Can early introduction of egg prevent egg allergy in infants? A population-based study

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Background: Infant feeding guidelines have long recommended delaying introduction of solids and allergenic foods to prevent allergy in high-risk infants, despite a paucity of evidence.
Objective: We aimed to determine whether confirmed egg allergy in 12-month-old infants is associated with (1) duration of breast-feeding and (2) ages of introducing egg and solids.
Methods: In a population-based cross-sectional study (HealthNuts) parents reported on infant feeding and potential confounding factors before skin prick testing for egg white. Egg-sensitized infants were then offered an egg oral food challenge. Multiple logistic regression was used to investigate associations between diet and egg allergy adjusted for possible confounding factors.
Results: A total of 2589 infants (73% response) participated. Compared with introduction at 4 to 6 months, introducing egg into the diet later was associated with higher risks of egg allergy (adjusted odds ratios [ORs], 1.6 [95% CI, 1.0-2.6] and 3.4 [95% CI, 1.8-6.5] for introduction at 10-12 and after 12 months, respectively). These findings persisted even in children without risk factors (OR, 3.3 [95% CI, 1.1-9.9]; 10-12 months). At age 4 to 6 months, first exposure as cooked egg reduced the risk of egg allergy compared with first exposure as egg in baked goods (OR, 0.2 [95% CI, 0.06-0.71]). Duration of breast-feeding and age at introduction of solids were not associated with egg allergy.
Conclusions: Introduction of cooked egg at 4 to 6 months of age might protect against egg allergy. Changes in infant feeding guidelines could have a significant effect on childhood egg allergy and possibly food allergy more generally. (J Allergy Clin Immunol 2010;126:807-13.)

Key words: *Egg allergy, food allergy, solids, breast-feeding, infant diet, weaning*

IgE-mediated food allergy often develops early in childhood and has a major effect not only on a child's quality of life but also that of his or her family.[1] An estimated 10% to 15% of the population report symptoms of food allergy, although the prevalence of IgE-mediated food allergies (ie, symptoms of food allergy in the context of a positive skin prick test [SPT] response) is reported to be lower at approximately 2% to 5%.[2] The apparent increase in the prevalence of food allergy appears to be a recent phenomenon of the last 20 to 25 years. Of concern are reports that hospitalizations for food allergy–related anaphylaxis, food allergy's most serious and life-threatening manifestation, have increased markedly since 1990 in the United Kingdom,[3] the United States,[4] and Australia,[5] most dramatically in 0- to 4-year-olds, with a 5-fold increase.

The reasons behind this apparent increase in serious food allergy are unknown, and to date, there is little evidence to guide effective prevention. Until very recently, expert guidelines for infants with a family history of allergy typically recommended delaying introduction of allergenic foods (including avoiding eggs until 2 years of age and nuts until 3 years of age), as well as delaying solid foods until after 6 months and breast-feeding for at least 12 months.[6]

Now, however, it has been acknowledged that few conclusions about infant feeding to prevent allergic disease can be reached from the currently available data.[7] No population study to date has directly examined the relationship between infant feeding in the first year of life and risk of confirmed infant food allergy. Despite this, there has been a progressive and dramatic delay in timing of first exposure to solid foods over the last 40 years. In the 1960s, most infants had been exposed to solids by 4 months of age.[8,9] The 1970s heralded guidelines recommending delayed introduction of solids until after 4 months based on possibly false assumptions that the increase in celiac disease was due to early introduction of gluten.[10] By the late 1990s, expert bodies began to recommend delaying solids until after 6 months of age.[11] These trends predate but accelerated with the food allergy epidemic. It is

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Supported by the Australian National Health & Medical Research Council, the Ilhan Food Allergy Foundation, and AnaphylaxiStop. K. J. A. is a Viertel Senior Medical Research Fellow, and L. C. G., M. W., M. C. M., A. J. L., A.-L. P., and S. C. D. hold National Health and Medical Research Council Awards. J. J. K., P. E. M., and T. D. are Australian Postgraduate Award scholars. T. T. is a recipient of a Malaysian Government Scholarship.

Disclosure of potential conflict of interest: N. J. Osborne and K. J. Allen have received research support from the Australian Egg Corporation Limited. M. Wake and L. C. Gurrin have received research support from the Australian National Health and Medical Research Council. M. L. K. Tang is on the Medical Advisory Board for Nestlé. S. C. Dharmage has received research support from the Clifford Craig Trust and the Sypkes Trust. The rest of the authors have declared that they have no conflict of interest.

