

## Is hen's egg allergy decreasing among Japanese children in nurseries?

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The prevalence of food allergies (FA) has been shown to be increasing in industrialized countries worldwide [1], although the exact reasons remain unknown. Since 2015, however, accumulating data have shown that early introduction of allergenic foods, such as peanuts [2], hen's eggs [3], and cow's milk [4], can prevent the development of FA. In accordance with these promising results, early introduction of allergenic foods to infants started to be recommended in guidelines around the world [5]. In Japan, a proposal for preventing hen's egg allergy was announced by the Japanese Society of Pediatric Allergy and Clinical Immunology (JSPACI) in 2017. Introduction of small amounts of boiled hen's egg from 6 months of age was recommended under doctor's supervision to infants with atopic dermatitis, who had higher risk of developing hen's egg allergy (HEA). Also in 2019, a Japanese guideline regarding lactation and weaning from the Ministry of Health,

Labour and Welfare (MHLW) was revised to indicate that weaning should be started at 5–6 months of age, and that no scientific evidence currently supports delaying the introduction of allergenic foods as a means of preventing FA. High levels of adoption of this advice can be expected [6], as many medical staff members have started to advise caregivers to follow these guidelines. Hence, the next important question is whether this recommendation can actually lead to reductions in FA.

In 2013, we performed a questionnaire-based survey of all licensed nurseries in Shiga Prefecture, Japan, regarding the management of food-allergic children [7]. In 2021, we repeated the same survey to identify changes in the situation. In both studies, the rate of children with FA was surveyed. We took advantage of this opportunity to determine the change in prevalence of FA among children attending nurseries between these time points, during which the proposal and revised guideline were issued in Japan.

In 2013 and 2021, a questionnaire regarding the management of children with FA was distributed to all licensed nurseries in Shiga Prefecture, Japan. The questionnaire included questions on the number and age of children with FA. In the questionnaire, we defined children with FA as those with food avoidance under physician's diagnosis and written instruction for avoidance of causative foods. Regarding those with FA, the kinds of foods that were avoided were also determined. The chi-squared test was used to compare results

between 2013 and 2021 using SPSS Statistics (version 27.0; IBM, Armonk, NY, USA).

Two-tailed values of  $P < 0.05$  were considered statistically significant. The study was approved by the Ethics Committee of Ryukoku University (approval no. 2021-15).

Written informed consent was obtained from all the nurseries involved.

Completed questionnaires were recovered from 237 of the 264 nurseries (recovery rate, 89.8%) surveyed in 2013, and from 261 of the 340 nurseries (recovery rate, 74.6%) surveyed in 2021, respectively. The numbers of children attending these nurseries were 26,210 in 2013 and 30,047 in 2021, respectively. The total prevalence of FA decreased from 6.1% in 2013 to 5.7% in 2021 ( $P = 0.044$ ) (Figure a). The prevalence increased among 4- and 5-year-old children, but decreased among 0-, 1-, and 2-year-old children. Statistical significance was observed at 1 year old ( $P = 0.002$ ), 2 years old ( $P = 0.002$ ) and 4 years old ( $P = 0.007$ ). When prevalences were compared according to avoided foods, significant decreases were observed for hen's egg ( $P < 0.001$ ), buckwheat ( $P < 0.001$ ), soybean ( $P < 0.001$ ) and others ( $P = 0.007$ ) (Figure b).

The declining trend in FA seen here is in line with a survey by Tokyo Prefecture showing a decline in FA at 3 years old from 17.1% in 2014 to 14.9% in 2019. Moreover, in our data, the decrease was most prominent for hen's egg. Interestingly, the prevalence of FA started to decrease among children 2 years old and younger. Children who were 2 years

old in 2021 were born in 2019, when the revised MHLW guideline for lactation and weaning was issued and 2 years had passed since the JSPACI proposal for early introduction of hen's eggs to the diets of children. It is therefore tempting to speculate that the decrease was, at least partially, caused by the adoption of these recommendations by caregivers. The data implies the effectiveness of these "early introduction" and/or "no delay of introduction" approaches for the prevention of FA.

One strength of this study was the high response rate obtained from licensed nurseries in Shiga Prefecture, and the data from large numbers of children in nurseries could be analyzed without selection bias. Also, data from different time points were obtained from the same area using the same methods, enabling analysis of trends over time. A limitation of the study was that the definition of FA was based solely on reports from the participating nurseries. Definitions were identical for the two time points and included strict avoidance of causative foods based on diagnosis and instructions from physicians, enabling direct comparisons. However, it is still possible that the decrease may be caused by the decrease of unnecessary avoidance, rather than real FA, due to early intake recommendation. In any case, the recommendation might work to decrease children with food avoidance. Another limitation was that the data were obtained from only one prefecture in Japan. A larger-scale nationwide survey is warranted to confirm this

declining trend.

In conclusion, based on two consecutive surveys of licensed nurseries in Shiga Prefecture, Japan, a decreasing prevalence of FA, most prominently for hen's egg allergy, was observed among children in nurseries. The trend was evident for children born in and after 2019, approximately the same time that "early introduction" and "no delay of introduction" guidelines for allergenic foods started to be promoted.

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### **Conflict of interests**

The authors declare that they have no relevant conflicts of interest.

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## Legends for Figure

Figure. Prevalence of food allergy among children in nurseries by age (a) and causative allergen (b).

