

Anthroposophic lifestyle and salivary cortisol are associated with a lower risk of sensitization during childhood

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To cite this article: Swartz J, Lindblad F, Arinell H, Theorell T, Alm J. Anthroposophic lifestyle and salivary cortisol are associated with a lower risk of sensitization during childhood. *Pediatr Allergy Immunol* 2015; **26**: 153–160.

Keywords

Allergic sensitization; anthroposophic lifestyle; children; salivary cortisol; stress

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Accepted for publication 5 January 2015

DOI:10.1111/pai.12342

Abstract

Background: Infants from anthroposophic families have low cortisol levels and low risk of IgE-sensitization during first 2 years of life. Our aim was to study the impact of an anthroposophic lifestyle and cortisol levels at 6 months on allergy sensitization up to age 5 years.

Methods: A total of 507 families participated from maternal healthcare centers. Parental lifestyle was categorized as anthroposophic, partly anthroposophic, or non-anthroposophic. Blood samples for analyzes of sensitization were obtained from parents at inclusion and from children at 6, 12, 24, and 60 months. Salivary samples were collected at home at 6 months.

Results: Sensitization increased from 2.9% to 26.0% in the anthroposophic group, from 8.4% to 26.8% in the partly anthroposophic group, and from 19.1% to 44.1% in the non-anthroposophic group. Children from anthroposophic families had lower cortisol levels in the morning, afternoon, and evening. The odds ratio (OR) for anthroposophic lifestyle was always <1 and lowest at 12 months (OR, 0.10; 95% CI, 0.03–0.36). Adjusting for cortisol levels at 6 months increased these ORs at 12 and 24 months. At the same ages, ORs for sensitization were elevated also for cortisol levels at 6 months. Analyzes in children not sensitized at 6 months confirmed the cortisol-related risk of sensitization.

Conclusions: Children from families with an anthroposophic lifestyle have lower risk than comparisons of developing sensitization up to 5 years. This risk is partially explained by low cortisol levels during infancy. High cortisol levels at 6 months predict sensitization up to 24 months.

Stressful experiences may induce the onset and/or the exacerbation of allergic disease (1–3). These findings seem to indicate that the HPA axis is involved in the pathogenesis (4). In infants with atopic disposition, both a hyper-responsiveness (5, 6) and hyporesponsiveness (7) of the HPA axis have been reported. However, underlying mechanisms associated to these HPA dysfunctions need to be demonstrated. Prospective studies are needed to separate the potentially etiological role of cortisol upon allergy development from possible HPA axis reactions to the sensitization.

In a previous prospective study, we found an association between various cortisol levels at age 6 months and sensitization

up to age 24 months (8). When only children who were not sensitized at 6 months and who did not have eczema were included, only a trend ($p = 0.051$) remained for an association between afternoon cortisol levels and sensitization (8). This study included anthroposophically reared children and comparisons. The anthroposophic lifestyle has several characteristics such as preference for home deliveries, a long period of breastfeeding, a diet of organic/biodynamic products emphasizing vegetarian components, a restrictive use of antibiotics and antipyretics and a postponed vaccination program as well as a holistic view of life, including spiritual values. Many aspects of this lifestyle are of relevance within the hygiene hypothesis (9).

Indeed, the prevalence of atopy is lower in children from anthroposophic families than in comparisons (10–12) and they have a lower risk of IgE-sensitization (13).

Notably, children from families with an anthroposophic lifestyle also have lower levels of cortisol than comparisons at ages 6, 12, and 24 months (14), which thus stand out as one possible explanation of their lower risk of developing allergy. As we now have access to sensitization data at 60 months from the same study groups, it is possible to investigate how our previous findings on both lifestyle and cortisol levels have developed. Thus, in this study, we investigate whether an anthroposophic environment and low cortisol levels at 6 months of age protect against sensitization at 5 years of age and whether these two background factors interact with each other in this process. We also re-investigate sensitization at 12 and 24 months of age, using a larger study group from a second recruitment wave.

Methods

Subjects

This study is based on Assessment of Lifestyle and Allergic Diseases During Infancy (ALADDIN), a prospective birth cohort study that focuses on the impact of lifestyle and environmental factors during pregnancy and childhood on the development of allergic disease (13). Families were recruited at anthroposophic maternal and child healthcare centers (MCHC) and from conventional MCHCs at two different start points—at September 2004 and January 2011. From a total of 552 families, finally 507 decided to participate (Fig. 1). The regional research ethics committee approved the study. Written informed consent was obtained from all families.

