

Letter to the Editor

Hen's egg, not cow's milk, sensitization in infancy is associated with asthma: 10-year follow-up of the PIAMA birth cohort

To the Editor:

Children of parents with allergies are at an increased risk of developing asthma. Early insight into the prognosis of these high-risk children is important for parents as well as for clinicians. Allergic sensitization is often used to predict asthma.¹ Previously, in the German Multicenter Allergy Study, children sensitized to hen's egg at age 1 year were at an increased risk of allergic sensitization at the age of 3 years.² Egg sensitization was previously associated with asthma in prospective studies.³⁻⁵ In a Dutch cohort of children with more repeated measurements and additional outcome measures, our study aimed to investigate whether sensitization to hen's egg allergen at age 1 year is more strongly associated with asthma development than is sensitization to other allergens.

The study population consisted of 565 children of mothers with allergies who participated in a birth cohort study and, around their first birthday, provided a serum sample for the determination of IgE level. Their mothers (reporting at least 1 of the following: asthma ever, pet allergy, house dust mite [HDM] allergy, or nasal allergy) were included during pregnancy in the Intervention study (total $n = 855$) of the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort.⁶ The PIAMA intervention consisted of mite-impermeable mattress covers (either "active" or placebo) on the parents' and child's bed.

At age 1 year, specific IgE level to cow's milk, hen's egg, HDM, cat, and dog was measured and sensitization was defined as a specific IgE level of 0.35 IU/mL or more. Atopy was defined as sensitization to any of these allergens.

Data on asthma and relevant covariables were available from annual questionnaires at ages 3 to 8 years and again at 11 years. Asthma was defined as the presence of at least 2 of 3 parental-reported criteria: (1) a doctor's diagnosis of asthma ever, (2) wheezing during the last 12 months, and (3) a prescription of inhaled corticosteroids in the last 12 months. At age 8 years, allergic asthma (asthma in combination with inhalant sensitization) and bronchial hyperresponsiveness (BHR) were available as additional outcome measures. BHR was defined as a decrease of 20% or more in FEV₁ at a cumulative dose of 0.61 mg or less of methacholine bromide.⁷

The associations between sensitization to hen's egg and cow's milk allergen and atopy, respectively, at age 1 year and asthma in the next 10 years were assessed by using generalized estimating equations. Log binomial regression analyses were used to obtain odds ratios (ORs) for the associations between sensitization at 1 year and BHR and sensitization at age 8 years. Although the risk of asthma symptoms was only temporarily reduced in the intervention group and no reduction in the risk of hay fever, eczema, and HDM sensitization up to age 8 years⁸ was found, we investigated possible modifications of the effect of sensitization on asthma by the intervention/placebo group. Bootstrap replications (1000) were used to test heterogeneity between the estimates of hen's egg and cow's milk allergen sensitization and atopy.

Atopy at age 1 year occurred in 159 (29.3%) children, and 142 (89.3%) of these children were sensitized to cow's milk; 36 (22.6%) children were sensitized to hen's egg, and 22 (13.8%) children were sensitized to hen's egg as well as cow's milk. As expected, sensitization to inhalant allergens was rare (3.0%) in this age group. The asthma prevalence ranged from 8.8% to 10.3% over the years in the total study group.

