"Doctor, Why Are My Patch Tests Negative?"

5

Denis Sasseville

Adopting the right attitude can convert a negative stress into a positive one.

Hans Selye

Not every patient referred for patch testing will end up with positive reactions. In his analysis of the cost-effectiveness of patch testing, Rietschel states that only about 53 % of patients suspected to have contact dermatitis will have one or more positive patch tests [1]. He also believes that a range of positive reactions between 30 and 65 % means appropriate utilization of patch testing. A yield below 30 % represents inadequate selection of patients and overuse of patch testing facilities. On the other hand, if the positivity rate is above 65 %, the patch testing physician is probably too selective and will likely not test many patients who would benefit from the procedure [1].

It is therefore quite normal that approximately half of patients undergoing patch testing will have no reaction. However, in a patient with true allergic contact dermatitis, patch testing may at times be falsely negative. This chapter will explore the causes of negative patch tests and give advice in order to maximize the yield of the procedure while avoiding false-negative reactions. The approach to the patient with negative tests will also be discussed.

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5.1 True-Negative Reactions

5.1.1 Not Contact Dermatitis

Patients with endogenous eczema such as atopic dermatitis, neurodermatitis, pompholyx, or stasis dermatitis are often referred for patch testing. These patients often have used numerous topical preparations to which they may have become sensitized. The procedure is indicated when the condition is long-standing, poorly responding to treatment, or localized to specific areas such as the eyelids, hands and feet, perianal area, or around leg ulcers, situations suggesting superimposed contact allergy. At times, patients with noneczematous conditions may need to be tested. These may include subjective ailments such as orodynia or vulvodynia or visible lesions of oral or cutaneous lichenoid reactions, eczematized psoriasis, and id reactions secondary to tinea pedis, etc. Under these circumstances, the physician is more or less expecting a negative reaction, and such a result does not come as a surprise.

5.1.2 Irritant Contact Dermatitis

Examples of contact dermatitis caused by exposure to strong or mild irritants include chemical burns, dermatitis caused by repeated hand washing, frictional dermatitis, and asteatotic eczema. These cases represent between 70 and 80 % of all cases of contact dermatitis [2]. Often, the diagnosis can be suspected based on the subacute to chronic morphology of the lesions, the predominance of burning pain over pruritus, and the history of exposure to known irritants. Some notorious irritants (formaldehyde, glutaral, metal salts, many biocides, etc.) are also potential allergens, and patch tests may be necessary to establish the distinction between irritant and allergic contact dermatitis or to prove the presence of both conditions. The importance of patch testing becomes paramount when dealing with occupational or medicolegal cases. Here again, negative patch testing is the expected result.

5.2 False-Negative Reactions

The causes of falsely negative patch tests are numerous and should always be kept in mind to avoid labeling patients as nonallergic when, in fact, they have an undiagnosed and easily curable condition. The consequences of such a misdiagnosis are more profound and far-reaching than those of a false-positive reaction, because patients will be prone to multiple recurrences of their dermatitis when they are reexposed to offending allergens.

5.2.1 Missed Allergen

This situation is the most common cause of negative patch tests in the presence of contact allergy. It occurs when a patient has not been tested to his allergen and could therefore be called a “false false-negative reaction.” Contact dermatitis should be

considered allergic until proven otherwise by comprehensive patch testing. Baseline series should be relied on as screening tools only. Larkin and Rietschel have shown that the European standard series will detect at best about 65 % of cases of allergic contact dermatitis [3]. More recently, Patel and Belsito, in a retrospective study of 2,088 patch-tested patients, found that only 27.6 % would have been fully evaluated by the two-panel TRUE Test and that 13.1 % would have been totally missed when tested to the more comprehensive North American Contact Dermatitis Group (NACDG) standard series of 65 allergens [4]. These screening tools need to be supplemented by additional series and personal products that reflect patients' exposures. When dealing with occupational contact dermatitis, it is imperative to review the composition of every product that may be deposited on the skin by direct or airborne exposure and to test patients with adequately prepared samples of workplace products [5].