Degree of adherence to an anthroposophic lifestyle

Parents' lifestyle was categorized, as anthroposophic if they had chosen an anthroposophic antenatal clinic, preferred an anthroposophic school, and reported anthroposophic views of life that also influencing daily living. If they reported opposite values on all these issues, the lifestyle was categorized as non-anthroposophic. Other report patterns were categorized as partly anthroposophic.

Family characteristics

A parental questionnaire concerning demography, health, and family aspects that may hypothetically differ between anthroposophic and other families was filled in at 2, 6, 12, 18, 24, and 60 months of age. The items of relevance for this study are presented in Table 1.

Procedures

Blood analysis

Blood samples were obtained from parents at inclusion and from child at 6, 12, 24, and 60 months of age. Samples were collected in heparin tubes, and plasma was stored at -20°C . Parental sensitization was analyzed by ImmunoCAP Phadia-top™ (Phadia AB, Uppsala, Sweden) for IgE to a mix of 11 inhalant allergens and from the children at 6, 12, and 24 months of age was analyzed by ImmunoCAP (Phadia AB for IgE to cow's milk, hen's egg, peanut, cat, dog, birch, and timothy). At 60 months, a food mix (fx5) (Phadia AB) and Phadiatop™ were used, adding the allergens codfish, wheat flour, soybean, *Cladosporium*, *D. farinae*, *D. pteronyssinus*,

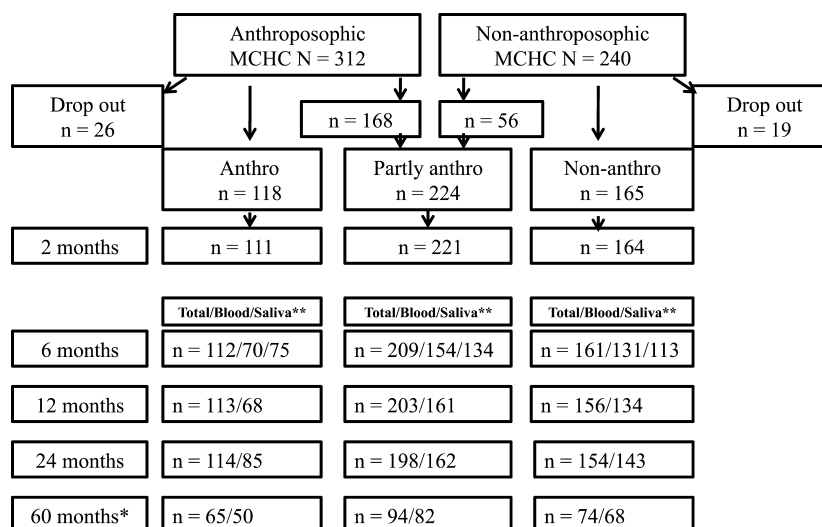


Figure 1 Flow chart of the recruitment process during the first 60 months in relation to participants with blood tests. n = number of families at each stage. MCHC, maternal and child healthcare center. **'Total/Blood/Saliva' means number of families who took part during a certain phase of this program/number of children with blood sample for sensitization tests during this phase/number of children with saliva samples for cortisol analyzes during this phase (only relevant at 6 months of age). *Only 233 families have an index child who has reached the age of 60 months.

Table 1 Demographic data and family characteristics for children up to 60 months of age arranged according to an anthroposophic, partly anthroposophic, or non-anthroposophic lifestyle