Received for publication May 10, 2010; revised June 30, 2010; accepted for publication July 20, 2010.

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0091-6749/$36.00

doi:10.1016/j.jaci.2010.07.028

Abbreviations used
OFC: Oral food challenge
OR: Odds ratio
SPT: Skin prick test

therefore entirely possible that recommendations to delay food introduction (with its associated effect on timing of various allergenic solids) not only are not protective against but also might actively contribute to the increasing prevalence of food allergy.

This article examines these issues with a focus on egg allergy, the most common IgE-mediated food allergy in infants and young children.[12] Although egg allergy itself can be outgrown, these children are at increased risk of other later atopic conditions, such as asthma and allergic rhinitis,[13-15] and many have comorbid food allergies that persist into adult life, such as peanut and tree nut allergy.[16] We could find no literature supporting an association between early exposure to egg and increased egg allergy.

To address this gap, we have drawn on data from HealthNuts, a single-center, population-based, cross-sectional study of food allergy in 12-month-old infants using food challenges to confirm allergy. Specifically, we aimed to determine whether confirmed egg allergy in 12-month-old infants is associated with (1) duration of breast-feeding and (2) ages of introducing egg and solids.

METHODS

Design and recruitment

The HealthNuts study's methods have been detailed previously.[17] In brief, 11- to 15-month-old infants were recruited as they attended 131 council-run immunization sessions across Melbourne, Australia, between June 2008 and January 2010. At the commencement of the study, statewide policy was to not introduce solids until 6 months of age and egg until 10 months of age. More than 90% of Melbourne infants receive their 12-month immunizations, with approximately half of these attending council-run immunization sessions.[18] The remaining infants are immunized by general practitioners or state/community health agencies. Infants were excluded if parents did not speak English, understand English, or both. Parents or guardians provided written informed consent.

Summary of procedures

During the compulsory 15- to 20-minute wait period after immunization, a study nurse administered an SPT using single-tine lancets to 4 foods, including egg white; 10 mg/mL histamine (positive control); and saline (negative control).[19] Before the SPT responses were read, parents completed a detailed interviewer-administered questionnaire that investigated the age at which egg and egg-containing products were introduced to the infant's diet. A second 8-page self-administered questionnaire collected information on duration of breast-feeding, age at introduction of solids, and potential confounders.

All infants with any detectable SPT wheal reactions to egg white (wheal size ≥1 mm after subtracting the negative control) were invited to the HealthNuts research follow-up clinic at Melbourne's Royal Children's Hospital (supervised by Dr Allen) within the next 4 to 8 weeks for a formal food challenge. Infants with a negative SPT response to all 4 foods (wheal size of 0 mm) in the context of a positive histamine control response were considered to be highly unlikely to have IgE-mediated allergy to these foods and did not undergo further testing.

Measures

Participants with a positive SPT response to egg underwent inpatient oral food challenge (OFC) to raw egg white. Doses were administered at 15-minute intervals as follows: 1 drop (inside lip), 0.5 mL, 1 mL, 2 mL, 5 mL, 10 mL, and then the remainder of the egg white from a 60-g egg. Nurses performing the OFCs were blinded to SPT wheal size, egg ingestion, and reaction history, and supervising clinicians were blinded to wheal size only.

Predefined criteria for a positive OFC response were at least 1 of the following: 3 concurrent, noncontact urticarial reactions lasting at least 5 minutes; severe persistent vomiting; periorbital angioedema; and/or anaphylaxis (evidence of circulatory or respiratory tract involvement; ie, wheeze, cough, change in quality of cry, or respiratory distress) within 1 hour of the last challenge dose.[17]

Infants were considered to have egg allergy (and thus not offered a food challenge) if a parent reported a definite reaction to egg consistent with the above OFC criteria in the previous month before the food challenge clinic plus a positive SPT response plus current avoidance of egg in the infant's diet.

To capture late reactions, research nurses telephoned all food challenge participants the next day. Parents of infants who tolerated 1 whole raw egg white were asked to administer a single serving of 1 whole raw egg white on a daily basis at home over the next 7 days and simultaneously to complete a daily symptoms questionnaire.

