

Breast feeding and allergic diseases in infants—a prospective birth cohort study

I Kull, M Wickman, G Lilja, S L Nordvall, G Pershagen

Arch Dis Child 2002;87:478–481

See end of article for authors' affiliations

Correspondence to:
Dr M Wickman,
Department of
Environmental Health,
Norrbäcka Building, Level
3, Karolinska Hospital,
SE-171 76 Stockholm,
Sweden;
magnus.wickman@smd.sll.se

Accepted 4 July 2002

Aims: To investigate the effect of breast feeding on allergic disease in infants up to 2 years of age.

Methods: A birth cohort of 4089 infants was followed prospectively in Stockholm, Sweden. Information about various exposures was obtained by parental questionnaires when the infants were 2 months old, and about allergic symptoms and feeding at 1 and 2 years of age. Duration of exclusive and partial breast feeding was assessed separately. Symptom related definitions of various allergic diseases were used. Odds ratios (OR) and 95% confidence intervals (CI) were estimated in a multiple logistic regression model. Adjustments were made for potential confounders.

Results: Children exclusively breast fed during four months or more exhibited less asthma (7.7% v 12%, $OR_{adj} = 0.7$, 95% CI 0.5 to 0.8), less atopic dermatitis (24% v 27%, $OR_{adj} = 0.8$, 95% CI 0.7 to 1.0), and less suspected allergic rhinitis (6.5% v 9%, $OR_{adj} = 0.7$, 95% CI 0.5 to 1.0) by 2 years of age. There was a significant risk reduction for asthma related to partial breast feeding during six months or more ($OR_{adj} = 0.7$, 95% CI 0.5 to 0.9). Three or more of five possible allergic disorders—asthma, suspected allergic rhinitis, atopic dermatitis, food allergy related symptoms, and suspected allergic respiratory symptoms after exposure to pets or pollen—were found in 6.5% of the children. Exclusive breast feeding prevented children from having multiple allergic disease ($OR_{adj} = 0.7$, 95% CI 0.5 to 0.9) during the first two years of life.

Conclusion: Exclusive breast feeding seems to have a preventive effect on the early development of allergic disease—that is, asthma, atopic dermatitis, and suspected allergic rhinitis, up to 2 years of age. This protective effect was also evident for multiple allergic disease.

To reduce the incidence and severity of allergic disease in children, preventive strategies have often focused on indoor environmental factors such as environmental tobacco smoke, allergens from furred pets, dust mites, and indoor humidity, as well as on early exposure to cows' milk and other foreign food proteins, and also on the possible protective effect of breast feeding.^{1–6} With the exception of tobacco smoke, the effect of such recommendations has sometimes been questioned.^{7–9} The influence of breast feeding on induction of asthma and other allergic diseases in children appears contradictory.^{10–12} Some studies indicate that prolonged breast feeding significantly decreases the risk of asthma and other allergic disease among children.^{13–15} However, other studies have failed to confirm this or even suggest that breast feeding is associated with an increased risk for childhood asthma in the presence of maternal asthma.^{16–18}

Since the scientific evidence on the effect of breast feeding for development of allergic disease is inconclusive, one aim of this prospective birth cohort study was to assess the role of breast feeding for development of allergic disease in infancy.

MATERIAL AND METHODS

Study subjects

From February 1994 until November 1996, 4089 newborn infants (2065 boys and 2024 girls) were included in a prospective study. These infants comprised 75% of all eligible children born in predefined areas of Stockholm, who fulfilled our inclusion criteria, for example, parents answering the first questionnaire and collecting samples of mattress dust during the child's first year of life. Study design, enrolment, criteria for inclusion, and the procedures of data collection are described in detail elsewhere.¹⁹

Questionnaire

Data on detailed residential characteristics, environmental factors, and allergic heredity were collected from the parental questionnaires when the children were about 2 months of age. Information was also obtained on parental education and employment. At 1 and 2 years of age a similar questionnaire, which focused on symptoms possibly related to allergic disease and respiratory infections, was mailed to the parents of all children (Q1 and Q2, respectively). A second part of Q1 and Q2 provided detailed information on breast feeding. The response rate of the questionnaire at 1 and 2 years of age was 96% and 94%, respectively. For this report it was required that the parents had answered all three questionnaires, leaving 3791 infants (93%).

