



The diagnostic value of atopy patch testing and prick testing in atopic dermatitis: facts and controversies

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Abstract We conducted a systematic Medline search of the literature (1998–2008) on the criteria for performing the skin prick test and atopy patch testing (APT) to determine their utility in atopic dermatitis (AD). The skin prick, scratch, and skin patch tests are performed to identify which allergen is causing eczematous skin symptoms in patients with AD, or sneezing, nasal congestion, itchy eyes, wheezing, skin rash, and swelling. Many allergens in foods, drugs, and environmental substances (eg, ragweed and fungus), as well as contact allergens, can elicit eczematous skin reactions after epicutaneous application. Because no gold standard exists for aeroallergen provocation in AD, the APT is currently used to evaluate allergen without comparison with another accurate and reliable method. The APT is presumed to reflect delayed-phase clinical reactions. Even with delayed onset of symptoms (more than 2 hours after food ingestion), APT findings were not consistent among AD children. The APT could be used in children with gastrointestinal reactions to foods as well as AD. After standardization, the APT may provide further diagnostic information in addition to the skin prick test and serum immunoglobulin E values and may be able to evaluate the actual clinical relevance of immunoglobulin E-mediated sensitizations for eczematous lesions. The European APT model used with standardization of allergen concentration and vehicle may provide an important diagnostic tool to select patients for avoidance and for procedures of allergen-specific immunotherapy, but the clinical relevance of positive APT reactions awaits standardized provocation and avoidance testing.

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Atopic dermatitis (AD) is a chronic intermittent inflammatory disease in which the individual reacts to environmental stimuli that elicit skin symptoms of different degrees of severity. Allergies have been the source of more controversy than any other subject among dermatologists in terms of how to resolve atopic conditions, especially AD.

AD is the most common skin manifestation of cow's milk protein allergy or intolerance and hens's egg allergy in infancy and childhood until late childhood, after which the prevalence remains stable at 1% to 2%. Allergy to the peanut is likely to be life-long for most but not all AD patients, and about 20% of children with peanut allergy will outgrow it. Soybean, wheat, and rice are the most common food allergens.

Immunologic findings in AD include increased levels of immunoglobulin E (IgE), eosinophils, spontaneous

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histamine release from mast cells, and Th2 cells secreting interleukin-4 (IL-4) and IL-5, and decreased numbers of Th1 cells secreting interferon- γ .

Diagnostic value of the SPT and the atopy patch test

The value of the skin prick test (SPT) in diagnosing food allergy in AD is variable. A 2000 study contended that the size of the SPT wheal could predict, with 100% accuracy, that the open food challenge would be positive.¹ The atopy patch test (APT) was traditionally used to investigate the association between AD and aeroallergen allergy and has recently been used to supplement the SPT in diagnosing food allergy in children with AD. These tests are useful in investigating delayed reactions to milk and in improving the accuracy of the SPT, because about one-half of the reactions after the ingestion of milk are not mediated by specific IgE antibodies to milk protein and are lost by the age of 3 years.¹

The SPT can diagnose an allergy to seven foods: milk, egg, peanut, soy, wheat, fish, and cashew.² Patch testing is more sensitive than the SPT for diagnosing food allergy in young children with AD.³ Many children who have a negative response to the SPT could have a positive result to patch testing, especially for cereals. A food allergy diagnosis should be confirmed by elimination.

Aeroallergens and contact allergens in AD patients are also relevant for eliciting sensitization and skin symptoms. The most common ones in some adults with long-lasting AD are house dust mite (*Dermatophagoides pteronyssinus* and *D. farinae*), animal epithelials (cat, dog), and pollens, but the relevance of triggering factors is difficult to determine.⁴ A study of the relevance of the APT, specific IgE tests, and the SPT observed multiplex positivity by the APT in extrinsic AD and proved it was clinically relevant to atopic skin symptoms and the patient's medical history.⁴ The question of which diagnostic tests are the most accurate and relevant in AD patients is still open.³⁻⁷

Diagnosis of AD

The history of the disease and the SPT values of specific IgE are important in the diagnosis of early sensitization, but the diagnosis is more problematic for late type of allergic manifestation, especially to food allergens. The late type requires a patch test, an APT skin application food test (SAFT), and an exposition test such as the open test, single-challenge test, or double-blind, placebo-controlled food challenge test (DBPCFC). The latter is the gold standard procedure for diagnosing food allergy.^{8,9} The APT result is frequently positive (75%) in individuals with challenge-proven allergy to peanuts, and may represent a useful supplementary test to SPT in peanut-allergic AD patients.⁹

