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Natural history of egg hypersensitivity

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SUMMARY Twenty-five children with clinical egg hypersensitivity, confirmed by double-blind challenge, were followed for between 2 and 2½ years. Clinical egg hypersensitivity was found to have resolved in 11 children but was persistent in 14. Skin prick test reactions to egg were initially of equivalent size in the resolved and persisting groups, but became negative or diminished in size with resolution of clinical egg hypersensitivity, while remaining positive in the group with persisting symptoms. Symptoms after egg ingestion were categorised as cutaneous, gastrointestinal, respiratory, and angioedema. The adverse reactions of the resolved group were either cutaneous or gastrointestinal symptoms. The persisting group had multisystem involvement and most of them developed angioedema and respiratory symptoms. These differences may be useful as prognostic indicators in clinical egg hypersensitivity.

Immediate hypersensitivity to hen's egg protein has been estimated to occur in about 0·5% of the childhood population and in about 5% of atopic children.[1] One of the first descriptions of idiosyncrasy to egg was given by Schloss[2] who described a 14-month-old boy who developed urticaria and facial oedema immediately after ingesting egg. Schloss clearly showed that the boy had a specific skin hypersensitivity to egg protein. Other manifestations of egg hypersensitivity are a red blotchy rash, laryngeal oedema, wheezing, nausea, vomiting, and abdominal pain.

The relationship of eczema to egg ingestion is less clear although instances of egg precipitating eczema are recorded[3] and a double-blind trial of dietary elimination has shown a beneficial effect on infantile eczema.[4]

The natural history of egg hypersensitivity is poorly documented. Ratner and Untracht[1] commented that the incidence of egg allergy wanes with age, and Stuart and Farnham[5] described 3 children to illustrate the variation in the outcome of egg hypersensitivity.

This study was undertaken to follow the natural history of egg hypersensitivity in children and relate its prognosis to clinical history, skin prick tests, and serum radio allergosorbent test (RAST) to egg protein.

Patients and methods

Twenty-five children were diagnosed as having acute clinical egg hypersensitivity by double-blind challenge.[6] This comprised all 17 children with positive egg challenges from an earlier study[6] and 8 additional children identified by the same challenge procedure. The children, 20 boys and 5 girls, were followed up after an interval of 2–2½ years from the initial challenge studies. Their ages at the initial study ranged from 7 months to 9¾ years, median age 17 months. Initial challenges were done in hospital, but subsequent challenges to determine evidence of persisting or resolved egg hypersensitivity were done at home or in hospital depending on the severity of the initial reaction. Egg hypersensitivity was assumed to have resolved when a whole egg could be eaten with no apparent symptoms.

At initial study all the children except one had associated eczema, 20 (80%) had asthma or allergic rhinitis, and 21 (84%) had positive prick tests to at least one inhalant allergen. Twenty-two (88%) had been breast fed at least partly and in 16 (64%) there was a history of milk hypersensitivity.

Twenty-two (88%) had histories of adverse reactions after their first exposure to egg. Facial angioedema, a blotchy erythematous rash or urticaria on the face, and sometimes on the body, were the most common manifestations of egg hypersensitivity. Twenty (80%) children had some combination of these cutaneous symptoms, 15 (60%) had vomiting, abdominal pain, or diarrhoea, and 10 (40%) had respiratory symptoms including 3 with laryngeal oedema, 7 with coughing or choking, 4 with allergic rhinitis, and 3 with wheezing.

Symptoms occurred within 30 minutes of egg ingestion in 19 (76%), between 30 to 90 minutes in 5 (20%), and in one child after 10 hours.

Skin prick tests were performed at enrolment and at follow-up with Bencard allergens to egg, milk, and control, and to the inhalant's house dust, house mite (*Dermatophagoides pteronyssinus*), and rye grass. These tests were done on the back with a 23 gauge needle. The same batches were used at enrolment and follow-up. Repeat testing with a fresh batch at follow-up confirmed the reproducibility of the skin tests and potency of the stored allergens.

Specific IgE to eggs and milk was measured by the RAST (Phadebas, Pharmacia) at follow-up only. All the specimens were measured at the same time with the same batch of reagents, and thus radioimmune assay counts could be used for analysis as well as RAST scores. Total IgE was measured by paper radioimmunosorbent test (PRIST) (Phadebas, Pharmacia), and IgG, IgA, and IgM by a nephelometric method. No blood was obtained from 2 children.

Statistics were done using Wilcoxon's rank sum test and Fisher's exact test. P values refer to the rank sum test unless specified.

Results

Between 2 and 2½ years after initial study clinical egg hypersensitivity had resolved in 11 (44%) but was persistent in 14 (56%). Factors associated with resolution of adverse symptoms after egg ingestion were assessed (Table 1).

