

ORIGINAL ARTICLE

Serum immunoglobulin A concentration in infancy, but not human milk immunoglobulin A, is associated with subsequent atopic manifestations in children and adolescents: a 20-year prospective follow-up study

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Summary

Background Serum and secretory IgA concentrations have been suggested to be inversely associated with allergic symptoms in children. Furthermore, low maternal milk IgA concentration has been suggested to be associated with the development of cow's milk allergy. **Objective** Our aim was to explore whether the serum IgA concentrations in infancy and the IgA concentration of maternal milk predict atopic manifestations in childhood and up to age 20 years.

Methods A cohort of 200 unselected full-term newborns was prospectively followed up from birth to age 20 years with measurement of serum total IgA at ages 2 and 6 months. The mothers were encouraged to maintain exclusive breastfeeding for as long as possible. Total IgA concentration of maternal milk was measured at birth (colostrum, $n = 169$) and at 2 ($n = 167$) and 6 ($n = 119$) months of lactation. The children were re-assessed at ages 5, 11 and 20 years for the occurrence of allergic symptoms, with skin prick testing and measurement of serum IgE.

Results Children and adolescents with respiratory allergic symptoms and sensitization had a higher serum IgA concentration at age 2 months than the non-atopic subjects. Colostrum and breast milk IgA concentrations were not associated with the development of allergic symptoms in the recipient infant. However, maternal milk IgA concentration at 6 months of lactation was inversely associated with elevated serum total IgE and positive skin prick test to tree pollen in the offspring at age 20 years.

Conclusions and Clinical Relevance Increased serum IgA concentration at age 2 months is associated with the development of subsequent allergic symptoms and sensitization in childhood and adolescence. Maternal milk IgA concentrations are not associated with subsequent allergic symptoms in the recipient infant. The present study provides novel information on the role of IgA in the development of respiratory allergy and sensitization.

Keywords adolescence, allergy, atopy, breast milk, children, colostrum, IgA

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Introduction

In infancy, the inexperienced immune system is challenged with a variety of microbes and protein antigens, which may influence the maturing immune system in a way that either predisposes or protects from the development of an allergic immune response [1]. The production of IgA, the main humoral effector of the mucosal

immunity, is a marker of the maturation of the immune system in infancy. The IgA production is induced after birth, and the serum IgA level rapidly increases in early infancy [2, 3].

The serum IgA is mainly produced in the bone marrow, whereas the secretory IgA is produced locally in mucosal tissues and glands [4, 5]. Mucosal and serum IgA responses are differentially regulated [6]. Children with low

levels of serum IgA can have a high salivary IgA secretion, as was demonstrated by a study in which the salivary IgA was measured in stimulated whole saliva collected by aspiration from the mouth [3]. However, in immunologically normal children, the number of IgA-producing plasma cells in the intestine has been shown to correlate with the serum IgA level [7].

Previous studies lend support to a possible association of secretory and serum IgA levels and the development of allergic symptoms and sensitization, although the results are inconsistent. Low levels of total secretory IgA and transient IgA deficiency have been associated with an increased risk of allergy [8, 9]. More recently, opposite results with high salivary IgA concentrations in resting saliva collected by aspiration from the mouth were reported in children with allergic sensitization during the first 2 years of life [10, 11]. Serum IgA of low normal range has been reported in children with allergic manifestations at age 18–23 months [12], and plasma IgA levels at age 4 months were reported to be inversely associated with the frequency of eczema at age 18 months [13]. However, in children with asthma, the serum IgA was found to be relatively high [14], although conflicting results exist [15].

Secretory IgA in human milk is an essential mediator of the passive antimicrobial protection provided by breastfeeding [16]. In early infancy, when the infant's intestinal production of secretory IgA is low or undetectable [17] and the intestinal barrier has not yet developed, the secretory IgA in human milk may prevent an excessive uptake of foreign antigens across the mucosa, thus possibly lowering the risk of allergic sensitization [18]. Low human milk IgA concentration has been shown to be associated with the development of cow's milk allergy in the recipient infant [18–20]. However, the total concentration of IgA in human milk was shown to be unrelated to the prevalence of allergies at age 4 years, while low levels of casein-specific IgA antibodies were associated with a risk of allergy development [21].

