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Bottle Feeding in the Bed or Crib Before Sleep Time and Wheezing in Early Childhood

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ABSTRACT. *Objective.* Bottle feeding in the bed or crib before sleep time has been associated with an increased risk of wheezing in the first year of life. We examined whether bottle feeding in the bed or crib before sleep time in the first year of life is associated with wheezing in the first 5 years of life.

Methods. In a prospective cohort study of 448 children with parental history of atopy followed from birth, we examined the relation between the number of bi-monthly parental reports of bottle feeding in the bed or crib before sleep time in the first year of life (range: 0–6 reports) and parental report of wheezing in the first 5 years of life. Additional outcome measures included recurrent wheezing (≥ 2 episodes of wheezing in the previous year) and asthma (physician-diagnosed asthma and ≥ 1 episode of wheezing in the previous year) at the age of 5 years.

Results. The risk of recurrent wheezing and asthma at 5 years of age increased significantly with each additional report of bottle feeding in the bed or crib before sleep time in the first year of life. The risk of wheezing between the ages of 1 and 5 years increased with each additional report of bottle feeding in the bed or crib before sleep time in the first year of life. As an example, a child whose parents reported bottle feeding in the bed or crib before sleep time on 3 occasions in the first year of life had 1.5 times higher risk of wheezing between the ages of 1 and 5 years than a child whose parents did not report bottle feeding in the bed or crib before sleep time in the first year of life (95% confidence interval for relative risk: 1.12–2.12).

Conclusions. Among children with parental history of atopy, bottle feeding in the bed or crib before sleep time in the first year of life is a risk factor for recurrent wheezing and asthma at 5 years of age and a risk factor for wheezing between the ages of 1 and 5 years. *Pediatrics* 2002;110(6). URL: <http://www.pediatrics.org/cgi/content/full/110/6/e77>; *bottle feeding, sleep time, wheezing.*

ABBREVIATIONS. IgE, immunoglobulin E; OR, odds ratio; CI, confidence interval; GER, gastroesophageal reflux.

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Received for publication May 16, 2002; accepted Aug 26, 2002. Reprint requests to (J.C.C.) Channing Laboratory, 181 Longwood Ave, Boston, MA 02115. E-mail: juan.celedon@channing.harvard.edu PEDIATRICS (ISSN 0031 4005). Copyright © 2002 by the American Academy of Pediatrics.

Wheezing in early childhood is a common problem that may or may not be related to the subsequent development of asthma or allergies.^{1,2} In most cases, wheezing that starts before the age of 3 years is transient and presumed to be related to viral infections in children with reduced airway caliber but not related to allergen sensitization or an elevated total serum immunoglobulin E (IgE) level at the age of 6 years. In a minority of infants, wheezing that starts before the age of 3 years persists up to the age of 6 years. Although children with persistent wheezing are more likely to have atopy and reduced lung function at the age of 6 years than nonwheezing children, persistent wheezing can occur in the absence of allergen sensitization.¹ Factors such as maternal smoking during pregnancy may influence the development of persistent wheezing through nonallergic mechanisms.³

The Home Allergens and Asthma Study is a prospective birth cohort study of children with a parental history of asthma or allergies in the Boston metropolitan area. We showed previously that parental report of bottle feeding the child in the bed or crib before sleep time in the 24 hours before the administration of a standardized questionnaire was associated cross-sectionally with an increased risk of wheezing in the first year of life.⁴ Given that infants who are bottle fed in the bed or crib before sleep time may be at greater risk for food regurgitation and aspiration-related wheezing, we were interested in examining the relation between bottle feeding in the bed or crib before sleep time in the first year of life and wheezing and asthma in the first 5 years of life among 448 children who were followed from birth to the age of 5 years.

METHODS

The 505 infants with a history of allergy or asthma in at least 1 parent were recruited between September 1994 and August 1996.⁵ Every 2 months, beginning when the child was 2 months of age, a telephone questionnaire was administered to the child's primary caregiver until the child's second birthday. Afterward, interviews were conducted every 6 months. Seven children were excluded from analysis because they were followed for ≤ 4 months during their first year of life. The study was approved by the Institutional Review Board of the Brigham and Women's Hospital.