Classification of exposure and outcome

Breast feeding

The roles of exclusive and partial breast feeding were assessed separately. Exclusive breast feeding denotes the period that the infants were only breast fed and that no formula, cows' milk, or solid foods had been introduced. Partial breast feeding implies that the child, in addition to breast milk, had also received infant formula, other formulas, or solid food.

Allergic diseases

As there is no golden standard for the classification of allergic diseases in this age group, a combination of symptoms was used to define asthma, atopic dermatitis, suspected allergic rhinitis, and food reactions apart from doctors' diagnoses.

Abbreviations: AD, atopic dermatitis; CI, confidence interval; OR, odds ratio; SAD, severe symptoms of allergic disease; SAR, suspected allergic rhinitis; SARS, suspected allergic respiratory symptoms

Table 1 Asthma, atopic dermatitis, suspected allergic rhinitis, and reactions to food among 3791 children up to 2 years of age in relation to various background factors

	Asthma n=321 (8.5%)			Suspected allergic rhinitis n=262 (7.0%)			Atopic dermatitis n=952 (25%)			Reactions to food n=768 (20%)		
	n	%	OR adj	95% CI	n	%	OR adj	95% CI	n	%	OR adj	95% CI
Gender												
Boys	196	10	1.6	1.27 to 2.05	150	7.9	1.1	1.05 to 1.77	486	25	1.0	0.88 to 1.19
Girls	125	6.7	1.0		112	6.0	1.0		466	25	1.0	
Heredity*												
Any	132	12	1.8	1.41 to 2.27	122	11	2.3	1.77 to 2.97	352	32	1.6	1.35 to 1.85
None	186	7.1	1.0		135	5.2	1.0		593	22	1.0	
Maternal age												
<26 years	65	14	1.8	1.31 to 2.39	58	13	1.9	1.33 to 2.58	126	27	1.1	0.88 to 1.39
≥26 years	256	7.7	1.0		204	6.2	1.0		826	25	1.0	
Maternal smoking†												
Yes	66	13	1.7	1.27 to 2.32	51	10	1.4	1.01 to 2.00	130	26	1.1	0.86 to 1.34
No	255	7.8	1.0		211	6.5	1.0		821	25	1.0	
Year of construction of home												
>1961	195	10	1.5	1.17 to 1.89	164	8.7	1.6	1.25 to 2.13	501	26	1.1	0.89 to 1.19
<1960	126	6.7	1.0		98	5.0	1.0		450	24	1.0	

For each of the five exposure variables adjustment has been made for the other four variables.

*Reported doctor's diagnosed asthma ever and/or doctor's diagnosed allergic rhinitis in any parent. In addition, allergy to furred pets or pollens was required.

†Maternal smoking during pregnancy and/or during the three first months of life of the child.

- *Asthma*. At least three reported episodes of wheezing during the first two years of life, and in addition, respiratory symptoms treated with inhaled glucocorticoids or signs of hyperreactivity (wheezing or severe coughing while exercising, cold weather, or disturbed coughing at night) without ongoing upper respiratory infection. Episodes of wheezing during the first three months were not included.
- *Atopic dermatitis (AD)*. Itchy rash for at least two weeks with typical distribution (face/outer limbs/folds of elbows, behind the knees/wrists, or fronts of ankles) and dry skin and/or doctor's diagnosis of eczema.
- *Suspected allergic rhinitis (SAR)*. Reported sneezing, runny/ blocked nose, and/or red and itchy eyes after contact with furred pets or pollen, and/or doctor's diagnosis of allergic rhinitis.
- *Suspected allergic respiratory symptoms (SARS)*. Wheezing and/or disturbing cough after exposure to furred pets or tree/grass pollen.
- *Reactions to food*. Any of the following symptoms reported to have appeared directly after consumption of food: atopic dermatitis, urticaria, oedema of lips/eyes, pruritus around the eyes, or running nose, asthma, and/or doctor's diagnosis of food allergy.
- *Severe symptoms of allergic disease (SAD)*. At least three of the five different outcomes above.

