

Letter to the Editor

Allergy-related disease in relation to early life exposures—the ALADDIN birth cohort

To the Editor:

Lifestyle is known to influence the risk of allergy-related disease, but the etiologic mechanisms for this influence remain unclear.¹ The Assessment of Lifestyle and Allergic Disease During Infancy (ALADDIN) birth cohort study aims to study the association between lifestyle exposures during pregnancy and early infancy and allergy-related disease in children. In previously published studies of the initial 330 children in the cohort, an anthroposophic lifestyle was associated with a markedly reduced risk of specific IgE sensitization.² Here, we report how the anthroposophic, partly anthroposophic, and nonanthroposophic lifestyles are associated with clinical allergy-related outcomes: parent-reported food hypersensitivity, recurrent wheeze, and eczema in the entire cohort of 490 children up to age 2 years. For description of methods and the distribution of 64 different early life exposures in the 3 lifestyle groups, see this article's Online Repository at www.jacionline.org.

Many early life exposures differed significantly between the lifestyle groups. For example, anthroposophic children more often had older siblings, were breast-fed to a higher extent, and were rarely vaccinated before age 6 months. Their parents were more commonly born outside Scandinavia. However, heredity, represented by parental IgE sensitization and reported history of allergy-related symptoms, did not differ significantly between the groups (see Table E1 in this article's Online Repository at www.jacionline.org).

The risk of parent-reported food hypersensitivity, recurrent wheeze, and IgE sensitization was reduced in both the anthroposophic and partly anthroposophic groups, compared with the nonanthroposophic group. The risk of eczema was similar in the 3 lifestyle groups (Table 1).

Having older siblings was associated with parent-reported food hypersensitivity (odds ratio [OR], 0.40; 95% CI, 0.17-0.96); however, adjusting for having older siblings had little impact on the effect of anthroposophic and partly anthroposophic lifestyle (see Table E2 in this article's Online Repository at www.jacionline.org). Significant associations were seen between recurrent wheeze and mother being university-educated (OR, 0.29; 95% CI, 0.14-0.58); having used olive oil as main cooking fat during pregnancy (OR, 0.45; 95% CI, 0.20-0.99); having been admitted to neonatal care (OR, 3.0; 95% CI, 1.2-7.3); and receiving milk formula during the first week of life (OR, 2.3; 95% CI, 1.2-4.6). When adjusting for these exposures, recurrent wheeze was not significantly associated with anthroposophic (OR, 0.59; 95% CI, 0.18-1.9) or partly anthroposophic (OR, 0.77; 95% CI, 0.33-1.8) lifestyle (see Table E3 in this article's Online Repository at www.jacionline.org). Four exposures were significantly associated with eczema: living in an apartment (OR, 1.6; 95% CI, 1.06-2.5); keeping pets in the household (OR, 0.59; 95% CI, 0.38-0.92); antibiotic use by mother during pregnancy (OR, 2.0; 95% CI, 1.2-3.3); and first body wash before age 7 days (OR, 1.6; 95% CI, 1.1-2.4) (see Table E4 in this article's Online Repository at www.jacionline.org). IgE sensitization was throughout all analyzes significantly associated with having a

mother who worked (gainful employment) during pregnancy (OR, 3.0; 95% CI, 1.1-8.1) and having had your first body wash before age 7 days (OR, 2.1; 95% CI, 1.2-3.5) (see Table E5 in this article's Online Repository at www.jacionline.org).

The main finding of this study was that anthroposophic lifestyle was associated with reduced risk of not only IgE sensitization but also parent-reported food hypersensitivity and recurrent wheeze up to age 2 years. No such association was determined for eczema. Wash of infant's whole body before age 7 days was associated with increased risk of eczema and IgE sensitization. This finding that delayed first wash of infant's whole body could reduce the risk of allergy-related outcomes is interesting and may support findings in a study of a subgroup of this cohort in which the protein composition of the vernix was associated with the development of eczema.³ In accordance with the original hygiene hypothesis,⁴ having older siblings was associated with reduced risk of both parent-reported food hypersensitivity and IgE sensitization but did not explain the risk reduction for anthroposophic lifestyle. There was no significant association between farming and IgE sensitization, which is interesting considering the strong evidence other studies have provided for an allergy-protective effect of farming in older children. A possible explanation could be that IgE sensitization at this young age is predominantly against food allergens, such as cow's milk and hen's egg, whereas the effect of farming on IgE sensitization has been mostly linked with inhalant allergens. The finding that anthroposophic lifestyle was inversely associated with recurrent wheeze is in line with other lifestyle studies in which farming has been inversely associated with not only atopy but also transient wheeze and nonatopic asthma in children.⁵ However, the exposures that seemed to largely explain the protective effect of anthroposophic lifestyle on recurrent wheeze in this study (maternal level of education, maternal consumption of olive oil during pregnancy, receiving milk formula during the first week of life, and having been admitted to neonatal care) are unlikely to be mediated by microbial exposure, which was the case for farming exposure and asthma.⁶ Heredity is a well-documented risk factor for allergy-related disease, yet we could not demonstrate any significant impact of parental allergy on allergy-related outcomes in the children of this cohort. This could indicate that lifestyle exposures are more important than genetics for allergy-related disease during early childhood.