	Anthro (A)	Partly anthro (B)	Non-anthro (C)	p	Post hoc
Number of children n/N (%)	118/507 (23.3)	224/507 (44.2)	165/507 (32.5)		
Demographics					
Sex (males)	57/118 (48.3)	109/224 (48.7)	79/165 (47.9)	0.988	
Mother sensitization	34/118 (28.8)	63/224 (28.1)	49/165 (29.7)	0.944	
Father sensitization	55/115 (47.8)	96/211 (45.5)	65/158 (41.1)	0.517	
Mother education high school	38/118 (32.2)	85/224 (37.9)	72/165 (43.6)	0.146	
Father education high school	46/117 (39.3)	85/218 (39.0)	92/164 (56.1)	0.002	C>A, B**
Mother education university	57/118 (48.3)	115/224 (51.3)	76/165 (46.1)	0.582	
Father education university	48/117 (41.0)	94/218 (43.1)	50/164 (30.5)	0.035	B>C*
Maternal smoking during pregnancy	7/117 (6.0)	11/221 (5.4)	11/165 (6.1)	0.775	
No siblings or other children living with the family	39/118 (33.1)	107/217 (49.3)	62/164 (37.8)	0.007	B>A**, C*
One sibling or other child living with the family	40/118 (33.9)	74/217 (34.1)	71/164 (43.3)	0.132	
> 2 siblings or other children living with the family	39/118 (33.1)	36/217 (16.6)	31/164 (18.9)	0.001	A>B, C**
Living on a farm with animals during pregnancy	21/113 (18.6)	18/219 (8.2)	13/163 (8.0)	0.006	A>B, C**
Exclusive breastfeeding 6 months	40/113 (35.4)	67/210 (31.9)	24/161 (14.9)	<0.001	A, B>C***

Categorical variables: n/N (%): p for comparisons of proportions. Significant pairwise differences between groups: *p < 0.05, **p < 0.01, and ***p < 0.001.

horse, and mugwort. Allergen-specific IgE-levels ≥ 0.35 kUA/l were categorized as 'IgE-sensitization'.

Cortisol analysis

Salivary samples were collected at home during 1 day at 6 months, in the morning, afternoon, and before going to bed by sterile rolls (braided cotton dental rolls; Richmond Dental, Charlotte, NC, USA), which the parents were instructed to keep in the mouth of the child until soaked with saliva (15). The samples were centrifuged and stored at -80°C until analyzed, using the SpectriaTM Cortisol RIA (125 l) kit from Orion Diagnostica Oy, Espoo, Finland.

Statistical analysis

Chi-square analyses and ANOVA were used for comparisons of sensitization and lifestyle factors between the groups. As salivary cortisol showed a skewed distribution in all studied groups and on all occasions, logarithmic transformation was used. Means were presented after back-transformation (geometric means). Logistic regression was used to analyze whether lifestyle could predict sensitization at 6, 12, 24, and 60 months of age in a model adjusted for sex of the child, parental sensitization, parental education, mother smoking during pregnancy, number of siblings or other children living with the family, family living on a farm with animals during pregnancy, and exclusive breastfeeding at age 6 months. A second model was adjusted also for cortisol. Logistic regression was similarly used to analyze whether salivary cortisol level at age 6 months in the morning, afternoon, and evening were related to sensitization at ages 6, 12, 24, and 60 months. A first model was adjusted for the variables mentioned above and a second model also for lifestyle. Odds ratios (ORs) and 95% confidence intervals (CI) were calculated. The Kaplan–Meier

method was used to illustrate the cumulative incidence of sensitization. Lifestyles as well as quartile-split cortisol levels at 6 months were used as main explanatory factors and differences in survival curves, that is, children not sensitized, were tested with log-rank (Mantel–Cox) statistics. p-values <0.05 were considered significant. spss Statistics 21.0 (IBM Software, Armonk, NY, USA) was used for the statistical analyses.

Results

Data on demographics and family characteristics are shown in Table 1. All 507 children were followed prospectively from birth until the age of 24 months and of these 233 (recruited until December 2013) up to 60 months of age. At age 6 months, blood was collected from 355/507 families (70%). At 12 months, the corresponding figures were 363 (72%), at age 24 months 390 (77%), and at 60 months 200 (39%; Fig. 1). There were large differences concerning prevalence of allergic sensitization in relation to lifestyle. Sensitization increased during the follow-up from 6 months until 60 months of age from 2.9% to 26.0% among children in the anthroposophic group, from 8.4% to 26.8% in the partly anthroposophic group, and from 19.1% to 44.1% in the non-anthroposophic group (Fig. 2).

