

LETTERS TO THE EDITOR

Allergic sensitisation in infants younger than one year of age

To the editor

Allergic sensitization, usually reported by specific immunoglobulin E (s-IgE) or skin prick test, is a significant predictor of asthma, allergic rhinitis, and food allergy.¹ Also, polysensitization as well as higher levels of s-IgE to any one particular allergen appears to be associated with severe and/or complex (comorbid) allergic disease.² However, information on early infant allergy sensitization is largely lacking, and with conflicting results. In the Danish DARC birth cohort, 12.5% of 3-month-old infants were sensitized, while 16.7% of the 404 infants were sensitized at 6 months.³ In contrast, the COPSAC₂₀₀₀ high-risk cohort⁴ reported that only 0.6% and 7.8% of around 330 6-month-old infants had s-IgE $\geq$ 0.35 kU/L to inhalant and food allergens, respectively. A recent study from Sweden observed that 11% of 6-month-old infants were sensitized (s-IgE $\geq$ 0.35 kU/L) to at least one of seven common food and inhalant allergens.⁵ Additionally, low sensitization (s-IgE 0.1–0.34 kU/L) to egg was found in 5%, to milk in 14%, and to peanut in 4% of the infants.

We therefore report the prevalence of allergic sensitization to common food and inhalant allergens in three age strata within the first year of life, as well as in relation to eczema. The Bronchiolitis ALL study, a randomized nine-center clinical trial of inhaled racemic adrenalin versus placebo for acute bronchiolitis,⁶

recruited 404 infants at admission to hospital. In addition, 240 infants were recruited from a non-selected general population.⁷ The present study included all infants with available serum for IgE analyses, 368 bronchiolitis patients (mean age 4.2 months) and 224 controls (mean age 6.6 months), with an overall mean age of 5.1 months. From a structured interview and clinical examination at enrollment, 11.1% of the infants had a doctor diagnosis of eczema, while 52% had parents reporting asthma and/or allergic rhinitis.

Phadiatop Infant screening was higher than 0.15 kU/L in 86 infants (14.5%), in whom we analyzed specific s-IgE to hens' egg, cow's milk, peanut, cat, dog, birch, timothy, and house dust mite. We found that 8.5% of all infants were sensitized to at least one allergen with similar rates among infants from the bronchiolitis (8.4%) and controls groups (8.5%), 6.9% with low sensitization, and 2.0% were sensitized to at least two allergens (polysensitized). As shown in Figure 1, allergic sensitization (s-IgE 0.35–30.4 kU/L) was similar in the two highest age strata, both with significantly higher prevalence than among infants younger than 4 months (122 days; $P = .01$).

Sensitization was most common toward food allergens (7.4%), including egg ($n = 25$), cow's milk ($n = 22$), and peanut ($n = 6$), whereas in infants younger than 4 months of age, sensitization to cow's milk