The APT was first used to diagnose AD in 1989 and was defined as a variant of the patch test.¹⁰ The APT is based on T cell-specific response to the application of allergens on the healthy skin of the patient's back or forearm, where an eczematous reaction is read after 48 and 72 hours when it is positive. That method is standardized only for aeroallergens. Patch test reaction on aeroallergens is specific in sensitized AD patients and is not aimed for healthy individuals, for asthmatic patients, or for patients with rhinitis.¹¹⁻¹³

Late skin reaction mediated by T cells has a very important role in the damaged skin of AD patients and in their APT reaction to aeroallergens.¹³ The morphologic picture of skin lesions and the microscopic analysis of biopsy specimens from lesional skin correlate well with the picture of positive APT reaction, thus indicating that the APT is an appropriate model for the analysis of an allergic reaction in AD.¹² The real value of the APT in food allergy in children remains unclear.¹⁴ The APT cannot predict hypersensitivity to hen's egg and cow's milk not identified by the SPT, or histamine release in unselected children 3 years of age with and without AD. As such, the APT cannot be recommended for daily practice in this setting.¹⁴

The APT has been increasingly recognized as a diagnostic method for food allergy in infants and children,^{14,15} in children with gastrointestinal allergy to cow's milk,¹⁶ and in those with eosinophilic esophagitis.¹⁷ The combination of the APT and the SPT and the determination of serum-specific IgE reduce the need for oral food challenges in children with AD.¹⁸ Positive APT results showed very good predictive values in food allergies compared with the SPT and the measurement of specific IgE in patients with wheat allergy and makes the DBPCFC superfluous for suspected cow's milk and hen's egg allergy. Combining the APT with specific IgE testing gives values of 100% for cow's milk and 94% for hen's egg. Adding SPTs to these two tests did not further improve results.¹⁸ The APT alone provided the best positive predictive values for wheat. The interpretation of an APT on food allergens is still subjective and not standardized.¹⁹⁻²¹

Many researchers have studied the APT to evaluate its possible use in the diagnosis of AD and to characterize an optimal standardized system for it in terms of airborne allergen concentrations and time of allergen exposure.^{13,22,23} The published data are conflicting.²³⁻²⁵ Aeroallergens and food allergens are able to elicit eczematous skin reactions after epicutaneous application. The APT with aeroallergens in AD patients may be a relevant test in addition to the SPT and specific IgE.²⁰ To investigate whether contact with aeroallergens exacerbates itching and eczematous skin lesions, one study used the APT with allergen concentrations exceeding 500, 3000, 5000, and 10,000 protein nitrogen units (PNU)/g in petrolatum on clinically uninvolved skin without irritating epidermal tape stripping.²⁵ The optimal concentration for an APT reaction was 5000 PNU/g.

The clinical relevance of positive APT reactions is suggested by comparison of APT findings with those of the SPT, specific IgE, the patient's history, and the eczema

pattern. The highest rate of positive APT results is found among the patients with eczema of skin lesions in air-exposed areas and with raised specific IgE (depending on the allergen), supporting the relevance of the test.²⁵ A study on food allergy and atopic eczema in infants reported that patch testing (26% of infants allergic to cow's milk were positive by patch testing) improved the accuracy of skin testing but noted that it needs to be standardized.²⁶ The study demonstrated that patch testing with cereals significantly increased the probability of early detection of cereal allergy in infants with AD. The specificity of the patch test was lower than that of the SPT and specific IgE measurements.²⁷

Other authors have also concluded that the APT seems to be a valuable additional tool in the diagnostic work-up of food allergy in children with AD, especially with regard to late-phase clinical reactions when APT results were positive (sensitivity 76%, specificity 95%). The APT test may help to prevent unnecessary restrictive diets among children with AD or in atopic eczema/dermatitis syndrome (AEDS).²⁸ AEDS is frequently associated with food allergy, which complicates the management in approximately 40% of affected children.