5.2.2 Technical Failure

Patch testing is the gold standard, time-honored technique to diagnose contact allergy. It is well known, however, that its results are not always reproducible [6, 7]. Even when properly performed, the technique remains a rather crude bioassay that does not exactly mimic real-life conditions: a 48-h application on intact skin, even under occlusion, is not equivalent to daily applications over large areas or on damaged integument. When allergy is strongly suspected, additional procedures such as repeat open application tests (ROATs), use tests, semi-open tests, scratch patch tests, or patch tests preceded by tape stripping may reveal sensitizers when regular patch testing is negative [8]. In addition, a number of technical errors may supervene and result in falsely negative tests [9, 10].

5.2.2.1 Insufficient Occlusion

The patch test strips may fall off or become loose if they have not been properly secured to the back. If they have not been applied with the patient sitting or standing in a neutral position, they may wrinkle or rip off when the patient straightens or bends. Extra tape may be required to ensure proper occlusion, especially in hot and humid weather conditions.

5.2.2.2 Insufficient Duration of Application

It is generally recommended to occlude the patches for 48 h in order to promote adequate penetration of the allergen. For years, numerous investigators have tried to compare the results of patch testing using different occlusion times [11–15]. Most of these parallel studies have shown no significant differences between occlusion times of 24 versus 48 h, even though some have not demonstrated perfectly concordant results [11, 12]. Positive reactions occurring only after 24-h occlusion periods were seen as often as those appearing only after 48 h. Later studies yielded concordant results in 86 and 93.3 % of the cases, respectively [13, 14]. They were, however, conducted on a relatively small number of patients, 15 in the Goh et al. study and 236 in the Macháckova and Seda study. A much larger multicenter, unpaired study involving 15,553 patients showed a statistically significant difference in the

reaction index when patches were applied for 24 or 48 h. The shorter application time gave better results and was associated with a lesser number of irritant reactions [15]. Commenting on previously published studies, Manuskiatti and Maibach state that no definite conclusion could be drawn and that it appears premature to recommend a 24-h application time as long as additional studies are not carried out in an ideal experimental design [16].

5.2.2.3 Insufficient Amount of Allergen

The ideal amount of a standardized, petrolatum-based allergen should be 20 mg per patch, corresponding to a strip, extruded from the syringe, that covers the diameter of an 8-mm Finn Chamber^{hyo0} [17]. False-negative reactions may also occur when the patch test technician, distracted by ambient conversations, forgets to fill a test chamber or fails to warn the attending physician that an allergen has run out. Maintenance of a constant supply of allergens and provision of a quiet environment for the preparation of the patches will reduce or eliminate these sources of errors.

5.2.2.4 Insufficient Concentration of Allergen

This situation is likely to arise when testing nonstandard allergens such as workplace chemicals or patients' personal products and topical medicaments. Diluting a product in order to avoid triggering an irritant reaction may render the final concentration of the offending allergen too low to elicit a positive reaction. Cosmetics that cause allergic contact dermatitis under real-life, daily usage may fail to react when patch tested for 48 h. Testing with a patient's own antibiotic preparation may be falsely negative because the concentration required to bring out a positive patch test reaction on intact skin is often 20–40 times that found in the finished product. This is why neomycin, framycetin, gentamicin, and bacitracin are tested at concentrations of 20 % in petrolatum. Rycroft correctly points out that "the first insurance against false-negative reactions is therefore the use of standardized patch test materials of reliable reactivity" [18]. Products brought by patients need to be prepared in nonirritant concentrations and mixed in the appropriate vehicle, according to existing literature [19]. When information is not available, multiple dilutions and vehicles must be used, as well as a number of controls.