Dietary exposures were reported at baseline (ie, before SPT results were known). Parents reported the ages at which they introduced egg and egg-containing products into the infant's diet. Because preliminary analysis showed a nonlinear relationship between the prevalence of egg allergy and age of egg introduction ($P = .03$, likelihood ratio test), we categorized age of egg introduction as 4 to 6, 7 to 9, 10 to 12, and greater than 12 months (including those infants who had not yet had egg introduced by recruitment). We further classified egg-exposed infants into 2 groups according to type of first egg exposure, defined as either cooked egg (boiled, scrambled, fried, or poached) or baked egg (egg-containing cakes or biscuits or similar products).

Duration of breast-feeding was categorized as less than 1, 1 to 3, 4 to 6, 7 to 9, 10 to 12, or greater than 12 months (including infants still breast-fed at the time of recruitment). Because most infants were introduced to solid foods between 4 and 6 months of age, this exposure was categorized more narrowly (<4, 4, 5, 6, or >6 months).

Confounders (also reported at baseline) were 3 factors previously shown to confound diet-allergy associations: parent-reported child reactions to foods, eczema, and family history of allergy.[19-21] Eczema was defined as parental report of a diagnosis of eczema. Separate variables were created for eczema occurring before the introduction of solids, before the introduction of egg, or during breast-feeding. A family history of allergy was defined as parent-reported asthma, eczema, hay fever, or food allergy in the child's parents or siblings. Other potential confounding variables were maternal consumption of eggs, maternal tobacco smoking during pregnancy, child's sex, preterm delivery, siblings, current smoking by any household member, parents' country of birth, and household income.

Statistical analysis

We used a separate multivariable logistic regression model for each of the 3 primary exposures (age at introduction of egg, duration of breast-feeding, and age at introduction of solids) to quantify their associations with egg allergy reported as odds ratios (OR) and 95% CIs. Each model was adjusted for the 3 main confounding variables provided they occurred before the exposure. The remaining potential confounders were retained only if they altered an OR by greater than 10%.

To examine trends across categorical variables, we assigned numeric values to the exposure categories and assumed a linear relationship with the log odds of the prevalence of egg allergy in the logistic regression models.

Models with and without interactions between each confounder (eczema, previous reaction to foods reported by parents, or family history of food allergy) and the dietary exposure variables were compared by using likelihood ratio tests. There was strong evidence of an interaction between type of first dietary egg exposure (cooked or baked) and age at first introduction of egg ($P = .01$), and therefore the logistic regression model of timing of egg introduction was stratified by first type of dietary egg exposure. No other interactions were evident.

Stata software (release 11.0; StataCorp, College Station, Tex) was used for all analyses.

Ethics approval

Ethics approval was obtained from the Victorian State Government Office for Children (reference no. CDF/07/492), the Victorian State Government Department of Human Services (reference no. 10/07), and the Royal Children's Hospital (reference no. 27047) Human Research Ethics Committees.

RESULTS

Study population

Of 3552 infants eligible for participation who were approached at immunization clinics, 2589 (73%) participated. Table I shows the characteristics of the 2589 recruited infants, and Fig 1 shows the participant flow. Of 448 infants with a positive egg-induced SPT response, 340 (76%) underwent an OFC. In total, 231 infants were classified as having egg allergy (Fig 1).

Relationship between timing of introduction of egg and egg allergy

Infants introduced to egg at 4 to 6 months had a lower risk of egg allergy than those introduced to egg after that time (Table II), particularly those introduced to egg at 10 to 12 months of age and after 12 months of age, even after adjusting for family history of allergy and infant allergy symptoms.

Infants with a family history of food allergy or a personal history of eczema or reactions to foods had a much higher risk of egg allergy than infants with none of these factors (OR, 6.7; 95% CI, 4.7-9.6). Only 30 infants with no risk factors (low-allergy-risk infants) had been given egg after 12 months of age, and none had egg allergy. Older age of introducing egg increased egg allergy risk among both low-allergy-risk infants ($P = .02$ for trend) and infants with 1 or more of eczema, history of reactions to foods, or a family history of food allergy ($P < .001$ for trend, both Table III).

Relationship between type of egg first introduced and egg allergy

After stratifying by first type of egg (baked or cooked) introduced, age at introduction of cooked, but not baked, egg was significantly associated with increased egg allergy (Table IV), even after adjustment for family history and the infant's allergy symptoms. These results were quantitatively unchanged (data not shown) after excluding those with a family history of egg allergy (n = 46), indicating that the association between age of introducing cooked egg and egg allergy were not due to those at higher risk of egg allergy introducing egg later.