Pityrosporum orbiculare fungus in AD patients can cause skin infections and induce specific IgE antibodies. It is also one of the triggers for inducing AD. In a study of 15 AD patients, positive reactions to *P. orbiculare* were found after 48 hours in eight, with significantly higher serum levels of *P. orbiculare* in 13. The study concluded that *P. orbiculare* can induce an eczematous reaction in sensitized AD patients and that the patch test can be of diagnostic value in this subgroup of AD patients.²⁹

In another study, a combination of the APT with defined levels of specific IgE was suggested for patients who are allergic to cow's milk and hen's eggs.³⁰ Because the role of food allergy in the pathogenesis of AD has not been completely elucidated, and given that not all children with AD have food allergy, one study concluded that about 80% of AD patients have increased total serum IgE levels and that this correlated with the severity of AD, a positive SPT, and positive-specific IgE to a number of inhaled allergens, especially house dust mite and food allergens that are found in most patients.³¹ SPT results are more frequently negative in young children than in older ones, and a positive SPT corresponds to a clinically detectable allergy (by a provocation test) in only about 25% of AD patients.³¹ In addition, the study demonstrated that inhaled allergens that are applied percutaneously by a patch test may penetrate the skin and induce eczematous skin lesions. These skin reactions that appear after 24 to 72 hour delay did not occur in allergic asthma and allergic rhinitis and seemed to be specific for AD.³¹

Positive APT reactions to *Malassezia furfur* in AD correlate with a T helper 2-like peripheral blood mononuclear cell response described in a 2002 study.³² SPT- or APT-positive reactions to the recombinant *M. furfur* allergens rMal f₁, rMal f₅, and rMal f₆ were observed in 7, 14, and 16,

respectively, of 40 AD patients. A correlation was also noted between productions of the T helper 2-related cytokines IL-4, IL-5, and IL-13 and stimulation indexes to *M. furfur* extract. These data strongly suggest a relationship between circulating specific T cells with a T helper 2-like cytokine profile and positive APT reactions.³²

The SPT and the measurement of specific IgE antibodies to food extracts, individual allergens, or allergenic peptides are helpful in the diagnostic workup of suspected food allergy. Eczema or gastrointestinal symptoms of cow's milk allergy in children may be a sign of undetected allergy to other food antigens. The SPT for cereals aids in diagnosing cereal allergy in small children, especially when used with patch testing.³³ AD patients require an early allergen avoidance regimen. It has also been suggested that a patient with positive skin reactivity to house dust mite in both the SPT and the APT should be considered being at risk of AD persistence and of possible development of allergic respiratory disorders.³⁴

Combined SPT and APT are needed to identify peanut allergy.³⁵ SPT reactivity proved to be higher in patients older than 12 years, whereas APT positivity was more frequent in children younger than 6 years. APT sensitivity proved significantly higher than SPT sensitivity, particularly in children younger than 12 years. APTs for peanuts may represent a useful integration of standard testing modalities for the diagnosis of peanut allergy in AD patients.³⁵

The role of SPT and APT in AD

A combination of SPT and APT can significantly enhance the accuracy in the diagnosis of specific food allergy in infants with AD or digestive symptoms, whereas the APT is useful in the diagnosis of delayed reactions in infants with AD.³⁶ A 1977 report suggested that measurements of IgE should be part of the diagnostic criteria for AD. AD severity was positively associated with the number of positive SPT responses or IgE antibody levels in seven of eight studies that measured both.³⁷ Complicating the interpretation of the results of some studies is that the number of positive SPT responses and the spectrum of IgE sensitization often changes in the same individual over time.³⁷ This applies to the number of allergens tested, and the age at which these measurements are performed will have a direct bearing on atopy prevalence. This is important in food-specific sensitization that tends to occur in infancy, bearing in mind that sensitization to aeroallergens is often transient.³⁷

APT was introduced to assess sensitization to inhalant allergens in AD and AEDS. The APT values were high in patients with mite-induced AEDS, which indicates that its routine use might also improve the diagnosis of respiratory allergy to house dust mites.³⁸ The APT was more frequently (n = 69) positive than the SPT (n = 24) in 89 patients with AEDS with only respiratory symptoms (86.5% vs 21.6%, respectively).³⁸

In a study that evaluated the diagnostic value of different skin tests in clinically egg-allergic children with AD, neither the SAFT nor the APT with fresh whole egg extract were able to increase the diagnostic accuracy in detecting egg-allergic children with AD compared with the SPT.³⁹ Nevertheless, the DBPCFC and open controlled food challenges remain the gold standard for diagnosing clinically relevant food allergy.³⁹

The APT is an informative and reliable diagnostic method to determine delayed-type allergic reactions in children with AD. The APT is necessary in infants and preschool children when the total IgE amount is within normal reference ranges and the SPT is negative. The most common food allergens determined by the SPT were soy, milk, peanuts, carrot, egg whites, wheat, and corn.⁴⁰ Delayed-type food allergy reactions were found in 50% of the tested children with AD. Another study compared humans with AD and cats with spontaneously occurring AD by studying the APT with two allergens in three different dilutions of *D. farinae*, *D. pteronyssinus*, *Tyrophagus putrescentia*, and a grass pollen mixture. The APT results were read after 10, 24, and 48 hours. Immunohistochemical evaluation from macroscopically positive APT reactions in punch biopsies in the cats revealed a high specificity and a macroscopically positive APT reaction in 50%, which is similar to what is seen in humans. Thus, the APT in cats might be a useful tool in studying the immunopathogenesis of feline AD.⁴¹

