Protective effect of breast feeding against infection

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Abstract

Objective—To assess the relations between breast feeding and infant illness in the first two years of life with particular reference to gastrointestinal disease.

Design—Prospective observational study of mothers and babies followed up for 24 months after birth.

Setting—Community setting in Dundee.

Patients—750 pairs of mothers and infants, 76 of whom were excluded because the babies were preterm (less than 38 weeks), low birth weight (less than 2500 g), or treated in special care for more than 48 hours. Of the remaining cohort of 674, 618 were followed up for two years.

Interventions—Detailed observations of infant feeding and illness were made at two weeks, and one, two, three, four, five, six, nine, 12, 15, 18, 21, and 24 months by health visitors.

Main outcome measure—The prevalence of gastrointestinal disease in infants during follow up.

Results—After confounding variables were corrected for babies who were breast fed for 13 weeks or more (227) had significantly less gastrointestinal illness than those who were bottle fed from birth (267) at ages 0-13 weeks ($p<0\cdot01$; 95% confidence interval for reduction in incidence 6·6% to 16·8%), 14-26 weeks ($p<0\cdot01$), 27-39 weeks ($p<0\cdot05$), and 40-52 weeks ($p<0\cdot05$). This reduction in illness was found whether or not supplements were introduced before 13 weeks, was maintained beyond the period of breast feeding itself, and was accompanied by a reduction in the rate of hospital admission. By contrast, babies who were breast fed for less than 13 weeks (180) had rates of gastrointestinal illness similar to those observed in bottle fed babies. Smaller reductions in the rates of respiratory illness were observed at ages 0-13 and 40-52 weeks ($p<0\cdot05$) in babies who were breast fed for more than 13 weeks. There was no consistent protective effect of breast feeding against ear, eye, mouth, or skin infections, infantile colic, eczema, or nappy rash.

Conclusion—Breast feeding during the first 13 weeks of life confers protection against gastrointestinal illness that persists beyond the period of breast feeding itself.

Introduction

Much evidence shows that compared with artificial feeding breast feeding protects infants from gastrointestinal infection in developing countries.[1 2] There is much less agreement about similar effects of breast feeding in developed countries. Recently Bauchner *et al* reviewed all the studies on this subject written in English since 1970.[3] The four important methodological criteria that they applied to these reports were avoidance of detection bias, adjustment for potential confounding variables, definition of the outcome events, and definition of infant feeding. They concluded that of the 14 cohort and six case-control studies, only two met all four criteria and four met three criteria; the two studies that met all four criteria had small numbers of subjects. Their overall conclusions were that most of the studies had major methodological flaws and that breast feeding had at most a minimal protective effect in industrialised countries. This conclusion has been vigorously disputed by Cunningham,[4] whose own data suggested that breast feeding had an important protective effect.[5]

We studied the effect of breast feeding on childhood illness in Scotland in a study of adequate size that met the methodological criteria of Bauchner *et al*.[3]

Subjects and methods

After a detailed oral explanation from the project coordinator supplemented by an explanatory leaflet women with singleton pregnancies were recruited as close to 36 weeks' gestation as possible at the antenatal clinic of this hospital. All women lived in Dundee and were in a stable relationship. Nearly all women are delivered in the single obstetric unit at this hospital. To avoid unmanageably large numbers requiring follow up at the same time recruitment took place during three periods—namely, September 1983 to December 1984; March to August 1985; and December 1985 to May 1986.

Planned home visits were made by the mothers' health visitor at two weeks and one, two, three, four, six, nine, 12, 15, 18, 21, and 24 months. By using a standardised form information was recorded at each visit about all episodes of infant illness, maternal health, and illness among siblings since the previous visit. In children with recurring episodes of the same illness a week of good health free from symptoms was required before a new episode of illness was considered to have occurred. The definitions used to define childhood illness were adapted from those used by Chandra.[6]

Gastrointestinal illness—vomiting or diarrhoea, or both, lasting as a discrete illness for 48 hours or more; episodes of vomiting were coded separately from persistent posseting or episodes of regurgitation. Diarrhoea was diagnosed on the basis of frequent unformed stools; these episodes were distinguished from chronic diarrhoeal disease, such as intolerance to cows' milk or malabsorption, which was coded separately.

Respiratory infections—coryza, accompanied by cough or wheeze, or both, lasting for 48 hours or more.

Ear infection—painful or discharging ear lasting for 48 hours or more.

Other infections—infections of mouth, ear, eye, and skin lasting for 48 hours or more.

Colic—intermittent attacks of abdominal pain when the baby screamed and drew up his or her legs but was well between episodes.

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Eczema—as diagnosed by clinical appearances by the attending medical staff.

Nappy rash—redness of the skin confined to the area covered by the nappy.

