

Original article

Early atopic disease and early childhood immunization – is there a link?

Background: There are frequent concerns about early immunizations among the parents of children at heightened risk for atopy. The study assessed the effect of vaccine immunization before the first birthday on eczema severity and allergic sensitization in the second year of life.

Methods: A total of 2184 infants, aged 1–2 years, with established atopic dermatitis and a family history of allergy, from 97 study centres in 10 European countries, South Africa and Australia were included. Exposure to vaccines (diphtheria, tetanus, pertussis, polio, *Haemophilus influenzae* Type B, hepatitis B, mumps, measles, rubella, varicella, BCG, meningococci and pneumococci) and immunization dates were recorded from immunization cards. Immunoglobulin E (IgE) was determined by RAST and eczema severity was assessed by scoring atopic dermatitis (SCORAD).

Results: Immunization against any target was not associated with an increased risk of allergic sensitization to food or inhalant allergens. Varicella immunization (only 0.7% immunized) was inversely associated with total IgE > 30 kU/l (OR 0.27; 95% CI 0.08–0.87) and eczema severity (OR 0.34; 95% CI 0.12–0.93). Pertussis immunization (only 1.7% nonimmunized) was inversely associated with eczema severity (OR 0.30; 95% CI 0.10–0.89). Cumulative received vaccine doses were inversely associated with eczema severity ($P = 0.0107$). The immunization coverage of infants before and after the onset of atopic dermatitis was similar.

Conclusion: In children at heightened risk for atopy, common childhood immunization in the first year is not associated with an increased risk of more severe eczema or allergic sensitization. Parents of atopic children should be encouraged to fully immunize their children.

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Atopic diseases are among the commonest chronic conditions in childhood. Atopic dermatitis, which develops in the first year of life (1), is frequently the initial manifestation of the atopic syndrome and is characterized by the development of immunoglobulin E (IgE) antibodies against food and inhalant allergens.

Parents of children at heightened risk for atopy are frequently concerned about the effect of immunizations in infancy. Apart from concerns about rare allergic reactions to the vaccine antigens themselves or vaccine contaminants (2), there exists a fear that immunizations may promote the development of atopic disease (3). This may lead to delayed or incomplete immunization of some children. In addition, the rising prevalence of atopic disease today has been attributed to a decline in infectious disease. In this context, early childhood immunizations

have been viewed as a promoter of the atopic career (4) or as a surrogate for infections with an inhibitory effect on atopy (5).

The primary aim of this study was to assess the potential effect of immunization, in a large population of infants, with common vaccines in the first year of life, on the severity of eczema and on IgE sensitization to environmental allergens in the second year of life.

Methods

Participants

Infants aged between 11.5 and 25.5 months with active atopic dermatitis were screened for recruitment into a randomized clinical trial, under the EPAAC study (Early Prevention of Asthma in the Atopic Child). The trial was designed to test the effect of levocetirizine on the onset of asthma. Included were infants with active dermatitis and a family history of allergy (first degree relative with a history of atopic dermatitis, bronchial asthma or hay fever), but no

Abbreviations: BCG, Bacille Calmette Guérin; CI, confidence interval; EPAAC, early prevention of asthma in the atopic child; OR, odds ratio; SCORAD, scoring atopic dermatitis; Th, T helper.

history of asthma or wheezing. The results presented in this study were obtained exclusively from the analyses of these screening data collected between March 2002 and March 2004 before randomization.

Atopic dermatitis and disease severity

Scoring atopic dermatitis (SCORAD) is a standard tool for measuring the severity of dermatitis (6) and measures the extent of the body area involved, the intensity of six different signs, and of itching. Investigators were trained for using the SCORAD, to ensure better homogeneity of the assessments. For the analysis, the total index was used as a dichotomous variable (mild, index < 25; moderate/severe, index $\geq$ 25) (7, 8).