Ages. At the start of the study there was no difference between the ages of the children in the two groups ($P>0.05$), but assuming egg hypersensitivity had been present since birth, there was a significant difference in the number of years of egg allergy between the groups at follow-up ($P<0.01$).

Symptoms. The symptoms produced by egg ingestion differed greatly between the two groups. The resolved group had only one system affected in their adverse reaction to egg, either cutaneous manifestations or vomiting. Only one child reacted with facial oedema and none had respiratory symptoms. However, the persisting group had multiple-system involvement frequently with angioedema and respiratory symptoms ($P<0.005$) (Table 2). The type of reaction remained unchanged during the follow-up period although 5 children had less severe reactions than at enrolment. At follow-up no child had a stronger reaction than at the initial study.

Skin prick tests. Twenty-three children had positive reactions to the skin prick test to egg at the

Table 1 *Clinical features of children with egg hypersensitivity*

Case	*Age at start*		*Duration of hypersensitivity*		*Egg prick test weal size (mm)*		*RAST score*	*Symptoms with egg ingestion*		
	Years	*Months*	*Years*	*Months*	*Start*	*Follow-up*	*Follow-up*	*Cutaneous*	*Gastro-intestinal*	*Respiratory*
Resolved hypersensitivity										
1	0	6	3	0	8	6	2	RU	—	—
2	0	7	2	0	6	0	0	R	—	—
3	0	7	3	0	10	2	0	R	—	—
4	0	9	3	0	16	6	2	U	—	—
5	0	11	2	0	3	0	1	—	V	—
6	1	0	3	0	9	0	0	ORU	—	—
7	1	2	3	0	3	0	—	—	V	—
8	1	6	3	0	7	1	0	—	V	—
9	1	7	4	0	9	2	4	U	—	—
10	2	7	3	0	3	0	0	U	—	—
11	3	2	5	0	7	0	2	—	V	—
Persisting hypersensitivity										
12	0	7	2	11	4	12	—	ORU	—	Rh W
13	0	8	3	1	8	12	4	OR	V	—
14	0	10	3	5	6	10	3	—	—	C Rh
15	1	0	3	11	16	9	3	R	V	C
16	1	5	4	3	9	25	4	R	—	LC
17	9	9	12	4	4	7	2	OE	V	—
18	1	8	4	4	20	12	4	OR	V	—
19	2	1	4	11	8	9	3	ORU	P	C L Rh
20	3	3	5	6	14	8	2	OR	V DP	C
21	3	8	6	3	12	6	2	ORU	DP	Rh W
22	5	4	7	11	5	7	4	OR	P	C L W
23	6	10	9	3	7	8	3	OR	V P	C
Egg prick test negative										
24	1	5	3	9	0	0	0	ORU	P	—
25	1	6	4	3	0	0	0	—	V DP	—

O=angioedema; R=rash; U=urticaria; E=eczema; V=vomiting; D=diarrhoea; P=abdominal pain; L=laryngeal oedema; C=coughing; Rh=rhinitis; W=wheezing.

Table 2 *Differences in symptoms between groups with resolved and persisting egg hypersensitivity*

	Symptoms with egg ingestion				
	Cutaneous	*Angioedema*	*Gastrointestinal*	*Respiratory*	*More than one system involved*
	No (%)	*No* (%)	*No* (%)	*No* (%)	*No* (%)
Resolved egg hypersensitivity (n=11)	7 (63)	1 (9)	4 (36)	0 (0)	0 (0)
Persisting egg hypersensitivity (n=12)	11 (92)	9 (75)	9 (75)	9 (75)	11 (92)
P values*	NS	<0·005	NS	<0·005	<0·001

*By Fisher's exact test. NS=not significant.

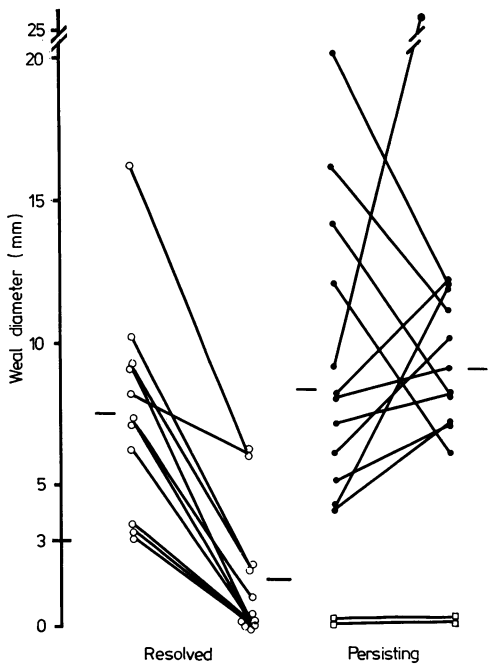

Figure *Egg skin prick weal diameter at enrolment and at follow-up. Bars denote arithmetic mean; closed circles, persisting group; open circles, resolved group; open squares, skin test negative children. A weal diameter of less than 3 mm considered as negative.*