5.2.2.5 Inactive Allergen

To induce allergic contact dermatitis, some chemicals must be oxidized. This is the case for D-limonene, tea tree oil, turpentine, linalool, etc. The substance used for patch testing therefore needs to be in the same oxidized state to reveal the allergic sensitization [20–22]. Many commercially available allergens such as metal salts are quite stable, but others degrade very easily and can disappear within days or even hours if kept at room temperature or applied in advance to test chambers. Such is the case with numerous isocyanates and acrylates that should be ideally stored in the freezer and thawed just prior to application [23, 24]. Additional examples of substances that may not be stable forever include corticosteroids, formaldehyde, sodium hypochlorite, and paraphenylenediamine. Every allergen should be refrigerated if not frozen and stored in the dark. Expiration dates should be respected, and allergens replaced in a timely manner in order to avoid falsely negative tests due to inexistent allergens.

5.2.2.6 Inadequate Vehicle

Penetration of the allergen in the epidermis may be impaired if the allergen is not released from the vehicle in which it is mixed. Negative patch tests to hydrocortisone-17-butyrate and other corticosteroids may be the result of testing in petrolatum instead of ethanol [25]. Acyclovir and minoxidil need to be tested in propylene glycol to elicit positive reactions [26, 27].

5.2.2.7 Compound Allergy

This term refers to the situation where a patient shows a positive patch test reaction to a product while testing of its individual ingredients remains negative [28, 29]. True compound allergy has rarely been documented. It may result from the interaction, inside the product, of separate ingredients to produce a new allergen or from metabolic transformation of one or more ingredients by cutaneous enzymes. Pseudocompound allergy is probably more common and may be due to irritancy of the finished product or to the selection of inadequate concentrations when testing the individual ingredients.

5.2.3 Patient-Related Failure

As an active participant in the testing procedure, the patient must understand and follow the given instructions. He or she must avoid sweating, showering, and exercising lest the patch test strips come loose, making the whole process a useless exercise. It is therefore important to meet patients beforehand for a verbal explanation of the patch test technique and to provide them with a written handout to refresh their memory, especially if there is a certain amount of delay between the initial visit and actual testing.

The damping effect of immunosuppression on patch testing reactivity should not be underestimated. It is at times necessary to test mildly or profoundly immunosuppressed patients. There is a general feeling among experts in contact dermatitis that if an immunosuppressed patient presents with active lesions of allergic contact dermatitis, he is still capable of mounting an immune reaction and patch tests should be positive. Patches should be applied on intact skin, and the site of application should not have been previously treated with topical corticosteroids, as these agents are known to dampen or suppress reactions [30, 31]. Members of the NACDG feel that topical application of corticosteroids should be avoided over the test site at least 3–7 days prior to patch testing [32].

The effect of systemic corticosteroid on patch testing reactions has also been evaluated [33–37]. O'Quinn tested 20 patients with known contact allergies and found that the administration of 40 mg of prednisone abolished reactions in 6 of them and diminished the intensity of reactions in 6 other individuals [33]. Suppressed reactions again became positive when the dose of prednisone was lowered to 20 mg. It should be noted that the initial reactions, off prednisone, were strongly positive. It is therefore possible that weak reactions could still be suppressed by the lower dose of prednisone. Feuerman and Levy found that a daily dose of 40 mg suppressed reactions in 3 of 12 patients, while 20 mg abolished reactivity in only 1 of

16 subjects [34]. After administration of an oral dose of 40 mg of prednisone, Condie and Adams were unable to suppress patch test reactions to *Rhus* antigen [35]. Urushiol is a notoriously potent allergen, however, and from this study no conclusion can be drawn on the effect of such a dose of prednisone on weak reactions. A recent multicenter study evaluated the outcome of nickel-allergic patients tested twice with nickel sulfate while on placebo and while receiving a daily dose of prednisone 20 mg [37]. There was a significant reduction in the total number of positive reactions from 171 on placebo to 63 on prednisone. In those who still reacted, there was a shift from strong to weak or doubtful reactions. Members of the NACDG believe that patients submitted to patch testing should not be taking a daily dose of more than 10 mg of prednisone [32].