Exposure to vaccines

Immunization details of the children were recorded retrospectively from their immunization cards. Immunization targets (diphtheria, tetanus, pertussis, *Haemophilus influenzae* type B, hepatitis B, polio, measles, mumps, rubella, tuberculosis, meningitis, pneumonia and other) were recorded, and their commercial name and the date of all administrations were coded with WHODRUG 2003Q4 (UMC Products and Services, Uppsala, Sweden). The available data did not allow classification into acellular/cellular pertussis vaccine with sufficient precision. Additionally, the cumulative number of administrations for each vaccine and the cumulative number of administrations summed for all vaccines were calculated. Exposure was calculated for the following intervals: at birth (during the first week of life), during the first 3, 6 and 12 months, during the last 3 months prior to screening and during the lifetime prior to the study visit.

Atopy

All IgE measurements were performed in three central laboratories with the Pharmacia ImmunoCAP fluorescence enzyme immunoassay technology (Pharmacia Diagnostics, Uppsala, Sweden). There was a high correlation of results from reference sera between the laboratories. The lower and upper detection limits were 0.35 and 100 kU_A/l, respectively. A specific IgE test was considered positive if $\geq$ 0.35 kU_A/l. To allow for quantitative analysis on serum concentration as a continuous variable, we used the following counting rules, based on visual extrapolations from the observed distribution: the specific IgE measurement was set to 0.175 when the record was < 0.35, or to 135 when the record was > 100. The following variables were derived for the purpose of the analyses:

- Inhalant: positive if any test was positive for house dust mite, cat, grass pollen or alternaria.
- Food: positive if any test was positive for milk, egg or peanut.
- Any: positive if a test was positive for inhalant or food.
- Total serum IgE was categorized as elevated if the measured value was > 30 kU_A/l.

Statistics

Descriptive statistics were reported in a standard way (number and proportion; mean and/or median, and standard deviation). Associations were measured by multiple logistic regressions. Exposure to vaccines (see above) was categorized according to the targets of immunization. Candidate confounding factors were selected based

on the current literature. They include: country, age, gender, birth weight, maternal age, family history of atopy, presence of siblings, breastfeeding, parental smoking, day care, exposure to pet animals and SCORAD total index. The candidate factors were first evaluated by univariate analysis and were retained in further analyses only if they were statistically significant in a consistent way. In subsequent multivariable analyses, the set of confounding factors was further optimized, separately for each outcome. Odds ratios were estimated by logistic regression (PROC LOGISTIC, SAS 8.2; SAS Institute Inc., Cary, NC, USA), either without any other factor than exposure (raw OR) or with the confounding factors (adjusted OR). The power was computed for detecting a significant OR = 2.0 given a total sample size of 2173 and a baseline proportion between 30 and 70%; no adjustment for covariates was assumed. The power was always above 80% when the smaller group (vaccinated or not) was larger than 4% of the population.

Ethical approval

The parents of all children involved in the study gave their informed consent. The research protocol was approved by the Ethics Committees in the institutions of every participating investigator.

Results

Study population

The study sample consisted of 2184 subjects screened in 94 study centres from 12 countries. A total of 2184 participants was recruited, from Australia ($n = 301$), Austria ($n = 8$), Belgium ($n = 85$), Czech Republic ($n = 315$), France ($n = 126$), Germany ($n = 223$), Italy ($n = 234$), the Netherlands ($n = 149$), Poland ($n = 505$), South Africa ($n = 161$), Spain ($n = 35$), and the UK ($n = 42$). 92.1% of the study subjects were caucasian. Further characteristics of the participants are summarized in Table 1.

Table 1. Epidemiological and clinical data of the study subjects

Groups	IR	PAR-P	PAR-HDM	HC
Subjects (n)	32	35	30	50
Age (years)	41 $\pm$ 18	28 $\pm$ 11	31 $\pm$ 12	37 $\pm$ 12
Disease duration (years)	7 $\pm$ 7	6 $\pm$ 5	8 $\pm$ 6	NA
Gender, n (%)				
Male	13 (41)	14 (40)	11 (37)	19 (38)
Female	19 (59)	21 (60)	19 (63)	31 (62)
FHA, n (%)	15 (46)	15 (43)	13 (43)	14 (28)
Dwelling, n (%)				
City	20 (62)	22 (63)	20 (67)	31 (62)
Country	12 (38)	13 (37)	10 (33)	19 (38)
Co-morbidity, n (%)				
Conjunctivitis	20 (62)	23 (65)	13 (43)	NA
Asthma	10 (31)	4 (11)	9 (30)	

Data expressed as mean $\pm$ standard deviation.

