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Infant feeding and childhood atopy: does early introduction of non-milk fluids matter?

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Studies on the role of non-milk fluids in the development of child atopic disease are scarce. We had a unique opportunity to investigate prospective association between the introduction of fruit syrup, orange juice, sterilized water, vitamins and honey at 1 month and the development of child atopic disease. The exposure of interest was measured by parental report of non-milk fluids introduction to infants aged 1 month at the Tasmanian Infant Health Survey, 1988–89, Tasmania. Data on the outcomes of interest (atopic sensitization, asthma, eczema and hay fever) were collected during the 1997 Childhood Allergy and Respiratory Health Study when children were 8 yr old. Relative risks were derived from generalized linear model with a log link function and binomial error structure. None of the non-milk fluids appeared to be a significant predictor of atopic sensitization. Only sterilized water was a significant risk factor for asthma (adjusted relative risk = 1.59; 95% confidence intervals: 1.14–2.22), which may be partly because of associated overall better hygienic conditions and decreased exposure to early infections in the household. In summary, we were unable to find evidence for an association between introduction of non-milk fluids in infancy and childhood atopic disease.

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A short duration of breastfeeding and introduction of supplementary foods at an early age has been implicated in many diseases, including allergies (1). Based on the effects of breastfeeding on child health, growth and development and on maternal health, the World Health Assembly adopted a resolution to recommend exclusive breastfeeding for 6 months to its member states (2). Other health bodies such as the American Academy of Pediatrics (3) also promoted exclusive breastfeeding for at least 6 months. However, the available evidence suggests that the duration of exclusive breastfeeding is shorter than that recommended in many countries (4–7).

With regard to atopic diseases, breastfeeding is recommended particularly in high-risk children (those with atopic heredity); in these children breastfeeding combined with avoidance of solid food and cow's milk for at least 4–6 months is recommended as the most effective preventative regimen (8). In the absence of breast milk, formulas with documented reduced allergenicity are recommended to at-risk infants for at least 4–6 months (8). Little advice is given concerning introduction of non-milk fluids, partially because of lack of prospective data.

Nevertheless, these fluids can be introduced early by some parents. A study from Lithuania found that herbal tea was given to approximately 60% of infants, plain water to 30% and juice to 3% of infants at 1 month of age (7). In a population-based cohort study from Finland (5), infants were introduced supplementary foods at the median age of 3.5 months; fruit/berries were introduced at the median age of 4 months. The early introduction of complementary foods and fluids may be disadvantageous as they often have a lower nutritional value than breast milk (9) and may shorten the duration of breastfeeding (10, 11). It is also possible that early introduced

non-milk fluids may influence the risk of child atopic disease directly. As infants cannot ethically be randomly assigned to potentially harmful feeding patterns, observational cohort data are required.

We had a unique opportunity to examine prospective association between the introduction of non-milk fluids at 1 month and the development of child atopic disease (atopic sensitization, asthma, eczema and hay fever) at 8 yr of age.

Materials and methods

This report utilizes data on infant feeding from the Tasmanian Infant Health Survey in 1988–89 (12) and childhood data on allergic sensitization and atopic disease (13) collected as part of a follow-up study, the Childhood Allergy and Respiratory Health Survey, which occurred later in 1997 (14).

The Tasmanian Infant Health Survey

The Tasmanian Infant Health Survey (TIHS) was a cohort study investigating sudden infant death syndrome (SIDS) and provided comprehensive baseline data on approximately one-fifth of infants born in Tasmania from 1988 to 1995 (12). A scoring system based on young maternal age, male sex, birth weight, autumn birth, maternal intention to bottle feed and duration of second stage of labour (known risk factors for SIDS) was used to recruit infant into the study (15). Singletons exceeding a scoring cut-off were eligible for inclusion. Multiple births were automatically eligible. Infants with severe neonatal disease or a major congenital malformation, or infants for adoption or who would not be residing in Tasmania at 1 month of age were excluded from the TIHS. Data were obtained by research assistants on three occasions: an in-hospital interview conducted on the fourth day of life, a home interview during the fifth postnatal week and a phone interview at approximately 10 wk postnatally. In 1988/89, 609 (88% of eligible) infants in Northern Tasmania had a TIHS home interview. The median age of the home interview was 5.14 wk (interquartile range: 4.57–6.68). At this stage, mothers were asked if the following non-milk fluids had been introduced: fruit syrup (predominantly diluted rosehip or blackcurrant), orange juice, sterilized water, vitamins and honey.