Every 2 months during the child's first 2 years of life, the primary caregiver was asked whether the child was bottle fed. For children who were bottle fed, we asked, "During the past 24 hours, was the child given a bottle in his/her bed or crib before napping or sleeping at night?" Bottle feeding in the bed or crib before sleep time in the first year of life was treated as an ordinal variable (range: 0–6 reports).

The following variables were considered for inclusion in the multivariate analysis: child's race,⁵ annual household income, day care in the first year of life,⁴ in utero exposure to smoking, breastfeeding (never, for <4 months, or for ≥4 months), maternal history of asthma (ever, and ever with current symptoms [active]), number of older siblings in the household, average number of cigarettes per day smoked by all adults in the household, physician-diagnosed lower respiratory illnesses (croup, bronchitis, bronchiolitis, or pneumonia) in the first year of life, physician-diagnosed upper respiratory illnesses (ear infections and sinus trouble) in the first year of life, and recurrent nasal catarrh (at least 3 vs fewer than 3 episodes of runny nose) in the first year of life.⁴

At every survey, we asked whether the child had experienced any wheezing or whistling in the chest since the previous interview. Every year, starting when the child was 2 years of age, we also asked, "How many attacks or episodes of wheezing has your child had in the past 12 months?" (0, 1, ≥2 but <1 per month, approximately 1 per month, approximately 1 every week, daily or nearly every day). At 5 years of age, we defined recurrent wheezing as 2 or more episodes of wheezing in the previous year, asthma as physician-diagnosed asthma and at least 1 episode of wheezing in the previous year, and allergic rhinitis as physician-diagnosed allergic rhinitis and a history of nasal discharge or sneezing apart from colds in the previous year.

Total serum IgE level at 2 years of age was measured by an enzyme-immunoassay based on the sandwich technique (UniCap, Pharmacia Diagnostics, Kalamazoo, MI). All values were converted to the log-natural scale for analysis.

Stepwise logistic regression was used to study the relation between bottle feeding in the bed or crib before sleep time in the first year of life and asthma, recurrent wheezing, and allergic rhinitis at 5 years of age while adjusting for potential confounders and examining interactions. In the final models, we included variables that were significant at $P < .05$ or that satisfied a change in estimate criterion (≥10%) in the odds ratio (OR). For the longitudinal analysis of the relation between bottle feeding in the bed or crib before sleep time in the first year of life and wheezing in the first 5 years of life, we used proportional hazard models, with repeated events on the same child being handled by the method of Anderson and Gill.⁶ To examine age-dependent associations, we calculated interaction terms between the age of the children at each survey and the variables in the model.

RESULTS

The characteristics of the 498 study subjects have been described in detail elsewhere.⁵ Of the 498 study participants, 448 (90%) were followed up to the age of 5 years. Subjects who dropped out of the study before the age of 5 years were significantly more likely to come from low-income families than were subjects who were followed up to the age of 5 years. Of the 448 children with 5-year follow-up, 246 (54.9%) were boys. Table 1 summarizes the main characteristics of study participants with 5-year follow-up. Of these 448 children, 355 (79.2%) were white, 40 (8.9%) were black, 21 (4.7%) were Hispanic, and 32 (7.2%) belonged to other racial groups.

Of the 498 original study subjects, 230 (46.2%) had a measurement of total serum IgE level at 2 years of age. No significant differences in bottle feeding in the bed or crib before sleep time in the first year of life were found between those with a total serum IgE measurement at 2 years of age and those without the measurement.

We found no significant cross-sectional association between bottle feeding in the bed or crib before sleep time and doctor-diagnosed lower respiratory illnesses in the first year of life (unadjusted OR for each additional report of bottle feeding in the bed or crib before sleep time: 0.9; 95% confidence interval [CI]: 0.76–1.09).