IR, idiopathic rhinitis; PAR-P, persistent allergic rhinitis to pollen; PAR-HDM, persistent allergic rhinitis to house dust mite; HC, healthy control group; n , number of subjects; FHA, family history of atopy; NA, not applicable.

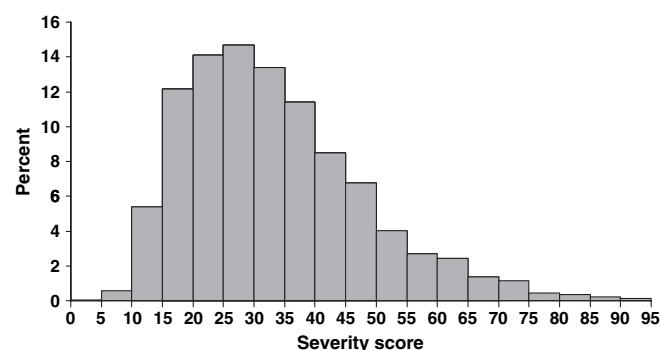


Figure 1. Distribution of the SCORAD total index.

The mean total SCORAD index for the study population was 33 (median, 31.0; range, 0.6–93.8). The proportion of children in the moderate/severe category (total index ≥ 25) was 68%. The distribution of the SCORAD total index is shown in Fig. 1.

Elevated total IgE ($> 30\text{kU}_\text{A}/\text{l}$) was detected in 52.9% of the children. Among the 2096 subjects possessing full specific IgE test results, 44.5% were without allergic sensitization to any of the tested allergens, 48.6% were sensitized to food allergen, 31.5% to inhalant allergen, 55.5% to any food or inhalant allergen. Overall, 65.1% of the children were atopic, based on raised total IgE and/or allergic sensitization.

Exposure to vaccines

Of the 2184 children screened, immunization data were available for 2173 children. Eleven children with all immunization data missing were excluded from further analyses. Hence, 2173 children were included in the final sample. For some calculations we received a slightly lower number of cases because immunization data (e.g. date of vaccination) were not available.

The mean age at first immunization was 1.1 month. There was wide variation among the countries for immunization coverage and timing. Overall, 63% of the children received some form of immunization at birth (range among countries: 0–98%); these were mostly immunizations for hepatitis B in Australia and Poland; polio in South Africa; and BCG in the Czech Republic and Poland. By 3 months of age, 90% of the children had received some form of immunization. On an average, the children had received eight different vaccines (range: 0–14), with up to four different vaccines given at birth. The average value ranged from 7.1 to 9.0 among the countries. On average, the children had received 16.7 ± 3.3 administrations at age of 1 year and 20.1 ± 4.4 administrations between birth and the study visit.

The proportion of children immunized varied considerably by country and by vaccine. More than 90% were immunized against diphtheria, tetanus, pertussis and polio. BCG was more frequently administered in the