The 1997 Childhood Allergy and Respiratory Health Study

In 1997, 596 TIHS participants born in 1988 or 1989 were identified in the northern region of Tasmania (excluding offshore islands) through school records (14). Of these, 499 (84%) agreed to participate in the 1997 Childhood Allergy and Respiratory Health Study (CARHS). Four hundred and fifty-six CARHS participants had both infant home visit and hospital interview data. The parental interview and child assessment were carried out in the Launceston General Hospital. The parental questionnaire included questions on asthma, wheeze, hay fever and eczema from the International Study of Asthma and Allergies in Childhood (ISAAC) (16), questions on child diet and diseases and other factors.

Skin-prick testing (SPT) was used to assess the cutaneous reaction to exposure to aeroallergens. The tested allergens included the house dust mites (HDM) *Dermatophagoides pteronyssinus* (Der p) and *Dermatophagoides farinae* (Der f), cat, dog, *Alternaria* (type of mould), ryegrass, cow's milk, egg and peanut (Hollister-Stier purified allergen extracts supplied by Bayer, Sydney, Australia) and positive (histamine 10 and 1 mg/ml) and negative (glycerine) controls. SPT was carried out on 498 children. The mean age at the time of SPT was 8.71 (SD 0.59) yr. The study methods are discussed in more detail elsewhere (17).

The disease outcomes of interest were categories of atopic sensitization (sensitization to any aeroallergens, ryegrass or HDM) and the asthma, eczema and hay fever phenotypes. A positive weal allergen reaction of ≥2 mm to any aeroallergen at 15 min was defined as skin test positivity. The term atopy was used for consistency with past work on child atopic disease (17–19). A positive response to the ISAAC question, 'Has your child had wheezing or whistling in the chest in the last 12 months?' (16) was defined as asthma. This question has a sensitivity of 0.81 and a specificity of 0.85 for the physician diagnosis of asthma in childhood (20). Eczema and hay fever were defined as positive responses to 'Has he/she ever had eczema in the creases (bends) of elbows, wrists, or knees?' and to 'Does he/she get attacks of 'hay fever' (i.e. sneezing, running or blocked nose, sometimes with itchy eyes or nose)?' respectively. Of 499 children, 498 had data on atopic sensitization, 497 on asthma and hay fever and 495 on eczema (Table 1).

The exposures of interest were the introduction of non-milk fluids at 1 month postnatally assessed by parental response to 'Does baby have any of the following non-milk fluids?' with fruit syrup (e.g. Delrosa/Ribena), orange juice, sterilized water, vitamins, honey and others as possible choices. Of the 499 CARHS children,

Table 1. Prevalence of exposure and outcome variables, the 1988–1989 Tasmanian Infant Health Survey and the 1997 Childhood Asthma and Respiratory Health Study

Variable	Overall % (n/N)	Among those with asthma % (n/N)
Non-milk fluids introduced at home visit (*c.* 1 month)		
Sterilized water	62.39 (287/460)	72.59 (98/135)
Fruit syrup	15.43 (71/460)	16.30 (22/135)
Honey	4.57 (21/460)	5.19 (7/135)
Vitamins	3.05 (14/459)	0.74 (1/135)
Orange juice	2.83 (13/460)	2.22 (3/135)
Other non-milk fluids	6.74 (31/460)	6.67 (9/135)
Respiratory and atopic outcome		
Any atopic sensitization	41.37 (206/498)	56.86 (87/153)
House dust mite sensitization	31.53 (157/498)	47.06 (72/153)
Ryegrass sensitization	23.29 (116/498)	37.25 (57/153)
Asthma	30.78 (153/497)	–
Eczema	23.84 (118/495)	33.55 (51/152)
Hay fever	25.15 (125/497)	46.05 (70/152)

See Materials and methods for description of the exposure and outcome variables.

the proportion of missing answers for the exposures was 8%.

Written informed consent was obtained from all the TIHS mothers and CARHS parents. Both these studies received ethical approval from the Human Ethics Committee of the University of Tasmania.

Statistical methods

Relative risks (RR) were calculated with test-based 95% confidence intervals (CI) (21). The effect of individual confounders was assessed by stratified analysis. To control simultaneously for multiple confounders and to obtain CI for RR estimates, a generalized linear model with a log link function and binomial error structure was used (22).

