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The association between infant feeding practices and subsequent atopy among children with a family history of asthma

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Clinical and Experimental Allergy

Summary

Background Although longer duration of breastfeeding and later introduction of solid foods are both recommended for the prevention of asthma and allergic disease, evidence to support these recommendations is controversial.

Objective To examine the relation between infant feeding practices and the risk of asthma and allergic disease at age 5 years.

Methods A cohort of children with a family history of asthma in Sydney, Australia, was followed from birth to age 5 years. Data on infant feeding practices and on early manifestations of eczema were collected prospectively. The presence of eczema, asthma and atopy (positive allergen skin prick tests) were determined at age 5 years.

Results In 516 children evaluated at age 5 years, there was no significant association between the duration of breastfeeding or timing of introduction of solid foods and protection against asthma or other allergic disease, after adjustment for confounding factors. However, breastfeeding for 6 months or more and introduction of solid foods after 3 months were both associated with an increased risk of atopy at age 5 years ($P = 0.02$ and 0.01 , respectively).

There was no significant association between the presence of eczema at 4 weeks and at 3 months and continued breastfeeding beyond those times.

Conclusion Longer duration of breastfeeding and later introduction of solid foods did not prevent the onset of asthma, eczema or atopy by age 5 years.

Keywords asthma, atopy, breastfeeding, eczema, infant feeding, reverse causality

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Introduction

The role of infant feeding practices, in particular duration of breastfeeding and timing of introduction of solid foods, in the prevention of asthma and allergic diseases remains controversial, despite a number of studies and some systematic reviews [1–5]. Most prospective studies have shown that breastfeeding is associated with reduced risks of asthma or allergic disease including eczema [6–12] whereas several others have suggested that breastfeeding may not offer a protective effect in later life or may even enhance the development of allergic disease [13–16]. Although later introduction of solids has been widely recommended as a preventative strategy for allergic dis-

ease there is little evidence to support this view and recent studies have not demonstrated a protective effect. In fact later introduction of solids has been associated with an increased prevalence of allergic disease among 5-year-old children [17]. It has been suggested that this may be due to deliberate delay in the introduction of solid foods among parents of children with early manifestations of allergic disease. This explanation for the observed association is sometimes described as 'reverse causality' [18].

The conflicting results and differences in the magnitude of observed effects may, in part, be explained by methodological differences. Particularly important in this regard, is the substantial variation in definitions and

measurement of breastfeeding (e.g. failure to distinguish between exclusive/full breastfeeding and complementary feeding), asthma and atopy, the differences in study populations with respect to family history of atopy [1, 19, 20] and differences in the analytical approach to selection bias resulting from extension of breastfeeding due to family history of allergic disease or early manifestations of allergic disease in the child.

The Childhood Asthma Prevention Study (CAPS) is a large randomized controlled trial investigating the effects of dietary supplementation with omega 3 fatty acids, and house dust mite (HDM) avoidance, among children from birth to 5 years, on the incidence of asthma and atopy in children with a family history of allergic disease. The findings of this trial have been reported elsewhere [21]. The pre-natal recruitment, explicit definitions of infant feeding practices, detailed and multiple measures of allergic outcomes, and longitudinal nature of the study provides a valuable opportunity to examine the relationship between infant feeding and measures of allergic disease, taking the issue of reverse causality into account.

Methods

Subjects

The subjects are members of a high-risk cohort who participated in the CAPS. This is a randomized, parallel-group controlled trial that separately tested HDM avoidance and omega-3 fatty acid supplementation for the primary prevention of asthma. The results of the randomized controlled trial [21] and further details of the study methods, including enrolment and randomization procedures, loss to follow up and generalizability of the cohort have been published elsewhere [22]. In brief, pregnant women, whose unborn children were at high risk of having asthma because one or more parents or siblings had asthma or wheezing, were identified at the antenatal clinics of six Sydney hospitals. Eligible women were enrolled from September 1997 to December 1999. Among the exclusion criteria were babies from multiple births, gestational age less than 36 weeks, hospitalization for >1 week, or serious illness. This report uses data from the whole cohort, which is representative of a high-risk cohort.