In the present study on healthy, unselected newborns prospectively followed-up from birth to age 20 years, we aimed at clarifying whether the serum IgA level in infancy and the IgA concentration of colostrum and mature breast milk are associated with subsequent atopic manifestations in childhood and adolescence.

Methods

Subjects

This investigation is a part of a nutritional follow-up study of 200 unselected newborns and their mothers, which was initiated in 1981 [22]. Healthy, non-smoking mothers with an uncomplicated pregnancy and an uncomplicated vaginal delivery and a full-term healthy infant with birth weight appropriate for gestational age

were invited to participate. All the mothers were encouraged to breast-feed exclusively for as long as it was nutritionally sufficient for the infant. During exclusive breastfeeding, the infants received exclusively human milk without any supplementary formula or solid foods; only water and routine vitamin A and D supplementations were allowed. All the infants received some duration of exclusive breastfeeding. The number of infants on strictly exclusive breastfeeding was 167 at 2, 116 at 6, 36 at 9 and 7 at 12 months of age. When exclusive breastfeeding became insufficient to the infant, the infant was gradually weaned to cow's-milk-based formula (Tutteli[®]; Valio, Helsinki, Finland) and after age 3 months to solid foods. After the exclusive breastfeeding was considered terminated, most infants still continued on partial breastfeeding. There were only 10 infants in whom breastfeeding was terminated before age 2 months.

Of the 200 infants, 42% had a family history of allergy, defined as the presence of at least one first-grade relative with allergic symptoms [23]. Two of the 200 infants were lost to follow-up during the first year. Of the remaining 198 children, 163 (82%) were re-assessed at age 5 years, 150 (76%) at age 11 years and 164 (83%) at age 20 years with skin prick testing, clinical examination and parental (at ages 5 and 11) and personal (at age 20) structured interviews by a physician (M. J. T. K. at the 5- and 11-year re-examinations, M. P. at the 20-year re-examination) unaware of the early feeding history and serum IgA levels. Before the 5- and 11-year visits, the parents filled in a questionnaire concerning the possible allergic symptoms in the child, and the information in the questionnaires was confirmed by personal interviews.

Measurement of serum immunoglobulin concentrations

Serum IgA concentrations at ages 2 ($n=166$) and 6 months ($n=197$) were determined nephelometrically in 1981 [24, 25]. Serum total IgE at ages 5 and 20 years was determined by the Pharmacia ImmunoCAP System IgE FEIA[®] (Pharmacia Diagnostics, Uppsala, Sweden). The serum samples were stored at -20°C until analysed in 2004. The samples at age 11 years were analysed by the Pharmacia CAP System IgE FEIA[®] in 1993. The cut-off for an elevated total IgE was set to 130 kU/L at ages of 11 and 20 years, and to 48 kU/L at age 5 years [26].

Measurement of immunoglobulin A in human milk

The human milk total IgA was measured in 1981 by the single radial immunodiffusion method using secretory IgA as a standard [19]. It was measured in the colostrum ($n=169$), and at 2 ($n=167$) and at 6 months ($n=119$) of lactation. The colostrum milk samples were obtained within 5 days post-partum. The milk samples consisted of

equal amounts of fore and hind milk collected during a 24 h period.

Measurement of plasma retinol concentration

The retinol concentration was repeatedly measured in infancy in every other infant entering the study. Therefore, the plasma concentration of retinol was determined in cord blood at birth in 97 infants and in 95 of these children at ages 2, 4 and 12 months by high-performance liquid chromatography [27].

