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Effect of Short-term Egg Exclusion Diet on Infantile Atopic Dermatitis and its Relation to Egg Allergy:

A single-blind test

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A unique, single-blind, controlled trial of egg exclusion was performed in infants under 3 years of age, with atopic dermatitis, and/or their breast-feeding mothers. All subjects were put on an exclusion diet, but assessment of the effect of egg exclusion was made without knowing the results of allergy the tests. Results showed that there was a statistically significant correlation between the effect of egg exclusion and egg allergy, but *only* in infants 3–6 months old. Combination with other allergies did not seem to affect the results at this age. These findings indicate that egg exclusion is effective in ameliorating skin symptoms of atopic dermatitis *only* in early infancy and in the presence of egg allergy, irrespective of combination with other food allergies. This may be correlated to high RAST scores to egg at this age. *Key words: Food allergy; IgE.*

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The relation of foods and infantile atopic dermatitis is still a subject of controversy. Despite the well-known report of Atherton (1) confirming the effect of egg exclusion diet on atopic children aged 2 to 8 years, most dermatologists still hesitate to introduce the exclusion diet as a treatment for atopic dermatitis (AD). Recent reports (2, 3) from the pediatric field suggest that the occurrence of AD can be suppressed by excluding eggs, cow's milk and fish or peanuts from the diet of breast-feeding mothers and of infants up to 6 months of age but not later than that.

However, whether the effect of diet manipulation is related to IgE allergy to foods has not yet been clarified. Sampson & McCaskill (4) reported that food restriction caused significant improvement in AD when it was based on food challenge tests. They dealt with subjects having a wide range of ages, from 4 months up to 24.5 years. On the other hand, our experience indicates that the most frequent and intense allergy seen in infantile AD is egg allergy (unpublished data). Therefore, we considered that egg exclusion only might be adequate if diet manipulation were effective against infantile AD. This prompted us to undertake the following single-blind controlled trial of a unique scheme to ascertain the relationship between the effect of egg exclusion, and egg allergy.

Table I. *Number of cases and reasons for exclusion and drop-out*

Age	3–6M	7–11M	1Y	2Y	Totals
Considered cases	(84	44	75	52)	(255)
Excluded cases	(17	8	11	6)	(42)
Taking a small amount of egg (already excluding eggs)	3	7	10	6	26
Solely milk-fed	9				9
Required immediate treatment	3	1			4
Unsuccessful venipuncture	2		1		3
Cases enrolled	(67	36	64	46)	(213)
Drop-out cases	(34	11	18	12)	(75)
(Reasons)					
Did not visit again	4	2	1	1	8
Did not exclude eggs as instructed	4	1	5	3	13
Restricted foods other than eggs	14	5	3	5	27
Change of symptom by infections	5	3	3	1	12
Change of treatment	6		2	1	9
Effect not indicated	1		4	1	6
Analysis cases	(33	25	46	34)	(138)

M = months. Y = years

PATIENTS AND METHODS

Newly visiting infants under 3 years of age, diagnosed as having infantile eczema or AD at our out-patient clinic during January to December 1988, were all considered as subjects for this investigation. Their breast-feeding mothers were asked how many eggs they or their infants had eaten. Purely milk-fed infants, infants already on egg exclusion diet, or those eating only a small amount of egg (less than 3 eggs per week for mothers of purely breast-fed babies, less than 1 egg per week for infants under one year of age and not taking breast milk, and less than 2 eggs per week for infants aged 1 and 2 years) were excluded from the study.

Skin symptoms and treatment were confirmed to have been unchanged during the preceeding 2 weeks. Infants with severe skin symptoms and who needed immediate treatment were also removed from the study.

The remaining cases were enrolled in the study. The whole body

Table II. *Ages of infants, effects of egg exclusion and their relation to allergy*

Age	3–6M		7–11M		1Y		2Y	
Effect	Yes	No	Yes	No	Yes	No	Yes	No
Allergy	Number of cases							
Egg (+) Others (+)	6	4	3	1	2	2	1	5
Egg (+) Others (−)	7	3	3	4	2	6	0	2
Egg (−) Others (+)	0	1	0	0	0	5	3	6
Egg (−) Others (−)	3	9	5	9	5	24	2	15
	16	17	11	14	9	37	6	28
Total 138	33		25		46		34	

Table III. *Comparison of the effects of egg exclusion between single egg allergic infants and all negative infants*

Age	3–6M		7–11M		1Y		2Y	
Effect	Yes	No	Yes	No	Yes	No	Yes	No
Allergy	Number of cases							
Egg (+) Others (−)	7	3	3	4	2	6	0	2
Egg (−) Others (−)	*3	9	5	9	5	24	2	15
	10	12	8	13	7	30	2	17
Total 99	22		21		37		19	

* $p<0.05$ (Fisher's exact test).

was examined and eruptions were sketched and photographed. Skin symptoms were graded into three categories (+1, +2, +3). Mothers were asked to stop using eggs for cooking and not to take or to give their infants eggs in any form for 2 weeks. This included egg-containing manufactured products such as cookies and cakes. The numbers of eggs and egg-containing products eaten by mothers and infants were recorded.

