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Original article

# Natural history of immediate-type hen's egg allergy in Japanese children

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*Abbreviations:*
EW, egg white; HE, hen's egg; Immunoglobulin E, IgE; OFC, oral food challenge; OM, ovomucoid; SEM, standard error of the mean

ABSTRACT

*Background:* Hen's egg (HE) allergy develops during infancy. We investigated tolerance acquisition in Japanese children allergic to HE aging <6 years.
*Methods:* In this retrospective study, 226 children born in 2005 with a history of immediate-type HE allergy underwent an oral food challenge (OFC). Tolerance was defined as no reaction to an OFC with half of whole heated HE or accidental HE consumption at home. Participants were divided into three groups based on age at tolerance acquisition: group I (<3 years) ($n = 66$), group II (3–6 years) ($n = 98$), and group III (prolonged allergic groups) ($n = 62$).
*Results:* Tolerance acquisition occurred in 30% (66/226) by 3 years of age, 59% (133/226) by 5 years of age, and 73% (164/226) at 6 years of age. At 3 years, incidences of allergy-related complications (bronchial asthma, $p = 0.02$; atopic dermatitis, $p = 0.04$) were higher in the group III than in the group I. Anaphylaxis to any food occurred more frequently in the group III than in the group I ($p = 0.03$); anaphylaxis to HE was more common in the group III ($p = 0.04$). Egg white (EW)- and ovomucoid (OM)-specific immunoglobulin E (IgE) levels were higher in the group III than in the group I ($p < 0.05$).
*Conclusions:* The group III experienced HE-related anaphylaxis and complications more frequently and exhibited sustained, high EW- and OM-specific IgE levels.


## Introduction

Diagnosis of a food allergy is associated with a significant deterioration in quality of life. In Japan, the most common food allergy is to hen's egg (HE).[1] Food allergies are common among infants aging <1 year and they diminish with age, indicating that tolerance develops with age. The estimated prevalence of food allergy in Japan is 5%–10% among infants and 1%–2% among schoolchildren.[1,2] The basis of food allergy treatment is elimination of the offending food from the diet.[3] Regarding the clinical practice of food allergy medicine, it is important to determine the timing of tolerance acquisition, so that elimination of the allergen from the diet is no longer necessary.

In Western countries, many investigators have studied the natural history of food allergy in children and have discussed the factors associated with the prolongation of food allergy.[4–14] In contrast, only two reports have been published so far about the natural history of food allergy in Japan.[15,16] Ikematsu *et al.*[15] investigated the rate of tolerance acquisition in children aging <3 years allergic to HE, cow's milk, and wheat, and Imai *et al.*[16] investigated the prolongation of food allergies in children up to 6 years who were diagnosed with food allergy to HE by a definitive history of positive food allergic reactions or food provocation tests.

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In this study, based on an oral HE challenge in Japanese children aged 6 and under years, and the large number of the study population in Japan, we retrospectively investigated tolerance acquisition and factors related to the prolongation of immediate-type HE allergy.

## Methods

### *Study population*

We conducted a retrospective study using the clinical records of children with HE allergy born in 2005 who presented at our hospital with a history of an immediate-type reaction. The cohort was followed up at our department until 6 years of age. HE allergy was defined as the presence of an allergic reaction after the ingestion of a raw or heated HE, or a positive physician-supervised OFC with HE.

The history of an immediate-type reaction to HE can vary from urticaria to severe responses, such as anaphylaxis. Children were included if they were instructed to eliminate HE from their diet after presentation, and if an immediate-type allergic reaction occurred following accidental ingestion of HE after HE elimination. Patients who were not given HE because of their levels of antigen-specific immunoglobulin E (IgE) or who did not ingest HE were excluded. Additionally, patients where follow-up to the age of 6 was impossible or who received oral immunotherapy were excluded. Moreover, children were excluded from this study if they presented at our department with severe atopic dermatitis and unstable asthma had no history of HE ingestion, or started an egg-elimination diet because of a high level of egg white (EW)-specific IgE but had a negative result to the OFC. This study was approved by the ethics committee of Sagamihara National Hospital.

