

Patch Testing with Egg Represents a Useful Integration to Diagnosis of Egg Allergy in Children with Atopic Dermatitis

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Abstract: Our aim was to investigate atopy patch and skin prick test reactions to egg in 85 children with atopic dermatitis, and to evaluate their relevance by performing repeated open challenges with egg. Thirty-one percent of our patients showed an eczematous response to the challenge. Positive reactions to atopy patch and skin prick tests were recorded in 37% and 19%, respectively. Atopy patch test sensitivity proved significantly higher than that of skin prick test (79.6% vs. 46.2%), whereas specificity was lower (81.4% vs. 93.2%). Our data suggest that combined skin prick and patch testing improves screening for egg allergy in affected children, identifying 92% of those who were challenge positive among our patients.

Atopic dermatitis (AD) is a recurring inflammatory skin disorder, which is often associated with food allergy, especially in infants and children. The most frequently offending foods are cow's milk, hen's egg, wheat, and soy, which can elicit both immediate and delayed (eczematous) skin responses. The results of skin prick tests or serologic assays as predictors of allergen-mediated skin reactions are frequently disappointing, since their correlation to the appearance of eczematous reactions may be poor. Recently, positive responses to food patch tests have been associated with the appearance of delayed reactions after food ingestion (1–6).

Our aim was to investigate skin prick test and atopy patch test responses to egg in Italian children with AD employing egg yolk and white separately, and to correlate these results to repeated open food challenges with egg.

MATERIALS AND METHODS

Eighty-five patients with AD (37 boys and 48 girls), aged from 6 months to 14 years (mean age $\pm$ SD = 6 ± 3.9) were studied. Skin prick tests (SPT) with egg yolk and egg white were performed on the volar forearm, according to the standard technique, using commercial allergens from Stallergènes (Antony, France). For atopy patch tests (APT), a mixture (2 : 1) was prepared every day with egg yolk or white and petrolatum oil. About 20 mg of each material were applied to the back by using large Finn Chambers on Scanpor tape (Epitest, Tuusula, Finland) for 72 h. The results were read 30 to 60 min after patch test removal according to the following scale: erythema and edema = 1; erythema, edema, and few papules = 2; erythema, edema, and papules covering most of the patch test area = 3; erythema, edema, and papules spreading outside the patch test area, or

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Figure 1. Positive APT reaction to egg yolk in a child with AD

vesicles = 4. Irritant or doubtful reactions included redness with no infiltration.

After a milk, egg, and peanut elimination diet for 3 to 4 weeks, when the eczema was in a stable phase, a repeated open food challenge (ROFC) with egg was performed. One spoon of cooked egg (yolk and white) was administered the first day at the hospital. One to two eggs had to be consumed during the following days at home. When a clinical reaction (cutaneous, respiratory, or gastrointestinal) appeared, the patient was promptly examined by the medical staff and the challenge discontinued. All patients were examined on day 7 of the challenge.

RESULTS

Skin prick tests and APT with egg white were positive in 15 and 16 children, respectively, the agreement between skin tests being 77%. As regards egg yolk, SPT proved positive in 11 patients, whereas APT was positive in 20. The agreement between egg yolk APT and SPT was 73%. Figure 1 shows an example of positive patch test reaction to egg yolk.

On the whole, SPT to egg yolk and/or white were positive in 18.8% of patients, whereas APT was positive in 36.5%. Twenty-six subjects (30.6%) had an eczematous response after challenge associated to immediate urticarial reactions in four instances and to gastrointestinal

symptoms in three. Among challenge-positive subjects, 77% showed positive APT, and 46% reacted to SPT. In particular, 12 children reacted only to APT, four did to SPT alone, eight to both skin tests, and two were negative. Eighteen percent of challenge-negative patients proved positive to APT, whereas 7% were positive to SPT. The frequency of positive skin tests was higher in infants (< 2 years of age) (Table 1). Figures referring to sensitivity, specificity, and positive and negative predictive values are illustrated in Table 2. APT sensitivity proved significantly higher than SPT sensitivity, whereas specificity was lower. In infants, both APT specificity and positive predictive value was significantly lower than those for SPT.