To identify possible confounders, first, the exposure–outcome associations were stratified by possible confounders which included the components of the perinatal scoring system for cohort entry and factors suggested by literature, and pooled Mantel–Haenszel estimates were obtained (23). Second, the magnitude and significance of the association between each factor and non-milk fluids introduction (Table 2) or each atopic outcome were estimated separately by generalized linear models. We used change-in-estimate strategy to control for confounding: covariates that met the criteria for confounding (23) and changed the RR of most of non-milk fluids and atopic disease associations by $>10\%$ were entered into the multivariate model (24). The statistical significance of interaction terms between the dependent variables was tested by likelihood ratio tests. All analyses were conducted using STATA 8 (25).

Table 2. Univariate associations between selected study variables and introduction of non-milk fluids, the 1988–1989 Tasmanian Infant Health Survey and the 1997 Childhood Asthma and Respiratory Health Study

	Fruit syrup		Orange juice		Sterilized water		Vitamins		Honey	
	Risk ratio	95% CI	Risk ratio	95% CI	Risk ratio	95% CI	Risk ratio	95% CI	Risk ratio	95% CI
Feeding with formula only at 1 month (reference)	1.00	–	1.00	–	1.00	–	1.00	–	1.00	–
Feeding with breast only at 1 month	0.21	0.10–0.43	0.45	0.12–1.60	0.76	0.64–0.89	0.85	0.25–2.85	0.57	0.21–1.58
Feeding with formula and breast at 1 month	0.63	0.30–1.29	–	–	0.75	0.57–0.99	2.14	0.57–8.00	1.16	0.34–3.91
Solids introduction at 11 months	2.18	1.42–3.35	0.17	0.02–1.27	0.98	0.84–1.14	1.11	0.38–3.25	1.33	0.56–3.19
Paternal unemployment at birth (yes vs. no)	0.97	0.52–1.79	1.27	0.28–5.74	1.09	0.91–1.31	0.95	0.22–4.16	1.43	0.49–4.14
Maternal education (low vs. high)	3.64	1.17–11.33	2.08	0.27–16.31	1.25	0.98–1.60	0.59	0.19–1.83	2.34	0.30–18.11
Maternal age (per year increase)	0.92	0.87–0.97	0.95	0.84–1.08	1.01	0.99–1.02	1.14	1.03–1.25	0.97	0.88–1.07
Family history of asthma at birth	0.92	0.59–1.46	1.47	0.50–4.29	1.13	0.98–1.31	0.95	0.32–2.79	1.40	0.59–3.31
History of maternal asthma when child is 8 yr old	1.13	0.71–1.81	0.22	0.03–1.64	0.98	0.84–1.16	0.71	0.20–2.49	1.60	0.68–3.76
History of paternal asthma when child 8 yr old	0.63	0.32–1.22	0.74	0.17–3.32	1.09	0.92–1.29	0.28	0.04–2.15	0.19	0.03–1.44
Infant's sex (male vs. female)	1.17	0.71–1.92	0.90	0.28–2.86	0.93	0.80–1.08	0.72	0.25–2.10	0.80	0.33–1.93
Birthweight (per 1 g increase)	0.89	0.73–1.07	1.65	0.97–2.79	1.07	1.00–1.13	0.45	0.25–0.81	0.96	0.66–1.38
Low birthweight (<2500 g vs. ≥2500 g)	0.94	0.55–1.62	0.32	0.04–2.43	0.81	0.66–1.00	14.05	4.00–49.35	1.20	0.45–3.19
Premature birth (<37 wk vs. ≥38 wk)	1.43	0.88–2.30	0.31	0.04–2.37	0.97	0.82–1.16	13.71	3.90–48.17	0.66	0.20–2.21
Firstborn (yes vs. no)	1.91	1.23–2.96	0.86	0.29–2.60	0.96	0.83–1.11	1.38	0.49–3.88	1.38	0.59–3.26
Any cigarette smoking in the same room with the infant	0.50	0.31–0.81	4.26	1.19–15.28	0.98	0.85–1.14	1.71	0.60–4.86	0.40	0.15–1.07
Any domestic gas used for cooking or heating in infancy	0.35	0.05–2.36	–	–	0.61	0.34–1.10	4.05	0.98–16.75	2.56	0.65–10.17
Any air freshener used at home at 1 month	0.97	0.85–1.10	1.15	0.84–1.57	1.01	0.97–1.05	0.79	0.56–1.11	0.91	0.70–1.17
Any child feather quilt use	0.90	0.58–1.39	1.53	0.51–4.59	1.07	0.92–1.23	1.72	0.59–5.06	0.48	0.20–1.16
Any fish intake in 1997	0.74	0.41–1.32	1.68	0.22–12.67	0.97	0.79–1.19	–	–	0.45	0.17–1.18
Number of siblings in 1997 (per sibling number increase)	0.84	0.69–1.03	0.98	0.62–1.56	0.99	0.93–1.06	0.83	0.50–1.36	1.13	0.83–1.53

