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Letter to the Editor

# Egg antigen was more abundant than mite antigen in children's bedding: Findings of the pilot study of the Japan Environment and Children's Study (JECS)

### Dear Editor,

Hen's egg is the most common cause of early childhood food allergy in Japan<sup>1</sup> and a major cause in Europe also.<sup>2</sup> A Japanese birth cohort study showed that eczema in early infancy considerably increased the risk of food allergy in childhood,<sup>3</sup> supporting the hypothesis that cutaneous exposure to food antigens is an important pathway of allergic sensitization.<sup>4</sup> Therefore, it is essential to demonstrate the existence of food antigens in children's environment to confirm this mechanism.

Peanut consumption is related to high amounts of peanut protein detected in house dust and secondarily to the possibility of the development of peanut allergy.<sup>5</sup> Egg and milk antigens were also detected in the mattresses of Norwegian homes,<sup>6</sup> and a recent study showed that egg protein levels in the household environment were clearly correlated to egg consumption.<sup>7</sup>

The Japan Environment and Children's Study (JECS) is a largescale, nationwide, multicenter, birth cohort study launched in 2011.<sup>8</sup> The pilot study of JECS started prior to the main study.<sup>9</sup> In this study, we evaluated the egg protein and house dust mite antigen levels detectable in the dust from the bedsheets of the participants in the JECS pilot study.

Between February 2009 and March 2010, parturients receiving outpatient care with cooperating health-care providers of the regional centers participating in the Pilot Study of IECS and their partners received an explanation of the Pilot Study, and 453 pregnant women (participating mothers) provided consent for participation. Of 440 participating children born from 436 participating mothers out of these 453 pregnant women, 94 agreed to participate in the study of home visit survey where dust samples were collected from the bedsheets of participating children aged 3. We analyzed dust samples (n = 94) for egg protein and house dust antigen. A dust filter mounted on a vacuum cleaner nozzle (Dyson handy cleaner DC34) was used. The proteins were extracted from the dust samples using PBS. The quantity of egg protein (wholeegg protein including ovalbumin, ovotransferrin, and ovomucoid) was measured by an ELISA kit (FASTKIT ELISA Version II; Nipponham Foods, Osaka, Japan). The house dust mite (HDM) protein from both Dermatophagoides farinae and D. pteronyssinus was measured by ITEA Der f 1/Der p 1 ELISA kits (ITEA, Tokyo, Japan). The upper limit of the quantitative value for egg protein and house dust mite protein was set to 60 µg/g. For statistical analysis, we defined 60  $\mu$ g/g and over was 60  $\mu$ g/g. Dermatophagoides 1 (Der 1) was defined as the sum of *D. pteronyssinus* (Der p 1) and *D. far-inae* (Der f 1), and the maximum level for Der 1 was set to 60  $\mu$ g/g, because the exact values over this point were not infallibly available for all the samples after the sum of the two parameters when one of them exceeded 60  $\mu$ g/g. Nonparametric statistical analysis was applied to compare the egg protein and HDM antigen levels.

The study protocol was reviewed and approved by the ethics committees of the National Center for Child Health and Development (approved number is 1562) and each institute. Written consent was obtained from all the caregivers.

Dust samples were collected from the bedsheets of 94 children, and egg protein was measured in 88 samples. The characteristics of children are shown in Table 1. As for the home environment, 52.3% were living in a detached house with more than two floors (47.7% were living in an apartment). A quarter of the children had no sibling, and 8.2% had a cat or dog at home.

Egg protein was detected in all the samples with the median egg protein level of 43.7  $\mu$ g/g dust (range 0.9–60  $\mu$ g/g). The median Der p 1, Der f 1 and Der 1 levels were 2.4  $\mu$ g/g dust (range 0.1–60  $\mu$ g/g), 1.4  $\mu g/g$  dust (range 0.1–60  $\mu g/g)$  and 7.8  $\mu g/g$  dust (range 0.1–60  $\mu$ g/g), respectively. In the dust samples, 73%, 98%, 99% and 97% of the results for hen's egg, Der p 1, Der f 1 and Der 1 were found above the upper limit of 60  $\mu$ g/g. The amount of egg protein was significantly greater than the amount of Der p 1, Der f 1, or Der 1 (Fig. 1) (p < 0.001, Wilcoxon rank-sum test). Furthermore, we found a higher concentration of egg protein in 80% of the dust samples comparing to HDM levels in the same ones. To be more specific, 59% samples showed a two-fold and higher level, 25% showed a ten-fold and higher level, and 7% showed more than a 100foldhigher level of egg protein than Der 1. No statistical association was found between the quantity of egg protein in the dust samples and the different background characteristics of the participants shown in Table 1.

The detection of food antigens in the household environment is essential to explain the cutaneous sensitization pathway in food allergy. Only a few studies of food antigen detection in household dust exist, most of which concern the peanut antigen.<sup>5</sup> A recent study showed the presence of egg protein in dust samples from various areas in the home following the cooking and consumption of eggs.<sup>7</sup> In this study, we found a high amount of egg protein in all the dust samples from the bedsheets of children. To our knowledge, this is the first study of reporting the detection of food antigens in the household environment of Japan. The preparation and

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### Table 1

Background characteristics of the study population.