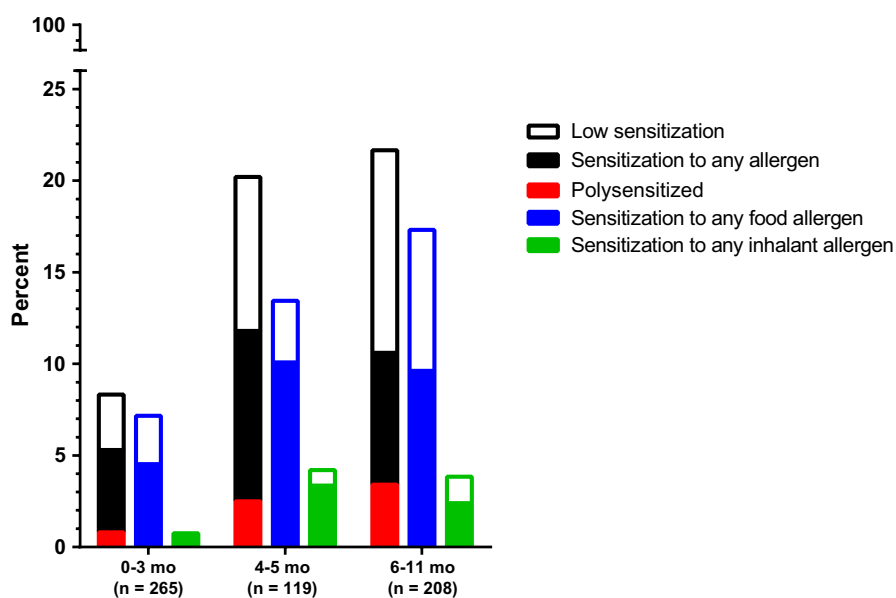


FIGURE 1 Allergic sensitization in a cross-sectional infant population. Low sensitization is defined as s-IgE of 0.10–0.34 kU/L and is displayed with borders only. Sensitization is defined as s-IgE $\geq$ 0.35 kU/L. Food allergens include egg, milk, and peanut. Inhalant allergens include birch, timothy, cat, dog, d. pteronyssinus, cladosporeum, and guinea pigs

($n = 11$) exceeded that of egg ($n = 2$). Among the 1.9% of infants sensitized to inhalant allergens, cat ($n = 8$) was most common, followed by dog ($n = 5$), birch ($n = 2$), timothy ($n = 1$), and house dust mite ($n = 0$). Five infants were sensitized to both food and inhalant allergens. Among infants younger than 4 months, 11 were sensitized to cow's milk, two to egg, one to cat, and two to dog (Figure 2). Among

the 12 polysensitized infants, eight were sensitized to two allergens, most commonly to egg ($n = 9$), followed by cat and milk (both $n = 6$) and peanut ($n = 5$).

The prevalence of allergic sensitization was significantly higher in infants with eczema (24.2%) compared to those without (5.8%) eczema ($P < .001$), as seen in all age strata in Figure 3, but our study was not designed to verify or refute the hypothesis that AD promotes sensitization through a reduced skin barrier function.⁸ The diagnoses of eczema were based upon parental reported physician diagnosed eczema, previously shown to correspond 75% with the Hanifin and Rajka diagnostic criteria.

However, sensitization rates were similar in infants with and without parental allergic rhinitis (9.2% vs 9.1%) and/or asthma (8.4% vs 8.7%).

Allergic sensitization to any allergen was not significantly different in boys (8.1%) versus girls (7.4%).

The prevalence of allergic sensitization to at least one allergen in our study is in line with the Swedish ALLADIN study⁵ and the COPSAC2000 high-risk cohort at 6 months of age.³ The DARC study, although population based, reported higher prevalence of allergic sensitization, by using an alternative analytical method (Magic Lite).⁴ The Canadian CHILD birth cohort study of more than 2000 individuals found that at least 13.5% was sensitized to at least one food or inhalant allergen at 12 months.⁹

Our study contributes to the low number of studies reporting s-IgE levels in very young infants.

The allergic sensitization and low sensitization present in the youngest strata, even with very few individuals with eczema (3/265), warrant further exploration of the sequence of the development of atopic features. The clinical relevance of low sensitization, observed more frequently in the oldest age stratum, is unclear.

Our observation that milk was predominant in infants younger than 4 months is in contrast in the DARC cohort, where egg dominated, as is the case in other studies later in childhood.

Polysensitization, associated with more severe or complex allergic disease,² was found in even the youngest strata, increasing with age. Similar data in the DARC cohort indicated 23 children <18 months of age, not specified for children <3 months.

The high rate of self-reported parental asthma/allergic rhinitis indicates that our cohort is somewhat skewed in an atopic direction, although the sensitization rates were similar in children with and without parental atopy.

The cross-sectional study design provides prevalence data, but limits causality.

All analyses were performed in one batch, specified with down to 0.10 kU/L, enabling classification of possible sensitization.

We conclude that already by 4 months of age, five percent of infants were sensitized to at least one allergen and further 2.8% were low sensitized, even in the absence of eczema. This study adds insight to sensitization patterns in young infants.