Salivary cortisol levels at age 6 months (Table 2) varied according to a circadian rhythm and showed lower levels of cortisol in children from anthroposophic families than from partly anthroposophic and non-anthroposophic on all sampling occasions. Logistic regression models of sensitization at 12, 24, and 60 months of age given different lifestyles and different cortisol levels at 6 months of age are presented in Table 3. The ORs—adjusted for demographic and family-related variables (Model 1)—for lifestyle were always below one for anthroposophic lifestyle with the lowest (OR, 0.10; 95% CI, 0.03–0.36) at 12 months of age as compared to

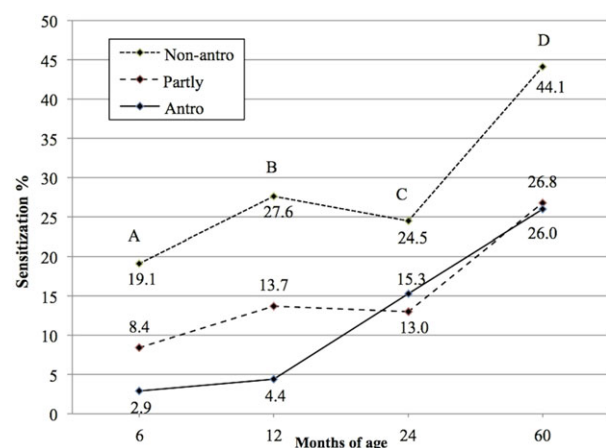


Figure 2 Prevalence (%) of sensitization in children at age 6, 12, 24, and 60 months from three lifestyle groups (anthroposophic, partly anthroposophic, and non-anthroposophic). Significant differences between the three groups: (a) non-anthro > partly anthro ($p < 0.01$) and anthro ($p < 0.001$). (b) Non-anthro > partly anthro ($p < 0.01$) and anthro ($p < 0.001$); partly anthro > anthro ($p < 0.05$). (c) Non-anthro > partly anthro and anthro ($p < 0.05$). (d) Non-anthro > partly anthro and anthro ($p < 0.05$).

non-anthroposophic lifestyle. They mostly reached—or were close to—significance both for the anthroposophic and/or partly anthroposophic group at all ages except at 24 months. In a model also adjusted for cortisol at 6 months of age (Model 2), the ORs increased for the anthroposophic group at 12 and 24 months (just as at 6 months) but decreased at 60 months of age (i.e. at an age when there were no correlations between cortisol at 6 months and sensitization). For the partly anthroposophic group, the ORs decreased in these fully adjusted models (Model 2). The ORs—adjusted for demographic and family-related variables—were increased for high (≥ 1 standard deviation [s.d.]) cortisol levels at 6 months of age at follow-ups at 12 and 24 months of age (just as at 6 months). In a model also adjusted for lifestyle, the ORs decreased slightly or were unchanged at these ages. Further analyses restricted to children not sensitized at 6 months of age were performed demonstrating associations between salivary cortisol levels in the morning,

afternoon, and evening at age 6 months and sensitization at 12 months. The adjusted odds ratio (OR) in the morning was 1.83 (95% CI, 1.04–3.23; $p < 0.05$), in the afternoon 1.65 (1.02–2.66; $p < 0.01$), and in the evening 1.73 (1.13–2.65; $p < 0.05$). The corresponding results for age 24 months were in the morning 1.89 (1.14–3.12; $p < 0.05$), in the afternoon 1.42 (0.96–2.11; $p = 0.081$), and in the evening 1.40 (0.98–2.01; $p = 0.067$). No association was found at age 60 months. No parents reported use of inhaled or systemic steroids up to age 6 months of the child.

Kaplan–Meier statistics was applied for analyzing the effects of lifestyle and cortisol levels upon the cumulative incidence of sensitization. The non-anthroposophic lifestyle showed significantly different development of sensitization from both the partly anthroposophic group ($\chi^2 = 5.03$; $p < 0.05$) and the anthroposophic group ($\chi^2 = 10.82$; $p < 0.01$; Fig. 3). The quartile with highest cortisol levels in the morning showed a development that differed significantly from the other quartiles. Similar results were obtained for the afternoon cortisol levels. For the evening levels, the only significant difference between the curves was between the highest and the lowest quartile (Fig. 4a–c).