The "anthroposophic effect" on sensitization was largely unexplained by the exposures measured in the study. Limited statistical power could lead to incorrect exclusion of variables from the adjusted model. However, it is also possible that the true explanations are not among the measured exposures. For example, environmental diversity⁷ and diversity of food in infancy⁸ have been associated with the risk of allergy-related outcomes. We had no information on usage of topical corticosteroids. Such treatment is commonly intentionally avoided in anthroposophic families, meaning that some children with no symptoms of eczema at examination could be misclassified. Wearing wool closest to the skin has been associated with more intense symptoms of eczema,⁹ yet despite being more common among anthroposophic infants we found no such association in our cohort.

In conclusion, we recorded a significantly reduced risk of parent-reported food hypersensitivity and recurrent wheeze up to

TABLE I. Allergy-related outcomes and overall risk estimates (ORs) in children up to age 2 years from families with anthroposophic, partly anthroposophic, or nonanthroposophic lifestyle, n/N (%)

	Whole cohort	Anthroposophic	Partly anthroposophic	Nonanthroposophic
Parent-reported food hypersensitivity				
1 y	17/474 (3.6)	3/113 (2.7)	5/204 (2.5)	9/157 (5.7)
2 y	19/466 (4.1)	3/114 (2.6)	5/197 (2.5)	11/155 (7.1)
OR (95% CI)	—	0.38 (0.12-1.24)	0.35 (0.13-0.92)*	1
Recurrent wheeze				
1 y	18/474 (3.8)	2/113 (1.8)	6/204 (2.9)	10/157 (6.4)
2 y	37/466 (7.9)	6/114 (5.3)	13/196 (6.6)	18/155 (11.5)
OR (95% CI)	—	0.38 (0.16-0.91)*	0.51 (0.26-0.99)*	1
Eczema				
2 mo	28/476 (5.9)	6/108 (5.6)	8/208 (3.8)	14/160 (8.8)
6 mo	51/470 (10.9)	14/110 (12.7)	18/201 (9.0)	19/159 (11.9)
1 y	52/470 (11.1)	12/112 (10.7)	23/203 (11.3)	17/155 (11.0)
2 y	55/461 (11.9)	11/109 (10.1)	23/198 (11.6)	21/154 (13.6)
OR (95% CI)	—	0.83 (0.49-1.4)	0.76 (0.49-1.2)	1
IgE sensitized†				
6 mo	39/357 (10.9)	2/70 (2.9)	13/152 (8.6)	24/135 (17.8)
1 y	62/372 (16.7)	3/70 (4.3)	22/165 (13.3)	37/137 (27.0)
2 y	69/395 (17.5)	13/85 (15.3)	21/164 (12.8)	35/146 (24.0)
OR (95% CI)	—	0.37 (0.19-0.70)*	0.45 (0.27-0.74)*	1

OR from general estimating equations, unadjusted.

* $P < .05$.†Specific IgE level > 0.35 kU/L toward at least 1 of the tested allergens (cow's milk, hen's egg, peanut, cat, dog, birch, and timothy).

age 2 years among children from families with an anthroposophic lifestyle, in addition to a reduced risk of IgE sensitization. Although among the factors associated with this reduced risk was delayed wash of infant's body, the "anthroposophic effect" still remains largely unclear. The cohort study is ongoing with 5- and 10-year follow-ups and includes an extensive biobank of placenta, vernix, breast milk, feces, saliva, and urine, in addition to blood, for further association studies.

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