The study was approved by the Human Research Ethics Committees of the University of Sydney, the Children's Hospital at Westmead and Western and South Western Sydney Area Health Services.

Feeding advice

All mothers were advised to breastfeed for as long as possible and were told that the benefits of so doing may include protection from asthma and other allergic condi-

tions. They were also advised verbally and in written material that cow's milk should not be introduced as a drink until after 12 months of age because of the protein's potential to cause allergic responses [23]. In addition, it was recommended that they avoid introducing solid foods before 4–6 months, as advised by the Australian guidelines for infant feeding at the time, to prevent replacement of breastmilk with less nutrient dense and possibly more allergenic sources of energy [24].

Sociodemographic and biomedical information

The ages of the child's mother and father, their employment status, educational level and smoking status, the mother's parity and gravidity, aspects of the mother's diet and the mother's intention to breastfeed were documented using an interviewer-administered questionnaire when the women were 36 weeks pregnant. Information about the child, including birth weight, gestational age and admission to neonatal intensive care unit or special care nursery were obtained from the hospital record after birth of the child.

Definitions and measurement of breastfeeding

Study families were visited at home by research nurses at around 1, 3, 6, 9 and 12 months to collect information and deliver supplies for the intervention and control groups. Breastfeeding practices were assessed using a series of standard questions that have been used in two Australian National Health Surveys [25, 26]. Questions related to 'ever breastfeeding', the age of the child when breastfeeding had stopped and the age when breastmilk substitutes and/or solid foods were first regularly given. The following definitions were used, adapted from recommended national breastfeeding definitions and indicators for Australia [27].

Ever breastfed infants were defined as children who had ever consumed any breastmilk (even once).

Duration of any breastfeeding was defined as the age, in weeks or months, that mother reported baby had stopped breastfeeding.

Early introduction of solid foods was defined as mother reporting regularly giving solid foods by the 3 month home visit.

An '*allergenic food*' was arbitrarily defined as cow's milk, eggs, nuts or fish.

Fully breastfed infants at 3 and 6 months were defined as those infants whose mothers reported at the 3 and at the 6 month visits, respectively, that they had not been fed solid foods or breastmilk substitutes.

Information on water and juice consumption was not recorded. Therefore, it was not possible to determine exclusive breastfeeding in this study.

Asthma and allergy outcomes

Allergic outcomes were assessed at age 5 years by questionnaire administered by an independent research nurse, who was not involved in collecting the data on infant feeding. Skin prick test (SPTs) to inhaled and ingested allergens and measurement of spirometric function before and after the administration of bronchodilator were performed as previously described [21]. The main outcomes were defined as follows.

Probable current asthma was defined as any wheeze in the preceding 12 months at age 5 years in children who either had asthma diagnosed by a doctor or at a hospital at any time during the first 5 years OR had a positive bronchodilator test at the 5 year assessment.

Eczema was defined as presence of flexural eczema on inspection OR a history of itchy rash coming and going for 3 months or more AND at least one of the following: seeking medical care in the last 12 months for diagnosed eczema/atopic dermatitis or using steroid or emollient creams in the last 12 months.

Atopy was defined as the presence of any allergen weal ≥ 2 mm and larger than the negative control.

HDM allergy was defined as an allergen weal ≥ 2 mm to *Dermatophagoides pteronyssinus* (DP).

Inhalant allergy was defined as having a weal ≥ 2 mm to one or more of the following allergens: DP, cockroach, cat, *Alternaria*, rye or grass mix.

Ingested allergy was defined as an allergen weal ≥ 2 mm to one or more of the following allergens: salmon, peanuts, cow's milk, egg white, egg yolk or tuna.

Statistical analysis

Data were entered into an Access database and imported into SPSS for Windows version 13.0 (SPSS Inc., Chicago, IL).

The relationship between infant feeding variables during the 5 year of life and respiratory and allergy outcomes measured at age 5 years was analysed using χ^2 tests and univariate odds ratios (ORs) with 95% confidence intervals (CIs).