Definitions of allergic symptoms

Information on the occurrence of allergic symptoms was obtained by personal interview with the child and the parents, and by clinical examination. Allergic rhinoconjunctivitis was defined as recurrent non-infectious rhinitis at pollen seasons or on aeroallergen exposure, and/or itching and watery discharge of the eyes at pollen seasons or on aeroallergen exposure during the preceding year. Recurrent wheezing was recorded if the subject had a diagnosis of bronchial asthma, or two or more separate episodes of respiratory distress and wheezing during the preceding year. Atopic dermatitis was defined as a chronic or relapsing itchy dermatitis with a characteristic morphology and distribution [28]. Atopic dermatitis was recorded if it was present at a follow-up examination or if atopic dermatitis had been diagnosed by a physician and there was a history of relapsing eczema with typical features and localization during the preceding year. Food hypersensitivity symptoms were defined as a history of repeated itching or swelling of the lips, the oral mucosa or the throat, urticarial eruption, or severe vomiting after ingestion of a specific food. At age 20 years, food hypersensitivity symptoms were no longer taken into account. The prevalences of allergic symptoms at ages 5, 11 and 20 years have been published previously [23].

Skin prick testing

We performed skin prick tests (SPTs) at ages 5 ($n = 160$), 11 ($n = 149$) and 20 years ($n = 164$) with standardized allergen extracts (ALK, Copenhagen, Denmark) of birch, alder, timothy, Kentucky blue, mugwort, cat, dog, *Dermatophagoides pteronyssinus*, cow's milk, egg and codfish; histamine hydrochloride (10 mg/mL) and a diluent control were included. A positive SPT was defined as at least one test reaction with a mean diameter equal to or greater than half of the diameter of the histamine weal [29].

Statistical analyses

The two-tailed unpaired Student's *t*-test was used for evaluating the significance of the differences between the

population means. A $P < 0.05$ was considered to be statistically significant. In order to improve normality, the IgA values were log-transformed before analyses. Statistical analyses were performed with StatView 5.0 (SAS Institute, Cary, NC, USA). Multivariate logistic regression analyses were performed in order to control for the effect of potential covariates. As potential covariates, gender, exclusive breastfeeding for the first 2 months, smoking in the household during the infant's first year, sibship size ≥ 3 and family history of allergy were taken into account. Spearman's rank correlation was used for analysis of the association of continuous values, i.e. IgA and retinol concentrations.

Ethical considerations

The Ethical Review Board of the Hospital for Children and Adolescents and the Ethical Review Board for Internal Medicine of the Helsinki University Hospital have approved the study. Written informed consent was obtained from the parents at the beginning of the study, and from the participants of the 20-year re-examination.

Results

Family history of allergy is associated with serum immunoglobulin A concentration in infancy

In our study population, the mean serum IgA concentration was 0.10 g/L (± 0.09) at age 2 months and 0.19 g/L (± 0.12) at age 6 months. Infants with a family history of allergy had a higher serum IgA concentration than those without a family history of allergy at age 2 months (Table 1). There was no statistically significant difference in the mean serum IgA concentrations at age 2 months of infants on exclusive breastfeeding at age 2 months and of those whose exclusive breastfeeding was considered terminated before age 2 months [0.10 g/L (± 0.09) and 0.09 g/L (± 0.05), respectively]. The 10 infants whose breastfeeding had been terminated before age 2 months had a mean serum IgA concentration at age 2 months of 0.08 g/L (± 0.04), which was not significantly different from the

Table 1. Serum IgA concentrations (mean $\pm$ SD) in infants with a family history of allergy (FHA+) and in those without a family history of allergy (FHA-)

Age	FHA+		FHA-		<i>P</i> *
	<i>n</i>	Serum IgA (g/L)	<i>n</i>	Serum IgA (g/L)	
2 months	69	0.112 (± 0.105)	97	0.087 (± 0.068)	0.03
6 months	83	0.200 (± 0.119)	114	0.188 (± 0.123)	NS

**P*-values calculated with unpaired *t*-test.

NS, not statistically significant; SD, standard deviation.

mean serum IgA concentration of the infants who continued on partial or exclusive breastfeeding [0.09 g/L (± 0.09)].