All values are from generalized linear model with a log link function and binomial error structure.

Results

The prevalence of the exposure and outcome variables in the study sample is shown in Table 1. Sterilized water was introduced to the majority (62%) and fruit syrup to 15% of children at 1 month of age. In contrast, orange juice was given to only 3% of the infants. Asthma was slightly more prevalent than hay fever or eczema. Forty-one per cent (206/498) of children were sensitized to at least one allergen. HDM sensitization was, however, more prevalent than ryegrass sensitization. Fifteen percent of children were sensitized to both ryegrass and HDM (mixed sensitization) (19).

Table 2 shows strength and significance of associations between selected study variables and early introduction of non-milk fluids. Having received non-milk fluids by 1 month was positively associated with the introduction of other complimentary foods such as formula ($p < 0.001$) and solids ($p = 0.02$) and negatively with the duration of breastfeeding in the first 12 wk ($p < 0.001$). Older and better-educated mothers tended to introduce the fluids later, except for vitamins. The percentage of breastfeeding mothers at the time of the telephone interview conducted on average at 11 wk was twice as high if the non-milk fluids had not been given at the home visit (65% vs. 33%).

None of the non-milk fluids introduced at 1 month appeared to be a significant predictor of atopic sensitization at 8 yr (Table 3). From the non-milk fluids, only sterilized water was a significant predictor of childhood asthma overall (Table 4) and among those with atopic sensitization (RR = 1.75; 95%CI: 1.17–2.62). Adjustment for early introduction of solids did not alter the results. Neither did additional adjustment for the composite perinatal score (including birthweight, season of birth, maternal age), multiple births, weight, head circumference and length at birth and home visit, length of gestation, birth order, any gas used for cooking or heating and any air freshener used at home at birth, cat and dog ownership and mould observed by research assistant in infancy, the number of siblings or fish intake in 1997 (data not shown).

We explored the positive association between sterilized water and asthma further. Additional adjustment for the manner of bottle cleaning did not substantially alter the finding (RR = 1.63; 95%CI: 1.16–2.28). Sterilized water was, however, no longer a risk factor for child asthma (RR = 1.50; 95%CI: 0.95–2.36) after additional adjustment for low maternal education. For the sterilized water–asthma association, the interaction term for family history of asthma at birth was not significant ($p = 0.40$); amongst children without family history the risk of asthma because of sterilized water was of borderline significance (RR = 1.52; 95% CI: 0.99–2.33) reflecting partly the reduced sample size.

Discussion

This novel report examines the role of early introduction of non-milk fluids in the development of atopic sensitization and atopic diseases such as asthma, eczema and hay fever in childhood. In this prospective study, among the examined exposures and outcomes, the only significant association was found between sterilized water and asthma. The observed positive association between sterilized water and child asthma may be partly because of overall better hygienic conditions in the household and decreased exposure to early infections. However, the association remained significant after additional adjustment for factors potentially indicative of hygiene level at the household such as the manner of sterilizing bottles, mould observed by research assistant and smoking hygiene. Adjustment for some social class variables including educational attainment pathway needs to be interpreted with caution as it may be part of the causal pathway – the effect of sterilized water on asthma risk may be mediated by a factor related closely to maternal education. This is unlikely in this setting as sterilized water was strongly, although non-significantly, associated with asthma among infants of university-educated mothers (RR = 3.12; 95% CI: 0.40–24.57).

Younger mothers with shorter education were significantly more likely to introduce the non-milk fluids and solid foods earlier and also bottle-feed. Interestingly, older and better-educated mothers introduced vitamins to their infants earlier. Infant's sex or positive family history at the child's birth were not significant predictors of the early introduction of the fluids. Mothers of premature and low birthweight babies were more likely to have given honey by 1 month.

