

Patch Testing for Noncontact Dermatitis: The Atopy Patch Test for Food and Inhalants

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Abstract The atopy patch test (APT) is defined as a patch test procedure to assess delayed type hypersensitivity reactions against those protein allergens known to elicit IgE-mediated type I reactions in atopic patients. This patch test procedure uses intact protein allergens instead of haptens in an optimized test setting and with a special reading key. It may be clinically useful especially for atopic dermatitis, as the currently available test procedures either target the wrong reaction type (type I and not type IV) or use the wrong allergens (haptens and not protein allergen). A positive APT reaction correlates with a positive lymphocyte transformation test and allergen-specific Th2 cells in the peripheral blood. As even small changes in the test procedure influence the sensitivity, specificity, and reproducibility of the APT, the European Task Force on Atopic Dermatitis (ETFAD) has developed a standardized APT technique: Intact protein allergens, purified in petrolatum, are applied in 12-mm-diameter Finn chambers mounted on Scanpor tape for 48 h to non-irritated, non-abraded, or tape-stripped skin of the upper back for 48 h; the evaluation of the test reaction is done after 48 and 72 h using the ETFAD reading key, assessing erythema as well as number and distribution pattern of the papules. The APT may reveal type IV sensitization in patients who are negative for the respective type I tests. Limited availability of the expensive test substances and limited reimbursement is among the factors restricting the routine use of the APT.

Keywords Atopic dermatitis · Patch test · ETFAD · Reading key · Atopy patch test · Standardization · Noncontact dermatitis · Inhalants · Immunology

Introduction

Atopic dermatitis (AD) is a very common, chronic inflammatory skin disease of great socioeconomic importance, and a heavy impact on the patient's quality of life. The non-lesional skin of patients with AD shows a disturbed epidermal barrier function, which results in malfunction of both the innate and adaptive immune system. The poor skin barrier function facilitates the penetration of allergens and may be quantified by measuring the transepidermal water loss. The presence of immediate-type sensitization to common protein allergens delineates extrinsic AD from intrinsic AD patients. Hence, performing allergy tests with the typical aero- and food allergens of AD is necessary to assign AD patients to either subgroup of AD. As the clinical presentation of AD is eczematous and not urticarial, tests for immediate type hypersensitivity do not assess major underlying disease mechanisms of AD.

On the other hand, there is an existing test procedure for the eczematous type IV reaction of contact dermatitis, and this is the patch test. Though this test would be appropriate in terms of disease mechanism, it is almost exclusively performed with the low molecular weight allergens of contact dermatitis known as haptens.

To detect delayed type sensitizations against intact protein allergens which are relevant to an AD patients' course of disease, a patch test procedure has been developed using protein allergens in an optimized patch test procedure [1]. This test may reveal information which is additive to skin prick tests and specific serum IgE tests, as it targets with a reasonable sensitivity and specificity the clinically relevant protein allergen sensitization to the cellular component of AD [2].

Definition of APT

The atopy patch test (APT) is defined as an epicutaneously applied patch test procedure with allergens known to elicit IgE-mediated reactions, in which the test sites are evaluated

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for a delayed hypersensitivity type, eczematous skin reaction after 48 to 72 h [3]. In other words, the APT is a patch test procedure using intact protein allergens instead of haptens in an optimized test setting and with a special reading key.

History of the APT

The first description of patch-testing with what is now known as haptens was done by Jadassohn in 1895. In 1937, Rostenberg and Sulzberger documented the application of native proteins for patch-testing including aeroallergens, but without commenting on the special aspects of atopy [4]. Mitchell and Platts-Mills dedicatedly performed patch test series with aeroallergens in AD patients and controls for the first time in 1982, but there was no exact definition of the test method or positive reactions at that time [5]. Different methods of improving allergen penetration through the epidermis such as tape stripping, abrasion of stratum corneum, or addition of sodium lauryl sulphate were investigated in larger series of patients [6–11]. In 1989, Ring coined the term “atopy patch test” for this test procedure [3]. In the following years, the APT was standardized regarding the allergen concentration, vehicle, time intervals, and preparation of the test site to develop a reliable diagnostic tool for the clinical routine use in AD patients in certain countries in Europe [1, 12–14]. Though a number of test protocols have been published, the standardized test protocol of the European Task Force on Atopic Dermatitis (ETFAD) has most widely been used during the last decade [14, 15]. Some exclusion criteria for the APT have been established for multicenter trials and should also be followed for a diagnostic APT procedure (Table 1). It must be noted that minor changes in the time of allergen application, pre-treatment of the skin at the test site, and allergen preparations may lead to quite different results [16–20]. Hence, the standardization of aeroallergen preparations and test performance by ETFAD has brought a good reliability of the APT for multicenter trials [12], which is not reached so well for food allergens.