Yours sincerely

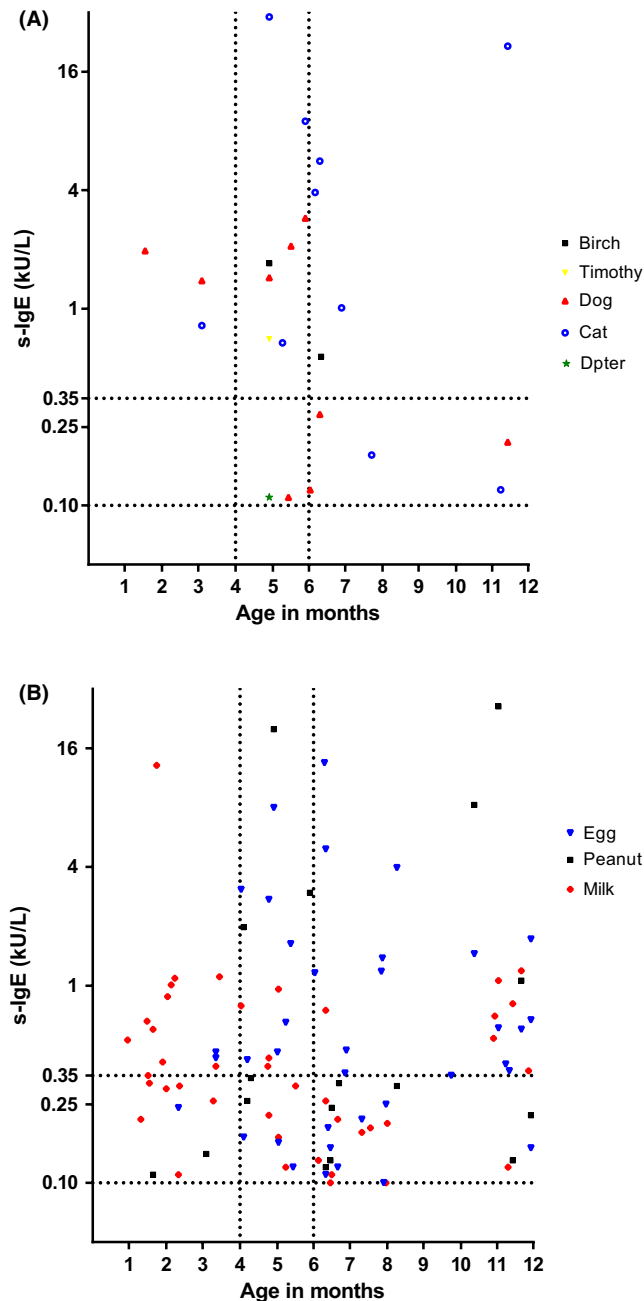
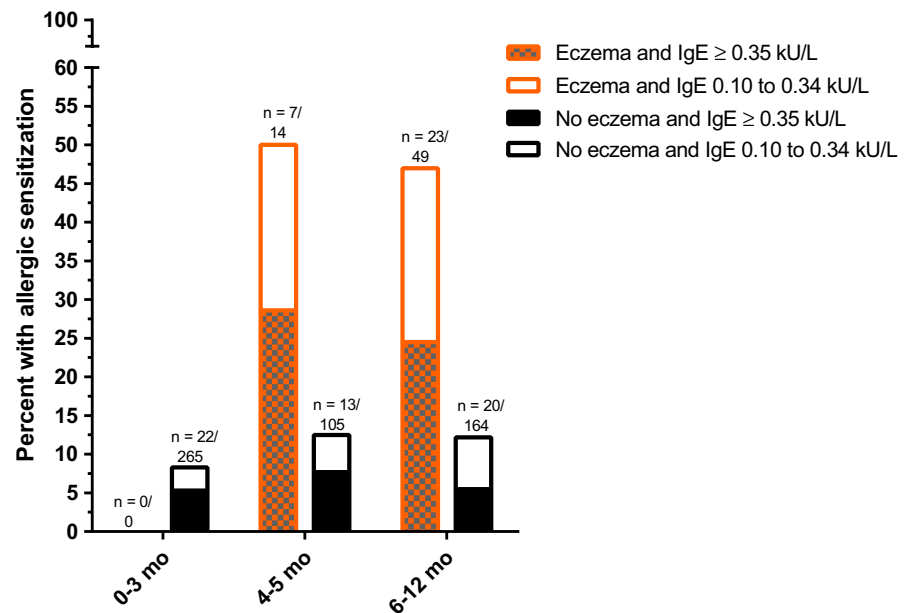