The lowest risk of egg allergy was found among infants whose first exposure to egg occurred at 4 to 6 months of age in the form of cooked egg compared with those introduced later. These infants also had a lower risk of egg allergy than those whose first exposure to egg occurred at 4 to 6 months of age in the form of baked goods containing egg (OR, 0.2; 95% CI, 0.06-0.71; $P = .012$).

To assess whether including infants with a parent-reported reaction within 4 hours of egg ingestion and a negative SPT response changed our results, we repeated the analysis assuming that all of these infants had egg allergy. The prevalence of parent-reported reactions to egg in infants with a negative SPT response who had egg introduced into their diet was 40 (2.0%) of 2023. When we repeated the analyses classifying these infants as having egg allergy, the reported associations between age at introduction of egg and egg allergy remained significant (data not shown).

Although more than 75% of eligible infants completed a food challenge, there were 100 infants with a positive SPT response whose parents declined challenge. It has previously been shown that a SPT wheal size of 5 mm or greater to egg has a greater than 95% positive predictive value for egg allergy in infants younger than 2 years.[22] We therefore repeated the analyses after classifying as having egg allergy all infants with an SPT wheal size of 5 mm or greater to egg (n = 23) and those with a parent-reported reaction to egg (n = 13). This did not change our findings (data not shown).

Relationship between duration of breast-feeding and timing of introduction of solids and egg allergy

Most infants (86.4%) were breast-fed for at least 1 month, and 29.5% were breast-fed for more than 12 months. Solid foods were generally introduced at 4 to 6 months of age, with only 3.7% of the infants given solids before 4 months of age and 5.0% after 6 months of age. In an unadjusted analysis longer duration of breast-feeding was associated with an increased risk of egg allergy (Table II). However, this association disappeared when adjusted for infant and family history of allergy and other factors (Table II). There was no evidence of an association between age at introduction of solids and egg allergy (Table II).

DISCUSSION

This is the first large-scale epidemiologic study to examine relationships between timing of infant feeding milestones and subsequent risk of challenge-proven food allergy in an unselected population. Introducing cooked egg into the infant's diet at 4 to 6 months of age was associated with a substantially lower risk of egg allergy than later introduction, even after controlling for family history of allergy and infant allergy symptoms. In contrast, any association between age at introduction of solids or duration of breast-feeding and egg allergy disappeared after controlling for the above potential confounding factors. These findings suggest that although many allergic associations might be due to reverse causation, timing and type of introduction of egg could alter the risk of egg allergy independently of reverse causation.

Strengths of the study include its large sample size, population nature, high recruitment rate, and the ability to control for a wide range of potential confounders. We selected infants for food challenge on the basis of objective SPT responses and rigorously determined our outcome of egg allergy by using confirmatory OFCs, obtaining very high participation rates. Limitations include the potential for recall bias because infants' diets were assessed retrospectively at 12 months. We minimized this by collecting infants' dietary information before the parent's knowledge of both SPT and food challenge outcomes.

A potential limitation of this study is that infants with a negative SPT response to egg (wheal size of 0 mm) did not undergo OFCs. However, the proportion of those with a 0-mm SPT wheal size with egg allergy is likely to be extremely low. In support of this assumption, only 2.0% of infants with a negative SPT response had a parent-reported reaction to egg possibly consistent with IgE-mediated egg allergy. When we repeated the analyses classifying these infants as having egg allergy, the reported associations between age at introduction of egg and egg allergy remained significant (data not shown).

The HealthNuts study involved a population-based sample of infants recruited from urban and suburban areas of Melbourne,

TABLE I. Demographic and lifestyle characteristics of the study cohort as defined by egg allergy status