Serum immunoglobulin A concentration in infancy is associated with subsequent atopic manifestations

We observed an association between the serum total IgA level at age 2 months and subsequent respiratory allergic symptoms, positive SPT and an elevated total IgE in childhood and young adulthood (Table 2).

Children with respiratory allergic symptoms at age 5 years, i.e. allergic rhinoconjunctivitis or recurrent wheezing, had a significantly higher serum IgA concentration at age 2 months than the symptom-free children ($P = 0.001$).

Allergic rhinoconjunctivitis at age 11 years was associated with an elevated IgA concentration at age 2 months ($P = 0.02$). Children with verified atopy at age 11 years had a higher serum IgA concentration at age 2 months than the children without verified atopy ($P = 0.03$). Furthermore, an elevated total IgE at age 11 years was associated with an elevated IgA concentration at age 2 months ($P = 0.02$).

Subjects with allergic symptoms at age 20 years had significantly higher serum IgA concentration at age 2 months than the symptom-free subjects ($P = 0.02$). Allergic rhinoconjunctivitis, recurrent wheezing and positive SPT at age 20 years were associated with an elevated IgA concentration at age 2 months ($P = 0.01$). Furthermore, verified atopy, i.e. allergic symptoms and positive SPT,

was associated with an elevated IgA concentration at age 2 months ($P = 0.01$). Subjects with an elevated total IgE at age 20 years tended to have a higher IgA concentration at age 2 months, with no significant difference. The association of serum IgA concentration at age 2 months and subsequent atopic manifestations remained significant when adjusted for the potential cofactors (Table 2). In order to control for the possibility of statistically significant results arising by change due to multiple comparisons, the Holm–Bonferroni method [30] was applied on the *t*-test results on the outcomes at age 20 years, with the cut-off for statistical significance set at 0.05. The results remained statistically significant after the Holm–Bonferroni correction (data not shown).

IgA concentrations at age 6 months were comparable in subjects without atopic manifestations and in those with subsequent allergic symptoms, positive SPT and an elevated total IgE at ages 5, 11 and 20 years.

In addition, we observed an inverse association of serum IgA and plasma retinol concentrations at age 2 months ($P = 0.01$ and $\rho -0.3$, Spearman's rank correlation), i.e. high concentrations of serum IgA were associated with low concentrations of plasma retinol (Fig. 1).

Human milk immunoglobulin A concentrations are not associated with subsequent allergic symptoms in the recipient infant

Human milk total IgA concentrations measured at birth and at 2 and 6 months of lactation were similar in atopic

Table 2. Serum IgA concentration at age 2 months and atopic manifestations at ages of 5, 11 and 20 years

	Mean serum IgA (g/L)			
	Atopics	Controls*	<i>P</i> (<i>t</i> -test)	<i>P</i> (adjusted) [†]
Outcomes at age 5 years				
Any allergic symptom (<i>n</i> = 36)	0.127 (0.14)	0.094 (0.07)	0.06	0.03
Respiratory allergy [‡] (<i>n</i> = 8)	0.260 (0.25)	0.094 (0.07)	0.001	0.03
Outcomes at age 11 years				
Total IgE ≥ 130 kU/L (<i>n</i> = 26)	0.126 (0.11)	0.086 (0.04)	0.02	0.05
Verified atopy [§] (<i>n</i> = 34)	0.129 (0.12)	0.086 (0.04)	0.02	0.05
Allergic rhinoconjunctivitis (<i>n</i> = 35)	0.135 (0.16)	0.086 (0.04)	0.03	0.05
Outcomes at age 20 years				
Any allergic symptom (<i>n</i> = 69)	0.107 (0.10)	0.075 (0.04)	0.02	0.04
Allergic rhinoconjunctivitis (<i>n</i> = 57)	0.113 (0.10)	0.075 (0.04)	0.01	0.02
Recurrent wheezing (<i>n</i> = 16)	0.144 (0.13)	0.075 (0.04)	0.01	0.02
Skin prick test positivity (<i>n</i> = 69)	0.110 (0.10)	0.075 (0.04)	0.01	0.01
Verified atopy [‡] (<i>n</i> = 55)	0.115 (0.10)	0.075 (0.04)	0.01	0.03

Standard deviation in parenthesis.