TABLE 1. Characteristics of Children in the Cohort ($n = 448$)

Variables	n (%)
Household income	
<\$30 000	28 (6.2)
>\$30 000	408 (91.1)
Unknown	12 (2.7)
Breastfeeding	
Never	106 (23.7)
Exclusively for <4 mo	259 (57.8)
Exclusively for ≥4 mo	83 (18.5)
Reports of bottle feeding in the bed or crib before sleep time in the first year of life	
0	330 (73.7)
1	48 (10.7)
2	29 (6.5)
3	20 (4.5)
4–6	21 (4.6)
Maternal history of asthma, ever	127 (28.3)
Maternal history of asthma, active	40 (8.9)
Maternal smoking during pregnancy	27 (6.0)
Daycare attendance in the first year of life	211 (47.1)
Number of older siblings	
0	212 (47.3)
1	158 (35.3)
2	59 (13.2)
3 or more	19 (4.2)
≥1 doctor-diagnosed LRI in the first year of life	119 (26.6)
≥1 doctor-diagnosed URI in the first year of life	289 (64.5)
Recurrent nasal catarrh (≥3 episodes of runny nose) in the first year of life	380 (84.8)

LRI indicates lower respiratory illness; URI, upper respiratory illness.

Sixteen (13.6%) of the 118 children whose parents reported bottle feeding in the bed or crib before sleep time at least once in the first year of life and 22 (6.7%) of the 330 children (6.7%) whose parents did not report bottle feeding in the bed or crib before sleep time in the first year of life had recurrent wheezing at 5 years of age. Fifteen (12.7%) of the 118 children whose parents reported bottle feeding in the bed or crib before sleep time at least once in their first year of life and 23 (7.0%) of the 330 children whose parents did not report bottle feeding in the bed or crib before sleep time in their first year of life had asthma at 5 years of age. Table 2 summarizes the results of the analysis of the relation between bottle feeding in the bed or crib before sleep time in the first year of life and recurrent wheezing and asthma at 5 years of age. After adjustment for other variables, children whose parents reported bottle feeding in the bed or crib before sleep time at least once in their first year of life had significantly higher odds of recurrent wheezing at 5 years of age than children whose parents did not report bottle feeding in the bed or crib before sleep time in the first year of life. In the adjusted analysis, the odds of both recurrent wheezing and asthma at 5 years of age increased significantly with each additional report of bottle feeding in the bed or crib before sleep time in the first year of life (P for linear trend = .01 for recurrent wheezing and .02 for asthma). We found no significant association between breastfeeding in the first year of life and either recurrent wheezing or asthma (unadjusted OR for exclusive breastfeeding for <4 months versus never: 1.1; 95% CI: 0.5–2.4; unadjusted OR for

TABLE 2. Relation Between Bottle Feeding in the Bed or Crib Before Sleep Time in the First Year of Life and Recurrent Wheezing and Asthma at Age 5 Years Among 448 Study Participants

Number of Reports of Bottle Feeding in the Bed or Crib Before Sleep Time	OR (95% CI)			
	Recurrent Wheezing (<i>n</i> = 38)*		Asthma (<i>n</i> = 38)†	
	Unadjusted	Adjusted‡	Unadjusted	Adjusted‡
0	1.0	1.0	1.0	1.0
1	1.3 (1.08–1.66)	1.3 (1.05–1.66)	1.4 (1.12–1.72)	1.3 (1.07–1.69)
2	1.8 (1.16–2.77)	1.8 (1.11–2.77)	1.9 (1.25–2.95)	1.8 (1.13–2.86)
3	2.4 (1.25–4.62)	2.3 (1.17–4.61)	2.7 (1.40–5.06)	2.4 (1.21–4.84)
4	3.2 (1.35–7.70)	3.1 (1.23–7.67)	3.7 (1.57–8.68)	3.3 (1.29–8.18)
5	4.3 (1.46–12.82)	4.1 (1.30–12.76)	5.1 (1.76–14.89)	4.4 (1.37–13.83)
6	5.8 (1.57–21.35)	5.4 (1.36–21.23)	7.1 (1.97–25.55)	5.9 (1.46–23.39)

* At least 2 episodes of wheezing in the previous 12 months.

† Physician-diagnosed asthma and at least 1 episode of wheezing in the previous 12 months.

‡ Adjusted for gender, household income, and active maternal history of asthma.

exclusive breastfeeding for ≥ 4 months versus never: 0.7; 95% CI: 0.2–2.1).