Immunology of the APT

Though AD is a clinically defined disease, it is currently best understood as a T cell-based, dendritic cell-mediated chronic

inflammatory skin disease with a variable component of IgE-mediated immune dysregulation [21, 22]. The epidermal skin barrier of AD patients is impaired in both damaged and apparently healthy skin. As a consequence, protein allergens may penetrate the stratum corneum, where they are taken up by Langerhans cells (LC) with low-level high-affinity IgE receptor (FcεRI) expression or inflammatory dendritic epidermal cells (IDEC) with high-level FcεRI expression [23].

The histological correlate of a positive APT reaction is a lymphohistiocytic infiltrate, which is accumulating within days after the test application. Positive APT reactions are characterized by a lymphohistiocytic infiltrate closely resembling the early stages of an AD lesion [24].

After 24 h of APT application, infiltrating T cells show a typical Th2 pattern with secretion of interleukin 4 and 13. Another 24 h later, a shift towards a Th1 pattern with secretion of Interferon gamma—as seen in chronic AD lesions—has been described [25–27]. In addition, IDEC are recruited into the APT lesions of both intrinsic and extrinsic AD patients [28]. Extrinsic AD patients with a positive APT reaction to house dust mite carry IgE on their Langerhans cells even in non-lesional skin [29], thus suggesting a role of IgE-bearing Langerhans cells in the development of the APT lesion. The description of positive APT reactions to house dust mite allergen in intrinsic AD patients lacking specific IgE to house dust mite antigen argues against a prerequisite of type I allergy for developing APT reactions [30]. Those AD patients with allergen-specific proliferation of peripheral blood lymphocytes show positive APT results more frequently than those with negative lymphocyte proliferation results [31].

Technical Aspects

Allergens: native food, prick test solutions on filter paper, purified allergens in hydrogel, and purified allergens in petrolatum have been used for APT [14, 32, 33]. Purified allergens with known protein content have demonstrated a better reproducibility in multicenter studies. A concentration between 5.000 and 7.000 protein nitrogen units (PNU)/g or 200 IR (biological units)/g petrolatum base yields the most useful ratio between sensitivity and specificity [14, 34]. The allergen concentration needed for an APT is higher than for SPT. In children, approximately half the adults' dose can be used with good success [34]. Petrolatum is preferred over hydrogel as vehicle for all aeroallergen lyophilisates, because the preparations are more stable and the reaction frequencies obtained are consistently higher [1]. A negative (petrolatum) vehicle control must be applied with each APT. No irritant reactions were found in APT using lyophilized and commercial food allergen extracts and commercial extracts of house dust mite and American cockroach in non-atopic subjects [35].

Table 1 The ETFAD exclusion criteria for APT

Test site free of topical steroids for 7 days
Test site without UV treatment for 4 weeks
Patient free of oral steroids
Patient free of oral Cyclosporin A or oral Tacrolimus
Avoidance of antihistamines for 5 days (to be evaluated)

Test chambers: throughout Europe, large Finn chambers (12 mm diameter) are generally preferred for APT over the smaller chambers (6 mm diameter) widely used for hapten PT, which is based on the better reaction rates for food allergens in a pediatric setting [36] and for aeroallergens [34]. In terms of pathophysiology, the larger occluded test area will allow for a better penetration and subsequent allergen presentation of the intact protein allergens. This is in line with our finding that most patients with a positive APT reaction using 12-mm chambers show a negative repeated open application test (ROAT) if retested without occlusion [13]. The recommended large Finn chambers on Scanpor (a hypoallergenic plaster tape) are available from commercial sources.