Discussion

In this prospective birth cohort of 507 families, we investigated the influence of an anthroposophic lifestyle and cortisol levels at 6 months of age on allergic sensitization up to age 24 months and in the initially reported part of the cohort, up to 60 months (Table 2). An anthroposophic lifestyle was associated with a lower risk of sensitization up to 60 months of age (although not significantly at 24 months). Higher cortisol levels were associated with an increased risk of sensitization at 12 and 24 months. The prevalence of allergic sensitization increased in all three lifestyle groups during the follow-up. The anthroposophic and partly anthroposophic groups developed along the same line. In analyses of the cumulative incidence, using Kaplan–Meier statistics, the development of sensitization was significantly different between the three groups. The strongest differences appeared early, during the first year of life.

There was an interaction between lifestyle and high cortisol levels. Thus, the lower risk of immunization associated with an

Table 2 Salivary cortisol levels at 6 months of child age in three lifestyle groups (anthroposophic, partly anthroposophic, non-anthroposophic) at all sampling occasions (morning, afternoon, and evening) with p-values corresponding to linear regressions with anthroposophic lifestyle group as explanatory and $\ln$ (cortisol concentration) as outcome variable. Geometric means (saliva cortisol, nmol/l) with confidence intervals (95%) and number of participants

	Anthroposophic		Partly anthroposophic		Non-anthroposophic		p
	Geometric mean	Confidence intervals	Geometric mean	Confidence Intervals	Geometric mean	Confidence Intervals	
Infant							
Morning	9.8 (73)	7.8–12.3	11.4 (127)	9.9–13.1	13.7 (108)	11.2–16.8	<0.05
Afternoon	3.2 (75)	2.5–4.1	5.4 (134)	4.6–6.2	5.6 (113)	4.4–7.0	<0.001
Evening	1.9 (73)	1.5–2.4	2.8 (127)	2.3–3.4	3.4 (112)	2.6–4.5	<0.01

Table 3 Logistic regression models of sensitization in children at 12, 24, and 60 months of age given different lifestyles (anthroposophic and partly anthroposophic with non-anthroposophic reference = 1) and different cortisol levels (high ≥ 1 s.d. [standard deviation] above mean with others as reference = 1) at 6 months of age (separate analyses for morning, afternoon, and evening samples presented). Bold ORs indicate statistical significance

	6 months		12 months		24 months		60 months	
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
Anthro	0.11 (0.02–0.50)	0.18 (0.03–0.96)*	0.10 (0.03–0.36)	0.16 (0.04–0.63)*	0.71 (0.34–1.51)	0.82 (0.31–2.14)*	0.38 (0.15–0.95)	0.27 (0.08–0.93)*
Partly	0.25 (0.11–0.58)	0.23 (0.07–0.72)*	0.28 (0.14–0.56)	0.24 (0.09–0.60)*	0.46 (0.24–0.88)	0.39 (0.16–0.93)*	0.49 (0.24–1.01)	0.32 (0.13–0.80)*
Cortisol morning	2.02 (1.27–3.22)	1.88 (1.19–2.98)†	2.12 (1.42–3.15)	1.99 (1.34–2.97)†	2.05 (1.40–3.00)	2.01 (1.37–2.95)†	1.14 (0.76–1.71)	1.10 (0.73–1.66)†
Anthro	0.11 (0.02–0.50)	0.22 (0.04–1.24)*	0.10 (0.03–0.36)	0.17 (0.04–0.70)*	0.71 (0.34–1.51)	0.93 (0.36–2.39)*	0.38 (0.15–0.95)	0.30 (0.09–1.03)*
Partly	0.25 (0.11–0.58)	0.19 (0.06–0.60)*	0.28 (0.14–0.56)	0.21 (0.08–0.52)*	0.46 (0.24–0.88)	0.46 (0.20–1.04)*	0.49 (0.24–1.01)	0.39 (0.16–0.94)*
Cortisol afternoon	1.86 (1.25–2.78)	1.86 (1.24–2.79)†	1.78 (1.29–2.46)	1.70 (1.23–2.36)†	1.54 (1.15–2.07)	1.54 (1.15–2.07)†	1.14 (0.82–1.59)	1.12 (0.80–1.55)†
Anthro	0.11 (0.02–0.50)	0.17 (0.03–0.89)*	0.10 (0.03–0.36)	0.15 (0.04–0.58)*	0.71 (0.34–1.51)	0.85 (0.33–2.17)*	0.38 (0.15–0.95)	0.27 (0.07–0.99)*
Partly	0.25 (0.11–0.58)	0.16 (0.05–0.55)*	0.28 (0.14–0.56)	0.20 (0.08–0.50)*	0.46 (0.24–0.88)	0.44 (0.19–1.02)*	0.49 (0.24–1.01)	0.36 (0.14–0.92)*
Cortisol evening	1.50 (1.10–2.06)	1.45 (1.04–2.01)†	1.58 (1.20–2.08)	1.49 (1.13–1.98)†	1.38 (1.07–1.78)	1.35 (1.04–1.75)†	1.35 (0.97–1.86)	1.32 (0.95–1.82)†