All diagnostic methods in food allergy, such as SPT, specific IgE measurements, APT, and DBPCFC, may sometimes be misleading. Irritative skin reactions can mimic IgE-mediated symptoms, some reactions are not mediated by IgE, and pitfalls occur from the way foods are prepared or processed and the effects of the route of exposure, among others.⁴² A diagnostic workup of suspected food allergy that includes the SPT, the measurement of food-specific IgE antibodies, and more recently, the APT may be helpful, especially when considered in combination with defined levels of specific IgE.⁴³

In a diagnostic and analytic evaluation of screening panels for allergy that consisted of four major respiratory and four nutritional allergens in 142 patients with respiratory or food allergies, or both, overall concordance was found between the SPT and specific IgE values for all tested allergens (*D. pteronyssinus*, *D. farinae*, birch and grass pollen, whole egg, cow's milk, soybean, and hazelnut).⁴⁴ Likewise, the combined APT and SPT provided a diagnostically relevant test for food allergy in AD.⁴⁵

To evaluate the usefulness of the APT in diagnosing cow's milk allergy, the SPT, the DBPCFC, and specific IgE measurements was performed in 37 children for a median of 11 months and proved that the APT may be a useful adjunct to SPT in excluding cow's mild allergy in children who have allergic manifestations other than AD.⁴⁶ In a study on 73 Singaporean patients with AD and 38 non-AD controls, the APT for house dust mite correlated with specific IgE, whereas the APT for cat fur correlated with the SPT,

indicating that the APT may be useful for evaluating aeroallergens in AD patients.⁴⁷

Another study investigated the effect of pretreatment with 1% pimecrolimus cream on the backs and forearms in a randomized subgroup of 20 patients with atopic eczema and positive APT and SPT reactions to aeroallergens (house dust mites, *D. pteronyssinus*, cat dander, grass or birch pollen).⁴⁸ The authors proposed the APT as an inflammation model for atopic eczema and aeroallergens as relevant eliciting factors for atopic eczema and concluded that the APT reaction (10 of 20 patients had strong suppression in the pimecrolimus area) can be used as a model for skin inflammation associated with atopic eczema.

Clinical relevance of ATP and SPT

A recent study that included 437 children (age range, 3 months-14 years),⁴⁹ of whom 399 (90%) had AD (43% mild, 25% moderate, 12% severe AD), evaluated the SPT and IgE measurement in the diagnosis of suspected food-related symptoms. There were 1700 separate APT reactions for 437 children, and 303 of 1700 results (18%) were positive (hen's egg, 37%; cow's milk, 16%; wheat, 9%; and soy, 9%). The 95% predicted probability for the SPT was 9.2 mm for cow's milk and 9.0 mm for hen's egg. The authors noted that the SPT is unpleasant for young children and their parents. In addition, eczematous involvement in the test area might make an SPT impossible in children with AD. An IgE test is helpful and easy to perform. The SPT should be given preference, however, because is cheaper, the result is obtained promptly, and specificity is generally higher as well. Specificity of the APT was higher than that for IgE measurement or the SPT for all four allergens in that same study.⁴⁹

SPTs have been used for decades to prove or exclude sensitization to allergens. For foods, fresh samples seem to be superior to commercially available extracts. The authors concluded that for daily clinical practice, the APT adds only a small predictive value to the standard SPT and IgE measurement in the diagnosis of suspected food-related symptoms.⁴⁹

In a 2006 study⁵⁰ of children and adults with a history of an allergic reaction to Brazil nut or evidence of sensitization, 56 were investigated by questionnaire, 53 with SPTs, 54 with measurement of specific IgE, and 19 with the DBPCFC. Those authors concluded that a combination of medical history, SPT findings, and serum-specific IgE measurements is adequate in achieving a diagnosis in 77% patients with suspected Brazil nut allergy, but they went on to state that no method of diagnosing Brazil nut allergic reaction is totally reliable because even an oral challenge gave a misleading result in one patient.⁵⁰ Other authors studied the APT results of 87 AD children with suspected food allergy. They reported that induration and at least seven papules at 72 hours in the APT reaction is needed to achieve the greatest accuracy for food allergy in children with AD.¹⁹