The effect of other systemic immunosuppressants on patch test reactivity is less well known. Wee et al. patch tested 38 patients who were taking azathioprine, methotrexate, cyclosporine, tacrolimus, mycophenolate mofetil, and the TNF-α inhibitors etanercept, infliximab, and adalimumab. Seventeen patients displayed reactions varying from + to +++. The authors conclude that, when indicated, patch testing should not be postponed in patients taking immunosuppressive drugs. Given that the allergic status of their patients prior to the introduction of immunosuppressants was unknown, they also state that "this study could not, however, shed light on what degree some allergic reactions may have been suppressed by particular immunomodulating drugs" [38]. Of the 11 patients tested while on immunosuppressants by Rosmarin et al., 10 had positive reactions graded + to +++ [39]. Only one patient, on mycophenolate mofetil, was retested after the drug was discontinued and showed positive reactions to formaldehyde, formaldehyde releasers, and MCI/MI that were not detected during the initial testing session. More recently, it was shown that ustekinumab, an inhibitor of interleukins 12 and 23, was ineffective in the treatment of allergic contact dermatitis and had no effect on patch testing [40, 41]. From the preceding studies, one can conclude that false-negative reactions can occur when testing patients taking immunosuppressants but that the risk may be less with biological immunomodulators.

Ultraviolet light irradiation is known to locally decrease the number of Langerhans cells and also induce a state of systemic immunosuppression susceptible to suppress weak patch test reactions [42]. It is recommended to avoid exposure to natural or artificial sources of ultraviolet light between 2 and 4 weeks prior to patch testing [32, 43]. Patients taking pentoxifylline, a methylxanthine derivative that has inhibitory activity against TNF-α, have been shown to experience a decrease in patch test response that could result in false-negative testing [44, 45]. A similar state of hyporeactivity has been alluded to with cimetidine, H1-antihistamines, diltiazem, and pentamidine [46].

5.2.4 Physician-Related Failure

Any health professional undertaking patch testing should have an in-depth knowledge of the pathophysiology of allergic contact dermatitis and of the methodology of patch testing, thereby minimizing or avoiding potential sources of false-negative reactions as described below.

5.2.4.1 Too Early Testing

The experienced patch tester knows that he needs to "treat first, test later" in order to avoid false-positive reaction or the occurrence of the "angry back syndrome." It is a less well-known fact that testing in the presence of active dermatitis can also lead to false-negative reactions [47, 48]. It appears that cutaneous inflammation, whether induced by irritant or allergic mechanisms, may induce changes in the composition of the thickness and barrier function of the epidermis, leading to hyporeactivity that may last up to 9 weeks [48].

5.2.4.2 Too Late Testing

With time, the number of memory or primed effector T cells may decrease, especially if the allergen responsible for the initial sensitization is rarely encountered. Testing months or years after an episode of allergic contact dermatitis may fail to elicit a positive reaction. The procedure, however, can awaken a dormant immune system, and retesting a few weeks later may then bring forth a positive reaction.

5.2.4.3 Failure to Perform Early Readings

When the patient's history suggests contact urticaria, open or occluded patch tests need to be closely watched, every 10–20 min for up to 2–3 h, lest an immediate reaction be missed if the tests are read in the usual fashion after 48 and 96 h.

5.2.4.4 Failure to Perform Late Readings

A single reading at 48 h, when patches are removed, will fail to reveal 25–30 % of positive reactions. Readings at 96 h should always be performed. Some allergens, such as corticosteroids and neomycin, are notorious late reactors that may become positive only after 5–7 days.

5.2.4.5 Failure to Perform Specific Procedures

The allergens responsible for photocontact dermatitis need to be activated by ultraviolet light to induce sensitization. Proceeding with patch testing instead of photopatch testing in such cases will obviously translate in false-negative results. Similarly, failure to perform prick testing in cases of protein contact dermatitis or a stepwise combination of patch, prick, and intradermal testing in cases of adverse drug eruptions will also lead to falsely negative tests.