The administered home visit questionnaire might have had some weaknesses in that the exact time when non-milk fluids were introduced, their amount, frequency and dilution were not recorded. It is also not clear whether the non-milk fluids were given in addition to or instead of breast feeds. Small numbers might have been one of the reasons for some of the non-significant associations. However, the administration of some fluids such as diluted fruit syrup were more

Table 3. Early introduction of non-milk fluids and likelihood of atopic sensitization in childhood, the 1988–1989 Tasmanian Infant Health Survey and the 1997 Childhood Asthma and Respiratory Health Study

	Any atopic sensitization				Any house dust mite sensitization				Any ryegrass sensitization			
	Prevalence of the disease if the non-milk not introduced at home visit % (n/N)	Prevalence of the disease if the non-milk introduced at home visit % (n/N)	Risk ratio	95% CI	Prevalence of the disease if the non-milk not introduced at home visit % (n/N)	Prevalence of the disease if the non-milk introduced at home visit % (n/N)	Risk ratio	95% CI	Prevalence of the disease if the non-milk not introduced at home visit % (n/N)	Prevalence of the disease if the non-milk introduced at home visit % (n/N)	Risk ratio	95% CI
Fruit syrup												
Crude	41.49 (161/388)	42.25 (30/71)	1.02	0.76–1.37	31.96 (124/388)	29.58 (21/71)	0.93	0.63–1.36	23.97 (93/388)	22.54 (16/71)	0.94	0.59–1.50
Adjusted*			0.99	0.73–1.34			0.87	0.59–1.29			0.98	0.60–1.59
Orange juice												
Crude	41.70 (186/446)	38.46 (5/13)	0.92	0.46–1.85	31.61 (141/446)	30.77 (4/13)	0.97	0.43–2.22	23.99 (107/446)	15.38 (2/13)	0.64	0.18–2.32
Adjusted*			0.86	0.43–1.73			0.88	0.38–2.03			0.60	0.16–2.17
Sterilized water												
Crude	41.86 (72/172)	41.46 (119/287)	0.99	0.79–1.24	31.98 (55/172)	31.36 (90/287)	0.98	0.74–1.29	26.16 (45/172)	22.30 (64/287)	0.85	0.61–1.19
Adjusted*			0.99	0.79–1.24			0.98	0.74–1.30			0.89	0.64–1.26
Vitamins												
Crude	40.99 (182/444)	57.14 (8/14)	1.39	0.87–2.22	30.86 (137/444)	50.00 (7/14)	1.62	0.94–2.79	23.20 (103/444)	42.86 (6/14)	1.85	0.99–3.46
Adjusted*			1.43	0.90–2.28			1.63	0.94–2.84			1.64	0.84–3.20
Honey												
Crude	41.10 (180/438)	52.38 (11/21)	1.27	0.84–1.95	31.05 (136/438)	42.86 (9/21)	1.38	0.83–2.31	23.29 (102/438)	33.33 (7/21)	1.43	0.76–2.68
Adjusted*			1.22	0.80–1.86			1.34	0.81–2.23			1.49	0.79–2.79

*Adjusted for age at home visit, infant's sex, any cigarette smoking in the same room with the infant, synthetic pillow use in infancy and any bottle-feeding at 1 month.
CI, confidence interval.

Table 4. Early introduction of non-milk fluids and likelihood of asthma, eczema and hay fever in childhood, the 1988–1989 Tasmanian Infant Health Survey and the 1997 Childhood Asthma and Respiratory Health Study