Table 2. Frequency and severity of symptoms during the pollen season

Symptom	IR (<i>n</i> = 32)	PAR-P (<i>n</i> = 35)	IR vs PAR-P <i>P</i> -value	HC (<i>n</i> = 50)
Itching (%)				
Frequency	24 (75)	23 (65)	NS	—
Mild	8 (25)	7 (20)		—
Moderate	12 (37)	11 (31)		—
Severe	4 (13)	5 (14)	NS	—
Sneezing (%)				
Frequency	25 (78)	28 (80)	NS	2 (4)
Mild	6 (19)	9 (26)		2 (4)
Moderate	11 (34)	16 (46)		—
Severe	8 (25)	3 (8)	<0.05	—
Anterior Rhinorrhoea (%)				
Frequency	28 (88)	27 (77)	NS	3 (6)
Mild	3 (9)	7 (20)		3 (6)
Moderate	15 (48)	19 (54)		—
Severe	10 (31)	1 (3)	0.002	—
Posterior Rhinorrhoea (%)				
Frequency	30 (96)	27 (77)	0.001	—
Mild	4 (13)	7 (20)		—
Moderate	15 (48)	19 (54)		—
Severe	11 (35)	1 (3)	0.002	—
Nasal obstruction (%)				
Frequency	20 (62)	24 (68)	NS	1 (2)
Mild	—	12 (34)		1 (2)
Moderate	12 (38)	7 (20)		—
Severe	8 (25)	5 (14)	NS	—
Hyposmia (%)				
Frequency	11 (34)	9 (26)	NS	—
Mild	5 (15)	9 (26)		—
Moderate	6 (19)	—		—
Severe	—	—	NS	—
Ocular symptoms (%)				
Frequency	20 (62)	21 (60)	NS	—
Mild	—	—		—
Moderate	8 (25)	10 (29)		—
Severe	12 (37)	11 (31)	NS	—

IR, idiopathic rhinitis; PAR-P, persistent allergic rhinitis to pollen; HC, healthy control group; NS, not significant.

Czech Republic, France, the UK, Poland and South Africa; in all other countries, less than 3% of the children had received BCG (Table 2). The immunization coverage by age is summarized in Table 3.

Association of atopy and immunization

Infants immunized against hepatitis B at birth were less likely to be IgE-sensitized to aeroallergens (adjusted OR 0.54, 95% CI 0.32–0.90, $P = 0.0181$). No effect was seen for hepatitis B immunization later on in life. Newborns immunized against polio were more likely to be sensitized to food allergens (adjusted OR 2.60, 95% CI 1.08–6.25, $P = 0.0324$), whereas either later in life or regarding sensitization to inhalants, no effect was

Table 3. Laboratory data during the pollen season in seasonal IR subjects regardless of response to NAPT

	IR	PAR-P	HC
Serum			
ECP, µg/l	23 ± 12*	38 ± 18†	18 ± 13
Total IgE, IU/ml	143 ± 178*	430 ± 507†	47 ± 59
slgE grass, kU/l	<0.35*	24 ± 43†	<0.35
slgE olive, kU/l	<0.35*	12 ± 18†	<0.35
Nasal Lavage			
Supernatant			
ECP, µg/l	12 ± 17†	48 ± 63†	2 ± 2
Total IgE, IU/ml	21 ± 28	23 ± 16†	8 ± 19
slgE grass	0.62 ± 0.40*	0.69 ± 0.86†	<0.35
slgE olive, kU/l	0.21 ± 0.37	0.28 ± 0.46	<0.35
Flow cytometry			
TCC	9218 ± 1766	9369 ± 1588	8758 ± 2316
CD45+	85 ± 16†	80 ± 19†	57 ± 29
N, %	16 ± 8	12 ± 10	17 ± 23
E, %	44 ± 25†	52 ± 22†	14 ± 8
B-MC, %	1.39 ± 1.20	1.47 ± 1.23†	0.77 ± 0.91
L, %	0.45 ± 0.42*	1.01 ± 0.64†	0.29 ± 0.34
CD3 + T cells, %	0.04 ± 0.04*	0.22 ± 0.26†	0.12 ± 0.25
CD4 + T cells, %	14 ± 22*	30 ± 29†	7 ± 13
CD8 + T cells, %	16 ± 26	32 ± 31	26 ± 32

Data represent mean ± standard deviation.

IR, idiopathic rhinitis; PAR-P, persistent allergic rhinitis to pollen; HC, healthy control group; slgE, specific IgE; ECP, eosinophil cationic protein; TCC, total cell count; N, neutrophils; E, eosinophils; B-MC, basophils-mast cells; L, lymphocytes.

*Significant differences between IR and PAR-P patients.

†Significant differences with HC.