*Adjusted for gender, duration of exclusive breastfeeding ≥ 2 months, family history of allergy, smoking in the household during the infant's first year and sibship size ≥ 3 . Smoking status at age 20 years was added for the outcomes at age 20 years.

[†]Controls: symptom-free and SPT negative subjects; *n* = 92, 54 and 55 at ages 5, 11 and 20 years.

[‡]Allergic rhinoconjunctivitis and/or recurrent wheezing.

[§]Allergic symptoms and skin prick test positivity.

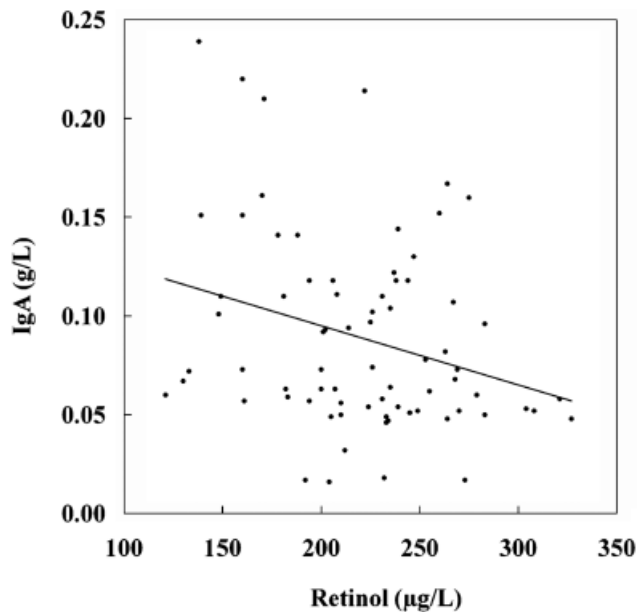


Fig. 1. Inverse association of serum IgA and plasma retinol concentrations at age 2 months. Linear regression. $R = 0.29$, $P = 0.01$.

Table 3. Concentration of IgA in colostrum and in breast milk at 2 and 6 months of lactation in atopic and non-atopic mothers

Months of lactation	Mean breast milk IgA (g/L)		
	Total population	Atopic mothers	Non-atopic mothers
0 ($n = 168^*$)	1.337 (1.067)	1.252 (1.090)	1.367 (1.062)
2 ($n = 167$)	0.339 (0.204)	0.324 (0.192)	0.344 (0.208)
6 ($n = 119$)	0.207 (0.074)	0.205 (0.078)	0.208 (0.073)

Standard deviation in parenthesis.

*One mother with exceptionally high colostrum IgA value (8.4 g/L) excluded.

and in non-atopic mothers (Table 3). Human milk IgA concentrations were not associated with the development of subsequent allergic symptoms in the recipient infant (data not shown). However, the maternal milk IgA concentration at 6 months of lactation was inversely associated with an elevated serum total IgE and positive SPT to tree pollen (birch, alder) in the offspring at age 20 years ($P = 0.01$ and 0.03 , respectively).