Multiple logistic regression was used to estimate ORs adjusted for confounders. The following variables were included in all regression models: the experimental intervention (study group allocation), gender of the child, maternal or paternal asthma entered separately into the model and maternal smoking in pregnancy. Other potential confounders, which were retained in the model if they changed the OR by 5% or more, included maternal or paternal history of hayfever and/or eczema, presence of older siblings, sibling history of asthma, post-natal household exposure to tobacco smoke, maternal age (expressed in quintiles), maternal and paternal education, pet ownership, day care attendance and anthropometric

characteristics at birth (birth weight, birth length and head circumference).

In order to elucidate the possible impact of early manifestations of allergic disease on subsequent infant feeding decisions, the effect of parental report of an itchy rash at age 4 weeks and at age 3 months on subsequent breastfeeding practices was assessed among the subgroups of children who were continuing to be breastfed at 4 weeks and at 3 months, respectively. The effect of parental report of itchy rash at 4 weeks on introduction of solid foods by age 3 months was tested in the cohort as a whole.

Results

Of the 616 children initially enrolled in the study, data were available for the following numbers of children for each of the indicators of breastfeeding: 601 (97.7% of total enrolled) for 'ever breastfed' status; 523 (84.9%) for duration of any breastfeeding; 520 (84.4%) for presence of full breastfeeding to at least 3 and 6 months and for introduction of solid foods by the time of the three month visit; and 500 (81.1%) for the introduction of infant formula before 6 months. Data were available for clinical and allergic outcome measures at age 5 years for 516 (83.7%) children. Reasons for incomplete data were withdrawal from the study and missed home visits. The socio-demographic characteristics of the study population have been described elsewhere [28].

The prevalence of various breastfeeding and infant feeding practices is summarized in Table 1. Most mothers breastfed their infants initially and over half were still breastfeeding at 3 months. However, less than half breastfed to 6 months, and only 20% were still breastfeeding at 12 months. Just over one-third of infants were fully breastfed to 3 months, well short of the national guideline of exclusive breastfeeding to 6 months. Solid foods were

Table 1. Infant feeding practices of the study population

Infant feeding variable		<i>n</i>	<i>N</i> (total)	%
Ever breastfed		539	601	89.7
Duration of breastfeeding (months)	1	388	523*	74.1
	3	318	523	60.6
	6	227	523	43.4
	9	156	523	29.8
	12	104	523	19.8
Fully breastfed (months)	1	328	593	55.3
	3	179	520	34.4
	6	13	563	2.3
Introduction of solid foods (months)	by 3	135	520	26.0

*Ninety-three missing data on duration of breastfeeding includes those who were never breastfed (62), those who said they had breastfed but do not have data on duration of breastfeeding (16) and those who have withdrawn from the study after the antenatal visit (15).

Table 2. Crude and adjusted ORs for the association between various infant feeding practices and asthma at age 5 years

	Probable current asthma <i>n/N</i> (%)	OR (95% CI)	Adjusted OR (95% CI)*
Ever breastfed			
Yes	97/467 (20.8)	0.54 (0.29–1.02)	0.59 (0.30–1.16)
No	16/49 (32.7)		
Breastfed for 6 months or more			
Yes	43/212 (20.3)	0.85 (0.55–1.31)	0.90 (0.58–1.40)
No	70/304 (23.0)		
Fully breastfed to 3 months			
Yes	29/147 (19.7)	0.90 (0.56–1.47)	0.93 (0.56–1.53)
No	74/345 (21.4)		
Missing	24		
Solid food introduction by 3 months			
Yes	19/111 (17.1)	0.70 (0.40–1.22)	0.65 (0.36–1.15)
No	79/348 (22.7)		
Missing	57		
Allergenic food by 9 months			
Yes	81/375 (21.6)	0.93 (0.58–1.48)	0.96 (0.60–1.54)
No	32/140 (22.9)		
Missing	1		

*Adjusted for intervention or control group allocation, mothers and fathers history of asthma, mother smoking in pregnancy and gender of the child. CI, confidence interval; OR, odds ratio.

introduced to most infants ($N = 542$ or 96.3%) before the recommended 6 months.