Table 4. Laboratory data during the pollen season in seasonal IR subjects with positive or negative response to NAPT

	IR-PosNAPT	PAR-P	IR-NegNAPT	HC
Serum				
ECP, µg/l	25 ± 12	38 ± 18‡	22 ± 10†	18 ± 13
Nasal Lavage				
Supernatant				
ECP, µg/l	19 ± 24‡†	48 ± 63‡	14 ± 21†	2 ± 2
Flow cytometry				
TCC	8638 ± 2725	9369 ± 1588	9354 ± 1130	8758 ± 2316
CD45+	80 ± 20‡	80 ± 19‡	86 ± 13‡	57 ± 29
N, %	12 ± 5	12 ± 10	16 ± 9	17 ± 23
E, %	56 ± 24‡	52 ± 22‡	40 ± 24‡	14 ± 8
B-MC, %	2.64 ± 0.69‡†	1.47 ± 1.23‡	1.11 ± 1.07	0.77 ± 0.91
L, %	0.78 ± 0.51	1.01 ± 0.64‡	0.39 ± 0.42†	0.29 ± 0.34
CD3 + T cells, %	0.50 ± 0.30*†‡	0.22 ± 0.26‡	0.02 ± 0.04†	0.12 ± 0.25
CD4 + T cells, %	33 ± 38	30 ± 29‡	11 ± 17	7 ± 13
CD8 + T cells, %	52 ± 14*	32 ± 31	19 ± 30	26 ± 32

Data represent mean ± standard deviation.

IR, idiopathic rhinitis; NAPT, nasal allergen provocation test; IR-PosNAPT, IR with positive response to NAPT; IR-NegNAPT, IR with negative response to NAPT; PAR-P, persistent allergic rhinitis to pollen; HC, healthy control group; TCC, total cell count; N, neutrophils; E, eosinophils; B-MC, basophils-mast cells; L, total lymphocytes.

*Significant with IR-NegNAPT.

†Significant differences with PAR-P patients.

‡Significant differences with HC.

observed. Immunization against any other target did not significantly influence allergic sensitization (Fig. 2).

Elevated total IgE was associated with immunization against hepatitis B in the first 6 months (adjusted OR 1.48, 95% CI 1.03–2.13, $P = 0.0343$), but not thereafter. Varicella immunization in the first year was inversely associated with elevated total IgE (adjusted OR 0.27, 95% CI 0.08–0.87, $P = 0.0284$), as was the immunization in the 3 months before screening (adjusted OR 0.28, 95% CI 0.14–0.56, $P = 0.0003$) and since birth (adjusted OR 0.37, 95% CI 0.21–0.65, $P = 0.0005$). A weak inverse association was also observed with rubella immunization since birth (adjusted OR 0.79, 95% CI 0.63–0.99, $P = 0.0425$) and with immunization against pneumococci since birth (adjusted OR 0.49, 95% CI 0.27–0.92, $P = 0.0265$) but not with immunization in earlier time intervals (Fig. 2). No significant association of vaccination status and atopy (as defined by any positive IgE test) was found.

Association of disease severity and immunization

A moderate to severe SCORAD index was inversely associated with immunization against polio in the first 6 months (adjusted OR 0.66, 95% CI 0.45–0.97, $P = 0.0335$) and pertussis in the first year (adjusted OR 0.30, 95% CI 0.10–0.89, $P = 0.0265$). Varicella immunization was also inversely associated with eczema severity if given in the first year (adjusted OR 0.34, 95% CI 0.12–0.93, $P = 0.0358$) or since birth (adjusted OR 0.56, 95% CI 0.33–0.93, $P = 0.0263$). A similar inverse association was observed for immunization against measles (adjusted OR 0.72, 95% CI 0.55–0.96, $P = 0.0226$), mumps (adjusted OR 0.72, 95% CI 0.54–0.94, $P = 0.0184$) and rubella, 3 months before screening (adjusted OR 0.73, 95% CI 0.55–0.96, $P = 0.0270$) and for immunization against measles (adjusted OR 0.63, 95% CI 0.49–0.80, $P = 0.0002$), mumps (adjusted OR 0.68, 95% CI 0.54–0.86, $P = 0.0010$) and rubella since birth (adjusted OR 0.69, 95% CI 0.55–0.87, $P = 0.0015$) (Fig. 2).