enrolment: all 11 in the resolved group and 12 of those with persisting symptoms at follow-up. Weal diameters were not significantly different between the two groups at enrolment (P>0·1). At follow-up all but 2 children in the resolved group had negative prick tests, while the group with persisting egg hypersensitivity maintained their positive prick tests (P<0·001). The 2 children with negative skin prick tests at both enrolment and follow-up had persisting symptoms (Figure).

There were no differences between the two groups in the rate of positive inhalant or milk prick test reactions.

Immunoglobulins. Throughout both groups there was a good correlation between RAST to egg and egg prick test weal diameter (r=0·69), when radioimmune assay counts were considered. However this correlation was increased to r=0·71 when RAST scores were used due to a clustering effect caused by the grouping. It was further raised to r=0·74 by grouping skin prick diameter sizes in grades. The 2 children in the resolved group with positive prick tests had correspondingly positive RASTs.

The total IgE levels tended to be higher in the persisting group at follow-up but this was not statistically significant, P>0·05. There were no differences between the groups in the levels of IgG, IgA, and IgM.

Prick test negative group. The 2 children with negative skin prick tests to egg but with a clinical egg hypersensitivity differed from the prick test positive children in several ways. As well as having negative egg prick tests they were the only children in whom there was a change of timing of the adverse reaction. Initially their reactions occurred within 30 minutes but at follow-up the onset was not until 3 or 4 hours. Their reactions were mainly gastrointestinal although Case 24 had cutaneous symptoms in the first 2 years. In both responses to RAST to egg were negative.

Discussion

Skin testing of foods is generally considered to be unreliable.[7] Perhaps this is because the scratch test has been used which is less sensitive than the prick test,[8] or perhaps small reactions have been overread. Others have found that skin prick testing with food allergens is helpful[6 9 10] although it depends on the type of food tested.[11]

The clinical significance of positive egg tests is unknown. About half of children with eczema have positive egg tests[1] although this varies from 12%[12] to 86%[13] depending on patient selection and the criteria used for reading the tests. Although a positive egg prick test does not necessarily imply a clinical sensitivity, if clinical sensitivity exists then this study

shows that the egg prick test may be a useful guide in following its course.

The 2 children with resolved egg hypersensitivity but persisting egg prick tests had been able to tolerate egg clinically for only a few months and had decreasing weal sizes. There seems to be an interval between the disappearance of clinical and skin sensitivity. Skin prick weal size at enrolment did not give any indication of the clinical course.

We found that RAST results for egg discriminated less well between the two groups than prick tests, but this is contrary to the findings of Gavani *et al.*[14] This may be because the RAST is a more sensitive measurement and persists after clinical sensitivity is lost and after the prick tests become negative. The two children (Cases 9 and 11) who had inappropriately high RAST scores for skin tests both had very high IgE levels, 5800 and 3020 IU/ml. This may have affected the RAST scores. Total IgE levels were otherwise unhelpful.

The number of years of egg allergy differs between the two groups. If children tend to outgrow their allergies then one would expect the resolved group to have been older than the persisting group. This was not the case and thus supports the observation that egg hypersensitivity is likely to persist in children who retain a positive egg prick test and in those children whose symptoms include angioedema or respiratory symptoms, or in those who have more than one system affected by the adverse reaction.

Egg hypersensitivity has often been regarded as contraindicating immunisation with attenuated measles virus vaccine. During this study several children were immunised with chick fibroblast cultured measles vaccine without any adverse local or systemic reaction, which confirmed earlier reports[15–17] on the complete safety of measles vaccine in egg-hypersensitive individuals. Acute reactions to measles vaccine have been reported in children who were not hypersensitive to egg.[18] In contrast, influenza and probably other vaccines which are produced *in ovo* have caused serious systemic reactions in egg-hypersensitive individuals.[19]

Angioedema, respiratory symptoms, multiple system involvement, and persistence of a positive egg skin-prick test may be useful as prognostic indicators of egg hypersensitivity and may reduce the need for frequent challenges with egg. Further follow-up is necessary to determine the natural history of the persisting group and to ensure that there is no reappearance of egg hypersensitivity in the resolved group. Also a prospective longitudinal study is needed to test the reliability of these proposed prognostic indicators.

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