Statistical analysis

Multiple regression models were used to determine whether outcome variables (asthma, atopic dermatitis, suspected allergic rhinitis, suspected allergic respiratory symptoms, and reactions to food) were associated with the independent variable (breast feeding). The 95% confidence intervals for odds ratios were calculated using standard algorithms. Adjustments were made for gender, heredity for allergic disease, mother's age, maternal smoking during pregnancy and/or during the first months of life of the baby, and year of construction of the home (table 1). The χ^2 test was used for statistical analysis of proportions. All statistical analyses were performed with STATA, Statistical Software, release 6.0 (Collage Station, Texas, USA). The ethical committee of Karolinska Institute, Stockholm, Sweden, approved the study.

RESULTS

The median duration of exclusive breast feeding was five months (25th and 75th centiles: four and six months, respectively) and for partial breast feeding eight months (25th and 75th centiles: six and eleven months, respectively). Eighty per cent of the children were exclusively breast fed during four months or more (fig 1). Maternal factors such as young age, short school education, and smoking were associated with shorter breast feeding of their babies. This was particularly evident for mothers with a combination or all of these characteristics. Atopic heredity did not affect the median duration of breast feeding (not shown in figure).

Table 1 gives the cumulative incidence for asthma and other allergic diseases in the cohort in relation to different background factors. Male sex, allergic heredity, mother's age, maternal smoking, and year of construction of the home were all significant risk factors for asthma and suspected allergic rhinitis. For atopic dermatitis and reactions to food, only heredity was associated with an increased risk.

Infants breast fed during four months or more exhibited a reduced risk of asthma (OR_{adj} = 0.66, 95% CI 0.51 to 0.87) and wheezing (OR_{adj} = 0.78, 95% CI 0.65 to 0.93) (table 2). A total of 186 children (4.9%) exhibited asthma in combination with at least one other suspected allergic manifestation. Among children who had been breast fed for four months or more, only 4.4% exhibited this combination, compared to 6.9%

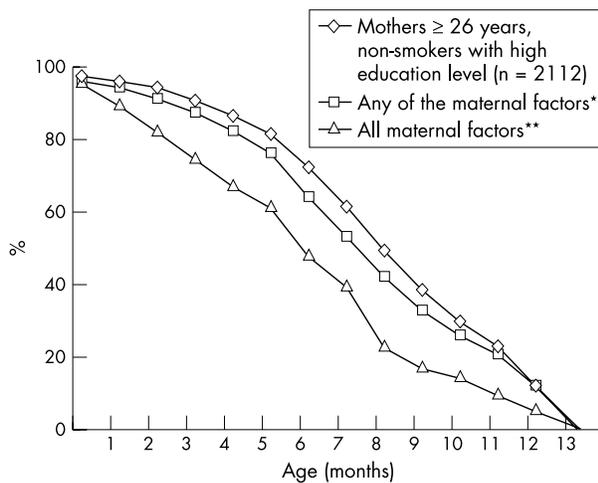


Figure 1 Duration of breast feeding (exclusive and partial) in relation to various maternal factors. *Either low maternal education (n = 1265), maternal smoking (n = 504), or mother <26 years of age (n = 459). **Low maternal education, mother <26 years of age, and maternal smoking (n = 68).

among those breast fed for a shorter period ($OR_{adj} = 0.69$, 95% CI 0.49 to 0.97). Partial breast feeding also seemed to reduce the risk of asthma up to the age of 2 years ($OR_{adj} = 0.69$, 95% CI 0.52 to 0.91). No difference was seen between boys and girls with regard to the effect on asthma of breast feeding (data not shown). The protective effect of partial breast feeding for six months was significantly stronger among infants with atopic heredity ($p = 0.018$). This effect was independent of whether the heredity for asthma or other allergic disease was on the mother's or on the father's side.