	Ν	%	Total available data (N)
Participants' allergic background			
Diagnosed bronchial asthma	10	11.8	85
Diagnosed atopic dermatitis	15	17.4	86
Elevated egg white specific IgE	18	20.5	88
Symptoms after egg consumption	10	11.4	88
Egg elimination diet (total and partial)	11	12.8	86
Family history of allergy			
Mother			
Bronchial asthma	7	8.5	82
Atopic dermatitis	3	3.7	82
Allergic rhinitis	19	23.2	82
Urticaria and others	3	37	82
Father	5	5.7	02
Bronchial asthma	24	31.6	76
Atopic dermatitis	24	31.6	76
Allergic rhinitis	28	36.8	76
Urticaria and others	0	0.0	76
Home environment characteristics	0		
Siblings			
No sibling	22	25.0	88
Older siblings	51	58.0	88
Younger siblings	27	30.7	88
Both older and younger siblings	16	18.2	88
Parental smoking		1012	
Maternal smoking	6	71	85
Paternal smoking	27	31.8	85
Pets		5110	
Total	12	14.1	85
Dogs or cats	7	82	85
Others	8	9.4	85
Dwelling characteristics	-		
Type of dwelling			
Detached house	46	52 3	88
Apartment	42	47.7	88
Time from construction			
Less than 5 years	23	28.8	80
From 5 to 20 years	35	43.8	80
More than 20 years	12	15.0	80
Dwelling size			
Smaller than 60 $m^2$	28	32.2	87
Between 60 $\text{m}^2$ and 120 $\text{m}^2$	41	47.1	87
Larger than 120 m <sup>2</sup>	18	20.7	87
Larger than 120 m <sup>2</sup>	18	20.7	8/



**Fig. 1.** Egg and house dust mite allergen (Der 1, Der p 1, and Der f 1) protein levels in the dust samples collected from the homes of participants aged 3 years in the JECS pilot study. The egg protein level was significantly higher than the Der 1, Der p 1, or Der f 1 proteins levels (p < 0.001, Wilcoxon rank-sum test).

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consumption of food containing egg as an ingredient is incontestably the source of the egg protein, but how it spread throughout the household environment is still unclear. The spread of vapors containing egg protein during cooking is one possibility in restricted areas close to the kitchen. However, the children's bed was not always located on the same floor as the kitchen, suggesting that another pathway for the spread of egg protein exists. The skin, hands, and saliva of people living in the house were reported to be possible vectors of peanut protein dispersion,<sup>5</sup> and egg protein may spread throughout a dwelling in the same way. Further investigation is needed to confirm this hypothesis.

The disparity found in the amount of egg protein may be related to several factors. Our samples were collected in accordance with a common protocol using a vacuum cleaner, but the sampling conditions were not strictly controlled. Differences in the participants' lifestyle, the frequency and the timing of egg consumption may also have influenced.<sup>7</sup>

In conclusion, egg protein was detected from all the samples collected from the bedsheets of participants in a cohort study in higher concentrations than HDM antigen. Further investigation into the biological characteristics of egg protein in household dust as well as more accurate epidemiological and biological investigation aimed at clarifying the environmental conditions of egg sensitization is needed.

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Conflict of interest

The authors have no conflict of interest to declare.

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#### References

- Ebisawa M, Ito K, Fujisawa T. Japanese guidelines for food allergy 2017. Allergol Int 2017;66:248–64.
- Nwaru BI, Hickstein L, Panesar SS, Roberts G, Muraro A, Sheikh A. Prevalence of common food allergies in Europe: a systematic review and meta-analysis. *Allergy* 2014;69:992–1007.
- Shoda T, Futamura M, Yang L, Yamamoto-Hanada K, Narita M, Saito H, et al. Timing of eczema onset and risk of food allergy at 3 years of age: a hospitalbased prospective birth cohort study. J Dermatol Sci 2016;84:144–8.
- Lack G. Update on risk factors for food allergy. J Allergy Clin Immunol 2012;129: 1187-97.
- Brough HA, Simpson A, Makinson K, Hankinson J, Brown S, Douiri A, et al. Peanut allergy: effect of environmental peanut exposure in children with filaggrin lossof-function mutations. J Allergy Clin Immunol 2014;134:867–75. e1.
- Bertelsen RJ, Faeste CK, Granum B, Egaas E, London SJ, Carlsen KH, et al. Food allergens in mattress dust in Norwegian homes - a potentially important source of allergen exposure. *Clin Exp Allergy* 2014;44:142–9.
- Trendelenburg V, Tschirner S, Niggemann B, Beyer K. Hen's egg allergen in house and bed dust is significantly increased after hen's egg consumption - a pilot study. *Allergy* 2018;**73**:261–4.
- Kawamoto T, Nitta H, Murata K, Toda E, Tsukamoto N, Hasegawa M, et al. Rationale and study design of the Japan environment and children's study (JECS). BMC Publ Health 2014;14:25.
- 9. Ayabe T, Yamamoto-Hanada K, Mezawa H, Konishi M, Ishitsuka K, Saito M, et al. Regional differences in infant 25-hydroxyvitamin D: pilot study of the Japan environment and children's study. *Pediatr Int* 2018;**60**:30–4.

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