Spoken and written guidance on these definitions were given to all participating health visitors at two meetings arranged for this purpose. For each episode of illness the health visitor was asked to record whether the general practitioner had been consulted and had confirmed the diagnosis of disease or prescribed treatment, or both. Hospital admissions were also recorded and the diagnosis confirmed from the hospital case records. If insufficient data were supplied by the health visitor on which to base a firm diagnosis further information was sought from the health visitor by the project coordinator and from the information recorded in the general practice records. If there was uncertainty about whether an episode of disease fulfilled the agreed criteria a decision was made by one of us (JSF) without knowledge of the method of infant feeding. After two years of follow up the general practitioners' records of the child were scrutinised to supplement the health visitors' data on childhood illness and any previously unrecorded episodes added to the record.

The methods of infant feeding from birth and at the time of discharge home were recorded from the hospital records. At each scheduled visit by the health visitor details of the infant feeding in the 24 hours before the visit were recorded: number of breast feeds, number and types of formula bottle feeds, number of juice and water feeds, and number of solid feeds a day. As appropriate the dates were recorded of the first formula feed, first cows' milk feed, first solid feed, and last breast feed. Supplementary feeding was defined as the introduction of formula feeds, cows' milk, or solid feeds specifically omitting the use of juice or water. Mothers were supplied with record cards for feeding and infant illness to help accuracy of recall. On the basis of the infant feeding record mothers were, for the purposes of comparison, allocated into one of four groups. Firstly, mothers who breast fed for 13 weeks or more and did not introduce supplements before that time (full breast feeders); secondly, mothers who breast fed for 13 weeks or more but introduced supplements before that time (partial breast feeders); thirdly, mothers who started breast feeding but discontinued before 13 weeks (early weaners); and fourthly, mothers who bottle fed from birth (bottle feeders).

After the baby was delivered we reviewed the obstetric records to abstract any obstetric, medical, and social data likely to be associated with the frequency of childhood illness. Data were collected on maternal factors (age, parity, social class, height, smoking habit, marital state, age at leaving school, complications in pregnancy, puerperal illness, previous medical illness), infant factors (sex of child, birth weight, gestational age, mode of delivery, duration of labour, Apgar score, neonatal jaundice, immunisation, illness in siblings, attendance at day care nursery), and paternal and social factors (age, social class, smoking habit, maternal reaction to pregnancy, planned or unplanned pregnancy, initial reaction to pregnancy, time of first antenatal attendance, defaults from antenatal clinic, and attendance at mothercraft classes).

Fergusson *et al* detected a difference in the rates of gastrointestinal illness (0-4 months) between bottle and breast fed infants of 8·7%.[7] To be 90% certain of detecting a difference of this magnitude at $p \leq 0.05$ we needed a sample of 280 initially breast fed and 280 initially bottle fed children. We therefore recruited 750 mothers to allow for an anticipated loss during follow up. We recorded and verified the data on IBM compatible microcomputers with the database program dBase III+. Checks for accuracy on a random sample of cases showed an error rate in key punching of <1%. The data were then transferred to a main frame computer for analysis. We used the statistical package for the social sciences (SPSS-X) to prepare tables to describe the incidence of illness and the distribution of risk factors. This also allowed any necessary recoding, calculation, and exclusion of cases. χ^2 Tests were used to compare differences in risk factors between feeding groups.

When we were investigating the relation of illness to several explanatory variables (typically a categorical variable indicating feeding type and some potential confounding variables such as mother's age and social class) we used multiple logistic regression. This method summarises the data by expressing the logarithmic odds of disease incidence as a linear function of the explanatory variables. We used generalised linear interactive modelling to perform the calculations and provide tests of significance and standard errors of the estimated variables in the function.[8] Standardised incidence rates for each feeding category were obtained by finding the average logarithmic odds resulting when all cases were imagined to be in that same category, while their other confounding variables were unchanged. The resulting average logarithmic odds were converted to give an adjusted incidence rate. The adjusted odds ratio was also used for comparisons. Comparisons were then made between the main feeding groups in respect of the adjusted rates of infant illnesses during the periods 0-13, 14-26, 27-39, and 40-52 weeks. To test the significance of the difference in incidence among two or more subgroups they were combined into one group and the corresponding change in deviance noted.

Ethical permission was granted by Dundee District Medical Ethical Committee.

Results

All mothers fulfilling the entry criteria were approached. A total of 126 refused to participate: 33 were leaving the area, 54 did not want to participate, 33 were planning to return to full time work, and six for other reasons. Recruitment continued until a total of 750 pairs of mothers and infants had been included in the study. Seventy babies who were delivered before 37 weeks' completed gestation, weighed <2500 g at birth, or stayed in the special care baby unit for more than 48 hours were not retained in the study. A further six mothers withdrew their consent to participate after delivery leaving a final cohort of 674 available for study.