Many developed countries have documented a rapid increase of food allergy disorders in recent years.⁵¹ Too few allergologists are available to assess so many children with allergies, and pediatricians should be retrained to diagnose and managing food allergy disorders.⁵¹

The diagnostic accuracy of the APT was higher (64.5% sensitivity, 95.8% specificity) with fresh food than with commercial food extracts tested in 60 children. A recent study documented 89 food challenges on 60 patients, and the SPT was positive in 31 for cow's milk, 19 for hen's egg, and 2 for wheat-specific IgE. The SPTs were also positive in 7 and 14 of 31 patients with cow's milk allergy and in 7 and 7 of 19 patients with hen's egg allergy.⁵²

Another study analyzed the predictive values of the SPT and the APT for eosinophilic esophagitis.⁵³ When the authors used the current positive predictive values and sensitivity for all of the foods, the combination of an SPT and an APT could correctly identify a correct diet in about 70% of the population, with resolution of the symptoms and biopsy specimens.⁵³

The correlation between the APT and the SPT and specific IgE for *D pteronyssinus* was evaluated in 32 atopic patients (8 men) with AD, 27 with AD and concomitant rhinitis (17 allergic), and 16 with concomitant bronchial asthma.⁵⁴ All were tested for specific IgE, the SPT and the APT for *D pteronyssinus*; of these, 17 had positive APT, 12 had positive-specific IgE antibodies, and 14 had a positive SPT.⁵⁴

Skin tests (the SPT, the APT, and the scratch test) are used for aeroallergens and rarely, food allergens.⁵⁵ In atopic infants, APT is useful in revealing food allergy and to aeroallergens.⁵⁶ The European Academy of Allergology and Clinical Immunology/Global Allergy and Asthma European Network position paper, "Present Status of the Atopy Patch Test," states there is a need of indications for testing with the APT, for delineating the choice of allergens (aeroallergens and foods), for test materials and technique in addition of the present knowledge on sensitivity and specificity, and for future research on the clinical use of the APT.

For example, a novel technique for APT with milk in a commercially available test kit was recently introduced in France (Diallertest, DBV Technologies, Paris, France) and compared with the Finn Chambre APT (Epitest Ltd Oy, Tuusula, Finland) in 49 children with milk allergy. The results showed good sensitivity and specificity without side effects.⁵⁶ A 2008 study investigated the reproducibility of a duplicate APT (left vs right side of the back) with native and commercially available food (cow's milk allergy, hen's egg, tomato, wheat flour) and with inhalant allergens (*D pteronyssinus*, mixed grasses) in a large unselected group of 277 children. For the four allergens, positive results with APT on one side and negative on the opposite side were for tomato and cow's milk allergy, and APT with inhalant allergens were invariably reproducible.⁵⁷

The relationship between the APT and clinical expression of the disease was studied in 297 children with AE/AEDS and respiratory symptoms. All the patients underwent SPT

and APT using the house dust mite extract.⁵⁸ The positivity rate was significantly higher for the APT, whereas significantly more positive results to the SPT were documented in the control group participants with neither past nor current AEDS.⁵⁸

Other authors used an epidemiologic approach to evaluate the APT with food allergens in two large groups of an unselected population of 380 children (of different ages) in Rome in 2005. The participants were tested with food allergens. Results of one similar age group with inhalant allergens shows that APT with both types of allergens can be found positive in about 4% to 11% for food allergens and in about 4% to 30% for inhalant allergens of an unselected population of children. The authors concluded that inhalant allergens probably induce a positive APT reaction through an IgE-linked process, whereas food allergens probably do not.⁵⁹

Other authors conducted a prospective clinical study to evaluate the additional clinical value of the APT in 135 AD children aged younger than 3 years.⁶⁰ The participants were tested using the SAFT, the APT with freshly prepared foods, commercially available cow's milk, the egg white of a hard boiled hen's egg, and peanuts in a saline solution. Specific serum IgE was also measured. The authors could not find enough support for the current addition of the APT to the standardized allergy workup in children younger than age 3 years who had AD and suspected food allergy.⁶⁰

Future trials on APT

Independent blind comparisons of the APT with other methods need to be made, and many such comparisons are necessary. There is no gold standard provocation test in AD for aeroallergens; therefore, the current state is the patient's clinical history for comparison and for the future, studies should evaluate and standardize topical *in vivo* challenge procedures in AD.⁶¹ The APT with food allergens can be compared with the DBPCFC. The recent European position paper provides guidelines for the standardization of food challenges in patients with immediate reactions to food.⁶² Individuals with AD sometimes show only delayed reactions to such challenges,^{63,64} however, it is also necessary to standardize the challenge procedures for delayed reactions, such as dosing and length of exposure and observation, and wash-out periods. Studies on the performance of the APT should reveal that the results can predict the long-term outcome of food and aeroallergen avoidance in patients with AD.