Outcome in relation to cumulative vaccine doses

Cumulative vaccine doses received by age 1 year were not associated with a clear-cut dose–response pattern of allergic sensitization or elevated total IgE (Fig. 3). Severity of atopic dermatitis, however, was inversely associated with cumulative vaccine doses administered in year 1 ($P = 0.0107$; Fig. 3) and since birth ($P = 0.0098$, data not shown). The same tendency was seen earlier in life, however, without achieving statistical significance (data not shown). No other consistent dose–response relationship of sufficient significance was found for any particular vaccine antigen in relation to any endpoint (data not shown).

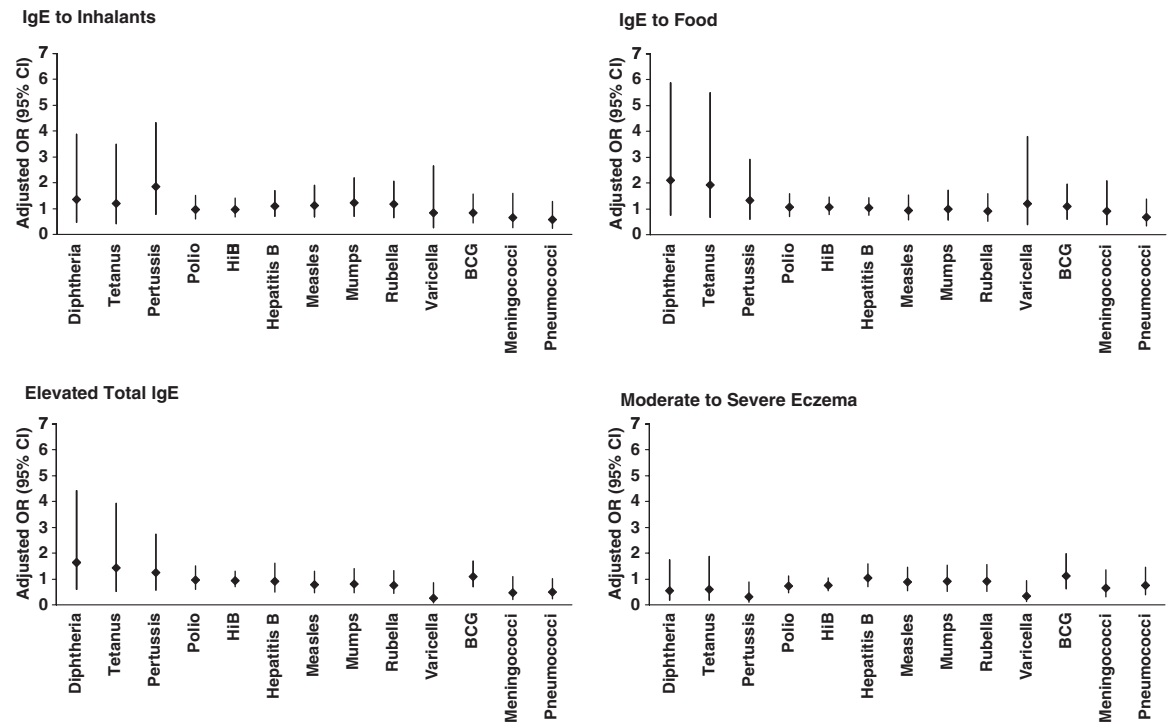


Figure 2. Exposure to vaccines administered in the first year and odds ratio for outcomes. Adjustment variables: country, gender, asthma of parents, day care, breast milk feeding, age, birth weight, SCORAD (IgE to inhalants, $n = 1461$); gender, siblings, atopic parents, animal contact in the first year, age, birth weight, breastfeeding duration, SCORAD (IgE to food, $n = 1455$); country, gender, atopic parents, breast milk, age, birth weight, breastfeeding duration, SCORAD (elevated total IgE, $n = 1464$); country, gender, siblings, atopic parents, age, mother's age, birth weight (eczema severity, $n = 1519$).