No additional treatment was given and the previous treatment was kept unchanged during 2 test weeks, especially regarding the frequency and day of application of local treatment. Radioallergosorbent test (RAST) was performed for egg white, milk, soybean, wheat, house dust and mites and scores of 2.0 or higher were regarded as positive. Infants in whom venipuncture for RAST was unsuccessful could not be included in the investigation.

When the mothers and infants visited 2 weeks later, it was ascertained that egg exclusion had been appropriate, that the infants had not experienced any acute infectious disease such as common cold and that the same treatment had been strictly adhered to. Patients who did not conform to these requirements were deemed to be drop-outs and were excluded.

In the remaining patients, skin conditions were judged as either better (effective) or not (unchanged and worse) (ineffective), without knowing the result of RAST, and with the help of sketches and photographs taken at the first visit. The subjects were then skin-tested with seven antigens (egg, milk, soy, wheat, rice and house dust) and the results were read by a conventional method. A patient was regarded as allergic when either RAST or skin test proved positive. The relation between the effect of egg exclusion and egg allergy with respect to other allergy was tested statistically.

RESULTS

Altogether 255 patients were considered for investigation,but 42 were later excluded for various reasons, as shown in Table I. The remaining 213 cases were enrolled in the study. Of these, however, 75 dropped out for reasons also listed in Table I, ultimately leaving 138 cases (age: 3–6 months, $n=33$; 7–11 months, 25; 1 year, 46; and 2 years, 34) for investigation.

Table IV. *Comparison of the effects of egg exclusion between egg-positive and egg-negative groups*

Age	3–6M		7–11M		1Y		2Y	
Effect	Yes	No	Yes	No	Yes	No	Yes	No
Allergy	Number of cases							
Egg (+)	13	7	6	5	4	8	1	7
Egg (−)	*3	10	5	9	5	29	5	21
	16	17	11	14	9	37	6	28
Total 138	33		25		46		34	

* $p<0.05$ (Fisher's exact test).

Table V. *Comparison of age between egg-positive and egg-negative groups in infants 3–6 months old*

Age (months)	3	4	5	6
Allergy	Number of cases			
Egg (+)	20	6	3	6	5
Egg (−)	13	5	3	1	4
Total	33	11	6	7	9

No statistical difference by χ^2-test.

In Table II, the ages and allergic states of the patients and the effects of egg exclusion are summarized. Egg allergy was frequent under 1 year of age; 3–6 months (60.6%) and 7–11 months (44.0%), as compared with 1 year (26.1%) and 2 years (23.5%). Single egg allergy was also common in young infants: 3–6 months (30.3%) and 7–11 months (28.0%), as compared with 1 year (17.4%), and was rare in 2-year-olds (5.9%).

Allergies other than egg allergy are also reported in Table II; 3–6 months (33.3%), 7–11 months (16.0%), 1 year (19.6%) and 2 years (44.1%). Of these, those observed in 3–6-month-olds and 7–11-month-olds were exclusively food allergies and most of them were present in combination with egg allergy. Conversely, inhalant allergies appeared in 1 year and increased in 2 years, whereas food allergies decreased with age (also seen in Table IX).

Subjects without any allergy formed a large proportion in all age groups except 3–6 months (36.4%); 7–11 months (56.0%), 1 year (63.0%), and 2 years (50.0%).

Judgement of egg exclusion as 'effective' was frequent in 3–6 months (48.5%) and 7–11 months (44.0%) but rare in 1-year-olds (19.6%) and 2-year-olds (17.6%). There was a significant difference (χ^2-test) between 3–6 months and 1 year or 2 years ($p<0.01$) and between 7–11 months and 1 year or 2 years ($p<0.05$).

The effect of egg exclusion was compared between the single egg allergy group and the all negative allergy group, in each age category (Table III). Fisher's exact test showed that there was a significant relation ($p<0.05$) between the effect and egg allergy *only* for 3–6-month-olds.

Table IV compares the effect of egg exclusion between egg-positive and -negative groups, irrespective of presence of absence of other allergies in each age category. The χ^2-test

Table VI. *Comparison of severity of skin symptoms between egg-positive and egg-negative groups in infants 3–6 months old*

Severity	+	++	+++	
Allergy	Number of cases			
Egg (+)	20	5	12	3
Egg (−)	13	6	5	2
Total	33	11	17	5

No statistical difference by χ^2-test.

Table VII. *Comparison between egg-positive and egg-negative groups of the amount of ingested egg by breast-feeding mothers of infants 3–6 months old*

Number of eggs ingested	Mother		
	–7 per week	7–5	5–3
Allergy	Number of cases		
Egg (+)	20	7	5	8
Egg (–)	13	3	4	6
Total	33	10	9	14

No statistical difference by χ^2-test.

indicated that a statistically significant relation between the effect and egg allergy was present *only* in 3-6-month-olds ($p<0.05$).