Conclusions

Aeroallergens and food allergens elicit eczematous skin reactions after epicutaneous application. Because there is no gold standard for aeroallergen provocation in AD, the APT is currently used to evaluate sensitivity to them, without

comparison with an accurate and reliable method. The APT is presumed to reflect delayed-phase clinical reactions. Even with a late onset of symptoms (ie, more than 2 hours after food ingestion), the APT findings were not consistent among AD children. The APT could be used in children with gastrointestinal reactions to foods as well as in AD patients. After standardization, the APT may provide further diagnostic information in addition to the SPT and serum IgE values, and it may be able to evaluate the actual clinical relevance of IgE-mediated sensitizations for eczematous lesions. The APT model used with standardization of allergen concentration and vehicle may provide an important diagnostic tool to select patients for avoidance procedures of allergen-specific immunotherapy, but the clinical relevance of positive APT reactions awaits standardized provocation and avoidance testing.

References

- Sporik R, Hill DJ, Hosking CS. Specificity of allergen skin testing in predicting positive open food challenges to milk, egg and peanut in children. *Clin Exp Allergy* 2000;30:1540-6.
- Burks AW, James JM, Hiegel A, et al. Atopic dermatitis and food hypersensitivity reactions. *Paediatrics* 1998;132:132-6.
- Strömberg L. Diagnostic accuracy of the atopy patch test and the skin-prick test for the diagnosis of food allergy in young children with atopic eczema/dermatitis syndrome. *Acta Paediatr* 2002;91:1044-9.
- Pónyai G, Hidvégi B, Németh I, Sas A, Temesvári E, Kárpáti S. Contact and aeroallergens in adulthood atopic dermatitis. *J Eur Acad Dermatol Venereol* 2008;22:1346-55.
- Cudowska B, Kaczmarek M. Atopy patch test in the diagnosis of food allergy in children with atopic eczema/dermatitis syndrome. *Rocz Akad Med Białymst* 2005;50:261-7.
- Isolauri 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.
- Turjanmaa K. The role of atopy patch tests in the diagnosis of food allergy in atopic dermatitis. *Curr Opin Allergy Clin Immunol* 2005;5:425-8.
- Sampson HA. The evaluation and management of food allergy in atopic dermatitis. *Clin Dermatol* 2003;21:183-92.
- Bock SA. Diagnostic evaluation. *Pediatrics* 2003;111:1638-44.
- Ring J, Kunz B, Bieber T, Vieluf D, Przybilla B. The 'atopy patch test' with aeroallergens in atopic eczema. *J Allergy Clin Immunol* 1989;82:195.
- 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;40:187-93.
- Langeveld-Wildschut EG, Thepen T, Bihari IC, et al. Evaluation of the atopy patch test and the cutaneous late-phase reaction as relevant models for the study of allergic inflammation in patients with atopic eczema. *J Allergy Clin Immunol* 1996;98:1019-27.
- Wistokat-Wülfling 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;29:513-21.
- Osterballe M, Andersen KE, Bindslev-Jensen C. The diagnostic accuracy of the atopy patch test in diagnosing hypersensitivity to cow's milk and hen's egg in unselected children with and without atopic dermatitis. *J Am Acad Dermatol* 2004;51:556-62.
- Niggemann B. Evolving role of the atopy patch test in the diagnosis of food allergy. *Curr Opin Allergy Clin Immunol* 2002;2:253-6.
- De Boissieu D, Wagué JC, Dupont C. The atopy patch tests for detection of cow's milk allergy with digestive symptoms. *J Pediatr* 2003;142:203-5.