Selection of test site and pretreatment: the test site on the patient's back must be non-lesional, must not have been treated with topical steroids for 5 days, and should not have received UV-radiation for several weeks. The washout period after systemic glucocorticosteroids depends on dose and duration of use and is handled similarly to hapten PT. As there are limited and conflicting data about influences of oral antihistamines on the APT, it is on the safe side to avoid them. An APT should not be performed during acute flares of AD or during pregnancy. It is known that mechanical or chemical disruption of the epidermal barrier of the test area immediately before application of the APT by tape stripping or acetone painting will increase the number of positive as well as irritative reactions [37, 38]. The ETFAD procedure favors a higher specificity over higher sensitivity, and consequently does not include any pretreatment of the skin [13, 14].

Test procedure: the test chambers are removed after 48 h from the patient's back and the first reading is done. The final reading is preformed at 72 h. In contrast to the conventional PT for allergic contact dermatitis, a decrescendo phenomenon between the first (48 h) and the second (72 h) reading is frequently observed in biologically meaningful, positive test reactions trials [12], which may be a consequence of the different allergen penetration kinetics. In our institutions, we follow the test criteria and reading key of the ETFAD (Table 2), which has been revised in October 2003 [12]. It is based upon the appearance of the erythema and the number and distribution pattern of the papules. Only palpable reactions with infiltration, but not erythema-only-reactions, are considered positive.

Table 2 The ETFAD APT reading key

–	Negative
?	Only erythema, questionable
+	Erythema, infiltration
++	Erythema, few papules
+++	Erythema, many or spreading papules
++++	Erythema, vesicles

Sensitivity, Specificity and Reproducibility

As the APT does not target immediate type reactions, it does not make sense to calculate sensitivity and specificity against SPT results or specific IgE levels. It is, however, biologically meaningful to assess sensitivity and specificity against the clinical data and challenge test results. As variations in the APT protocol will strongly influence the test results, sensitivity, specificity, and reproducibility must be assessed for each test procedure separately and must not be assumed the same for different procedures.

The sensitivity of the ETFAD procedure (Table 3), as determined against the history of exacerbation due to provocation factors obtained before testing, ranges for different allergens from 75 % in monocentric to 42–56 % in multicentric settings, whereas the specificity lies between 84 and 69–92 % [14, 39]. In a pediatric setting, the clinical study of Niggemann et al. showed a sensitivity of 76 % and specificity of 95 % of APT to late-phase clinical reactions and is therefore considered to be a helpful, additional diagnostic tool [18]. Evidence for a good predictive value showed the APT of patients with delayed reactions in food challenge tests, which were positive in 89 % of patients. In contrast, only 26 % of cow's milk allergic children were detectable by APT using a test protocol from Finland [40, 41].

The results for monitoring the progress of food allergy using the APT are quite diverse: The APT has been used to follow the course of an elimination diet in children with cow's milk allergy with sensitivity of 67.95 %, and specificity of 88.3 % [42]. In contrast, the APT had a very low sensitivity of 11.8 %, and a specificity of 85.7 % for testing children with food protein-induced enterocolitis [43].

In AD patients, the ETFAD protocol developed by Darsow et al. showed a reproducibility of 94 % of all positive APT reactions within a mean 16-month observation period using non-commercial high standard APT preparations of house dust mite, grass pollen, and birch pollen in petrolatum, 12-mm-diameter Finn chambers on non-irritated, non-abraded, or tape-stripped skin [34]. Comparing a tape-stripped and an unstripped technique with 3 standard allergens from 2 different suppliers, the reactions were reproducible upon retesting after 4–12 weeks in 56 % of AD patients.

Table 3 The ETFAD protocol for APT

Test area upper back
No tape stripping or acetone treatment
Large Finn chambers on Scanpor
Purified allergen in petrolatum as test substance
Allergen concentration standardized in biological units or µg/ml major allergen content
Reading at 48 and 72 h

The re-test was performed with the previously positive tested substances on tape-stripped and unstripped test skin. The first APT was performed on the patients' back, whereas the retest site was on the forearms. The correlation of results achieved with the same allergens from different providers was remarkably low [44].