Age of patient (Table V), severity of skin symptom (Table VI), amount of egg eaten by mother (Table VII) and method of ingestion (Table VIII) were all compared between the egg allergy group and the egg-negative group in the age category 3–6 months, by χ^2-test, but no statistical difference was found in any test. These were also compared between the single egg allergy group and the all-negative group (not shown), but here too there was no significant difference. The tests in other age categories also showed no significant difference (not shown).

Table IX reports food and inhalant allergies other than egg observed in the infants studied in this investigation. The total number of milk, wheat and soy allergies were statistically more frequent in 3-6-month-olds than in 1-yers-olds ($p<0.01$) or 2-year-olds ($p<0.05$), by χ^2-test, but house dust and mite allergies were only observed in 1-year-olds and 2-year-olds.

RAST scores for egg white in egg-allergic infants in each age category are shown in Table X. Scores were compared between different age categories and found to be significantly higher in 3–6-month-olds than in 7–11-month-olds ($p<0.05$) and 1-year and 2-year-olds ($p<0.01$) by median value test.

DISCUSSION

The purpose of this study was to learn the effect of egg exclusion in atopic dermatitis and its relation to the age of infants and to egg allergy. A double-blind controlled trial is an ideal way to examine the effect of any kind of treatment in diseases.

Table VIII. Comparison of nutrition between egg positive and egg negative groups in 3–6 months of age

		Nutrition	
		Breastfed *n*	Breast & milkfed, *n*
Allergy			
Number of cases			
Egg (+)	20	15	5
Egg (–)	13	10	3
Total	33	25	8

No statistical difference by χ^2-test.

Table IX. *Comparison of allergies other than egg allergy in each age group*

Age	3–6M		7–11M		1		2	
Egg allergy	(+)	(–)	(+)	(–)	(+)	(–)	(+)	(–)
Number of cases	20	13	11	14	12	34	8	26
Total	33		25		46		34	
Number of allergy			*		**		*	
Food	15		5		6		6	
milk (+)	8	1	3	0	1	1	3	1
wheat (+)	4	0	1	0	2	1	1	0
soy (+)	2	0	1	0	1	0	1	0
Inhalant	0		0		7		17	
house dust (+)	0	0	0	0	2	2	2	6
mite (+)	0	0	0	0	1	2	2	7
Number of cases with other allergy	10	1	4	0	4	5	6	6

Statistical difference of total number of food allergies from 3–6 months: $^*p<0.05$, $^{**}p<0.01$ by χ^2-test.

It is especially important in atopic dermatitis because the clinical course of this disease is influenced by many factors, such as infections, sleeplessness, lassitude and psychic stresses. But it is well known that a double-blind test is difficult to apply to a diet restriction study because compliance rates are usually low in this kind of study (5). Moreover, an increasing number of mothers of atopic children are restricting foods (mainly egg and milk) of their own volition, these days in Japan. In such circumstances, a double-blind study seemed difficult to accomplish within a limited period of time. These are the reasons why we started this single-blind study of a unique scheme.

In our study, all subjects were known to belong to the diet group. Assessment of the effect might be influenced by previous knowledge, but its relation to the allergy was 'blind'. Egg-negative patients served as controls. Therefore, our study is a kind of 'single-blind' controlled study.

Results indicated that the effect of egg exclusion was related egg allergy *only* in infants 3–6 months of age. Since none of these infants were taking solid foods and were nourished exclusively by breast-feeding (75.8%) or combined with milk-

Table X. *RAST scores to egg white in egg allergic infants in four age groups*

Age	3–6M	7–11M	1	2
Number of cases	20	11	12	8
RAST score		*	**	**
>4.0	3	1	0	0
3.5	9	1	2	0
3.0	1	1	0	1
2.5	3	2	1	2
2.0	2	2	7	2
<2.0	2	4	2	3

Statistical difference from 3–6 months: $^{**}p<0.01$, $^*p<0.05$ by median value test.

feeding, exclusion of egg from breast-feeding mothers seems to be an important factor in this effect. More interestingly, the diet effect in this age group was not influenced by the presence of other food allergies. We cannot make any other comment on this, since ingestion of other foods was not recorded in this study. But this give us hope that such a simple diet as egg exclusion might well ameliorate skin symptoms of egg-allergic infantile atopic dermatitis.

Reasons of the failure to demonstrate the diet effect and consequently its relation to egg allergy in other age groups are not known, a lower intensity of egg allergy, or combination with inhalant allergy might explain this.

To summarize, this study is still a preliminary step to achieve full understanding of the role of food allergy in atopic dermatitis. However, it suggests that treatment of atopic dermatitis by diet manipulation is effective only in early infancy, in relation to IgE allergy.

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