- Spergel JM, Beausoleil JL, Mascarenhas M, Liacouras CA. The use of skin prick tests and patch tests to identify causative foods in eosinophilic esophagitis. *J Allergy Clin Immunol* 2002;109:363-8.
- 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.
- Heine RG, Verstege A, Mehl A, Staten V, Rolinck-Werninghaus C, Niggemann B. Proposal for a standardized interpretation of the atopy patch test in children with atopic dermatitis and suspected food allergy. *Pediatr Allergy Immunol* 2006;17:213-7.
- Darsow U, Laifaoui J, Kerschenlohr K, 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;59:1318-25.
- Heinemann C, Schliemann-Willers S, Kelterer D, et al. The atopy patch test—reproducibility and comparison of different evaluation methods. *Allergy* 2002;57:641-5.
- Czarnecka-Operacz M, Bator-Weger M, Silny W. Atopy patch test reaction to airborne allergens in the diagnosis of atopic dermatitis. *Acta Dermatovenereol Croat* 2005;13:3-16.
- Czarnecka-Operacz M. Rola Dermatophagoides pteronyssinus w patomechanizmie atopowego zapalenia skóry. [Doctoral dissertation (Praca doktorska)]. Poznań, Poland: Poznan University of Medical Sciences; 1994.
- Darsow U, Vieluf D, Ring J. Concordance of atopy patch test, prick test and specific IgE in patient with atopic eczema. *J Dermatol Sci* 1993;6:95-9.
- Darsow U, Abeck D, Ring J. Allergie und atopisches Ekzem: Zur Bedeutung des Atopie-Patch-Tests. *Hautarzt* 1997;48:528-35.
- Kekki OM, Turjanmaa K, Isolauri E. Difference in skin-prick and patch test reactivity are related to the heterogeneity of atopic eczema in infants. *Allergy* 1997;52:755-9.
- Majamaa H, Moisiö P, Turjanmaa K, Holm K. Wheat allergy: diagnostic accuracy of skin prick and patch tests and specific IgE. *Allergy* 1999;54:851-6.
- 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.
- Tengvall Linder M, Johansson C, Scheynius A, Wahlgren C. Positive atopy patch test reactions to *Pityrosporum orbiculare* in atopic dermatitis patients. *Clin Exp Allergy* 2000;30:122-31.
- Niggemann B. Atopy patch test (APT)—its role in diagnosis of food allergy in atopic dermatitis. *Indian J Pediatr* 2002;69:57-9.
- van Bever H. Atopic dermatitis: is food important in its pathogenesis? 2002;27/MITA (P) No:157/05/2002. http://www.nuh.com.sg/_kids/files/medicalEducation/sharedCaredProgramme/bulletin_27.pdf. Accessed: Mar 31, 2009.
- Johansson C, Eshaghi H, Linder MT, Jakobson E, Scheynius A. Positive atopy patch test reaction to *Malassezia furfur* in atopic dermatitis correlates with a T helper 2-like peripheral blood mononuclear cells response. *J Invest Dermatol* 2002;118:1044-51.
- Järvinen KM, Turpeinen M, Suomalainen H. Concurrent cereal allergy in children with cow's milk allergy manifested with atopic dermatitis. *Clin Exp Allergy* 2003;8:1060-6.
- Pajno GB, Peroni DG, Barberio G, Pietrobelli A, Boner AL. Predictive features for persistence of atopic dermatitis in children. *Pediatr Allergy Immunol* 2003;14:292-5.
- Seidenari S, Giusti F, Bertoni L, Mantovani L. Combined skin prick and patch testing enhances identification of peanut-allergic patients with atopic dermatitis. *Allergy* 2003;58:495-9.
- de Boissieu D, Dupont C. Patch tests in the diagnosis of food allergies in the nursing infant. *Eur Ann Allergy Clin Immunol* 2003;35:150-2.
- Flohr C, Johansson SGO, Wahlgren CF, Williams H. How atopic is atopic dermatitis? *J Allergy Clin Immunol* 2004;113:150-8.