5.3 Approach to the Patch Test-Negative Patient

All patients are anxious to find the cause of their dermatitis. The best case scenario is when patch testing uncovers one or more allergens that are easy to avoid and are the cause of the patient's condition. In this case, avoidance is synonymous with cure, and everyone is happy, including the physician, who envisions a publication if he has discovered a new allergen. Patients who are told that their patch tests are negative will display a wide range of emotions [49]. Some will be beaming with joy and relief, especially those who feared that a positive test would make them lose their job or prevent them from receiving a metallic implant. For the majority, however, the news

of negative testing is a source of disappointment and frustration, often manifested by incredulity, sadness, and sometimes tears or anger, always accompanied by multiple questions, especially from those who have scribbled on their referral note "you are my last hope." They will often ask if more tests can be done, what is the cause of their condition if there is no external cause, how can it be cured, etc. Often, they see themselves in a dead end, with an incurable, lifelong disease.

Prevention should begin early, as soon as patch testing is considered. It should be emphasized to the patient that there are many causes of dermatitis and that, sometimes, different conditions may overlap. A careful preliminary history and physical examination are mandatory and will help establish a diagnosis of endogenous eczema or other personal dermatosis. When patch testing appears justified, it is important to explain not only the technique but also the purpose of the test. Patients should be told that patch tests will only disclose contact allergies but not irritant contact dermatitis or food and inhalant allergies. When looking for allergic contact dermatitis superimposed on endogenous eczema, it is imperative to warn patients that finding and eliminating contact allergens may help but not cure their condition. They will therefore come to the patch testing session with more realistic expectations and hopefully will not be floored by negative results.

Conclusion

Any patient with negative patch testing should be reassessed. The history should be reviewed, in search of a missed allergen from the workplace, household, or hobbies. Potential causes of false-negative reactions should not be overlooked and additional procedures such as repeat patch testing, photopatch and prick testing, ROATs, skin biopsy and cultures, etc., undertaken as needed. When the investigation is complete and the final diagnosis is one of endogenous eczema, it will be necessary to provide support, hope, and guidance. Patients need to be told that, even though there is no cure for their disease, it can be treated and often well controlled with adequate treatment. I often tell patients who have been suffering over many years from recurrent bouts of eczema that they did not have this condition during all of their past life and that it is very likely that they will experience long-lasting periods of remission. I also tell them that neither they nor I can predict the future and that we need to tackle the problem one day at a time. At that point, many patients will feel reassured that patch testing, even if it ended up being negative, was not done in vain.

Practical Tips

- Make sure to look for and test every possible allergen that your patient is exposed to.
- Use comprehensive series of standardized allergens.
- Prepare nonstandardized allergens in appropriate concentrations and vehicles.
- Perform early and late readings, photopatch tests, prick tests, and repeat open application tests and use tests as the situation requires.
- Do not hesitate to repeat procedures if your working diagnosis remains allergic contact dermatitis.