Of the 674 pairs available for analysis, 267 mothers chose to bottle feed from birth, 180 chose to breast feed but stopped before 13 weeks (early weaning group), and 227 breast fed for 13 weeks or more. The women who breast fed for 13 weeks or more were subdivided into 130 who introduced supplements before 13 weeks (partial breast feeders) and 97 who did not (full breast feeders). Only 18 mothers stopped breast feeding because of illness in their babies.

Table I shows the characteristics of the population according to the method of early feeding. Comparisons among the groups show that mothers who breast fed were older, were more often married, were of lower parity, were from higher social classes, smoked fewer cigarettes, and had had longer secondary education. Other factors not listed that were significantly commoner in mothers who bottle fed were initial adverse reaction to pregnancy, non-attendance at mothercraft classes, defaults from the antenatal clinic, short maternal stature, and paternal smoking. Factors showing no significant differences between breast and bottle feeding groups included the number of complications in pregnancy, maternal puerperal illness, sex of baby, birth weight, mode of delivery, Apgar score, duration of labour, time of first antenatal attendance, or attendance at day care nursery.

A stepwise multiple logistic regression excluding feeding type identified three variables that explained important amounts of variation in the incidence of gastrointestinal infection in the babies during the first three months: these were father's social class, maternal age, and whether either or both parents smoked. We adjusted for these three factors in analysis of differences between feeding groups.

Table II, shows the numbers of babies who had one or more episodes of gastrointestinal illnesses in the first 13 weeks of life for each main category of feeding. Both the observed rates and the adjusted rates (corrected for social class, maternal age, and parental smoking) are given. Twenty seven cases were excluded from the calculation of adjusted rates because of incomplete data on either social class or parental smoking. The adjusted rates for gastrointestinal illness for the full (2·9%) and the partial (5·1%) breast feeders were not significantly different and were combined into a single group for comparison with bottle feeders. The bottle feeding and the early weaning groups had a similar adjusted rate of gastrointestinal illness (15·7% and 16·7% respectively). The mean rate of the two breast feeding groups combined (4·0%) was significantly lower ($p<0·001$; 95% confidence interval for difference 7·9% to 16·5%) when compared with the other methods of feeding.

In relation to other infections (respiratory, ear, mouth, eye, and skin) and colic, eczema, and nappy rash there were no significant differences during the first 13 weeks between bottle feeders and early weaners or between full and partial breast feeders. The adjusted rate of respiratory infection in bottle feeders (37·0%) was, however, significantly greater than in partial (24·2%) and full (25·6%) breast feeders ($p<0·05$). No significant differences were found between bottle and breast fed babies in respect of the other illnesses studied.

Analysis of infant illness from 14-26, 27-39, and 40-52 weeks of life (table III and IV) was confined to those 617 pairs of mothers and infants in whom there was full follow up data for one year. Compared with the 246 bottle fed babies, the 210 babies who had been partially or fully (89) breast fed in the first 13 weeks of life had

TABLE I—*Characteristics of parents according to methods of feeding baby. Figures are numbers (percentages) of parents in each characteristic group*

Characteristic	Infant Feeding Group: Bottle feeders (n=267)	Infant Feeding Group: Early weaners (n=180)	Breast feeders: Partial (n=130)	Breast feeders: Full (n=97)
Maternal age (years):				
<20	19 (53)	13 (36)	4 (11)	
20–	122 (48)	74 (30)	42 (16)	18 (7)
25–	88 (33)	69 (26)	57 (22)	50 (19)
30–	30 (33)	15 (16)	22 (24)	24 (26)
≥35	8 (30)	9 (33)	5 (19)	5 (19)
Parity:				
0	88 (29)	104 (34)	67 (22)	43 (14)
1+	179 (48)	76 (20)	63 (17)	54 (15)
Marital state:				
Married	238 (38)	165 (27)	123 (20)	96 (15)
Other	29 (56)	15 (29)	7 (13)	1 (2)
Mother's age at leaving school:				
≤16	228 (50)	133 (29)	59 (13)	35 (8)
≥17	39 (18)	47 (21)	71 (32)	62 (28)
No of cigarettes smoked by mother a day:				
0	144 (33)	113 (26)	99 (22)	85 (19)
1–	54 (49)	29 (26)	18 (16)	10 (9)
≥15	69 (57)	38 (31)	13 (11)	2 (2)
Social class of father:				
I	9 (12)	13 (17)	19 (25)	34 (45)
II	22 (19)	29 (25)	36 (31)	31 (26)
III Non-manual	19 (33)	17 (30)	13 (23)	8 (14)
III Manual	127 (48)	72 (27)	49 (18)	19 (7)
IV	65 (55)	42 (36)	7 (6)	4 (3)
V	23 (85)	2 (7)	2 (7)	0
Unknown	2 (17)	5 (42)	4 (33)	0 (8)