### *Oral food challenge*

For patients on an egg-elimination diet, OFC using heated whole HE yolk was conducted in our department. In our department, OFC was undertaken based on the Japanese Guideline for Food Allergy. It was undertaken more than 1 year after the last immediate allergic responses to HE because of confirmed tolerance to HE allergy. The age at which OFC could be undertaken was decided by a primary doctor. However, if the diagnosis of HE allergy was unclear, we confirmed it by performing OFC.[2] If the result was negative, OFC using pumpkin cake containing half of whole heated HE was undertaken. The half of whole heated HE was cooked at 1000 W for 90 s in a microwave. The result of the OFC was deemed positive or negative based on the presence or the absence of clear objective symptoms on the skin or of the respiratory, digestive, cardiovascular, and nervous systems. Patients with objective symptoms who did not require treatment were designated undetermined. Undetermined patients were considered negative when no clear objective symptoms were observed after repeated ingestion of HE at home. Tolerance acquisition was recorded when a negative or undetermined response to the OFC was achieved after a 2- to 4-week period when half of whole heated HE was regularly ingested at home.

OFC to determine tolerance acquisition was conducted when more than 1 year had passed since the last episode of symptoms caused by accidental ingestion of egg, or if OFC was requested by parents or guardians on the precondition that a reduction in the level of EW-specific IgE was measured during the elimination period. Open challenges are routine at our clinic for very young children and follow the recommendations of the European Academy of Allergology and Clinical Immunology.[17]

### *Study selection*

OFC with half of whole heated HE at home was only conducted in children that had no history of anaphylaxis when an immediate-type reaction occurred more than 12 months before the OFC and measurement of the level of HE-specific IgE was found to be reduced or below 0.70 $kU_A/L$. Participants underwent OFC using half of whole heated HE and ingested half of whole heated EW as a trial at home (Fig. 1). The participants were divided into three groups based on the age at which tolerance to half of whole heated HE was acquired: group I (<3 years), group II (3–6 years), and group III (prolonged allergic groups), the individuals in which continued to present allergic symptoms after the OFC. The rate of tolerance acquisition against half of whole heated HE was investigated over time according to age.

### *Clinical information*

We recorded patient characteristics (gestational age, body weight at birth, type of delivery, sex, breast-feeding during infancy, age at weaning, presence of pets in the home, passive smoking, number of siblings, age at first presentation, presence of symptoms of bronchial asthma, atopic dermatitis, and allergic rhinitis or allergic conjunctivitis at 3 years), family history of complications of allergic diseases (bronchial asthma, atopic dermatitis, allergic rhinitis, and allergic conjunctivitis), and food allergy factors (disease type, age of occurrence, age at which food elimination diets were started, and any history of anaphylaxis caused by any foods or triggered by HE).

### *Serologic findings*

Serologic findings (changes in antigen-specific IgE levels over time) were obtained by measuring specific IgE antibodies to EW and ovomucoid (OM) (ImmunoCAP; Phadia AB, Uppsala, Sweden) after the OFC. However, skin tests were not performed in all participants.

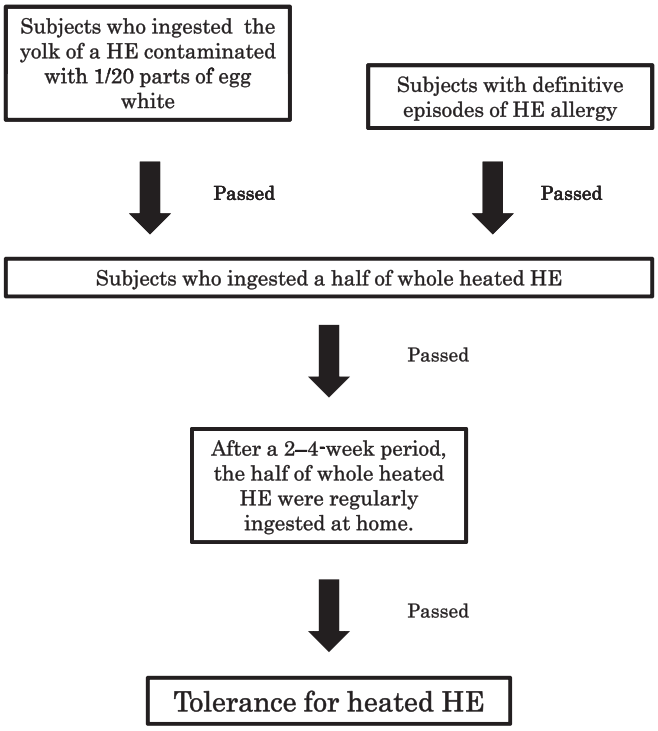


**Fig. 1.** Oral food challenge and tolerance.