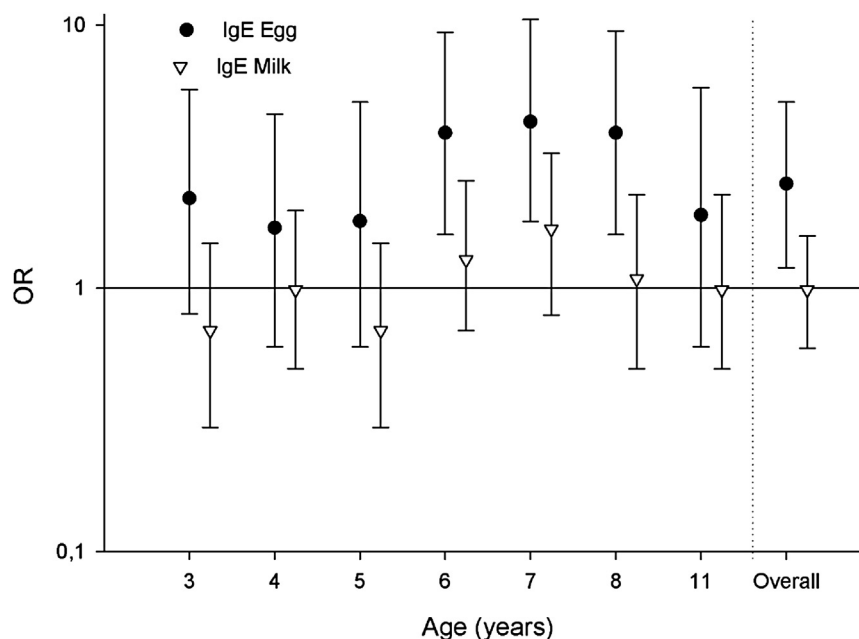


FIG 1. Odds ratios and 95% CIs for the associations of sensitization to hen's egg and cow's milk at age 1 year and asthma at following ages.

TABLE I. Odds ratios and 95% CIs for the associations of sensitization to hen's egg, cow's milk, and any allergen at age 1 year and BHR and allergic asthma at age 8 years

	BHR 8 y	Allergic asthma 8 y*	Nonallergic asthma 8 y	Inhalant allergen sensitization 8 y
Prevalence, n (%)	148 (48.5)	40 (10.6)	15 (4.0)	130 (39.4)
Hen's egg sensitization 1 y, OR (95% CI)	2.8 (1.1-6.9)	4.8 (1.9-12.1)	NA	2.1 (1.6-2.8)
Cow's milk sensitization 1 y, OR (95% CI)	1.1 (0.7-1.8)	1.5 (0.7-3.0)	0.5 (0.1-2.2)	1.1 (0.8-1.4)
Atopy 1 y, OR (95% CI)	1.3 (0.8-2.2)	2.1 (1.1-4.0)	0.4 (0.1-1.8)	1.3 (1.0-1.7)

NA, Not analyzed because this group was too small. Odds ratios in boldface represent statistically significant values.

*Allergic asthma 8 y: asthma and specific IgE ≥ 0.35 IU/mL against 1 of the following allergens: HDM, cat, dog, grass (*Dactylis glomerata*), birch pollen, and *Alternaria alternata*.

Children sensitized to hen's egg in infancy were at an increased risk of asthma later in childhood (OR, 2.5; 95% CI, 1.2-5.1), with significant age-specific associations at age 6 (OR, 3.9; 95% CI, 1.6-9.4), 7 (OR, 4.3; 95% CI, 1.8-10.5), and 8 (OR, 3.9; 95% CI, 1.6-9.5) years; (Fig 1). Sensitization to cow's milk at age 1 year was not statistically significantly associated with asthma in later years (OR, 1.0; 95% CI, 0.6-1.6) (Fig 1), neither was atopy. Children sensitized to hen's egg in infancy were at an increased risk of BHR at age 8 years (OR, 2.8; 95% CI, 1.1-6.9), and of allergic asthma (OR, 4.8; 95% CI, 1.9-12.1) (Table I). Sensitization to cow's milk in infancy was not associated with BHR and allergic asthma (Table I). Atopy was associated with allergic asthma (OR, 2.1; 95% CI, 1.1-4.0), but not with BHR. Potential confounders (sex, maternal smoking during pregnancy, breastfeeding, presence of older siblings, and paternal allergy) did not change the association of sensitization with asthma and BHR and 8-year-allergic asthma. There were no significant differences in sensitization prevalence at age 1 year between the intervention group and the placebo group, and no modification of the effect of sensitization on asthma by the intervention/placebo group was observed. The results from the bootstrap analyses showed statistically significant differences between the associations of asthma with hen's egg and cow's milk sensitization, respectively.

In our study population of high-risk children, the pattern of sensitization at age 1 year was strongly dominated by sensitization to cow's milk, as opposed to the Multicenter Allergy Study in which sensitization to hen's egg was more prevalent than sensitization to cow's milk. Sensitization to inhalant allergens was rare. Sensitization to cow's milk, and as a result atopy, was not associated with increased asthma risk during follow-up. Sensitization to hen's egg was less prevalent than sensitization to cow's milk, but despite the relatively small numbers in our study, strong associations were observed with asthma, BHR, and allergic asthma during follow-up. However, the most relevant specific type of sensitization may well differ between populations and age groups. In a recent article, Lazic et al⁹ argue that multiple atopy phenotypes exist, which may be more relevant in predicting asthma at later ages than conventionally defined atopy.

Our findings suggest that in predicting asthma risk, it may be important to consider sensitization to a particular allergen as a candidate predictor, besides atopy. We observed hen's egg sensitization at age 1 year to be more important than milk sensitization in association with asthma in later years.

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