Correlation of APT Results to Clinical Features

Though a positive APT reaction is frequently observed in patients with corresponding type I sensitizations in SPT or in vitro IgE tests, there is no need for a positive SPT or in vitro IgE test in a patient to develop a positive APT reaction [30]. A standardized APT shows a higher specificity for an allergen regarding clinical relevance for AD than the SPT, though the APT has a lower sensitivity [45]. At high levels of allergen-specific IgE, APT often reacts positively. Remarkably, in 7 % of AD patients, APTs are positive without evidence of specific IgE or positive SPT. Especially in those patients, the APT may play an important role for the detection of a relevant sensitization [30].

A German multicenter study involving 571 patients patch tested for allergic contact dermatitis showed 33 % positive APT reactions to *Dermatophagoides pteronyssinus* or *D. farinae* extracts in petrolatum (Mx 21B 20 %; Chemotechnique Diagnostics, Malmö). In this study, the allergens were applied for 24 h in small Finn chambers as used for routine hapten patch testing [46]. Using this technique, no correlation was found between a positive APT and an atopic diathesis, as defined by a history of AD, hay fever or allergic asthma, positive skin prick test results, or an elevated total serum IgE. The remarkable high percentage of positive *Dermatophagoides* patch tests suggests that some irritative reactions may have been counted positive, whereas the smaller Finn chamber size may have decreased the number of truly positive reactions.

An Italian study performed APTs in 75 subjects to compare patch test reactions to house dust mite in atopic and non-atopic patients. Reactivity to house dust mite was found in 23 % of non-atopic patients in comparison to 49 % of the atopic patients. The non-AD patients showed a lower reaction strength of APT reactions than the AD patients [47]. Another Italian study also found that the APT with house dust mite is more frequently positive in extrinsic (47.4 %) and intrinsic (66.6 %) AD patients than in non-atopic individuals (12.2 %) [48]. Most positive APT reactions are seen with house dust mite (*D. pteronyssinus*) 36 %, cat dander 22 %, and grass pollen 16 % [1].

Patients with AD clinically involving "air-exposed" areas have significantly positive results more often in APT (69 %) than patients with an AD elsewhere (39 %) [49]. In cases of worsening or flare-up of AD during spring and summer, the APT more often showed significantly positive reactions to

grass pollen (75 %) than in patients without such a history (16 %).

In children, where sensitizations against food allergens are more common, the patch testing of certain food proteins can be helpful to avoid unnecessary diets and sometimes make an oral food challenge unnecessary [32, 40].

Evidence for another valuable use of the APT comes from Greece, where the APT was positive in 32/54 children suffering from chronic constipation. After withdrawing the APT-positive foods, constipation had improved in 28/32 children. There was no correlation of APT with IgE levels [50]. During infancy and childhood, age does not seem to have an influence on the APT result [51]. A study from Italy suggests that the APT has a better sensitivity for peanut allergy than the SPT, especially in children younger than 12 years [47].

Evidence from a laboratory study performed in patients with a positive APT to *Malassezia sympodialis* revealed a strong correlation between the presence of circulating *Malassezia*-specific T cells with a Th2 profile in the peripheral blood and positive APT reactions to *M. sympodialis* [52]. Sensitization to cockroach could also be shown with the APT without a significant relationship between cockroach and house dust mite sensitivity. This positive APT to cockroach in 43 % of the atopic patients had no significant correlation with SPT or specific IgE levels [53].

Outlook and Conclusions

The APT has been used in an experimental setting as a model for early AD lesions [28]. In addition, the APT seems to be a valuable additional tool for the diagnosis of food allergies in AD patients [54], whereas it is clearly not suitable for diagnosing immediate type food allergy—this is reflected in different guidelines. A standardized APT, such as the ETFAD procedure, may show a higher specificity than SPT and specific IgE levels. The reliability of such a standardized APT with aeroallergens is very high, while the positive predictive value of food APTs must be improved to avoid unnecessary diets [55]. Ongoing clinical and experimental trials may further optimize various aspects of this technique. The routine use of APT will increase only if reimbursement for APT becomes adequate, because stable and good quality APT substances are considerably more expensive than standard hapten PT allergens.

Compliance with Ethics Guidelines

Conflict of Interest Andreas Wollenberg declares that he has no conflict of interest.

