

The role of the atopy patch test (APT) in diagnosis of food allergy in infants and children with atopic dermatitis

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Introduction

Food allergy has been demonstrated to play an important role in the pathogenesis of atopic dermatitis (AD), affecting around one-third of children (1). The most commonly offending foods are cow's milk (CM), hen's egg (HE), wheat, and soy. While immediate type clinical reactions to food (e.g. urticaria, bronchial obstruction after 10–20 min) can be identified quite easily, late phase reactions (e.g. worsening of eczema on the next day) still present diagnostic difficulties. Even double-blind, placebo-controlled oral food challenges (DBPCFC) – the gold standard of diagnosis in food allergy (2) – are not always easy to interpret, particularly in polysensitised children with atopic dermatitis (3).

The atopy patch test (APT) with aeroallergens has been studied for years (4–12). The first report on a possible role of the APT in food allergy came from a Finnish group (13, 14). The hypothesis has been raised that the skin prick test (SPT) and measurement of specific immunoglobulin E (IgE) in serum may reflect early clinical reactions (clinical symptoms within 2 hours) to the offending food, while the APT may have a high predictive capacity for late phase clinical reactions during DBPCFC (13–15).

Pathomechanism

The close macroscopic and microscopic similarities between the specimens from APT sites and lesional skin of patients with AD indicate that the APT is a valid model to study allergic inflammation in AD (11). In atopic dermatitis – especially in food sensitive AD – T-cells obviously play an important role, as shown in recent studies (16, 17). Our clinical investigations, showing that positive APTs (with T-cell infiltration of the skin) correlate with clinical late phase responses (15), support the previous findings. Additional evidence came from a recent study showing that APT-reactions are associated with T lymphocyte-mediated allergen-specific immune responses (12).

Performance

In our centre, the APT is performed in infants and children admitted to our hospital for the diagnosis of food allergy (15). APTs are performed on uninvolved skin – usually on the children's back. Twelve mm aluminium cups (Finn Chambers on Scanpor, Hermal, Reinbek, Germany) are used. One drop of fresh cow's milk containing 3.5% fat, native hen's egg (white of egg

and yolk), wheat-powder (Körner, Ibbenbüren, Germany) dissolved in water (1 g/10 ml) and soy milk are put on the filter paper. The occlusion time is 48 hours, and results are read 20 minutes and 24 hours after removal of the cups.

After 72 hours, reactions are classified as positive if erythema plus clear infiltration occurred. Reading of the APT is performed using a classification of + for erythema and slight infiltration, ++ for erythema and papules, and +++ for erythema and vesicles.

Recent clinical studies

Isolauro et al. first showed that positive APTs reflect late phase reactions during oral food challenges in cow's milk allergic children with atopic dermatitis (13). The authors conclude that combined skin prick and patch tests significantly enhances the accuracy in diagnosis of specific dietary allergies in children with atopic dermatitis.

We investigated 75 children (median age 2.1 years) with suspected food allergy by double-blind, placebo-controlled food-challenges, specific IgE in serum, SPT, and APT (15); 69/75 suffered from atopic dermatitis. Of 209 oral challenges, 133 were performed with allergen and 76 with placebo. 77/133 allergen and 2/76 placebo-challenges were assessed as positive. In 66 of 77 (86%) positive oral challenges specific IgE in serum to the corresponding allergen was positive, in 64/77 (83%) the SPT and in 42/77 (55%) the APT was positive. Immediate type clinical reactions were associated with positive SPT and proof of specific IgE in serum. While sensitivity of late phase clinical reactions reactions was 76% and specificity was 95%, corresponding figures for the SPT were 58% and 70%, and for the specific IgE in serum 71% and 29%, respectively (15).

Majamaa et al. (18) and Vanto et al. (19) investigated the performance of allergologic tests in suspected cow's milk allergy. In the first study, the atopy patch test was positive in 44% of challenge proven CM allergy; APT was found to have a PPV of 63% in this study, which is comparable to our PPV of 70%. Similar to their findings, we found the APT being the best predictor for positive challenges to CM. Vanto et al. (19), investigating 301 children with suspected CM allergy, found a PPV of 40% for the APT for immediate reactions, but no data could be provided for late phase reactions. The authors conclude that ATP results with cow's milk were not related to acute or delayed challenge reactions.