Characteristic	Egg allergy status		
	Negative SPT or negative OFC response (not allergic), n = 2249,* no. (%)	Positive SPT + positive OFC response (allergic),† n = 231,* no. (%)	Positive SPT response + declined OFC (uncertain),‡ n = 109,* no. (%)
Infant dietary variables			
Age at introduction of egg (mo)			
<4	15 (0.7)	1 (0.5)	1 (1.0)
4-6	496 (23)	30 (14)	31 (30)
7-9	911 (42)	77 (36)	36 (34)
10-12	698 (32)	79 (37)	30 (29)
>12	74 (3.4)	27 (13)	7 (6.7)
First type of egg given in diet			
Cooked egg white	1006 (48)	82 (44)	46 (47)
Baked goods containing egg	1099 (52)	104 (56)	51 (53)
Age at introduction of solids (mo)			
<4	81 (3.7)	5 (2.2)	7 (6.5)
4	362 (16)	38 (17)	17 (16)
5	647 (29)	69 (30)	30 (28)
6	1001 (45)	106 (47)	48 (44)
>6	113 (5.1)	9 (4.0)	6 (5.6)
Duration of breast-feeding (mo)			
<1	316 (14)	19 (8.3)	9 (8.4)
1-3	325 (15)	28 (12)	15 (14)
4-6	334 (15)	36 (16)	15 (14)
7-9	282 (13)	33 (14)	24 (22)
10-12	299 (14)	36 (16)	14 (13)
>12	641 (29)	77 (34)	30 (28)
Maternal diet			
Mother ate eggs while breast-feeding	1692 (79)	195 (86)	87 (84)
Mother ate eggs during pregnancy	1991 (94)	215 (94)	98 (94)
Other infant variables			
Male sex	1173 (53)	130 (57)	60 (56)
Preterm delivery (<37 wk)	147 (7.0)	7 (3.2)	7 (7.3)
Infant's family variables			
≥1 sibling	1177 (53)	98 (42)	49 (45)
Immediate family history of allergy			
Asthma	666 (30)	86 (38)	32 (29)
Hay fever	1095 (49)	140 (61)	46 (42)
Eczema	681 (30)	92 (40)	29 (27)
Food allergy	272 (12)	38 (17)	15 (14)
Egg allergy	41 (1.8)	17 (7.4)	4 (3.7)
Any	1538 (69)	184 (80)	71 (65)
Maternal smoking during pregnancy	121 (5.4)	2 (0.9)	3 (2.8)
Any household member currently smokes	524 (23)	43 (19)	17 (16)
Parents' country of birth			
One or both born in Australia	1894 (85)	175 (76)	65 (61)
Both born in Europe	43 (1.9)	6 (2.6)	4 (3.7)
Both born in Asia	197 (8.8)	40 (17)	29 (27)
Other	107 (4.8)	8 (3.5)	9 (8.4)
Household income (y)			
<$50,000	252 (14)	30 (15)	16 (19)
$50,000-$100,000	896 (49)	93 (47)	46 (55)
>$100,000	680 (37)	75 (38)	21 (25)
Infant allergy variables			
Parent-reported reactions to any food in the infant	411 (18)	130 (57)	52 (48)
Parent-reported reaction to egg	68 (3.1)	71 (32)	17 (16)
Eczema diagnosis in the infant			
Any	460 (22)	135 (61)	54 (53)
During breast-feeding	256 (12)	108 (49)	41 (41)
Before solids introduced	256 (12)	93 (43)	38 (38)
Before egg introduced	350 (17)	109 (53)	45 (45)

*Numbers might not add up to total because of missing data.

†This includes 8 infants who were not food challenged because of a previous definite reaction to egg consistent with the predefined criteria for a positive OFC response occurring in the previous month before the food challenge clinic.

‡This includes 9 infants with an inconclusive oral food challenge result.

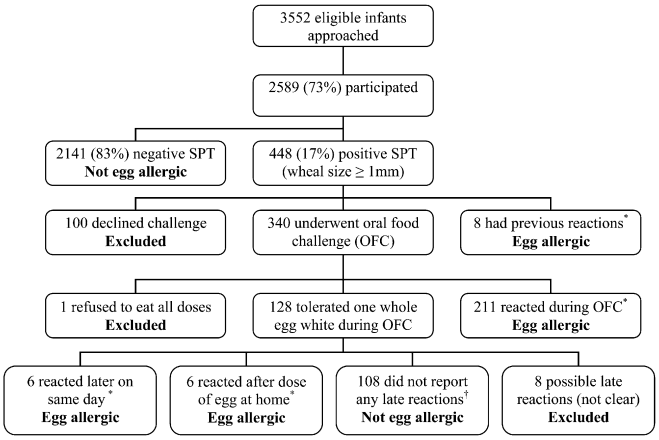

FIG 1. Study participation and assignment of egg allergy status. *Reactions included objective symptoms (defined as ≥1 of the following: 3 or more noncontact nontransient urticarial reactions, vomiting, angioedema, or anaphylaxis). †Thirty-six (28%) participants did not return their 1-week postchallenge questionnaire; however, no egg reactions were reported at their day 1 postchallenge nurse-administered telephone call.

and the results are therefore generalizable to similar areas. Because we did not recruit infants from rural areas, our findings should be generalized to rural populations with caution.