Sandra Vogel declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

- Darsow U, Vieluf D, Ring J. Atopy patch test with different vehicles and allergen concentrations: an approach to standardization. *J Allergy Clin Immunol*. 1995;95(3):677–84.
- Wüthrich B. Atopic dermatitis flare provoked by inhalant allergens. *Dermatologica*. 1989;178:51–3.
- Ring J, Kunz B, Bieber T, et al. The “atopy patch test” with aeroallergens in atopic eczema (Abstr.). *J Allergy Clin Immunol*. 1989;82:195.
- Rostenberg A, Sulzberger MB. Some results of patch tests. *Arch Dermatol*. 1937;35:433–54.
- Mitchell EB, Crow J, Chapman MD, Jouhal SS, Pope FM, Platts-Mills TA. Basophils in allergen-induced patch test sites in atopic dermatitis. *Lancet*. 1982;1(8264):127–30.
- Platts-Mills TA, Mitchell EB, Rowntree S, Chapman MD, Wilkins SR. The role of dust mite allergens in atopic dermatitis. *Clin Exp Dermatol*. 1983;8:233–47.
- Reitamo S, Visa K, Kahonen K, Kayhko K, Stubb S, Salo OP. Eczematous reactions in atopic patients caused by epicutaneous testing with inhalant allergens. *Br J Dermatol*. 1986;114:303–9.
- Reitamo S, Visa K, Kahonen K, Kayhko K, Lauerma AI, Stubb S, et al. Patch test reactions to inhalant allergens in atopic dermatitis. *Acta Derm Venereol Suppl (Stockh)*. 1989;144:119–21.
- Adinoff AD, Tellez P, Clark RA. Atopic dermatitis and aeroallergen contact sensitivity. *J Allergy Clin Immunol*. 1988;81:736–42.
- Imayama S, Hashizume T, Miyahara H, Tanahashi T, Takeishi M, Kubota Y, et al. Combination of patch test and IgE for dust mite antigens differentiates 130 patients with atopic dermatitis into four groups. *J Am Acad Dermatol*. 1992;27:531–8.
- Seidenari S, Manzini BM, Danese P, Giannetti A. Positive patch tests to whole mite culture and purified mite extracts in patients with atopic dermatitis, asthma, and rhinitis. *Ann Allergy*. 1992;69:201–6.
- Kerschenlohr K, Darsow U, Burgdorf WH, Ring J, Wollenberg A. Lessons from atopy patch testing in atopic dermatitis. *Curr Allergy Asthma Rep*. 2004;4(4):285–9.
- Darsow U, Laifaoui J, Kerschenlohr K, Wollenberg A, Przybilla B, Wüthrich B, et al. The prevalence of positive reactions in the atopy patch test with aeroallergens and food allergens in subjects with atopic eczema: a European multicenter study. *Allergy*. 2004;59(12):1318–25.
- Darsow U, Vieluf D, Ring J. Evaluating the relevance of aeroallergen sensitization in atopic eczema with the atopy patch test: a randomized, double-blind multicenter study. *J Am Acad Dermatol*. 1999;40(2 Pt 1):187–93.
- Darsow U, Ring J. Airborne and dietary allergens in atopic eczema: a comprehensive review of diagnostic tests. *Clin Exp Dermatol*. 2000;25:544–51.
- Bruijnzeel-Koomen C. The role of IgE in the pathogenesis of atopic dermatitis. *Allergy*. 1998;53:29–30.
- Johansson C, Sandstrom MH, Bartosik J, Sarnhult T, Christiansen J, Zargari A, et al. Atopy patch test reactions to *Malassezia* allergens differentiate subgroups of atopic dermatitis patients. *Br J Dermatol*. 2003;148:479–88.
- Niggemann B, Reibel S, Wahn U. The atopy patch test (APT)—a useful tool for the diagnosis of food allergy in children with atopic dermatitis. *Allergy*. 2000;55:281–5.
- Niggemann B, Reibel S, Roehr CC, Felger D, Ziegert M, Sommerfeld C, et al. Predictors of positive food challenge outcome in non-IgE-mediated reactions to food in children with atopic dermatitis. *J Allergy Clin Immunol*. 2001;108:1053–8.
- Niggemann B. The role of the atopy patch test (APT) in diagnosis of food allergy in infants and children with atopic dermatitis. *Pediatr Allergy Immunol*. 2001;12 Suppl 14:37–40.
- Wollenberg A, Bieber T. Atopic dermatitis: from the genes to skin lesions. *Allergy*. 2000;55:205–13.