The effect of breastfeeding for greater than 6 months on the presence of atopy or asthma at age 5 years did not differ between children with and without a maternal of asthma, a paternal history of asthma, a history of maternal smoking during pregnancy or between children in the active vs. control diet interventions groups (all $P > 0.3$). However, the effect of breastfeeding for 6 months or more on the risk of having eczema at age 5 years did differ between children with and without a maternal history of asthma ($P = 0.044$). Among children whose mothers had asthma, those who were breastfed for longer than 6 months were more likely to have eczema at 5 years than those who were not [adjusted OR (aOR) 2.30, 95% CI 1.30–4.06]. Paternal history of asthma, maternal smoking during pregnancy and the diet intervention group status did not influence the effect of breastfeeding for 6 months or more on the risk of having eczema at age 5 years (all $P > 0.3$). The effect of introduction of solid foods before age 3 months on the presence of atopy, asthma or eczema at age 5 years did not differ between subgroups of the study population defined as above (all $P > 0.05$).

After adjustment for confounding factors, we found no significant association between infant feeding practices and the presence of probable current asthma (Table 2) or eczema (Table 3) at age 5 years. However, breastfeeding for <6 months and introducing solid foods before age 3 months were both associated with a decreased risk of atopy at age 5 years (Table 4). These associations of various infant-feeding practices with any atopy were also evident for atopy to inhalant allergens and for atopy to

HDM allergen (data not shown). These positive associations were also tested after excluding infants with parental report of itchy rash at 4 weeks and at 3 months, respectively. The lower risk of atopy among children in whom solid foods were introduced before 3 months remained significant even after excluding those with a rash at 4 weeks (aOR 0.49, 95% CI 0.30–0.81). The higher risk of atopy among children who were breastfed for 6 months or more remained significant after excluding children with a rash at 4 weeks (aOR 1.62, 95% CI 1.11–2.38) but was no longer significant after excluding additional children who had a rash at 3 months (aOR 1.38, 95% CI 0.90–2.11). When duration of breastfeeding was examined as a continuous variable there was a linear effect of breastfeeding duration on risk of atopy at 5 years; for every month of breastfeeding up to 12 months there was a 1.047 (95% CI 1.009–1.087) increased odds of atopy at 5 years of age ($P = 0.015$).

Among children who were breastfed to at least 4 weeks of age, parental report of an itchy rash did not significantly affect the decision to fully breastfeed to 3 months of age, to breastfeed for 6 months or more, or to delay the introduction of solid foods beyond 3 months (Table 5). Similarly, among children who were breastfed to at least 3 months of age, the presence of an itchy rash at that age was not associated with a significantly increased prevalence of breastfeeding for 6 months or more [52/65, 80% in those with an itchy rash at 3 months vs. 175/253 (69.2%) in those without an itchy rash, $P = 0.09$]. However, these analyses were limited by the relatively small numbers of breastfed infants who manifest a rash at 4 weeks and at 3 months (15 and 65, respectively) and in all cases

Table 3. Crude and adjusted ORs for the association between various infant feeding practices and eczema at age 5 years

	Eczema <i>n/N</i> (%)	OR (95 CI)	Adjusted OR (95% CI)*
Ever breastfed			
Yes	122/467 (26.1)	1.81 (0.83–3.97)	1.38 (0.61–3.12)
No	8/49 (16.3)		
Breastfed for 6 months or more			
Yes	64/212 (30.2)	1.56 (1.05–2.33)	1.42 (0.94–2.16)
No	66/304 (21.7)		
Fully breastfed to 3 months			
Yes	47/147 (32.0)	1.72 (1.12–2.65)	1.52 (0.96–2.40)
No	74/345 (21.4)		
Missing	24		
Solid food introduction by 3 months			
Yes	19/111 (17.1)	0.56 (0.32–0.97)	0.59 (0.33–1.04)
No	94/348 (27.0)		
Missing			
Allergenic food by 9 months			
Yes	98/375 (26.1)	1.19 (0.76–1.89)	1.14 (0.71–1.83)
No	32/140 (22.9)		
Missing	1		

*Adjusted for intervention or control group allocation, mothers and fathers history of asthma, mother smoking in pregnancy and gender of child. CI, confidence interval; OR, odds ratio.