Model 1 adjusted for sex of the child (males), parental sensitization, parental education, mother smoking during pregnancy, number of siblings or other children living with the family, family living on a farm with animals during pregnancy, exclusive breastfeeding at age 6 months.
Model 2 adjusted also for cortisol at 6 months of age* or lifestyle†.

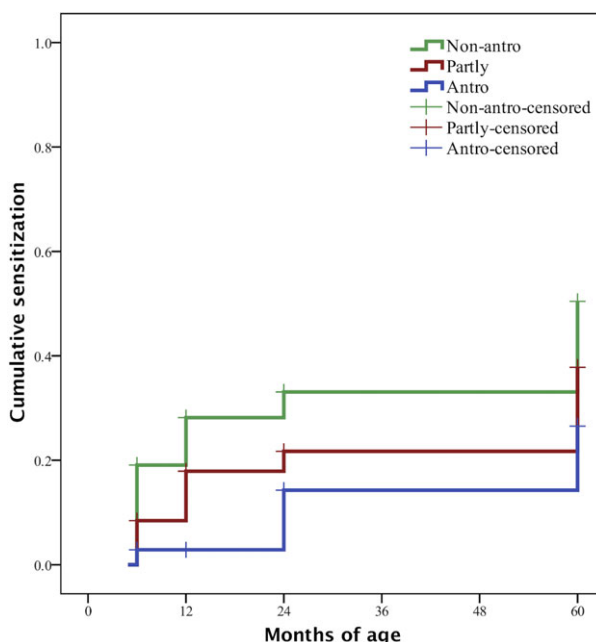


Figure 3 Kaplan–Meier curves illustrating cumulative proportions of sensitization over time. The curves differed significantly for the anthroposophic lifestyle group vs the partly anthroposophic group ($\chi^2 = 5.03$; $p < 0.05$) and vs the non-anthroposophic group ($\chi^2 = 10.82$; $p < 0.01$). Censored represents sensitized cases.

anthroposophic environment was to a substantial degree statistically explained by its negative association with cortisol levels. Still, most of this lower risk seemed to be related to unknown aspects of this lifestyle. Along the same line, an anthroposophic environment statistically explained part of the increased risk assigned to high cortisol levels but most of the risk remained after adjustments for lifestyle. The effect of high cortisol levels faded away over the years.

In line with our finding of an association between high levels of cortisol at 6 months and subsequent sensitization, high cortisol levels during infancy have been reported in two previous studies of children at risk of allergy (5, 6). Other studies have reported low cortisol levels and a reduced reactivity to stressors in children with allergy (7, 16), and this hypofunctioning has in turn been linked to an inadequate inflammatory response (17, 18). Buske-Kirschbaum (4) has suggested that hyperactivity of the HPA axis may be characteristic of early phases of the allergy development. This hyperactivity may influence the immunologic system in several ways, inter alia through the T helper (Th) cell responses, Th1 and Th2, which represent different immunologic processes. In neonates, Th2 dominate while a shift to Th1 immunity gradually occurs during the first 2 years of life (19). In allergy predisposed children, this shift seems to be delayed (19). Glucocorticoids may promote the Th2 response in several ways, which in turn stimulate allergy-promoting processes (4). Glucocorticoids also induce IgE secretion (4). Hypothetically, the hyperactive HPA axis may gradually turn hypoactive due to negative feedback processes (4). Following this theoretic and