- Leung DY, Bieber T. Atopic dermatitis. *Lancet*. 2003;361:151–60.
- Wollenberg A, Kraft S, Hanau D, Bieber T. Immunomorphological and ultrastructural characterization of Langerhans cells and a novel, inflammatory dendritic epidermal cell (IDEC) population in lesional skin of atopic eczema. *J Invest Dermatol*. 1996;106(3):446–53.
- Eckert F. Histopathological and immunohistological aspects of atopic dermatitis. In: Ruzicka T, Ring J, Przybilla B, editors. *Handbook of atopic dermatitis*. Berlin: Springer; 1991. p. 127–31.
- Ramb-Lindhauer C, Feldmann A, Rotte M, Neumann C. Characterization of grass pollen reactive T-cell lines derived from lesional atopic skin. *Arch Dermatol Res*. 1991;283:71–6.
- Sager N, Feldmann A, Schilling G, Kreitsch P, Neumann C. House dust mite-specific T cells in the skin of subjects with atopic dermatitis: frequency and lymphokine profile in the allergen patch test. *J Allergy Clin Immunol*. 1992;89:801–10.
- van Reijssen FC, Bruijnzeel-Koomen CA, Kalthoff FS, Maggi E, Romagnani S, Westland JK, et al. Skin-derived aeroallergen-specific T-cell clones of Th2 phenotype in patients with atopic dermatitis. *J Allergy Clin Immunol*. 1992;90:184–93.
- Kerschenlohr K, Decard S, Przybilla B, Wollenberg A. Atopy patch test reactions show a rapid influx of inflammatory dendritic epidermal cells in patients with extrinsic atopic dermatitis and patients with intrinsic atopic dermatitis. *J Allergy Clin Immunol*. 2003;111(4):869–74.
- Langeveld-Wildschut EG, Bruijnzeel PL, Mudde GC, Versluis C, Van Ieperen-Van Dijk AG, Bihari IC, et al. Clinical and immunologic variables in skin of patients with atopic eczema and either positive or negative atopy patch test reactions. *J Allergy Clin Immunol*. 2000;105:1008–16.
- Kerschenlohr K, Decard S, Darsow U, Ollert M, Wollenberg A. Clinical and immunologic reactivity to aeroallergens in ‘intrinsic’ atopic dermatitis patients. *J Allergy Clin Immunol*. 2003;111:195–7.
- Wistokat-Wulfing A, Schmidt P, Darsow U, Ring J, Kapp A, Werfel T. Atopy patch test reactions are associated with T lymphocyte-mediated allergen-specific immune responses in atopic dermatitis. *Clin Exp Allergy*. 1999;29(4):513–21.
- Roehr CC, Reibel S, Ziegert M, Sommerfeld C, Wahn U, Niggemann B. Atopy patch tests, together with determination of specific IgE levels, reduce the need for oral food challenges in children with atopic dermatitis. *J Allergy Clin Immunol*. 2001;107:548–53.
- Turjanmaa K. “Atopy patch tests” in the diagnosis of delayed food hypersensitivity. *Allerg Immunol (Paris)*. 2002;34:95–7.
- Darsow U, Ring J. Atopie-Patch-Test. *Atopisches Ekzem und Allergie. Hautarzt*. 2003;54:930–6.
- Boonyaviwat O, Pacham P, Piboonpocanun O, Vichyanond P, Visitsunthorn N. Comparison of irritant reactions between using lyophilized and commercial food allergen extracts in atopy patch tests in a normal population. *Asian Pac J Allergy Immunol*. 30(2):158–61.
- Niggemann B, Ziegert M, Reibel S. Importance of chamber size for the outcome of atopy patch testing in children with atopic dermatitis and food allergy. *J Allergy Clin Immunol*. 2002;110:515–6.
- Langeland T, Braathen LB, Borch M. Studies of atopic patch tests. *Acta Derm Venereol Suppl (Stockh)*. 1989;144:105–9.
- Taskapan O, Dogan B, Harmanyeri Y. Atopy patch test reactivity to house dust mites in patients with scabies. *Int J Dermatol*. 2003;42:246–8.
- Darsow U, Behrendt H, Ring J. Gramineae pollen as trigger factors of atopic eczema: evaluation of diagnostic measures using the atopy patch test. *Br J Dermatol*. 1997;137:201–7.
- Isolaure E, Turjanmaa K. Combined skin prick and patch testing enhances identification of food allergy in infants with atopic dermatitis. *J Allergy Clin Immunol*. 1996;97:9–15.