Table 4. Crude and adjusted ORs for the association between various infant feeding practices and atopy at age 5 years

	Atopy <i>n/N</i> (%)	OR (95% CI)	Adjusted OR (95% CI)*
Ever breastfed			
Yes	199/467 (44.7)	1.12 (0.60–2.12)	0.89 (0.45–1.76)
No	18/49 (41.9)		
Breastfed for 6 months or more			
Yes	105/201 (52.2)	1.71 (1.19–2.46)	1.56 (1.07–2.27)
No	112/287 (39.0)		
Missing	28		
Fully breastfed to 3 months			
Yes	72/139 (51.8)	1.55 (1.04–2.31)	1.36 (0.90–2.07)
No	134/327 (41.0)		
Missing	50		
Solid food introduction by 3 months			
Yes	32/104 (30.8)	0.49 (0.31–0.79)	0.54 (0.33–0.87)
No	156/330 (47.3)		
Missing	82		
Allergenic food by 9 months			
Yes	150/355 (42.3)	0.71 (0.48–1.06)	0.67 (0.45–1.02)
No	67/132 (50.8)		
Missing	29		

*Adjusted for intervention or control group allocation, mothers and fathers history of asthma, mother smoking in pregnancy and gender of child. CI, confidence interval; OR, odds ratio.

there were trends indicating a tendency to prolong breast-feeding and delay the introduction of solid foods among children with early features of eczema.

Children whose mothers or fathers had asthma were not more likely to be breastfed for longer than 6 months than children whose mothers or fathers did not have asthma (36% vs. 43%, $P=0.07$ for mothers and 40% vs. 39%, $P=0.8$, for fathers). Similarly, children whose mothers had a history of eczema or hayfever were not more likely to be

breastfed for 6 months or longer than children whose mothers did not have a history of eczema or hayfever (34% vs. 41%, $P=0.13$ for eczema history and 42% vs. 37%, $P=0.27$ for hayfever history).

Discussion

This study has shown that, in a cohort of children at high risk of allergic disease, infant feeding practices were not

Table 5. Infant feeding practices by presence of an itchy rash at 4 weeks of age

	Children with parent reported itchy rash at 4 weeks	Children without parent report of itchy rash at 4 weeks	P value*
Breastfed for 6 months or more [†]	7/15 (46.7%)	220/374 (58.8%)	0.35
Fully breastfed to 3 months [†]	4/15 (26.7%)	150/347 (43.2%)	0.20
Solid food introduction by 3 months	5/24 (20.8%)	131/496 (26.4%)	0.54

*P value based on Pearson's χ^2 without continuity correction.

[†]In children breastfed to at least 4 weeks of age.

related to the presence of asthma or eczema at age 5 years. Contrary to expectations, children who were breastfed for 6 months or more and those in whom the introduction of solid foods occurred after age 3 months, were at increased risk of having atopy, as identified by positive SPTs to allergens at age 5 years. This observation was independent of the specific history of asthma and other allergic disease in the child's mother and father.

In contrast to the present study, a number of previous observational studies have found that breastfeeding is associated with a reduced risk of allergic disease in early life. A recently published multi-disciplinary review examined over 4000 articles relating to breastfeeding and allergic disease [2] and concluded that exclusive breastfeeding reduces the risk of asthma and that the protective effects increase with the duration of breastfeeding up to at least 4 months of age. In addition it concluded that breastfeeding protects against the development of atopic dermatitis and that the protective effects on the development of allergic disease seemed to persist for at least the first decade of life. Of the 20 studies of effects of breastfeeding in children with a history of allergic disease, which were considered satisfactory in design, 18 were interpreted to show a beneficial effect on atopy or asthma. Similarly an inverse relation between exclusive breastfeeding in the first 3 months and eczema was found in a meta-analysis of prospective studies [5]. These findings are based on observational studies where maternal choice has dictated the occurrence and duration of breastfeeding. Individually randomized controlled trials are not feasible. However, a cluster randomized trial of breastfeeding promotion in Belarus did achieve differences in breastfeeding rates between intervention communities and control communities. Infants in the former were more likely to be exclusively breastfed at 3 months and at 6 months (43.3% vs. 6.4%; $P=0.001$; 7.9% vs. 0.6%; $P=0.01$, respectively) and significantly more likely to be breastfed at 12 months (19.7% vs. 11.4%; aOR, 0.47; 95% CI 0.32–0.69). At the sites where breastfeeding was promoted there was a significantly lower prevalence of atopic eczema (3.3% vs. 6.3%; aOR, 0.54; 95% CI 0.31–0.95).