	Asthma				Eczema				Hay fever			
	Prevalence of the disease if the non-milk not introduced at home visit % (n/N)	Prevalence of the disease if the non-milk introduced at home visit % (n/N)	Risk ratio	95% CI	Prevalence of the disease if the non-milk not introduced at home visit % (n/N)	Prevalence of the disease if the non-milk introduced at home visit % (n/N)	Risk ratio	95% CI	Prevalence of the disease if the non-milk not introduced at home visit % (n/N)	Prevalence of the disease if the non-milk introduced at home visit % (n/N)	Risk ratio	95% CI
Fruit syrup												
Crude	29.12 (113/388)	31.43 (22/70)	1.08	0.74–1.58	24.35 (94/386)	24.29 (17/70)	1.00	0.64–1.56	24.03 (93/387)	28.17 (20/71)	1.17	0.78–1.77
Adjusted*			0.97	0.66–1.43			1.22	0.77–1.92			1.19	0.78–1.81
Orange juice												
Crude	29.66 (132/445)	23.08 (3/13)	0.78	0.29–2.12	24.60 (109/443)	15.38 (2/13)	0.63	0.17–2.26	25.17 (112/445)	7.69 (1/13)	0.31	0.05–2.02
Adjusted*			0.75	0.27–2.06			0.67	0.19–2.40			0.29	0.04–1.92
Sterilised water												
Crude	21.39 (37/173)	34.39 (98/285)	1.61†	1.16–2.23	22.67 (39/172)	25.35 (72/284)	1.12	0.80–1.57	23.84 (41/172)	25.17 (72/286)	1.06	0.76–1.47
Adjusted*			1.60†	1.15–2.24			1.22	0.86–1.72			1.08	0.77–1.51
Vitamins												
Crude	30.25 (134/443)	7.14 (1/14)	0.24	0.04–1.57	24.49 (108/441)	21.43 (3/14)	0.88	0.32–2.42	24.83 (110/443)	21.43 (3/14)	0.86	0.31–2.38
Adjusted*			0.22	0.03–1.48			1.01	0.35–2.87			0.84	0.30–2.36
Honey												
Crude	29.22 (128/438)	35.00 (7/20)	1.20	0.65–2.21	25.00 (109/436)	10.00 (2/20)	0.40	0.11–1.50	24.49 (107/437)	28.57 (6/21)	1.17	0.58–2.34
Adjusted*			1.12	0.61–2.06			0.44	0.12–1.65			1.31	0.65–2.64

*Adjusted for age at home visit, infant's sex, any cigarette smoking in the same room with the infant, synthetic pillow use in infancy and any bottle-feeding at 1 month.
†$p = 0.005$.
CI, confidence interval.

prevalent than expected and this cohort had more than 80% power to detect an odds ratio (OR) greater than 2 at $p < 0.05$ for either fruit syrup or any non-milk fluids and asthma. Nevertheless, this first report is not powered to detect low magnitude risk effects and further larger prospective studies are required.

The cohort had good initial participation and follow-up rates, reducing the likelihood of selection bias. Given the prospective design and the lack of any specific dietary recommendations regarding non-milk fluids, reporting bias because of infant's birthweight, prematurity or other infant characteristics is unlikely. Furthermore, additional adjustment for birthweight and other variables did not alter the results (data not shown). Nevertheless, as in all observational studies, the possibility of residual confounding cannot be ruled out. Although the cohort is not representative of all live births in Tasmania at that time, adjustment for the components of the perinatal scoring system did not alter the findings and there is no reason to believe that the study population was substantially different from the general population with regard to the development of allergy and atopy.

Sterilized water, fruit syrup, honey, vitamins and orange juice have all lower nutritional value than breast milk. Sugary beverages reduce the infant's appetite for more nutritional foods and may soften the stools (26). The American Academy of Paediatrics recommends a maximum of 240 ml/day of fruit juices, to avoid competition with nutritionally richer foods (26). In Lithuania, the Soviet recommendations promoting liquids, e.g. water and tea, from the first few days after birth, juice from 1 month of age, and strained fruits from 1.5 months (27) were replaced by recommendations of exclusive breastfeeding for 4–6 months with fruit juice, strained fruits and gluten-free cereal porridge introduced thereafter (28).

Vitamins were uncommonly administered, so we were unable to examine the association between vitamin D supplementation and atopic disease. Based on recommendations from the National Academy of Science and studies from the United States, Norway and China, in 2003, the American Academy of Pediatrics recommended 200 IU/day vitamin D for all infants and children (29).

A recent study from Finland (30) found a positive link between vitamin D supplementation in infancy and the risk of atopy, allergic rhinitis and asthma at 31 yr of age. Although the findings were the first to suggest such an association and were not confirmed by other studies, the majority of the infants in the Finnish cohort received 2000 IU of vitamin D per day, which is 10 times greater compared with current US recommendations. However, the association between vitamin D and atopic disease requires further evaluation.

In western societies, the duration of exclusive breastfeeding is shorter than the recommended 6 months (4–7). Here, the negative association between the duration of breastfeeding and non-milk fluids, if causal, supports current recommendations (26, 28) that their early introduction should be discouraged. However, they were not prospectively associated with a marked increased risk of atopic disease in this population-based cohort.

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