References

1. Rietschel RL. Is patch testing cost-effective? J Am Acad Dermatol. 1989;21:885–7.
2. Nosbaum A, Vocanson M, Rozières A, Hennino A, Nicolas JF. Allergic and irritant contact dermatitis. Eur J Dermatol. 2009;19(4):1–8.
3. Larkin A, Rietschel RL. The utility of patch testing using larger screening series of allergens. Am J Contact Dermat. 1998;9:142–5.
4. Patel D, Belsito DV. The detection of clinically relevant contact allergens with a standard screening tray of 28 allergens. Contact Dermatitis. 2012;66:154–8.
5. Rycroft RJG. Problems in occupational allergy. Semin Dermatol. 1982;1:43–7.
6. Gollhausen R, Przybilla B, Ring J. Reproducibility of patch tests. J Am Acad Dermatol. 1989;21:1196–202.
7. Brasch J, Henseler T, Aberer W, Baüerle G, Frosch PJ, Fuchs T, et al. Reproducibility of patch tests. A multicenter study of synchronous left versus right-sided patch tests by the German Contact Dermatitis Research Group. J Am Acad Dermatol. 1994;31:584–91.
8. Lachapelle JM, Maibach HI. Additional testing procedures and spot tests. In: Lachapelle JM, Maibach HI, editors. Patch testing and prick testing. 3rd ed. Berlin/Heidelberg: Springer; 2012. p. 113–28.
9. Rietschel RL, Fowler Jr JF. Fisher's contact dermatitis. 6th ed. Hamilton: B.C. Decker Inc; 2008. p. 15.
10. Lindberg M, Matura M. Patch testing. In: Johansen JD, Frosch PJ, Lepoittevin JP, editors. Contact dermatitis. 5th ed. Berlin/Heidelberg: Springer; 2011. p. 439–64.
11. Skog E, Forsbeck M. Comparison between 24- and 48-h exposure time in patch testing. Contact Dermatitis. 1978;4:362–4.
12. Kalimo K, Lammintausta K. 24- and 48-h allergen exposure in patch testing. Comparative study with 11 common contact allergens and NiCl2. Contact Dermatitis. 1984;10:25–9.
13. Goh CL, Wong WK, Ng SK. Comparison between 1-day and 2-day occlusion times in patch testing. Contact Dermatitis. 1994;31:48–50.
14. Machácková J, Seda O. Reproducibility of patch tests. J Am Acad Dermatol. 1991;25:732–3.
15. Brasch J, Geier J, Henseler T. Evaluation of patch test results by use of the reaction index. An analysis of data recorded by the Information Network of Departments of Dermatology (IVDK). Contact Dermatitis. 1995;33:375–80.
16. Manuskiatti W, Maibach HI. 1- versus 2- and 3-day diagnostic patch testing. Contact Dermatitis. 1996;35:197–200.
17. Bruze M, Isaksson M, Gruvberger B, Frick-Engfeldt M. Recommendations of appropriate amounts of petrolatum preparations to be applied at patch testing. Contact Dermatitis. 2007; 56:281–5.
18. Rycroft RJG. False reactions to nonstandard patch tests. Semin Dermatol. 1986;5:225–30.
19. De Groot A. Patch testing. Test concentrations and vehicles for 4350 chemicals. 3rd ed. Amsterdam: AC Degroot Publishing; 2008.
20. Matura M, Sköld M, Börje A, Andersen KE, Bruze M, Frosch P, et al. Selected oxidized fragrance terpenes are common contact allergens. Contact Dermatitis. 2005;52:320–8.
21. Hausen BM. Evaluation of the main contact allergens in oxidized tea tree oil. Dermatitis. 2004;15:213–4.
22. Sköld M, Börje A, Harambasic E, Karlberg AT. Contact allergens formed on air exposure of linalool. Identification and quantification of primary and secondary oxidation products and the effect on skin sensitization. Chem Res Toxicol. 2004;17:1697–705.
23. Frick M, Zimerson E, Karlsson D, Marand A, Skarping G, Isaksson M, et al. Poor correlation between stated an found concentrations of diphenyl methane-4,4'-diisocyanate (4,4"-MDI) in petrolatum patch test preparations. Contact Dermatitis. 2004;51:73–8.
24. Mose KF, Andersen KE, Christensen LP. Stability of selected volatile contact allergens in different patch test chambers under different storage conditions. Contact Dermatitis. 2012;66: 172–9.
25. Wilkinson SM, Beck MH. Corticosteroid contact hypersensitivity: what vehicle and concentration? Contact Dermatitis. 1996;34:305–8.