Our findings are consistent with those of Nwaru et al,[23] who recently observed that infants introduced to egg later in life were more likely to be sensitized to egg at age 5 years. However, Nwaru et al's study did not consider the clinically relevant outcome of egg allergy or control for important potential confounders, including early symptoms of allergic disease in infants and family history of food allergy. HealthNuts addresses all of these weaknesses.

It is possible that a similar relationship exists between delayed introduction of other foods and food allergy. A study mounted to investigate the relationship between celiac disease and diabetes reported that children exposed to wheat after 6 months of age had higher rates of parent-reported wheat allergy than children exposed before 6 months of age,[24] but the study was limited by small numbers (16 had parent-reported wheat allergy, of whom only 4 had wheat-specific IgE). In an ecologic study, Du Toit et al[25] observed that Israeli infants are introduced to peanut at a young age, yet Israeli schoolchildren experience a low prevalence of peanut allergy, whereas the opposite is observed in the United Kingdom. However, direct associations between timing of introduction of peanut and the risk of peanut allergy could not be quantified because the exposures and outcomes were measured in different cohorts.

Our finding that the lowest risk of egg allergy occurred among infants exposed to cooked egg between 4 and 6 months of age is consistent with the new concept of a window of opportunity during which exposure to potentially allergenic foods promotes the development of persistent oral tolerance.[26] Alternatively, continued exposure to low doses of egg from 4 to 6 months of age might have induced desensitization in infants who previously had undiagnosed egg allergy by the time egg challenges were conducted after 12 months of age, as seen in early reports of egg oral immunotherapy for the treatment of egg allergy.[27,28] We initially anticipated that those who introduced baked egg early might be protected from egg allergy because of the hypothesis that tolerating baked egg might induce tolerance in those with raw egg allergy.[29] In fact, we found that initial exposure to cooked egg, but not baked egg, appeared protective. This has implications for future randomized controlled trials of egg introduction to prevent egg allergy because the type of egg exposure, in addition to

TABLE II. Association between infant dietary factors and egg allergy at 1 year of age

			Unadjusted		Adjusted	
Variable	**No.***	**Egg allergy (%)**	**OR (95% CI)**	***P* value, trend**	**OR (95% CI)**	***P* value, trend**
Age at introduction of egg (mo)†						
4-6	485	5.6	1.0	<.001	1.0	<.001
7-9	933	7.8	1.4 (0.9-2.3)		1.3 (0.8-2.1)	
10-12	730	10.1	1.9 (1.2-3.0)		1.6 (1.0-2.6)	
>12	98	27.6	6.5 (3.6-11.6)		3.4 (1.8-6.5)	
Age at introduction of solids (mo)‡						
<4	69	4.4	1.0	.70	1.0	.16
4	354	9.0	2.2 (0.7-7.4)		1.7 (0.5-6.0)	
5	636	8.8	2.1 (0.6-7.0)		1.2 (0.4-4.3)	
6	996	9.4	2.3 (0.7-7.4)		1.2 (0.4-4.2)	
>6	106	5.7	1.3 (0.3-5.5)		0.7 (0.2-3.0)	
Duration of breast-feeding (mo)§						
<1	293	5.5	1.0	.005	1.0	.088
1-3	311	7.7	1.4 (0.8-2.8)		1.1 (0.5-2.2)	
4-6	328	10.4	2.0 (1.1-3.7)		1.1 (0.6-2.3)	
7-9	285	10.9	2.1 (1.1-4.0)		0.9 (0.5-1.9)	
10-12	312	11.5	2.3 (1.2-4.2)		0.9 (0.4-1.8)	
>12	655	11.0	2.1 (1.2-3.7)		0.7 (0.4-1.4)	

*Numbers in each analysis differ because of missing data.
†Adjusted OR based on logistic regression model adjusted for family history of allergy, eczema diagnosis before the introduction of egg, and parent-reported reactions to 1 or more foods in the infant.
‡Adjusted OR based on logistic regression model adjusted for family history of allergy, age at introduction of egg, duration of breast-feeding, maternal smoking during pregnancy, parents' country of birth, and eczema diagnosis before the introduction of solids.
§Adjusted OR based on logistic regression model adjusted for family history of allergy, maternal consumption of egg during breast-feeding, maternal smoking during pregnancy, and eczema diagnosis before ceasing breast-feeding.