To assess whether the observed association between bottle feeding in the bed or crib before sleep time in the first year of life and asthma at 5 years of age could be mediated by an increased risk of allergy as a result of bottle feeding itself, we examined the relation between bottle feeding in the bed or crib before sleep time and markers of allergy. There was no significant difference in geometric mean total serum IgE level at 2 years of age between children whose parents reported bottle feeding in the bed or crib before sleep time at least once in the first year of life (16.5 [± 1 standard deviation = 4.3, 63.6] IU/mL) and those whose parents did not (15.2 [± 1 standard deviation = 4.0, 57.2] IU/mL). In addition, we found no significant association between bottle feeding in the bed or crib before sleep time in the first year of life and allergic rhinitis at 5 years of age (*n* = 45; unadjusted OR for 1 vs 0 reports of bottle feeding in the bed or crib before sleep time: 0.8; 95% CI: 0.6–1.2; *P* > .2).

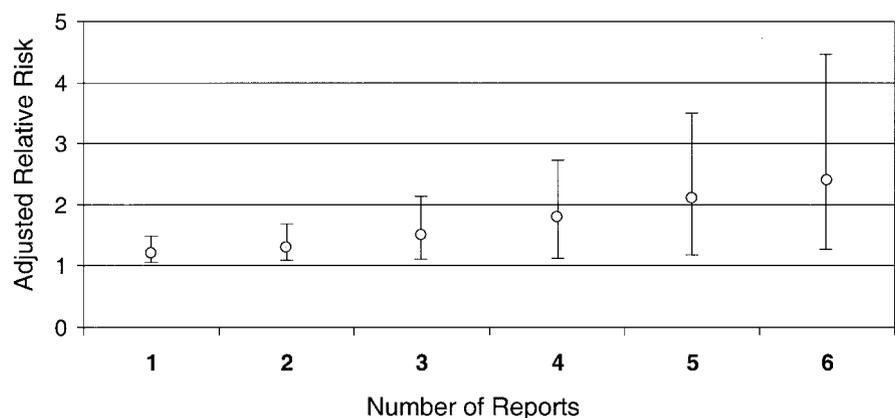
In the longitudinal bivariate analysis, the risk of wheezing between the ages of 1 and 5 years increased significantly with each additional report of bottle feeding in the bed or crib before sleep time in the first year of life. The results of the multivariate longitudinal analysis of the relation between the number of reports of bottle feeding in the bed or crib

before sleep time in the first year of life and wheezing between the ages of 1 and 5 years are shown in Fig 1. Bottle feeding in the bed or crib before sleep time in the first year of life was associated with an increased risk of wheezing that did not change significantly between the ages of 1 and 5 years (*P* for interaction with age > .2). The risk of wheezing between the ages of 1 and 5 years increased with each additional report of bottle feeding in the bed or crib before sleep time in the first year of life (*P* for linear trend < .01). In the multivariate analysis, the risk of wheezing associated with child care attendance in the first year of life decreased significantly from the ages of 1 to 5 years (*P* for interaction with age < .01).

We found no significant association between breastfeeding and wheezing between the ages of 1 and 5 years (unadjusted relative risk for exclusive breastfeeding for < 4 months versus never: 0.9; 95% CI: 0.7–1.3; unadjusted relative risk for exclusive breastfeeding for ≥ 4 months versus never: 0.9; 95% CI: 0.6–1.3).

Because we also had information on bottle feeding in the bed or crib before sleep time in the second year of life, we were interested in examining whether this parental behavior in the child's first year of life continued during the child's second year of life. Of the 118 parents who reported bottle feeding their children in the bed or crib before sleep time at least once in the first year of life, 73 (61.9%) reported bottle

Fig 1. Adjusted relative risk of wheezing between the ages of 1 and 5 years among children whose parents reported bottle feeding in the bed or crib before sleep time in the first year of life, as compared with children whose parents did not report bottle feeding in the bed or crib before sleep time in the first year of life. Relative risks were adjusted for gender, household income, daycare in the first year of life, recurrent nasal catarrh in the first year of life, and having at least 1 doctor-diagnosed lower respiratory illness in the first year of life. The increased risk of wheezing associated with bottle feeding in the bed or crib before sleep time in the first year of life did not change significantly between the ages of 1 and 5 years. The I bars represent the 95% CIs.



feeding their children in the bed or crib before sleep time at least once in the second year of life.