26. Serpentier-Daude A, Collet E, Didier AF, Touraud JP, Sgro C, Lambert D. Dermites de contact aux antiherpétiques locaux. Ann Dermatol Venereol. 2000;127:191–3.
27. Whitmore SE. The importance of proper vehicle selection in the detection of minoxidil sensitivity. Arch Dermatol. 1992;128:653–6.
28. Kellet JK, King CM, Beck MH. Compound allergy to medicaments. Contact Dermatitis. 1986;14:45–8.
29. Le Coz CJ, Sasseville D. Interprétation et pertinence des patch tests: faux positifs et faux négatifs, allergies composées, allergies croisées. Ann Dermatol Venereol. 2009;136:610–6.
30. Sukanto H, Nater JP, Bleumink E. Influence of topically applied corticosteroids on patch test reactions. Contact Dermatitis. 1981;7:180–5.
31. Clark R, Rietschel R. The effect of triamcinolone acetonide ointment 0.1% on positive patch tests. Arch Dermatol. 1982;118:163–5.
32. Fowler Jr JF, Maibach HI, Taylor JS, DeKoven JG, Sasseville D, Warshaw EM, et al. Effects of immunomodulatory agents on patch testing: expert opinion 2012. Dermatitis. 2012;23:301–3.
33. O'Quinn SE, Isbell KH. Influence of oral prednisone on eczematous patch test reactions. Arch Dermatol. 1969;99:380–9.
34. Feuerman E, Levy A. A study of the effect of prednisone and an antihistamine on patch test reactions. Br J Dermatol. 1972;86:68–71.
35. Condie MW, Adams RM. Influence of oral prednisone on patch test reactions to Rhus antigen. Arch Dermatol. 1973;107:540–3.
36. Olupona T, Scheinman P. Successful patch testing despite concomitant low-dose prednisone use. Dermatitis. 2008;19:117–8.
37. Anveden I, Lindberg M, Andersen KE, Bruze M, Isaksson M, Liden C, et al. Oral prednisone suppresses allergic but not irritant patch test reactions in individuals hypersensitive to nickel. Contact Dermatitis. 2004;50:298–303.
38. Wee JS, White JML, McFadden JP, White IR. Patch testing in patients treated with systemic immunosuppression and cytokine inhibitors. Contact Dermatitis. 2010;62:165–9.
39. Rosmarin D, Gottlieb AB, Asarch A, Scheinman PL. Patch-testing while on systemic immunosuppressant's. Dermatitis. 2009;20:265–70.
40. Bangsgaard N, Zachariae C, Menné T, Skov L. Lack of effect of ustekinumab in treatment of allergic contact dermatitis. Contact Dermatitis. 2011;65:227–30.
41. Nosbaum A, Rozières A, Balme B, Goujon C, Nicolas JF, Bérard F. Blocking T helper 1/T helper 17 pathways has no effect on patch testing. Contact Dermatitis. 2013;68:58–9.
42. Cruz PD. Effects of UV light on the immune system: answer to five basic questions. Am J Contact Dermat. 1996;7:47–52.
43. Lachapelle JM, Maibach HI. Patch testing methodology. In: Lachapelle JM, Maibach HI, editors. Patch testing and prick testing. 3rd ed. Berlin/Heidelberg: Springer; 2012. p. 35–77.
44. Schwarz T, Schwarz A, Krone C, Luger TA. Pentoxifylline suppresses allergic patch test reactions in humans. Arch Dermatol. 1993;129:513–4.
45. Balato N, Patruno C, Lembo G, Cuccurullo FM, Ayala F. Effect of pentoxifylline on patch test response. Contact Dermatitis. 1996;34:153.
46. Collet E, Didier AF. Ce qu'il ne faut jamais faire en dermato-allergologie. In: Le Coz CJ, Jelen G, Lepoittevin JP, editors. Progrès en dermato-allergologie- Strasbourg 2003. Paris: John Libbey Eurotext; 2003. p. 153–9.
47. Lammintausta K, Maibach HI. Human cutaneous irritation: induced hyporeactivity. Contact Dermatitis. 1987;17:193–8.
48. Koehler AM, Maibach HI. Skin hyporeactivity in relation to patch testing. Contact Dermatitis. 2000;42:1–4.
49. Beck MH. The patient with negative patch tests – what now? In: Guin JD, editor. Practical contact dermatitis. New York: McGraw-Hill Inc; 1995. p. 659–72.