Majamaa et al. also investigated the usefulness of SPT, APT and specific IgE in 39 patients with wheat allergy, most of whom suffered from AD (20). In their collective, 56% showed positive challenges, as in our patient group where 51% reacted to wheat. Regarding the APT these authors found a PPV to wheat of 63% compared to 94% in our study.

Open questions

Does the APT only work in patients with AD?

The patch test reactions to aeroallergens seem to be specific for sensitised AD patients, and do not occur in healthy volunteers or in patients suffering from asthma or rhinitis (5). In our study, six of 75 study children had no history of skin symptoms and especially did not suffer from AD: none of these children showed a positive APT (15); however, the numbers are very small and more data are warranted to prove whether the Dutch results in adults also are valid for children with food-sensitive AD.

Are results of APT testing age-dependent?

Our study indicates that age has no influence on the outcome and the APT may be performed in infants as well as in older children (15).

For what allergens has the APT been proven to be helpful?

In our studies, the APT was performed with cow's milk, hen's egg, wheat and soy which represent the four most common food allergens in childhood. Other studies used the same food allergens (13, 18–20). There is no reason to doubt that many other allergens will also work.

What is the optimal test material?

The good percentages of sensitivity and specificity for the APT in our studies may be explained by the fact that we used the identical native allergen source and concentration as for DBPCFC and SPT. Native food seems therefore be most suitable for performing APT.

What kind of a chamber should be used?

Unpublished data from our group show that the use of 6 mm aluminium cups may result in a decreased sensitivity compared to the use 12 mm aluminium cups, which should therefore be preferred. No data exist on the use of alternative materials such as quadratic plastic cups, recently available on the market.

What is the optimal concentration of the allergen?

Due to the fact that there is little information about the optimum concentration of the food used for the APT and to exclude falsely positive results by irritative reactions, all allergens were tested in a 1:10 solution in parallel (15). We observed 18/77 (23%) positive results in the 10% diluted APT, and these were seen in the patients with the strongest reactions to the undiluted ones. Furthermore, all these patients showed late eczematous reactions in the DBPCFC, mostly (n=10) to wheat (15). This indicates that our APT results are not biased by unspecific, irritative reactions and native foods may be used undiluted.

What is the best reading time?

For aeroallergens, studies have been performed comparing different reading times; it was concluded that an occlusion time of 48 hours and a reading time of 72 hours should be preferred (21). For food allergens, to our knowledge, no comparative data are available so far; however, good predictive capacities could be gained by our group and others using a 48-hour occlusion and 72-hour reading time.

Are there side-effects of the APT?

Six children could not be included in our study (15) because they showed clinical relevant reactions with acute local urticarial wheals and itching (contact urticaria) 5–15 minutes after administering the APT. In these six cases egg was the allergen. Otherwise, no side effects were observed.

Can the APT make DBPCFC superfluous?

In a recent study (22) we investigated whether the combination of the APT, SPT and specific IgE in serum could improve the diagnostic value. Evaluating suspected CM allergy, the APT was the best single predictive test (PPV 95%), and the combination of a positive APT with evidence of specific IgE, or APT together with a positive SPT, optimised the PPV to 100%. Concerning HE allergy, the APT was also the best single predictive test (PPV 94%). The combination of two or more tests did not exceed the APT's predictive value. In both CM and HE challenges, the predictability of oral challenges depended on the level of specific IgE. For wheat allergy, the APT proved to be the most reliable test and the PPV of 94% could not be improved by a combination with other allergological tests. Therefore, the combination of positive atopy

patch tests together with defined levels of specific IgE (cow's milk ≥ 0.35 kU/l and hen's egg ≥ 17.5 kU/l) makes DBPCFC superfluous for suspected cow's milk and hen's egg allergy.

Conclusions

The APT seems to be a valuable additional tool in the diagnostic work up of food allergy in infants and children with atopic dermatitis – especially concerning late phase clinical reactions. A positive APT may help to prevent restrictive and unnecessary diets which may be the consequence of misjudging late reactions by clinical assessment alone. Furthermore, the combination of positive atopy patch tests together with defined levels of specific IgE (cow's milk ≥ 0.35 kU/l and hen's egg ≥ 17.5 kU/l) makes DBPCFC superfluous for suspected cow's milk and hen's egg allergy.

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