów płatkowych dokonuje się po 48, 72, a nawet po 96 godzinach od momentu ich nałożenia. W pracy opisano przypadek bardzo późnej reakcji na jeden z alergenów kontaktowych: parafenylendwuaminę (odczyn obecny po 15 dniach od chwili nałożenia testów). Ścisły patomechanizm tego zjawiska, jak również wszystkie czynniki sprawcze stanowią wciąż aktualny i do końca niewyjaśniony problem. Właściwe poinstruowanie chorego w razie pojawienia się bardzo późnej reakcji na alergen kontaktowy ułatwi proces diagnostyczny i pozwoli na poprawną interpretację wyników.