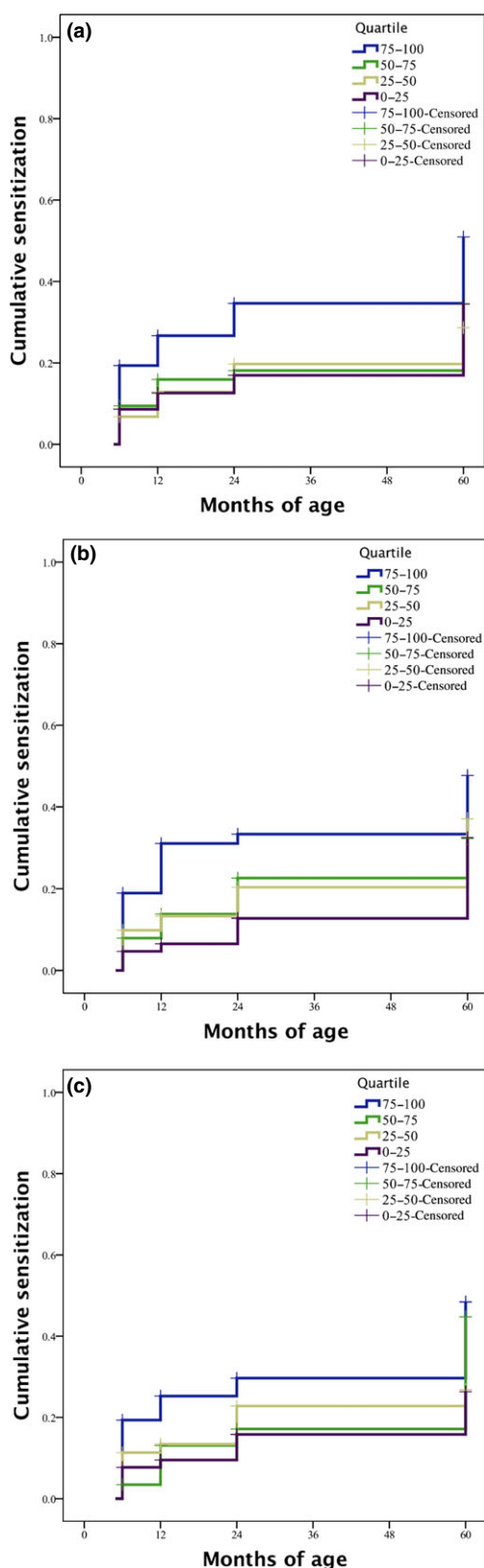


Figure 4 (a) Kaplan–Meier curves illustrating cumulative proportions of sensitization over time in quartile-split morning cortisol level at age of 6 months. The highest quartile (75–100) differed significantly vs q50–75 ($\chi^2 = 3.92$; $p < 0.05$), q25–50 ($\chi^2 = 4.65$; $p < 0.05$) and q0–25 ($\chi^2 = 4.09$; $p < 0.05$). Censored represents sensitized cases. (b) Kaplan–Meier curves illustrating cumulative proportions of sensitization over time in quartile-split afternoon cortisol level at age of 6 months. The highest quartile (75–100) differed significantly vs q0–25 ($\chi^2 = 6.06$; $p < 0.05$). Censored represents sensitized cases. (c) Kaplan–Meier curves illustrating cumulative proportions of sensitization over time in quartile-split evening cortisol level at age of 6 months. The highest quartile (75–100) differed significantly vs q0–25 ($\chi^2 = 4.76$; $p < 0.05$). Censored represents sensitized cases.

empirical path, we hypothesize that low cortisol levels may protect against allergy in predisposed children and/or that high cortisol levels increase the allergy-promoting processes in medium or high disposed children. Taking off from the Bradford Hill criteria (20), the *plausibility* of a causal link between high cortisol levels and subsequent sensitization thus receives some support from these empirical and theoretic sets of hypotheses. Further, the association in our study was statistically significant up to 24 months of age (*strength*) and remained after adjustments for a large number of variables such as parental sensitization, maternal smoking during pregnancy, and lifestyle (*specificity*). To draw more firmly established conclusions about *temporality*, we also performed analyzes restricted to children not sensitized at 6 months of age. The associations between high salivary cortisol levels at 6 months of age and sensitization at age 12 months remained (just as for high morning cortisol levels at 6 months of age and sensitization at age 24 months). We believe that the hypothesis of a causal relation between infancy cortisol levels and subsequent sensitization would benefit from replications in other settings (*consistency*), samples with same lifestyle but different levels of cortisol (*biologic gradient*) and designs including clinical outcomes (*coherence*), which were not available in this study.