38. Fuiano N, Incorvaria C. Value of skin prick test and atopy patch test in mite-induced respiratory allergy and/or atopic eczema/dermatitis syndrome. *Minerva Pediatr* 2004;56:537-40.
39. Hansen TK, Høst A, Bindslev-Jensen C. An evaluation of the diagnostic value of different skin tests with egg in clinically egg-allergic children having atopic dermatitis. *Pediatr Allergy Immunol* 2004;15:428-34.
40. Rokaitė R, Labanauskas L, Vaideliienė L. Role of the skin patch test in diagnosing food allergy in children with atopic dermatitis. *Medicina (Kaunas)* 2004;40:1081-7.
41. Roosje PJ, Thepen T, Rutten VP, van den Brom, Bruijnzeel-Koomen CA, Wilemse T. *Vet Immunol Immunopathol* 2004;101:143-51.
42. Niggemann B, Beyer K. Diagnostic pitfalls in food allergy in children. *Allergy* 2005;60:104-7.
43. Niggemann B, Rolinck-Werninghaus C, Mehl A, Binder C, Ziegert M, Beyer K. Controlled oral food challenges in children – when indicated, when superfluous? *Allergy* 2005;60:865-70.
44. Herzum I, Blümer N, Kersten W, Renz H. Diagnostic and analytical performance of a screening panel for allergy. *Clin Chem Lab Med* 2005;43:963-6.
45. Beyer K, Teuber SS. Food Allergy diagnostics: scientific and unproven procedures. *Curr Opin Allergy Clin Immunol* 2005;5:261-6.
46. Keskin O, Tuncer A, Adalioglu G, Sekerel BE, Sackesen C, Kalayci O. Evaluation of the utility of atopy patch testing, skin prick testing, and total and specific IgE assays in the diagnosis of cow's milk allergy. *Ann Allergy Asthma Immunol* 2005;94:553-60.
47. Goon A, Leow YH, Chan YH, Mg SK, Goh CL. Atopy patch testing with aeroallergens in patients with atopic dermatitis and controls in Singapore. *Clin Exp Dermatol* 2005;30:627-31.
48. Weissenbacher S, Traidl-Hoffmann C, Eyerich K, et al. Modulation of atopy patch test and skin prick test by pretreatment with 1% pimecrolimus cream. *Int Arch Allergy Immunol* 2006;140:239-44.
49. Mehl A, Rolinck-Werninghaus C, Staden U, et al. The atopy patch test in the diagnostic workup of suspected food-related symptoms in children. *J Allergy Clin Immunol* 2006;118:923-9.
50. Ridout S, Matthews S, Gant C, Twiselton R, Dean T, Arshad SH. The diagnosis of Brazil nut allergy using history, skin prick tests, serum-specific immunoglobulin E and food challenges. *Clin Exp Allergy* 2006;36:226-32.
51. Niggemann B, Heine RG. Who should manage infants and young children with food induced symptoms? *Arch Dis Child* 2006;91:379-82.
52. Canani RB, Ruotolo S, Auricchio L, et al. Diagnostic accuracy of the atopy patch test in children with food allergy-related gastrointestinal symptoms. *Allergy* 2007;62:738-43.
53. Spergel J, Brown-Whitehorn T, Beausoleil J, Shuker M, Liacouras C. Predictive values for skin prick test and atopy patch test for eosinophilic esophagitis. *J Allergy Clin Immunol* 2007;119:509-11.
54. Mandazhieva-Pepelanova M, Berova N. Is atopic dermatitis really atopic. Abstracts of the XX World Allergy Congress™ 2007, December 2-6, 2007, Bangkok, Thailand. *World Allergy Organization Journal*; 2007. p. S49.
55. Lipozenčić J, Ljubojević S. Atopic dermatitis. *Rad Med Sci Zagreb* 2008;499:77-103.
56. Turjanmaa K, Darsow U, Niggemann B, Rance F, Vanto T, Werfel T. EAACI/GA2LEN position paper: present status of the atopy patch test. *Allergy* 2006;61:1377-84.
57. Ronchetti R, Jesenak M, Barberi S, et al. Reproducibility of atopy patch tests with food and inhalant allergens. *J Biol Regul Homeost Agents* 2008;22:27-33.
58. Fuiano N, Incorvaia C, Prodam F, Procaccini DA, Bona G. Relationship between the atopy patch test and clinical expression of the disease in children with atopic eczema/dermatitis syndrome and respiratory symptoms. *Ann Allergy Asthma Immunol* 2008;101:174-8.
59. Ronchetti R, Jesenak M, Trubacova D, Pohanka V, Villa MP. Epidemiology of atopy patch tests with food and inhalant allergens in an unselected population of children. *Pediatr Allergy Immunol* 2008;19:599-604.
60. Devillers AC, de Waard-van der Spek FB, Mulder PG, Oranje AP. Delayed- and immediate-type reactions in the atopy patch test with food allergens in young children with atopic dermatitis. *Pediatr Allergy Immunol* 2009;20:53-8.
61. Tupker RA, De Monchy JG, Coenraads PJ, Homan A, van der Meer JB. Recognition of pathogenically relevant house dust mite hypersensitivity in adults with atopic dermatitis: a new approach. *J Allergy Clin Immunol* 2002;109:1012-8.
62. Bindslev-Jensen C, Ballmer-Weber BK, Bengtsson U, et al. Standardization of food challenges in patients with immediate reactions to foods – position paper from the European Academy of Allergology and Clinical Immunology. *Allergy* 2004;59:690-7.
63. Breuer K, Hetatizadeh A, Wulf A, et al. Late eczematous reactions to food in children with atopic dermatitis. *Clin Exp Allergy* 2004;34:817-24.
64. Werfel T, Breuer K. Role of food allergy in atopic dermatitis. *Curr Opin Allergy Clin Immunol* 2004;4:379-85.