However, the demonstrated beneficial effects of breastfeeding on the risk of allergic disease in unselected populations are relatively modest in magnitude. In the

Swedish BAMSE cohort comprising 4089 infants, exclusive breastfeeding for 4 months or more was associated with an OR of 0.7 for asthma [7] and an OR of 0.8 for eczema [8]. A population based cohort of 2602 Australian children found that cessation of exclusive breastfeeding before 4 months of age was associated with an OR of 1.28 for the presence of asthma at 6 years of age [29]. Furthermore, the longer term benefits of breastfeeding on the risk of asthma are more uncertain. A prospective study in Dunedin, New Zealand, in which subjects were followed from 9 years until 26 years of age, concluded that breastfeeding did not protect children against atopy and asthma and may even increase the risk in early adult life [15]. Hence, the finding in this study that longer duration of breastfeeding did not have a protective effect against asthma and eczema at age 5 years in a cohort with a positive family history of asthma is consistent with some previously published data.

The present study found that breastfeeding for 6 months or more was associated with a higher risk of atopy, as measured by positive SPTs to inhalant allergens at 5 years of age. In contrast, the Swedish BAMSE study found that exclusive breastfeeding for 4 months or more did not have any effect on sensitization to airborne allergens at 4 years [7]. The BAMSE study differed from the present study in that it was conducted in an unselected population-based cohort, in contrast to the present study, in which all participants had a family history of asthma. Also in BAMSE 99% of children were ever breastfed (vs. 90% for the present study) and 89% were breastfed for one month or more (vs. 74% for the present study). The present study is consistent with the New Zealand cohort study, referred to above, which found that children who were reported to have been breastfed for 4 weeks or more had a significantly increased prevalence of atopy to inhalant allergens at age 13 years [15].

It is important to note that the effects of breastfeeding on the development of atopy may differ according to family history of atopy. A recently published general population cohort study from Finland found that a longer duration of exclusive breastfeeding was associated with an increased risk of atopic dermatitis and allergic symptoms in those with a positive family history of allergic disease, but not in those without a family history of

allergic disease [30]. Unfortunately, data on SPT positivity were not separately reported as outcomes. In the present study, the entire cohort was selected on the basis of a family history of asthma and the specific maternal and paternal history of asthma did not influence the effect of infant feeding practices on the risk of developing atopy at age 5 years. However, the finding that, in the sub-group with a maternal history of asthma, longer duration of breastfeeding was associated with an increased risk of eczema, emphasizes the importance of familial factors in modifying the impact of breastfeeding on allergic outcomes. The mechanism for, and implications of, these familial effects remain unclear.

An unexpected finding in this study was that the introduction of solid foods before 3 months of age was associated with a significant protective effect against atopy at 5 years. Australian guidelines for infant feeding previously recommended introduction of solids at 4–6 months of age [24], and were revised in 2003 to recommend introduction be delayed until 6 months [31], based on evidence of range of beneficial effects. Guidelines for the prevention of allergic disease currently suggest that the introduction of complementary foods (including cow's milk-based formulas) should be delayed for at least 4–6 months in infants with a family history of atopy, such as the present cohort [32]. However, evidence to support delayed introduction of solid foods for the prevention of allergic disease is inconclusive. In a birth cohort comprising 671 children in Dundee there was no relation between the timing of the introduction of solids foods and the occurrence of eczema or wheeze during the first year of life [33]. More recent studies suggest that the delayed introduction of solids does not necessarily prevent, and might even increase, sensitization or manifestations of atopic disease [34]. A study of 642 children in the United Kingdom found that the introduction of any solid foods before age 3 months did not increase the risk of atopy, wheezing or eczema at age 5 years [17]. In fact, they found an increased risk for eczema (aOR 1.6, 95% CI 1.1–2.4) and a non-significant increased risk for wheezing (aOR 1.5, 95% CI 0.92–2.4) in those pre-school children who had been introduced to egg after age 8 months. Introduction of cow's milk after age 6 months was also associated with an increased risk of eczema (aOR 1.7, 95% CI 1.1–2.5). These associations were not influenced by the allergic status of the parents. In the United Kingdom study timing of introduction of solid foods was assessed retrospectively at age 1 year in contrast to the present study where this was assessed prospectively. Although the earlier introduction of solid foods is likely to be correlated with the early cessation of breastfeeding, and hence the similar associations of both these feeding practices with atopy may not be independent of one another, the present study does support the conclusion of previous studies that the earlier introduction of solid foods does not increase the risk of