TABLE II—*Numbers (percentages and percentages adjusted for social class, maternal age, and parental smoking) of babies with illness during first 13 weeks according to method of feeding*

Infant illness	Bottle feeders (n=257)	Early weaners (n=169)	Breast feeders: Partial (n=126)	Breast feeders: Full (n=95)	χ^2 For adjusted rates: Bottle feeders *v* early weaners	χ^2 For adjusted rates: Partial *v* full breast feeders	χ^2 For adjusted rates: Bottle feeders *v* breast feeders	95% Confidence interval for difference between bottle feeders and breast feeders
Infections:								
Gastrointestinal	50 (19·5, 15·7)	31 (18·3, 16·7)	6 (4·8, 5·1)	2 (2·2, 2·9)	0·08	0·56	11·89***	6·6 to 16·8
Respiratory	100 (38·9, 37·0)	54 (32·0, 31·7)	29 (23·0, 24·2)	22 (23·2, 25·6)	1·22	0·05	6·35*	3·9 to 20·3
Ear	8 (3·1, 2·4)	5 (2·9, 2·5)	4 (3·1, 3·3)	2 (2·1, 2·7)	0·01	0·04	0·18	−3·5 to 2·3
Mouth	41 (16·0, 15·0)	25 (14·8, 14·0)	11 (8·7, 8·3)	11 (11·6, 11·6)	0·08	0·63	2·57	−0·8 to 10·9
Eye	44 (17·1, 17·3)	34 (20·1, 20·0)	27 (21·4, 21·0)	18 (18·9, 18·2)	0·46	0·27	0·42	−9·2 to 4·6
Skin	34 (13·2, 11·9)	21 (12·4, 11·2)	14 (11·1, 11·3)	5 (5·3, 5·9)	0·04	1·77	0·60	−2·0 to 8·6
Colic	27 (10·5, 9·9)	19 (11·2, 11·2)	8 (6·4, 6·6)	8 (8·4, 8·6)	0·16	0·30	0·78	−2·7 to 7·3
Eczema	10 (3·9, 2·3)	3 (1·8, 1·6)	6 (4·8, 3·9)	2 (2·1, 1·5)	2·36	1·98	0·77	−3·2 to 2·4
Nappy rash	55 (21·4, 16·7)	30 (17·8, 15·9)	18 (14·3, 15·4)	12 (12·6, 16·3)	0·05	0·03	0·06	−5·8 to 7·5

*=p<0·05; **=p<0·01; ***=p<0·001.

TABLE III—*Numbers (percentages and percentages adjusted for social class, maternal age, and parental smoking) of babies with infections up to 1 year according to method of feeding in first 13 weeks*