Children exclusively breast fed during four months or more exhibited significantly less AD during their first two years of life than children breast fed for a shorter period. The duration of exclusive breast feeding also had an impact on the occurrence of suspected allergic rhinitis and suspected allergic respiratory symptoms. However, partial breast feeding did not significantly reduce the risk for AD, suspected allergic rhinitis, or suspected allergic respiratory symptoms.

At least three of five possible suspected allergic manifestations were found in 6.5% of the children during their first two years of life. Among infants exclusively breast fed for four months or more, 5.9% fulfilled these criteria compared to 9.2% among those breast fed for a shorter period ($OR_{adj} = 0.66$, 95% CI 0.48 to 0.90). Duration of partial breast feeding also had a significant effect on SAD. Among infants partially breast fed for six months or more, 5.9% exhibited SAD compared to 9.5% breast fed for a shorter period ($OR_{adj} = 0.69$, 95% CI 0.50 to 0.95).

DISCUSSION

In this prospective birth cohort survey we have shown a significant preventive impact of breast feeding on development of asthma, suspected allergic rhinitis, atopic dermatitis, and suspected allergic respiratory symptoms associated with exposure to pollen and/or pets during the first two years of life. This protective effect could also be shown for severe symptoms of allergic disease. The risk reduction was clearest in relation to duration of exclusive breast feeding. There also appeared to be a preventive effect for partial breast feeding. However, because of considerable overlap between the two groups in the analysis, the effects of exclusive and partial breast feeding were difficult to disentangle.

In many other studies a protective effect of breast feeding against wheezing early in life has been shown.^{20–23} Wright *et al* found a statistically significant lower prevalence of recurrent

Table 2 Length of exclusive and partial breast feeding in relation to reported asthma and allergic symptoms among 3791 children up to 2 years of age

	Exclusive breast feeding				Partial breast feeding				95% CI	OR adj*	95% CI
	<4 months (n=773)		≥4 months (n=3013)		<6 months (n=680)		≥6 months (n=3110)				
	n	%	n	%	n	%	n	%			
Wheezing ever	251	33	797	27	219	32	830	27	0.65 to 0.93	0.81	0.67 to 0.97
Asthma according to definition	90	12	231	7.7	81	12	240	7.7	0.51 to 0.87	0.69	0.49 to 0.95
Doctor's diagnosis of asthma	71	9.2	174	5.8	64	9.4	181	5.8	0.49 to 0.90	0.69	0.50 to 0.95
Asthma combined with any other allergic manifestation†	53	6.9	133	4.4	46	8.9	140	4.5	0.49 to 0.97	0.77	0.54 to 1.1
Suspected allergic rhinitis	70	9.0	192	6.5	61	9.0	201	6.5	0.54 to 0.99	0.80	0.58 to 1.09
Suspected allergic respiratory symptoms‡	58	7.5	137	4.6	48	7.0	148	4.8	0.47 to 0.92	0.80	0.56 to 1.15
Atopic dermatitis	209	27	742	25	181	27	770	25	0.71 to 1.0	0.88	0.72 to 1.05
Adverse reaction to food	166	22	601	20	135	20	632	20	0.75 to 1.1	1.0	0.85 to 1.31
Severe symptoms of allergic disease§	71	9.2	173	5.8	64	9.5	178	5.9	0.49 to 0.90	0.69	0.50 to 0.95

* Adjustment has been made for gender, heredity, maternal age, smoking during pregnancy and/or during the three first months of life of the child, and year of construction of home of the family.

† Asthma in combination with one or more of the following: atopic dermatitis, suspected allergic rhinitis, suspected allergic respiratory symptoms after exposure to pollen or pets, or adverse reactions to food.