Discussion

From a 20-year prospective follow-up study on healthy, unselected newborns, we report a positive association between the serum IgA concentration at age 2 months and subsequent allergic symptoms, positive SPT and elevated total IgE in childhood and at age 20 years. The IgA concentration of colostrum and mature breast milk

was not significantly associated with subsequent atopic symptoms in the recipient infant. However, the breast milk IgA concentration at 6 months of lactation was inversely associated with elevated serum total IgE and positive SPT to tree pollen in the offspring at age 20 years. Several previous studies [9, 12–14, 31, 32] indicate that low levels of secretory and serum IgA in infancy may be a risk factor for allergy development early in life. Infants with a high faecal IgA concentration at age 6 months were shown to be at a reduced risk of allergic diseases during the first 2 years of life [33]. In our study, the subjects who developed subsequent atopic manifestations had a higher serum IgA concentration at age 2 months than those who remained symptom free. The divergence in the results of our study and the previous ones may be due to the fact that we studied the association of serum IgA in infancy with atopic manifestations at ages 5, 11 and 20 years, i.e. at a considerably later age than the previous studies. Furthermore, in our cohort, all the infants received exclusive breastfeeding from birth, and a majority of the infants were still on strictly exclusive breastfeeding at age 2 months. This mode of feeding is likely to modulate the maturation of the gut immune responses as well as the intestinal bacterial colonization. In addition, the serum IgA was measured at an earlier age in our study than in the previous studies.

The IgA concentrations of colostrum and mature milk observed in the present study were similar to the previously reported concentrations of human milk IgA. The concentration of secretory IgA in human milk is highest, 1–2 g/L, in the first few days post-partum, i.e. in the colostrum. The concentration then falls to a basal level of 0.2–0.3 g/L [18, 34, 35]. In early infancy, when the intestinal production of secretory IgA is low or undetectable [17] and the intestinal barrier has not yet developed, the secretory IgA in human milk may compensate for the relative IgA deficiency and prevent excessive uptake of foreign antibodies across the mucosa. Therefore, lack of IgA in human milk might lead to an increased intestinal allergen exposure and enhance the risk of allergies [18]. Low human milk IgA concentration has been shown to be associated with the development of cow's milk allergy in the infant [18–20]. However, we now report that the IgA concentration of colostrum and mature milk is not significantly associated with allergic sensitization or symptoms during the first 2–4 years of life [35, 36, 21]. This suggests that although a low IgA level of breast milk may be associated with cow's milk allergy, it is unlikely to have an effect on the development of allergic symptoms emerging at a later age.

The maternal IgA does not cross the placenta, and IgA concentration in cord blood is low [3, 37, 38]. After birth,

the IgA production is induced and a rapid increase of the serum IgA is seen during the first month of life [2]. The adult level of serum IgA is reached at puberty [39]. However, in the intestinal lamina propria, the adult levels of IgA are reached as early as by the age 2 years [7]. The mucosal IgA secretion is triggered by intestinal colonization by the commensal flora [40, 41]. Recently, a transient colonization with a pathogenic microbe, i.e. toxigenic *Staphylococcus aureus* strains, was shown to be associated with a comparatively high systemic IgA level [13]. However, the serum IgA levels do not necessarily reflect the IgA function at mucosal surfaces, which should be kept in consideration while interpreting the results of the present and the previous studies.

The secretory IgA serves as the first line of defence in mucosal areas against pathogenic microbes and foreign proteins [38, 42–44, 45], and it may also have a role in the induction of immunological tolerance to food antigens [46, 47]. Because the binding of secretory IgA to antigens does not trigger inflammatory processes, it is considered a non-inflammatory antibody [46]. In contrast, serum IgA and IgA-containing immune complexes are capable of initiating immune effector functions by interacting with the IgA-Fc receptor (CD89) on cells of the myeloid lineage [38, 48]. Interaction of serum IgA with CD89 on tissue phagocytic cells has been suggested to act as a second line of defence in the case of bacterial infections penetrating through the mucosal barrier [49].