Infection	Weeks	Bottle feeders (n=246)	Early weaners (n=161)	Breast feeders: Partial (n=121)	Breast feeders: Full (n=89)	χ^2 For adjusted rates: Bottle feeders *v* early weaners	χ^2 For adjusted rates: Partial *v* full breast feeders	χ^2 For adjusted rates: Bottle feeders *v* breast feeders	95% Confidence interval for difference between bottle feeders and breast feeders
Gastrointestinal	14-26	47 (19·1, 17·9)	33 (20·5, 20·2)	8 (6·6, 6·9)	7 (7·9, 8·7)	0·33	0·21	8·06**	4·0 to 16·2
	27-39	55 (22·3, 21·8)	35 (21·7, 21·1)	20 (16·5, 16·5)	7 (7·9, 8·5)	0·03	2·79	4·03*	2·5 to 16·1
	40-52	55 (22·4, 22·7)	21 (13·0, 12·8)	19 (15·7, 15·2)	6 (6·7, 6·6)	6·23*	3·85*	6·70**	5·1 to 18·5
Respiratory	14-26	116 (47·1, 46·0)	76 (47·2, 47·2)	42 (34·7, 35·5)	34 (38·2, 39·9)	0·06	0·40	2·80	−0·8 to 17·4
	27-39	112 (45·5, 42·9)	85 (52·8, 52·6)	57 (47·1, 49·5)	32 (35·9, 39·6)	3·48	1·89	0·31	−10·8 to 7·5
	40-52	133 (54·1, 53·3)	72 (44·7, 44·6)	46 (38·0, 38·6)	38 (42·7, 44·2)	2·79	0·63	5·57*	2·7 to 21·1
Ear	14-26	11 (4·4, 4·1)	5 (3·1, 2·7)	5 (4·1, 3·7)	9 (10·1, 8·9)	0·59	2·61	0·40	−6·4 to 2·0
	27-39	26 (10·6, 10·7)	17 (10·6, 10·5)	16 (13·2, 12·7)	11 (12·4, 11·2)	0·00	0·12	0·19	−7·1 to 4·6
	40-52	36 (14·6, 15·1)	19 (11·8, 11·8)	14 (11·6, 11·0)	13 (14·6, 13·5)	0·89	0·29	0·75	−3·5 to 9·2
Mouth	14-26	12 (4·9, 5·0)	13 (8·1, 7·8)	1 (0·8, 0·7)	2 (2·2, 1·7)	1·23	0·59	4·82*	0·7 to 6·9
	27-39	6 (2·4)	5 (3·1)	1 (0·8)					
	40-52	8 (3·2, 2·5)	2 (1·2, 1·0)	1 (0·8, 0·1)		1·48	0·91	1·96	
Eye	14-26	23 (9·3, 9·6)	22 (13·7, 13·7)	11 (9·1, 7·8)	6 (6·7, 5·9)	1·04	0·32	0·83	−2·3 to 7·8
	27-39	17 (6·9, 5·8)	13 (8·1, 7·5)	9 (7·4, 8·1)	6 (6·7, 8·7)	0·50	0·02	0·87	−7·4 to 2·2
	40-52	22 (8·9, 8·4)	13 (8·1, 7·6)	8 (6·6, 6·2)	4 (4·4, 4·1)	0·08	0·51	1·23	−1·3 to 7·8
Skin	14-26	17 (6·9, 6·0)	11 (6·8, 6·4)	9 (7·4, 8·0)	4 (4·4, 5·3)	0·02	0·49	0·16	−5·1 to 3·8
	27-39	14 (5·7, 5·7)	6 (3·7, 3·7)	11 (9·1, 8·5)	4 (4·4, 4·0)	0·83	1·85	0·20	−4·9 to 3·8
	40-52	14 (5·7, 5·7)	11 (6·8, 6·6)	5 (4·1, 4·0)	5 (5·6, 5·7)	0·16	0·32	0·19	−3·3 to 5·0

*p<0·05; **p<0·01.

TABLE IV—*Numbers (percentages and percentages adjusted for social class, maternal age, and parental smoking) of babies with illness up to 1 year according to method of feeding in first 13 weeks*

Illness	Weeks	Bottle feeders (n=246)	Early weaners (n=161)	Breast feeders: Partial (n=121)	Breast feeders: Full (n=89)	χ^2 For adjusted rates: Bottle feeders *v* early weaners	χ^2 For adjusted rates: Partial *v* full breast feeders	χ^2 For adjusted rates: Bottle feeders *v* breast feeders	95% Confidence interval for difference between bottle feeders and breast feeders
Colic	14-26	7 (2·8, 2·4)	3 (1·8, 1·7)	4 (3·3, 3·4)	3 (3·4, 3·5)	0·22	0·00	0·38	−4·2 to 2·1
	27-39	3 (1·2)	1 (0·6)	0	0				
	40-52	4 (1·6)	0	0	0				
Eczema	14-26	16 (6·5, 6·3)	6 (3·7, 3·6)	7 (5·7, 5·4)	2 (2·2, 1·9)	1·52	2·07	0·89	−1·3 to 6·6
	27-39	11 (4·5, 4·2)	7 (4·3, 3·9)	9 (7·4, 6·5)	6 (6·7, 5·1)	0·02	0·23	0·58	−3·6 to 3·6
	40-52	13 (5·3, 5·1)	7 (4·3, 4·2)	4 (3·3, 3·2)	6 (6·7, 5·9)	0·15	0·94	0·12	−3·5 to 4·6
Nappy rash	14-26	42 (17·0, 14·9)	33 (20·5, 19·7)	12 (9·9, 10·8)	7 (7·9, 9·7)	1·60	0·06	1·63	−1·4 to 10·7
	27-39	32 (13·0, 10·9)	20 (12·4, 11·0)	14 (11·6, 12·0)	3 (3·4, 4·0)	0.00	3·86*	1·48	−2·4 to 8·2
	40-52	35 (14·2, 13·8)	16 (9·9, 9·6)	12 (9·9, 9·8)	3 (3·4, 3·6)	1·62	3·02	3·52	−1·7 to 12·5

*p<0·05; **p<0·01.