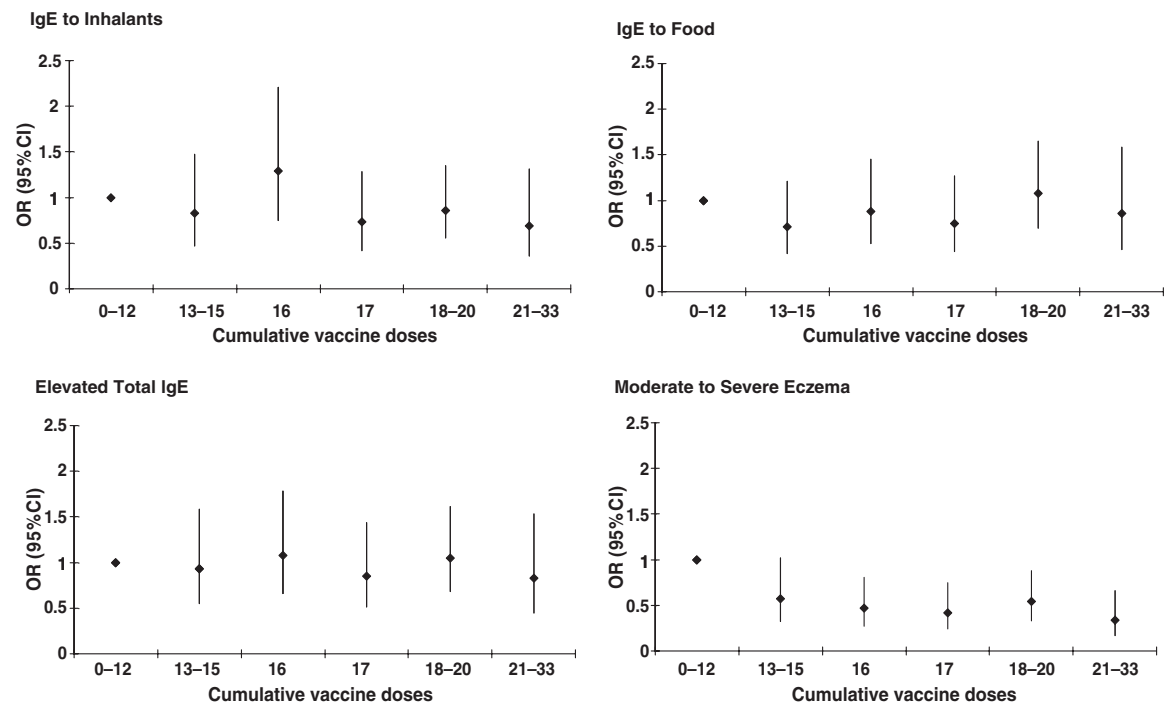


Figure 3. Number of cumulative vaccine doses administered before the age of 1 year in relation to the outcome.

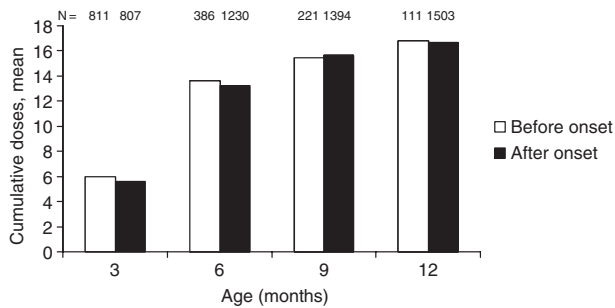


Figure 4. Cumulative vaccine doses among infants with already-established or not-yet-established atopic dermatitis (AD). No statistically significant group difference was found.

Onset of atopic dermatitis and immunization

The cumulative vaccine dose was compared between infants already afflicted from atopic dermatitis at a given age and infants who were still free from atopic dermatitis. There was no significant difference in the cumulative immunization dose between both the groups (Fig. 4).

Discussion

We found no association between either eczema severity or allergic sensitization and exposure to common vaccines in the first year of life in this exploratory study of a large population of young children with active atopic dermatitis. Cumulative calculated doses of immunizations received in the first year of life, however, were inversely associated with eczema severity (Fig. 3).