TABLE III. Relationship between timing of introduction of egg and egg allergy stratified by low-risk versus high-risk infants as defined by the presence of a positive family or personal history of food allergy, a personal history of eczema in infants, or both

	Low-allergy-risk infants*				High-allergy-risk infants†			
Age introduced to egg (mo)	No.	Allergic (%)	OR(95% CI)	*P* value, trend	No.	Allergic (%)	OR (95% CI)	*P* value, trend
4-6	289	1.4	1.0	.022	206	12.6	1.0	<.001
7-9	514	2.9	2.1 (0.7-6.5)		438	13.7	1.1 (0.7-1.8)	
10-12	404	4.5	3.3 (1.1-9.9)		341	17.3	1.4 (0.9-2.4)	
>12	30	0.0	ND		69	39.1	4.5 (2.4-8.4)	

ND, Not determined.
*Low-allergy-risk infants were defined as those without a family history of food allergy and with no history of eczema or parent-reported reactions to foods in the infant.
†High-allergy-risk infants were defined as those with 1 or more of the following: a family history of food allergy, a history of eczema in the infant, or a parent-reported reaction to 1 or more foods in the infant.

TABLE IV. Type and timing of egg introduction and relationship with egg allergy

			Unadjusted		Adjusted*	
Variable	No.	Allergic (%)	OR (95% CI)	*P* value, trend	OR (95% CI)	*P* value, trend
Cooked egg given first†						
4-6 mo	162	1.9	1.0	002	1.0	.003
7-9 mo	459	7.6	4.4. (1.3-14.4)		4.4 (1.3-15.1)	
10-12 mo	394	10.2	6.0 (1.8-19.6)	.	5.9 (1.7-19.9)	
Baked egg given first‡						
4-6 mo	321	7.2	1.0	.22	1.0	.63
7-9 mo	468	7.9	1.1 (0.6-1.9)		1.0 (0.5-1.7)	
10-12 mo	325	9.9	1.4 (0.8-2.5)		1.1 (0.6-2.1)	

*Adjusted for family history of allergy, eczema diagnosis before introduction of egg, and parent-reported reactions to foods in the infant.
†Infants whose first exposure to egg was in the form of cooked egg, which was defined as consumption of egg white in the form of hard-boiled, soft-boiled, fried, or poached eggs. If parents reported ingestion of both cooked and baked egg in the same month, infants were categorized as "cooked egg first" for the purpose of this analysis.
‡Infants whose first exposure to egg was in the form of baked egg, which was defined as consumption of baked goods containing egg, such as cakes and biscuits. Note that the "cooked egg first" and "baked egg first" groups are mutually exclusive.

dose and timing, is likely to be critical. We were unable to assess the effect of egg dosage in our study because allergic reactions after the first exposure (provided a sufficient threshold dose has been achieved) will affect decisions on whether to continue eating egg.

Our findings represent the first clear evidence to support a paradigm shift in infant feeding by challenging the notion that delaying egg introduction might protect against egg allergy. They go so far as to suggest that previous expert recommendations (eg, to delay egg introduction until age 2 years[6]) might in fact have contributed to the epidemic of the apparent increase in food allergy over the last 20 years.

In conclusion, our results have major implications for both practice and future research. Our data strongly suggest that introducing cooked egg at 4 to 6 months of age might protect against egg allergy and that delaying introduction to 10 to 12 months of age might in fact exacerbate it. Confirmation that early introduction is protective might result in radical changes in infant feeding guidelines and have the potential to reverse the epidemic of childhood food allergy.

We thank the HealthNuts safety committee: Associate Professor Noel Cranswick (Australian Paediatric Pharmacology Research Unit/Murdoch Childrens Research Institute), Dr Jo Smart (Department of Allergy and Immunology, Royal Children's Hospital, Melbourne, Australia), and Associate Professor Jo Douglass (Head of Allergy, Alfred Hospital, Melbourne, Australia). We also thank the additional members of the HealthNuts team, Margaret Sutherland, Helen Czech, Kirsten Aurich, and Margaret Gibson, and the parents and children who participated in the study.

Clinical implications: Our data suggest that early introduction of egg might protect against egg allergy. If this finding is confirmed, changes in infant feeding guidelines might reduce the prevalence of egg allergy.

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