TABLE V—*Numbers (percentages and percentages adjusted for social class, maternal age, and parental smoking) of babies with gastrointestinal illness up to 1 year according to duration of breast feeding*

Age of baby (weeks)	Duration (weeks) of breast feeding (full + partial): Never (n=246)	1-13 (n=161)	14-26 (n=49)	27-39 (n=71)	40-52 (n=60)	>52 (n=30)	χ^2 For adjusted rates: Never *v* 1-13 weeks (1df)	14-26 *v* 27-39 *v* 40-52 *v* >52 weeks	Never *v* 14->52 weeks (1df)	95% Confidence interval for never *v* 14−>52 weeks
0-13	49 (19·9, 15·7)	30 (18·6, 16·6)	1 (2·0, 2·2)	2 (2·8, 3·5)	3 (5·0, 6·3)	2 (6·7, 7·7)	0·06	1·63	11·02***	4·8 to 10·1
14-26	47 (19·1, 18·0)	33 (20·5, 20·3)	4 (8·2, 8·6)	6 (8·5, 9·1)	4 (6·7, 7·2)	1 (3·3, 3·5)	0·32	1·09	8·06**	4·8 to 16·7
27-39	55 (22·4, 21·6)	35 (21·8, 21·0)	7 (14·3, 13·7)	9 (12·7, 13·4)	9 (15·0, 16·0)	2 (6·7, 7·4)	0·02	1·28	4·03*	2·2 to 16·0
40-52	55 (22·4, 22·3)	21 (13·1, 12·7)	4 (8·1, 7·9)	10 (14·1, 14·2)	7 (11·7, 11·7)	4 (13·4, 13·4)	6·02*	1·25	6·70**	3·6 to 17·4

*p<0·05; **p<0·01; ***p<0·001.

TABLE VI—*Numbers (percentages) of babies admitted to hospital in first year with odds ratios adjusted for social class, maternal age, and parental smoking according to duration of breast feeding*

Infant illness	Overall No (%) admitted to hospital in first year (n=617)	Duration (weeks) of breast feeding (full + partial): Never (n=246)	0-13 (n=161)	14-26 (n=49)	27-39 (n=71)	40-52 (n=60)	>52 (n=30)	χ^2 For adjusted rates: Never *v* 0-13 weeks (1df)	14-26 *v* 27-39 *v* 40-52 *v* >52 weeks	Never *v* 14−>52 weeks (1df)
Gastrointestinal	35 (5·7)	19 (7·7)	13 (8·0)	1 (2·0)	0	2 (3·3)	0			
Odds ratio		1·0	1.08	0.29		0·30		0·04	2·39	5·64*
Respiratory	30 (4·9)	18 (7·3)	6 (3·7)	1 (2·0)	4 (5·6)	0	1 (3·3)			
Odds Ratio		1·0	0·53	0·36	0·83		0·57	1·83	3·83	2·16

*p<0·05.

Average odds ratio (95% confidence interval) for 1−>52 weeks *v* never 0·16 (0·036 to 0·726) for gastrointestinal illness and 0·44 (0·149 to 1·31) for respiratory illness.

significantly lower rates of gastrointestinal illness at 14-26 weeks (p<0·01), 27-39 weeks (p<0·05), and 40-52 weeks (p<0·01). No other consistent differences were found, though in comparison with bottle fed babies the breast fed babies had significantly lower rates (p<0·05) of respiratory infection at 40-52 weeks and mouth infection at 14-26 weeks. The only significant difference (p<0·05) between the early weaning group (161) and the bottle feeders was a lower rate of gastrointestinal infection at 40-52 weeks. Similarly, the rates of illness showed no significant differences between the full and partially breast fed groups except a lower rate of nappy rash at 27-39 weeks (p<0·05) (table IV) and gastrointestinal illness at 40-52 weeks in the fully breast fed group (p<0·05) (table III). During the second year of life the rate of gastrointestinal illness in the early weaning group (54·8%) was significantly higher than the rate of 41·4% in the bottle feeders (p<0·05), but no other differences were found for any other disease categories among the groups.

To assess how the duration of breast feeding influenced the rate of gastrointestinal illness mothers were divided into mutually exclusive groups of those who did not fully or partially breast feed (bottle feeders) and those who did so for 0-13 weeks (early weaners), 14-26 weeks, 27-39 weeks, 40-52 weeks, or ⩾52 weeks. Table V shows the adjusted rates of gastrointestinal illness for each 13 week period of the first year expressed according to the duration of breast feeding. Overall, the rates of gastrointestinal illness tended to rise during the first year, but, apart from in the period 40-52 weeks, the adjusted rates in babies who had never been breast fed showed no significant differences when compared with those who were breast fed for 13 weeks or less. By contrast, the adjusted rates of gastrointestinal illness for all the babies who were breast fed for 14 weeks or more were consistently lower than those in the bottle feeders, though the rates among the subgroups of those breast fed for 14 weeks or more showed no significant differences among themselves. Those babies who were breast fed for less than 13 weeks (the early weaning group) were further split into those who were breast fed for less than one week, from 1 to 6 weeks, and from 7 to 13 weeks; their odds ratios of gastrointestinal illness as compared with the bottle fed group were 1·3, 1·0, and 0·7 respectively, which were not significantly different, while the odds ratio for those breast fed for 13 weeks or more was 0·12 (p<0·01); all rates were adjusted for the three principal confounding variables.