For some of the vaccines, we had no sufficiently sized control group at the first birthday and it became important to evaluate immunization at other age intervals when more controls were available. Using this approach, we found no evidence for a worse outcome among infants already immunized in the first 3 months against diphtheria, tetanus and pertussis or among infants immunized against measles, mumps and rubella shortly before the study visit. Immunization against some targets such as pneumococci or varicella has been integrated recently into immunization schedules. Analysis of possible effects on atopy may be possible with more confidence in the near future when larger samples of immunized infants are available.

On account of the retrospective design of our study, we could not rule out the possibility that avoidance of immunization procedures, because of atopic dermatitis might have influenced our results. However, such a 'reverse causation' appears to be unlikely as the immunization coverage among infants before and after onset of atopic dermatitis is similar (Fig. 4). As some of the vaccines are usually administered simultaneously, it should be kept in mind that dependence among exposure cannot be ruled out completely in this study when conclusions are drawn with regard to particular vaccine antigens.

We controlled our calculations for a variety of confounding factors, including atopic family history, eczema severity, gender, age, breastfeeding duration, indicators of exposure to infections and animal dander and country. We cannot rule out the possibility that further factors influenced our results, such as vaccine adjuvants or contaminants for which no exact dose calculations were possible.

Impact of immunization on atopic dermatitis

Previous studies investigated the association of immunization status in relation to the occurrence of atopic dermatitis. A recent longitudinal survey reported a higher incidence of atopic dermatitis in measles-immunized children than in nonimmunized children, but the incidence of atopic dermatitis among measles-infected children was similar (9). Pertussis immunization does not seem to have any effect (10). A large international cross-sectional study showed a weak negative association of atopic dermatitis and better diphtheria–tetanus–pertussis or measles immunization coverage (11). In a German atopy risk-enhanced birth cohort, measles/mumps immunization was inversely associated with atopic dermatitis up to age of 5 years and a dose-dependent inverse association between better immunization-coverage rate in general and atopic dermatitis was noted (5). These studies do not suggest that avoidance of immunization prevents eczema. Our study shows in addition that severity of atopic dermatitis is unlikely to be increased by common childhood immunization and may even be decreased (Fig. 2).

Impact of immunization on IgE

Some vaccines have been previously investigated for their impact on allergic sensitization. Cellular pertussis immunization has been shown to frequently induce IgE to pertussis toxin, but to down-regulate IgE responses to co-administered antigens in children and to allergens in mice (12–14). In this study, most administered vaccines were acellular vaccines and no effect against IgE to allergens was observed. As mycobacteria are classic Th2-antagonists in experimental models, BCG has been investigated extensively as a potential immune modifier of atopy development (15). Consistent with most of the published epidemiological studies, no influence of BCG on allergic sensitization or elevated total serum IgE was noted in this study. We found isolated associations of hepatitis B immunization in the first 6 months with elevated total IgE and of hepatitis B immunization at birth with allergic sensitization to aeroallergens in our study. These conflicting results were not supported by findings within similar outcomes or in other age intervals and should thus be viewed with great caution. Immunization against varicella may be indicated more frequently among infants with more severe eczema. In our study, varicella immunization was inversely associated with

elevated total IgE and atopy. The risk of a type I error is certainly possible on account of the large number of measures of associations investigated in our study, but the consistency of results points to varicella immunization as a target for future research on inhibition of atopy development.

Clinical implication

Families tend to link causally events occurring around the same time in the life of their child such as the emergence of eczema and primary immunization. On the basis of currently available data (2, 16, 17), families of children at heightened risk for atopy can be reassured that early childhood immunization is unlikely to promote their child's eczema or allergic sensitization as a risk factor for later respiratory allergy and that the risks of infection by vaccine avoidance outweigh by far the risks of immunization.

Conclusion

No strong causal link between the occurrence or severity of early atopic disease and early immunization could be

demonstrated. Conversely, there was limited evidence of a mild inhibitory effect of cumulative vaccine doses on atopic dermatitis. As vaccines educate the immune system by mimicking infections (18) and skew the immune system away from Th2 immune profile (14), they may be helpful as a surrogate rather than as a barrier to infection in the defence against allergic sensitization and severity of Th2-dependent atopic disease.

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Competing interests

None declared.

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