DISCUSSION

To date, a double-blind, placebo-controlled food challenge (DBPCFC) remains the gold standard for diagnosing food allergy, although there is no universally accepted standard for performing it (7,8). This procedure is time consuming, costly, and must be performed over several days. In fact, skin reactions in AD patients sometimes appear more than 48 h after food ingestion, and require repeated administration of the foodstuff. The ROFC may represent an alternative to DBPCFC. Comparing DBPCFC performed for 1 week with ROFC in AD affected infants, Isolauri et al (1) found a high correlation between these two challenge modalities. In our experience, ROFC associated to careful follow-up seems to be adequate and well accepted (6) (although cooking denatures proteins comprising antigens, we perform ROFC with cooked egg, because of low compliance and possible health damage by challenging with raw egg). By means of this method, 30.6% of our AD patients had results indicating egg allergy, showing delayed reactions. Egg intake was associated with the appearance of immediate responses, such as urticaria and gastrointestinal symptoms only in seven children. According to Niggemann et al (7), who considered AD children with a median age of 21 months, hen's egg allergy presents primarily with immediate-type reactions. This discrepancy may be resulting both from the age of

TABLE 1. Skin Tests in Subjects of Varying Age Undergoing Challenge with Egg

Age (number of patients)	CH + (%)	APT + (%)	% agreement APT/CH	SPT + (%)	% agreement SPT/CH	% agreement SPT/CH
6 months–2 years (21)	10 (35.5)	10 (47.6)	71.4	6 (28.6)	66.6	71.4
3–6 years (33)	8 (24.2)	11 (32.4)	78.8	7 (21.2)	84.8	63.6
7–14 years (31)	8 (25.8)	10 (32.3)	87.1	3 (9.7)	70.9	58.1
Total (85)	26 (30.6)	31 (36.5)*	80	16 (18.1)	78.8	63.5

CH = food challenge; APT = atopy patch tests; SPT = skin prick tests; *Significant differences in comparison with SPT.

TABLE 2. Sensitivity, Specificity, Positive, and Negative Predictive Values (%) of Skin Tests with Egg on Patients of Varying Age

Age (number of patients)	Atopy patch tests				Skin prick tests			
	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV
6 months–2 years (21)	70	72.7*	70*	72.7†	60†	100	100†,‡	73.3
3–6 years (33)	75	80	54.5	90.9	62.5†	92	71.4†	88.5
7–14 years (31)	87.5*	86.9	70*	95.2	12.5	91.3	33.3	75
Total (85)	76.9*	81.4*	64.5	88.9	46.2	93.2	75	79.7

*Significant differences in comparison with SPT, †Significant differences in comparison with children aged 7 to 14 years, ‡Significant differences in comparison with children aged 3 to 6 years.

PPV = positive predictive value; NPV = negative predictive value.

our patients (median age = 5 years), and to the prolonged challenge and observation period enabling the detection of delayed reactions.

Roehr et al (4) found that the APT was the best single predictive test (PPV = 94%) compared to serum IgE and SPT in 42 AD children undergoing DBPCFC with egg. They concluded that the combination of specific IgE levels and APT results makes DBPCFC superfluous for suspected hen's egg allergy. In an APT study performed on 75 children with suspected food allergy, a sensitivity of 76% for late phase clinical reactions and a specificity of 95% were reported, while the corresponding figures for SPT were 58% and 70% (3).

Regarding our patients who had eczematous responses to challenge, both SPT and APT proved helpful diagnostic tools. However, APT sensitivity proved higher than that of SPT, whereas APT specificity was significantly lower, particularly in infants.

To assess possible differences in skin reactivity to egg yolk and white, we performed separate testing with the two egg components. (The correlation to challenge with the whole egg was studied taking together the responses both to egg yolk and white.) In our patients, positive responses to egg yolk and white were equally distributed among challenge positive and challenge negative patients and among immediate and delayed reactors. According to data in the literature, specificity figures for skin tests vary according to age. From our results, APT and SPT positivity are more frequently found in subjects under 2 years of age. Positive challenges were more frequently encountered in this age group as well.

According to our data, APT represents a useful integration to standard testing modalities employed for the diagnosis of egg allergy, enabling the identification of 77% of our challenge-positive AD children. The combined use of skin prick and patch tests further improves the detection rate, probably because several immunologic mechanisms are involved in food allergy

in AD. However, when considering these results we should take into account that methodologic problems are still present when performing food atopy patch testing. Unfortunately, commercial preparations for food APT are still lacking, and allergen concentration in preparations for SPT is considered too low and not suitable for patch testing. Therefore, we are obliged to employ fresh products. When considering patch testing with fresh egg, problems such as possible variations in allergen content according to diet of the hens and hen species, as well as contamination of yolk by white and vice versa cannot be avoided.

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