Among the babies observed throughout the first year of life, 35 (5·7%) and 30 (4·9%) were admitted to hospital with gastrointestinal and respiratory infections respectively (table VI). Babies who were breast fed for more than 13 weeks had a significantly lower odds ratio for hospital admission because of gastrointestinal infection (p<0·05) but not for respiratory infection when compared with bottle fed babies. The cases in which breast feeding was stopped because of infant illness were reclassified into the group who breast fed for 13 weeks and over to see if selecting these cases invalidated the comparison between feeding types. The odds ratio of gastrointestinal illness in the first 13 weeks for the group who were breast fed for more than 13 weeks versus the remaining groups changed from 0·26 (χ^2 = 11·99) to 0·36 (χ^2 = 7·97); this indicated that even after transferring these cases to the breast feeding group there was still a significant difference in gastrointestinal illness between the group who breast fed for more than 13 weeks and the remainder.

Discussion

We have shown that after confounding variables were considered babies who were breast fed for the first 13 weeks of life had substantially reduced rates of gastrointestinal illness and this benefit persisted for up to 1 year of age. During the first 13 weeks the rate of gastrointestinal illness in breast fed babies was less than a third of that of bottle fed babies. During the first year of life breast fed babies were less likely to require hospital admission for gastrointestinal illness.

The study design was in keeping with the important methodological criteria recommended by Bauchner *et al*.[3] Detection bias occurs when the outcome event of infection is detected more readily in one group than another. This can be minimised by frequent, regular surveillance.[3] In our study a combined approach was used in which participating mothers were visited regularly at home by health visitors and the general practice records were scrutinised retrospectively. The possibility of detection bias will therefore affect only those disease episodes that were both forgotten by the mother and unrecorded by the general practitioner. During the first four months, when the main hypothesis was being tested, home visits took place monthly but thereafter the size of the cohort made it necessary to reduce the frequency of home visits to two and then three monthly intervals. By this later stage of the study mothers were well acquainted with its plan and objectives and probably our strategy would have failed to identify only a small number of episodes of disease. If detection bias had played a major part in the observed differences between feeding groups in respect of gastrointestinal disease similar differences might have been expected in other disease categories, but these were not observed. Probably the observed differences were therefore true differences in the incidence of disease rather than artefacts of detection bias.

The definitions of disease outcomes were based on those used by Chandra,[6] and to increase standardisation as far as possible health visitors were given both spoken and written instructions of the definitions; they were also given written instructions on the format of words to be used when asking their questions. Whenever there was any doubt about whether a disease episode fulfilled the agreed definition or not, a decision was made on the basis of the information available to one of us (JSF) without knowledge of the feeding class of the subject. The classification of infant feeding categories was also determined in advance and based on detailed contemporaneous data collected by the health visitors during their home visits. Only 18 mothers stopped breast feeding because of illness, and when they were reallocated to the breast feeding group the overall conclusions were unchanged.

While standardisation was performed for three principal covariates identified by stepwise multiple regression, there were several potential confounding variables that could have been allowed for, though with some loss of numbers of cases due to missing values. The main analyses were repeated, allowing for marital state, parity, mother's height, father's age, reaction to pregnancy, attendance at mothercraft classes, default at antenatal clinics, mode of delivery, number of rooms in house, and number of older children in the family. When this was done the adjusted rates differed little from the rates adjusted for the three main confounding variables. Thus, even after allowing for potential confounding variables, our findings support the conclusion that breast feeding has a substantial protective effect against illness in a developed country. Of the papers reviewed by Bauchner *et al*,[3] 10 of the 14 cohort studies reported the effects of breast feeding on gastrointestinal infection but only three contained more than 500 subjects,[5 7 9] the minimum number that we calculated to have sufficient power to investigate the relation fully. One of the three studies showed no significant benefit,[9] but as data were collected by interview when the child was five years old maternal recall would probably have been poor, which would undermine confidence in the findings. The two other studies of greater than 500 subjects showed that breast feeding protects against gastrointestinal infection in the first four months of life,[5 7] conclusions compatible with our own. Breast milk has a number of beneficial properties that may explain why it should protect against gastrointestinal infection in infants.[10 11] Colostrum in particular has a high concentration of secretory IgA,[10] which may protect through the enteromammary[12] and bronchomammary pathways.[13] We did not find any evidence, however, to suggest that brief periods of breast feeding were sufficient to offer any significant protection. By contrast, our results indicated that babies who were breast fed for between 13 and 26 weeks had had as much protection as babies who were breast fed for longer periods of time. Furthermore, the early introduction of supplements did not undermine the protective effect, suggesting that it was some positive factor in breast milk rather than the avoidance of potentially infected feeds that reduced the incidence of gastrointestinal illness.