We have previously hypothesized that the low cortisol levels of the anthroposophic children are due to early family environmental aspects with, for example, lower exposure to stressful stimuli (21). Our findings in this and previous studies point at this early phase as a crucial period for future development. Alternatively—or complementarily—influences may emanate from the prenatal period (19, 22–24). It has been argued that the low levels of cortisol previously reported from our group may reflect a dull and understimulating lifestyle (25). The results from this study anyway support the positive aspects of a lifestyle related to low levels of cortisol, but future studies should approach this question from other research perspectives.

Children in families with a partly anthroposophic lifestyle also had substantially lower risk of sensitization than children in the non-anthroposophic group. This is particularly interesting as it seems to imply that some characteristics of the anthroposophic environment may be incorporated into a more

typical Swedish lifestyle and still keep the sensitization preventing capacity. This, in turn, means that some aspects of the anthroposophic lifestyle may be of public health importance, if they would be used for intervention purposes. A closer investigation of the partly anthroposophic group stands out as one interesting future scientific line.

The strengths of this study include the prospective design with families recruited already during pregnancy and data collected longitudinally up to 24 months, and for part of the cohort up to 60 months of age. Cortisol levels and sensitization data were based on well established and objective measurements, which are independent of each other. The collection of salivary samples did not coincide with the healthcare visits or blood drawing. None of the families received any information about the results of the sensitization or cortisol analyses during the study period before all children had reached the age of 24 months. Our controls may be considered representative of the general population, as the prevalence of traditional risk factors and sensitization was similar to other publications (26, 27).

As to limitations, the information about lifestyle was based mainly on parental reports. Cortisol data were based on samplings from one single day at each sampling age, which should be taken into consideration when conclusions are drawn. Clinical allergy data from 60 months of age were not available for this study. As we agree that total IgE is not a specific marker of allergic sensitization, we only used allergen-specific IgE as an outcome in this study.

To conclude, children from families with an anthroposophic lifestyle—or a partly anthroposophic lifestyle—run a lower risk of developing sensitization during the first 60 months of life compared with peers from families with a conventional lifestyle. This is to a certain degree statistically explained by saliva cortisol levels (lower levels in anthroposophic children) but most of the effect remains unexplained and merits further studies on which aspects of this lifestyle that may contribute to this allergy preventing capacity. High cortisol levels at age 6 months are associated with sensitization up to age

24 months. This effect is only to a minor degree statistically explained by the above-mentioned association between cortisol levels and an anthroposophic lifestyle.

Acknowledgments

The authors thank the families participating in the ALADDIN study for their trust and contribution and the ALADDIN team for their involvement in this work, especially nurse and coordinator Margareta Eriksson, doctors Fredrik Stenius and Helena Marell Hesla, biomed. Analysts Carina Wallén and Ann-Christine Sjöbeck.

Funding

Supported by the Centre for Allergy Research Karolinska Institutet, the 'Mjölkdroppen' Society, the Swedish Asthma and Allergy Research Association, the Swedish Research Council, Swedish Research Council for Working Life and Social Research, the Swedish Society of Medicine, the Cancer and Allergy Fund, the Ekhsaga, the 'Frimurare Barnhuset' in Stockholm, the Gyllenberg, the Vidar, the Hesselman, the Samariten and the Vårdal Foundation. Thermo Fischer Scientific provided the study with free reagents.

Contributions

Jackie Swartz was involved in family recruitment, performed the first statistical analyses, managed the literature searches in collaboration with Frank Lindblad (FL), and wrote the first draft of the manuscript in collaboration with FL. Johan Alm started the ALADDIN study and has the main responsibility for its development. Töres Theorell supervised. Hans Arinell had the main responsibility for statistical analyses, with support from Töres Theorell. Frank Lindblad supervised the manuscript preparation. All authors contributed to the continuous processing of the analyses and the text and all approved the final version.

Conflict of interests

Jackie Swartz is involved in several ways in the anthroposophic community. There are no other relevant conflict of interests from any of the co-authors.

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