Influence of age on the outcome of the atopy patch test with food in children with atopic dermatitis

To the Editor:

In recent years, the atopy patch test (APT) has established itself as a tool in the diagnostic work-up of food allergy in infants and children with atopic dermatitis,[1-3] especially because of its high predictive capacity for late phase clinical reactions in children with atopic dermatitis.[1,4] A positive atopy patch test result might help to avoid imposing restrictive and unnecessary diets after misjudging late reactions on the basis of clinical assessment alone.[1] Furthermore, the combination of positive atopy patch test results together with defined levels of specific IgE makes double-blinded, placebo-controlled food challenges (DBPCFCs) superfluous in some cases.[2] In spite of this, some questions still remain, and no data are available about the influence of age on the outcome of APT.

This study therefore aimed to investigate whether age could have an influence on the outcome of the APT in various pediatric age groups. We retrospectively considered 498 DBPCFCs performed in 255 patients (145 boys and 110 girls) ranging in age from 3 to 148 months (median, 12 months). These patients were subdivided into 4 age groups: group 1 (0 to 11 months, n = 113), group 2 (12 to 35 months, n = 86), group 3 (36 to 59 months, n = 39), and group 4 (60 months or older, n = 17). All children had atopic dermatitis, as defined by the criteria of Sampson[5] and Seymour et al,[6] modified from Hanifin and Rajka.[7]

To calculate sensitivity, specificity, positive and negative predictive values, and efficiency for APT, we used DBPCFC as a gold standard for diagnosing food allergy.[8-11] The oral provocations and the APTs were performed with the 4 foods that most commonly cause allergic reactions in children with atopic dermatitis: cow's milk, hen's egg, soy, and wheat.

Inclusion criterion for performing oral food challenges was suspicion of food-related symptoms by parents or physicians. These foods were challenged in a double-blinded, placebo-controlled manner as recently described.[9] Briefly, every 20 minutes successive doses (0.1, 0.3, 1.0, 3.0, 10.0, 30.0, and 100.0 mL) of fresh pasteurized cow's milk, soy milk, wheat powder, or placebo (Neocate SHS, Liverpool, United Kingdom) were administered. Beaten raw hen's egg was given in a similar fashion up to a 30.0-mL dose. The provocation was stopped when clinical symptoms were observed or the highest dose was reached. The food challenges were scored as positive by a pediatric allergy specialist if 1 or more of the following objective clinical reactions were noted: urticaria, angioedema, wheezing, vomiting, diarrhea, abdominal pain, shock, or exacerbation of eczema. The latter reaction was defined as a worsening of the SCORAD score of at least 10 points and always occurred as a late phase reaction 3 to 48 hours after the oral challenge.

Aluminum cups on adhesive tape (Finn Chambers on Scanpor; Hermal, Reinbek, Germany) with a diameter of 12 mm were used.[12] Fifty microliters of fresh cow's

TABLE I. Predictive capacity of the APT in the different age groups

Allergen and parameter	0-11 mo	12-35 mo	36-59 mo	≥60 mo	All
Cow's milk	n = 98	n = 65	n = 29	n = 13	n = 205
Sensitivity (%)	38	41	25	17	37
Specificity (%)	98	70	96	100	95
PPV (%)	95	81	50	100	88
NPV (%)	54	61	89	58	62
Efficiency (%)	63	66	86	62	67
Hen's egg	n = 30	n = 49	n = 23	n = 9	n = 111
Sensitivity (%)	42	49	27	25	42
Specificity (%)	82	88	92	100	89
PPV (%)	80	89	75	100	85
NPV (%)	45	45	58	63	50
Efficiency (%)	57	61	61	67	60
Soy	n = 39	n = 34	n = 13	n = 4	n = 90
Sensitivity (%)	40	43	67	*	47
Specificity (%)	88	93	90	*	91
PPV (%)	33	60	67	*	50
NPV (%)	91	86	90	*	90
Efficiency (%)	82	82	85	*	83
Wheat	n = 36	n = 35	n = 15	n = 6	n = 92
Sensitivity (%)	40	25	50	0	35
Specificity (%)	90	93	100	75	32
PPV (%)	75	50	100	0	67
NPV (%)	68	81	85	60	75
Efficiency (%)	69	77	87	50	74

PPV, Positive predictive value; *NPV*, negative predictive value.
*Predictive capacity could not be calculated, because no child had a positive oral food challenge with soy in this age group.

milk, of whisked hen's egg, soy milk, and of wheat powder solution was put on filter paper and applied on the unaffected skin of each child's back. The occlusion time was 48 hours, and results were read 20 minutes after removal of the cups and again 24 hours later for the final evaluation of the test. Final reactions (72 hours) were classified as positive if there was erythema together with infiltration.[1,2] Topical steroids were not allowed for at least 48 hours before the APT.

Statistical analyses were performed with SPSS for Windows software (version 8.0; SPSS, Chicago, Ill). Two-by-two tables were used to calculate sensitivity, specificity, positive predictive value, and negative predictive value. Sensitivity was defined as the proportion of true positives detected, specificity as the proportion of true negatives detected, positive predictive value as the proportion of symptomatic individuals among test positives, negative predictive value as the proportion of nonsymptomatic individuals among test negatives, and efficiency as the proportion of tested individuals correctly classified by the test. Ninety-five percent confidence intervals were calculated to investigate differences between the 4 age groups. *P* values less than .05 were considered statistically significant.

In the 255 patients, a total of 498 verum provocations were performed with the 4 foods: 205 with cow's milk, 111 with hen's egg, 90 with soy, and 92 with wheat. Two hundred nine of 498 oral challenges were assessed as positive and 289 of 498 as negative. One hundred twenty-two of 209 positive challenges were observed as early (urticaria, gastrointestinal, respiratory symptoms), 45 of 209 as late (worsening of eczema), and 42 of 209 as combined clinical reactions (worsening of eczema plus urticaria or gastrointestinal symptoms).

APTs were performed with the 4 allergens in all 255 patients. By using two-by-two tables for the outcome of the oral food challenges, data were calculated for sensitivity, specificity, positive predictive value, negative predictive value, and efficiency (Table I). Calculating 95% confidence intervals showed no significant differences for the 4 allergens between the 4 age groups.

Specificity seems to be the most reliable parameter to assess the outcome of APTs, reaching highest values for all 4 allergens investigated. However, sensitivity showed a low predictive capacity and a great variability in the various age groups. Relatively high values (70% to 100%) for all allergens were found in the 3 age groups up to 60 months, and the fourth age group (60 months or older) showed the widest variability. This might be explained by the small number of children in this age group. The age within this highest group ranged from 60 to 148 months, with a median age of 97 months and a mean age of 94 months.

Considering the 4 allergens, there were no marked differences concerning cow's milk, hen's egg, or wheat. As

can be seen in Table I, we observed no positive oral challenge to soy in children older than 60 months. Because most food allergies occur before the age of 60 months,[10,13] this does not result in diagnostic problems.

APTs with aeroallergens have mostly been performed in adults; no consideration of the influence of age was made. The only study that addresses this topic in children and young adults found that the frequency of the APT with house dust mite allergen showed more positive test results in children younger than 10 years with atopic dermatitis[14]; however, one might hypothesize that sensitization and clinical allergy to house dust mites are more often seen in younger children.

In conclusion, the outcome of the APT with food does not seem to be influenced by age in infancy and childhood. APTs might therefore be performed in the diagnostic work-up of food allergy in children with atopic dermatitis up to 12 years of age with unimpaired accuracy.

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doi:10.1067/mai.2003.1656