developing allergic disease. In fact, in this study, the earlier introduction of solid foods was associated with a reduced risk of atopy at age 5 years.

One advantage of the present study design was the standardization of advice to parents about infant feeding. All parents were recommended to continue breastfeeding for as long as possible and were given specific advice concerning the introduction of solid foods. This would be expected to reduce the impact of extraneous factors on infant feeding practices. A further strength was the prospective collection of information on infant feeding, which gave a valid measure infant feeding practices without risk of recall bias.

We considered the possibility that the apparent positive association of longer duration of breastfeeding and later introduction of solid foods with the presence of atopy at age 5 years could be attributable to the influence of early manifestations of atopic disease or risk factors for atopic disease on infant feeding practices, in other words the outcome may have influenced the exposure. There is evidence of this reverse causality in other studies. In an observational birth cohort study of 1314 infants the prevalence of atopic eczema in the first 7 years increased with each additional month of breastfeeding (1.03; 95% CI 1.00–1.06 for each additional month) [14]. However, the observation that the duration of breastfeeding increased if at least one parent had eczema implied that reverse causality may have played a role in that observed association. In the BAMSE cohort, when children with early signs of atopic disease during breastfeeding were excluded from analyses, the protective effects of breastfeeding on asthma [7] and eczema [8] were strengthened, providing further evidence of reverse causality. In a closely followed birth cohort from Melbourne, Australia, early manifestations of atopic disease were associated with prolongation of exclusive breastfeeding but were not associated with any change in the duration of any breastfeeding [35]. In a German cohort comprising 2500 children, those with cutaneous symptoms during the first 6 months of life were more likely to delay the introduction of egg and non-breastmilk products beyond 6 months of age [18]. In the present study, the number of children with features of eczema at 4 weeks and 3 months of age was relatively small. Although they did tend to be more likely to breastfeed for longer and introduce solid foods later, none of these differences were statistically significant. Furthermore, the exclusion of these children did not substantially alter conclusions about the effects of early introduction of solid foods and breastfeeding beyond 6 months on the risk of atopy at age 5 years. Hence, we could not confirm that early manifestation of allergic disease in this cohort contributed to changes in infant feeding practices. It is unlikely that family history of asthma or allergic disease influenced our findings for two reasons. First, our study population was limited to subjects with a family history of

asthma. Second, although we did not find that a specific maternal history of asthma, eczema or rhinitis influenced mothers to breastfeed for longer than 6 months, the analyses were adjusted for parental history of asthma and other atopic disease. Hence, we could not establish that, in this cohort, the observed positive association of longer duration of breastfeeding and later introduction of solid foods with increased risk of atopy at age 5 years was attributable to either early manifestations of allergic disease or a family history of asthma or allergic disease.

We have shown that, in a cohort of children with a family history of asthma, earlier introduction of solid foods and earlier cessation of breastfeeding were not associated with an increased risk of developing asthma or allergic disease. In the context of other evidence, we conclude that the beneficial effects of breastfeeding may be limited to early respiratory illness that occurs independently from atopy and familial factors that promote persistent asthma. In later childhood, and among children with a family history of asthma, the risk factors for asthma and allergic illness are dominated by other factors, unrelated to breastfeeding. The explanation for the higher prevalence of sensitization to inhalant allergens among those who were breastfed for 6 months or more and those in whom solid foods were introduced after 3 months of age remains uncertain. However, it is consistent with some recently reported observations in other cohorts. Reverse causality, which could contribute to the observed association, was not established in this cohort. However, alternative explanations, either due to unmeasured confounding or due to unexpected immunological effects of the duration of breastfeeding or the timing of introduction of solid foods need to be considered.

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