‡ Wheezing and/or disturbing cough, after contact with furred pets or tree/grass pollen.

§ At least three of the five different outcomes: asthma, atopic dermatitis, suspected allergic rhinitis, suspected allergic respiratory symptoms after exposure to pollen or pets, or adverse reactions to food.

wheeze up to 2 years of age in children who were exclusively breast fed for four months or more.¹⁸ However, at follow up at the age of 6 years they found that breast feeding was associated with an increased risk of asthma and wheeze for atopic children with asthmatic mothers. In our study, the group of children that benefited the most from breast feeding were those with parental history of atopic disease independently of maternal asthma. Further follow up of our cohort will show whether the protective effect of breast feeding remains.

One strength of this study is its design: use of a well defined participant base with a high response rate and collection of exposure data before onset of disease.²⁴ Furthermore, the average duration of breast feeding—that is, duration of exposure, was relatively long compared to many other studies. A sufficient duration of breast feeding has been considered as important, as there may be a threshold below which the effect is difficult to detect.¹⁰ The results of our study presented here encompass only the first two years of life, a period when diagnosis of allergic disease is often difficult. However, our data indicate that breast feeding at least postpones the onset of symptoms possibly related to allergic disease in infancy.

Social factors such as maternal age and education as well as maternal smoking, were all important risk factors for asthma.¹⁹ These risk factors co-varied with one another as well as with short duration of breast feeding. Thus, the impact on induction of allergic disease in early childhood by several different risk factors needs to be stressed. Early onset of atopic dermatitis has been found to be predictive for asthma later in childhood.²⁵ There are also studies indicating that asthma in combination with any other allergic manifestation in early life increases the risk of having the disease over many decades.²⁶ Since there was a preventive effect of exclusive breast feeding on atopic dermatitis as well as on the risk of having three or more allergic manifestations up to 2 years of age, the effects seen for breast feeding might be long lasting.

Conclusion

Our results indicate that exclusive breast feeding for four months or more reduces the risk of symptoms of allergic diseases up to 2 years of age. This protective effect was also evident if the child had symptoms of several allergic disorders. A risk reduction also appeared for partial breast feeding on development of asthma and severe symptoms of allergic disease. However, the effects of exclusive and partial breast feeding were difficult to disentangle because of overlap between the groups.

ACKNOWLEDGEMENTS

We would especially like to thank all children and parents in the BAMSE cohort and all nurses at the Child Care Health Centres. We are also grateful to Niklas Berglind for statistical advice, and Eva Hallner, André Lauber, and Lena Tollin at the Department of Environmental Health, Stockholm County Council. This study was founded by the Swedish Asthma and Allergy Association and the Swedish Foundation for Health Care Science and Allergy Research.

Authors' affiliations

I Kull, M Wickman, Department of Environmental Health, Stockholm County Council, Stockholm, Sweden
G Lilja, Sachss' Children's Hospital, Institutet of Södersjukhuset, Karolinska Institutet, Stockholm