Salivary total IgA concentration in resting saliva has been shown to be high in children who developed allergy during the first 2 years of life [10], and allergic sensitization at age 12 months has been shown to be associated with a higher salivary total IgA concentration in resting saliva at age 6 months [11]. The B cells derived from human nasopharynx-associated lymphoid tissue (NALT) have been shown to express a distinct homing-molecule profile, which directs them to the upper aerodigestive tract mucosa and associated glands rather than to the gut [50]. Thus, NALT-derived B cells might migrate to the parotid glands, which might, in turn, be reflected as elevated salivary IgA secretion stimulated by airway infection. Respiratory infections in early life, e.g. respiratory syncytial virus (RSV) bronchiolitis, have previously been suggested to be associated with an increased risk of developing subsequent allergic symptoms. Thus, the observed increase of serum IgA in infants with subsequent atopy might be due to an immune response directed against an infection. However, studies on the relationship between early respiratory infections and subsequent allergic sensitization and atopic symptoms have yielded conflicting results [51–55].

We observed an inverse association of serum IgA and plasma retinol (i.e. vitamin A) concentrations in infants at age 2 months. Previously, we have reported from the present follow-up cohort an inverse association of retinol

concentration in infants and the subsequent development of clinical and laboratory manifestations of atopy [56]. However, the retinol concentration at age 2 months was measured only in half of the infants in our study cohort. The low number of subjects did not permit a further analysis of the possible effect of the retinol concentration on the association of IgA at age 2 months and the subsequent atopy.

Retinoic acid, a vitamin A metabolite produced by the intestinal dendritic cells, imprints the gut tropism on T and B cells by inducing the expression of the gut-homing receptors integrin $\alpha 4\beta 7$ and the chemokine receptor CCR9 [57, 58]. Retinoic acid has also been shown to enhance the switch of B cells to the IgA isotype and to enhance the IgA production [58–60]. In addition, it enhances the expression of human polymeric Ig receptor (pIgR), which transports polymeric IgA across the epithelium into external secretions as secretory IgA [61, 62]. In vitamin A-deficient rats, the transport of IgA to external secretions was reduced, although the amount of plasma cells secreting IgA was normal [63]. In children and rats with vitamin A deficiency, the levels of secretory IgA were decreased, whereas the serum IgA levels were normal or elevated [63, 64]. However, vitamin A deficiency is an unlikely explanation to our results, because all the infants of the study cohort received vitamin A supplementation [56]. We find it more likely that the comparatively low level of retinol in infants who later developed atopic manifestations may be due to an inborn regulation of retinol metabolism. The comparatively low retinol level in infancy might result in a reduced expression of pIgR and possibly also interfere with the gut-homing of IgA-secreting plasma cells, resulting in an increased serum IgA instead of the IgA being transported to external secretions. In support of this is a previous follow-up study, in which the development of allergy tended to be associated with low levels of salivary secretory IgA [10]. A reduced expression of pIgR might lead into a decreased concentration of secretory IgA on the mucosal surfaces, which might in turn interfere with the induction of immunological tolerance to foreign antigens, therefore predisposing the infant to the development of subsequent atopic manifestations. We found that the serum IgA concentration at age 2 months was inversely associated with the subsequent development of sensitization and respiratory allergic symptoms, whereas the serum IgA at age 6 months was not. In the newborn, the functionally and immunologically immature gut mucosa is more permeable to antigens than it is later in infancy [65, 66]. Our finding might imply that there is a particularly vulnerable period in the postnatal maturation of the gut immune system in early infancy, when exposure to foreign antigens might more easily induce sensitization and subsequent clinical symptoms in individuals with genetic predisposition.

Conclusions and clinical relevance

Our results from a long-term prospective follow-up study provide novel information on the possible role the infants' own IgA secretion as well as the maternal milk IgA concentration might have in the development of clinical and laboratory manifestations of atopy. Serum IgA concentration at age 2 months is associated with subsequent atopic symptoms in childhood and adolescence in a cohort of unselected, exclusively breast-fed infants prospectively followed from birth to age 20 years. Maternal milk IgA concentration at 6 months of lactation is inversely associated with elevated serum total IgE and

positive SPT to tree pollen in the offspring at age 20 years. However, the concentration of IgA in colostrum and in breast milk at 2 and 6 months of lactation is not associated with subsequent allergic symptoms in the recipient infant.

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Conflict of interests: None to declare.

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