41. Kekki OM, Turjanmaa K, Isolauri E. Differences in skin-prick and patch-test reactivity are related to the heterogeneity of atopic eczema in infants. *Allergy*. 1997;52:755–9.
42. Nocerino R, Granata V, Di Costanzo M, Pezzella V, Leone L, Passariello A et al. Atopy patch tests are useful to predict oral tolerance in children with gastrointestinal symptoms related to non-IgE-mediated cow's milk allergy. *Allergy*. 2013;68(2):246–8.
43. Jarvinen KM, Caubet JC, Sickles L, Ford LS, Sampson HA, Nowak-Wegrzyn A. Poor utility of atopy patch test in predicting tolerance development in food protein-induced enterocolitis syndrome. *Ann Allergy Asthma Immunol*. 2012;109(3):221–2.
44. Heinemann C, Schliemann-Willers S, Kelterer D, Metzner U, Kluge K, Wigger-Alberti W, et al. The atopy patch test - reproducibility and comparison of different evaluation methods. *Allergy*. 2002;57:641–5.
45. Benhamou PH, Kalach N, Soulaïnes P, Donne N, Dupont C. Ready-to-use house dust mites atopy patch test (HDM-Diallertest), a new screening tool for detection of house dust mites allergy in children. *Eur Ann Allergy Clin Immunol*. 2009;41(5):146–51.
46. Brasch J, Uter W, Dibo M, Stockfleth E, Swensson O, Christophers E. Positive patch tests with a dermatophagoides mix relate to an increased responsiveness to standard patch test allergens. *Contact Dermatitis*. 2002;46:253–7.
47. Seidenari S, Giusti F, Pellacani G, Bertoni L. Frequency and intensity of responses to mite patch tests are lower in nonatopic subjects with respect to patients with atopic dermatitis. *Allergy*. 2003;58:426–9.
48. Ingordo V, D'Andria G, D'Andria C, Tortora A. Results of atopy patch tests with house dust mites in adults with 'intrinsic' and 'extrinsic' atopic dermatitis. *J Eur Acad Dermatol Venereol*. 2002;16:450–4.
49. Darsow U, Vieluf D, Ring J. The atopy patch test: an increased rate of reactivity in patients who have an air-exposed pattern of atopic eczema. *Br J Dermatol*. 1996;135(2):182–6.
50. Syrigou EI, Pitsios C, Panagiotou I, Chouliaras G, Kitsiou S, Kanariou M et al. Food allergy-related paediatric constipation: the usefulness of atopy patch test. *Eur J Pediatr*. 2011;170(9):1173–8.
51. Perackis K, Celik-Bilgili S, Staden U, Mehl A, Niggemann B. Influence of age on the outcome of the atopy patch test with food in children with atopic dermatitis. *J Allergy Clin Immunol*. 2003;112:625–7.
52. Johansson C, Ahlborg N, Andersson A, Lundeberg L, Karlsson MA, Scheynius A, et al. Elevated peripheral allergen-specific T cell response is crucial for a positive atopy patch test reaction. *Int Arch Allergy Immunol*. 2009;150(1):51–8.
53. Michel S, Yawalkar N, Schnyder B, Fischer B, Helbling A. Eczematous skin reaction to atopy patch testing with cockroach in patients with atopic dermatitis. *J Investig Allergol Clin Immunol*. 2009;19(3):173–9.
54. Chung BY, Kim HO, Park CW, Lee CH. Diagnostic usefulness of the serum-specific IgE, the skin prick test and the atopy patch test compared with that of the oral food challenge test. *Ann Dermatol*. 2010;22(4):404–11.
55. Nosbaum A, Hennino A, Berard F, Nicolas JF. Patch testing in atopic dermatitis patients. *Eur J Dermatol*. 2010;20(5):563–6.