FIGURE 2 Scatterplot of individual sensitization levels. Each point represents a single sensitization value. Each individual may be represented several times. Levels below 0.10 kU/L are not displayed. Dotted x-axis lines represent low sensitization (0.10 kU/L) and sensitization (≥ 0.35 kU/L)

FIGURE 3 Allergic sensitization in infants with and without eczema. Allergic sensitization (s-IgE ≥ 0.35 kU/L) to any allergen is stratified by reported doctor diagnosis of atopic dermatitis and age groups: 0 through 3 mo, 4 through 5 mo, and 6 through 11 mo of age. Low sensitization is defined as s-IgE of 0.10–0.34 kU/L and is displayed with borders only. Sensitization is defined as s-IgE ≥ 0.35 kU/L



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CONFLICT OF INTEREST

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Preschool wheezing diagnosis and management—Survey of physicians' and caregivers' perspective

To the Editor,

Preschool children with wheezing disorders represent a diagnostic and therapeutic challenge, and consume disproportionately large amounts of healthcare resources.¹⁻³ Most wheezing episodes are triggered by viral respiratory tract infections, occurring in 30%-50% of all preschool children.^{4,5} In the majority of cases, episodes of wheezing are mild and transient and are managed in non-hospital settings; however, some infants develop recurrent episodes severe enough to require medical review, hospital admission and further referral to specialist paediatricians for diagnosis and management.^{6,7}

Although there is an abundance of guidelines on asthma,⁸ there is no consensus on diagnostic workup in preschool children with wheezing.⁹ Therefore, the Task Force on Preschool Wheeze, established by the European Academy of Allergy and Clinical Immunology (EAACI), initiated a survey to identify the most common problems physicians face around the diagnosis and management of preschool wheeze, in order to inform future recommendations.

We carried out two consecutive surveys among physicians: an open survey (A), to study physicians' perception of the problem, and subsequently specifying all problems in the second survey (B) and a patients' opinion survey (C).

The preliminary international Survey A consisted of 5 open-ended questions (Appendix S1) and was conducted in winter 2017/2018 upon invitation to EAACI's Paediatric Section members. The answers were analysed and divided into appropriate categories by two independent researchers.

The full Survey B was addressed to physicians, based on the results of the Survey A, and involved a demographic survey with 5 closed-ended clinical questions, identical to those from the pilot survey (created using Google Forms). The estimated time of completing the survey was 5 minutes. The form circulated from May through September 2018 among EAACI Paediatric Section and Asthma Section members. The survey was also translated and distributed via a Polish, physician-exclusive, medical social network—www.konsylium24.pl, accessible from the website in August 2018.

Survey C was addressed to preschool wheezers' caregivers. The respondents were recruited by patient associations or in hospital

wards. The questions were discussed with parents, as many questions from the survey were written in professional language. Their responses were compared to those received from physicians to investigate agreements. All surveys were entirely anonymous and voluntary.

The results of the surveys were analysed using descriptive statistics. Chi-square test with the Bonferroni correction was used for categorical analyses.

A total of 2132 members of the EAACI Paediatric Section and Asthma Section were mailed, out of whom 55 (2.6%) completed Survey A and later 226 (10.6%) completed Survey B (Table S1). The National Survey B in Poland was viewed by 1324 unique users of the www.konsylium24.pl portal, 504 (38.1%) of whom completed the survey (Table S2). The detailed characterization of the participants of both surveys is available in Appendix S1.

Nearly uniform responses were observed across the different specialties and practice setting. Some significant differences were noted, however, and are described below.

1 | QUESTION 1: TROUBLES IN THE DIAGNOSIS OF 'PRESCHOOL WHEEZE' OR ASTHMA IN PRE-SCHOOLERS

The most pressing problem with the diagnosis of wheezing in preschoolers is lack of diagnostic tools, pointed out by the largest group of responders (36.4%, Figure 1), followed by fluctuation of symptoms (26.6%), doubts about the diagnosis significance (25.5%) and clear definition problems (21.9%).

2 | QUESTION 2: DIAGNOSTIC OPTIONS IN PRESCHOOL WHEEZERS

The most frequent response (50.7%) points out response to treatment, while allergy tests were also very popular, having been chosen by 34.1%. (Figure 2). Other relevant answers include number