S L Nordvall, Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden

G Pershage, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden

REFERENCES

- Rylander E, Pershagen G, Eriksson M, *et al*. Parental smoking and other risk factors for wheezing bronchitis in children. *Eur J Epidemiol* 1995;**9**:517–26.
- Wickman M, Nordvall SL, Pershagen G. Risk factors in early childhood for sensitization to airborne allergens. *Pediatr Allergy Immunol* 1992;**3**:128–33.
- Melen E, Wickman M, Nordvall SL, *et al*. Influence of early and current environmental exposure factors on sensitization and outcome of asthma in pre-school children. *Allergy* 2001;**56**:646–52.
- Sporik R, Holgate S, Platts-Mills T, *et al*. Exposure to house dust mite allergen (Der p I) and the development of asthma in childhood. A prospective study. *N Engl J Med* 1990;**323**:502–7.
- Wickman M, Nordvall SL, Pershagen G, *et al*. House dust mite sensitization in children and residential characteristics in a temperate region. *J Allergy Clin Immunol* 1991;**88**:89–95.
- Höst A, Husby S, Österballe O. A prospective study of cow's milk allergy in exclusively breast-fed infants. *Acta Paediatr Scand* 1988;**77**:663–70.
- Foucard T. Is prevention of allergy and asthma possible? *Acta Paediatr Scand* 2000;**89**(suppl 434):71–5.
- Peat JK. Can asthma be prevented? Evidence from epidemiological studies of children in Australia and New Zealand in the last decade. *Clin Exp Allergy* 1998;**28**:261–5.
- Pearce N, Douwes J, Beasley R. Is allergen exposure the major cause of asthma? *Thorax* 2000;**55**:424–31.
- Kramer, Michael S. Does breast feeding help protect against atopic disease? Biology, methodology and a golden jubilee of controversy. *J Pediatr* 1988;**112**:81–90.
- Vandenplas Y. Myths and facts about breastfeeding: does it prevent later atopic disease? *Acta Paediatr Scand* 1997;**86**:283–7.
- Gdalevich M, Mimouni D, Mimouni M. Breast-feeding and the risk of bronchial asthma in childhood: review with meta-analysis of prospective studies. *J Pediatr* 2001;**139**:261–6.
- Tariq SM, Matthews SM, Hakim EA, *et al*. The prevalence of and risk factors for atopy in early childhood: a whole population birth cohort study. *J Allergy Clin Immunol* 1998;**10**:587–93.
- Oddy WH, Holt PG, Sly PD, *et al*. Association between breast-feeding and asthma in 6-year-old children: findings of a prospective birth cohort study. *BMJ* 1999;**319**:815–19.
- Saarinen UM, Kajosaari M. Breastfeeding as prophylaxis against atopic diseases, prospective follow-up study until 17 years. *Lancet* 1995;**346**:1065–9.
- Wjst M, Dold S, Reitmeier P, *et al*. Does breast feeding prevent asthma and allergies? Results of the Munich asthma and allergy study. *Monatsschr Kinderheilk* 1992;**140**:769–74.
- Savilahi E, Tainio V-M, Salmenperä L, *et al*. Prolonged exclusive breast feeding and heredity as determinants in infantile atopy. *Arch Dis Child* 1987;**62**:269–73.
- Wright AL, Holberg CJ, Taussig LM, *et al*. Factors influencing the relation of infant feeding to asthma and recurrent wheeze in childhood. *Thorax* 2001;**56**:192–7.
- Lannerö E, Kull I, Tollin L, *et al*. Environmental risk factors for allergy and socio-economic status in a birth cohort (BAMSE). *Pediatr Allergy Immunol* 2002;**13**:182–7.
- Burr ML, Limb ES, Maguire MJ, *et al*. Infant feeding, wheezing, and allergy: a prospective study. *Arch Dis Child* 1993;**68**:724–8.
- Lewis S, Richards D, Bynner J, *et al*. Prospective study of risk factors for early and persistent wheezing in childhood. *Eur Respir J* 1995;**8**:349–56.
- McConnochie Mk, Roghmann K. Breast feeding and maternal smoking as predictors of wheezing in children age 6 to 10 years. *Pediatr Pulmonol* 1986;**2**:260–8.
- Wright AL, Holberg CJ, Taussig LM, *et al*. Relationship of infant feeding to recurrent wheezing at age 6 years. *Arch Pediatr Adolesc Med* 1995;**149**:758–63.
- Pershagen G. Challenges in epidemiological allergy research. *Allergy* 1997;**52**:1045–9.
- Bergmann RL, Edenharter G, Bergmann KE, *et al*. Atopic dermatitis in early infancy predicts allergic airway disease at 5 years. *Clin Exp Allergy* 1998;**28**:965–70.
- Csonka P, Kaila M, Laippala P, *et al*. Wheezing early in life and asthma at school age: predictors of symptom persistence. *Pediatr Allergy Immunol* 2000;**11**:225–9.