DISCUSSION

To our knowledge, this is the first study to demonstrate an association between bottle feeding in the bed or crib before sleep time in the first year of life and asthma at the age of 5 years and wheezing between the ages of 1 to 5 years. Because bottle feeding in the bed or crib before sleep time in the first year of life was associated with wheezing and asthma but not with allergic rhinitis or total serum IgE, a likely explanation for our findings is bronchospasm resulting from repeated irritation of the airways as a result of postprandial reflux and microaspiration in the recumbent position. Given that bottle feeding the child in the bed or crib before sleep time in the first year of life was correlated with the same behavior in the second year of life, this feeding habit may continue in some cases as the children grow older. In rabbits, weekly aspiration of a small volume of milk for 5 weeks is associated with an increased proportion of neutrophils in bronchoalveolar lavage and increased airway responsiveness to methacholine.⁷ Gastroesophageal reflux (GER) and microaspiration of liquids in early childhood may result in chronic inflammation of the airways, recurrent bronchoconstriction, and, perhaps, airway remodeling. In addition, GER may cause reflex bronchospasm mediated by stimulation of vagal pathways in the esophagus.^{8,9} Because it is known that adults with asthma have a high prevalence of esophageal dysfunction and GER,^{10,11} a plausible alternative explanation for our results is that infants with frequent wheezing in early life may have concurrent esophageal dysfunction and GER leading to persistent wheezing.

GER has protean manifestations in infants, including regurgitation, failure to thrive, crying resulting from esophagitis, stridor, or lower respiratory symptoms such as wheezing.¹² The most common symptom of GER in infants is overt regurgitation, a problem that usually resolves in the second year of life and that was not associated with respiratory symptoms in a recent case-control study.¹³ However, some infants with wheezing have coexisting GER,¹⁴ and a significant proportion of infants with GER may come to medical attention because of respiratory symptoms.¹⁵ In a study of infants who were referred to a pediatric pulmonary clinic for evaluation of daily wheezing that did not respond to conventional asthma therapy, 54 (64%) of 84 subjects had GER disease diagnosed by a positive 24-hour esophageal pH study.¹⁶ Of the 54 infants with GER disease and wheezing, 24 (44%) had no gastrointestinal symptoms (silent GER disease). The proportion of infants who have GER disease and respiratory symptoms and will have GER disease as older children and adults is unknown.

We considered confounding by type of feeding and/or socioeconomic status as an alternative explanation for our findings. However, we found no association between breastfeeding and any of the outcomes of interest. Given that there could be residual

confounding by bottle feeding itself, we also examined the relation between either the intensity (number of months) or month of initiation (<2 months, 2–4 months, >4 months) of bottle feeding in the first year of life and wheezing and asthma in the first 5 years of life, finding no significant association (data not shown). Furthermore, inclusion of variables indicating type of feeding and/or socioeconomic status in the multivariate models did not change our results appreciably.

We recognize several limitations to our findings. First, we had no information about the presence of nonrespiratory symptoms of GER or a test of esophageal pH, and thus we cannot examine whether the observed association between bottle feeding in the bed or crib before sleep time and wheezing was present in all children or only in children with GER. Second, our findings may not be applicable to children in the general population of Boston because we selected a stable population with parental history of atopy. Our results, however, are generalizable to a group of children at high risk for the development of asthma and atopy. Third, we do not know whether a proportion of the participating children with asthma or recurrent wheezing at the age of 5 years will become asymptomatic later in childhood. However, finding modifiable risk factors for wheezing in the first 5 years of life is important, as it may decrease respiratory morbidity in early childhood. Fourth, we asked only about bottle feeding in the bed or crib before sleep time in the 24 hours preceding the administration of the bimonthly questionnaire to minimize recall bias. It is likely, however, that an answer to this question reflects a pattern of parental behavior.

CONCLUSION

Bottle feeding in the bed or crib before sleep time was a risk factor for asthma and recurrent wheezing at 5 years of age and a risk factor for wheezing in the first 5 years of life among children with parental history of atopy. Avoidance of large-volume liquid meals in the bed or crib before sleep time and perhaps avoidance of the supine position immediately after bottle feeding may reduce wheezing in the first 5 years of life among children with parental history of atopy.

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