We found a similar but smaller protective effect of breast feeding against respiratory illness at the time periods of 0-13 and 40-52 weeks. The observed differences between bottle and breast feeding groups narrowed considerably but remained significant after allowing for confounding variables. Fergusson *et al*, whose study design was similar to our own, found that the observed differences between bottle and breast fed babies for respiratory illness disappeared after allowing for confounding variables.[7] Our study entailed more frequent home visits, and possibly a more effective detection strategy may account for our different findings, though the trends of the results were similar in the two studies.

No other consistent benefits of breast feeding were shown, and some of the other significant differences may have been chance findings. In particular, breast feeding did not seem to protect against either infantile colic or eczema. There is conflicting evidence about the protective effect of breast feeding against eczema and other allergic conditions,[14] but the data from this study did not show any significant reduction of eczema in either fully or partially breast fed babies. Our findings have implications for infant feeding policies. Mothers should be told without ambivalence that breast feeding offers a clear advantage to their babies by reducing gastrointestinal and respiratory infection but to obtain that advantage they should maintain breast feeding for at least three months. Currently, it is recommended that babies should be fully breast fed for four to six months and nothing in this study undermines that view.[15] Nevertheless, many mothers who discontinue breast feeding prematurely because they feel that they have insufficient milk[14] wean their babies completely from the breast; our data suggest that in such circumstances there would be advantages in continuing to give breast milk as part of the diet for at least three months. Thus, those health professionals, such as health visitors, midwives, and general practitioners, who are responsible for lactating mothers should encourage them to persevere if they encounter problems during the first few weeks.

Some women who are planning to return to full time work elect to bottle feed from birth on the grounds that a short period of breast feeding will not be worth while. Our findings suggest that if such mothers were encouraged to breast feed for at least three months their babies would benefit and suggest that maternity leave allowances should reflect this. Our data suggest that a minimum of 12 weeks should be allowed after delivery and probably more. In addition, there is also a strong case for the provision of creche facilities at work to allow nursing mothers to continue breast feeding. The present arrangement puts pressure on mothers who have to return to work either to choose bottle feeding from the start or to discontinue breast feeding prematurely.

The American Academy of Pediatrics reported that despite methodological imperfections most studies have found a protective effect of breast feeding against gastrointestinal infection and none have found an adverse effect.[16] Studies with methodological flaws may suggest spurious advantages of breast feeding but may also obscure true benefits due to negative biases.[2] Our study, which attempted to meet basic methodological requirements, strongly suggests that breast feeding still has an important part to play in preventing infection among infants in developed countries.

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Monitoring of blood glucose concentration in subjects with hypoglycaemic symptoms during everyday life

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Abstract

***Objective*—To study the persistence of hypoglycaemic symptoms, changes in blood glucose concentrations, and the relation between reported symptoms and measured blood glucose values in functional hypoglycaemia.**

***Design*—Re-evaluation of symptoms in patients admitted consecutively with suspected hypoglycaemia followed by a case-control study.**

***Setting*—The Steno Memorial Hospital in Gentofte, Denmark, which specialises in the diagnosis and treatment of and research on endocrine disorders, including hypoglycaemia.**

***Patients*—21 Subjects admitted consecutively with hypoglycaemic symptoms that were relieved by eating in whom insulinoma and other organic disorders presenting with hypoglycaemia had been ruled out. Twelve of these subjects with persistent symptoms entered the case-control study, as did a matched control group.**

***Interventions*—Four days of monitoring blood glucose concentrations at home, six daily samples being taken in fixed relation to meals by the finger prick method. Extra samples were taken when symptoms occurred.**

***Main outcome measures*—Blood glucose concentration, glycated haemoglobin concentration, and within subject variation in measured values.**

***Results*—After one to three years of observation 19 of the 21 subjects still had symptoms. Six out of 12 subjects experienced hypoglycaemic symptoms during the controlled study. Blood glucose concentration ranged from 3·7 mmol/l to 7·5 mmol/l during these episodes. Changes in blood glucose concentration, mean blood glucose concentrations at each time point, within subject variation in the measured values, and glycated haemoglobin concentration were not significantly different in all patients compared with the control subjects and in patients with symptoms during the study compared with controls.**

***Conclusion*—Hypoglycaemic symptoms during everyday life in apparently healthy subjects are persistent but are not related to chemical hypoglycaemia.**

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Introduction

Denmark, unlike Britain, has not been spared the epidemic of functional hypoglycaemia seen in the United States during the past two decades.[1 2] We share the widespread scepticism about whether functional hypoglycaemia is a disease.[3 4]

Subjects complaining of hypoglycaemic symptoms during their everyday life that disappear after eating are regularly evaluated in our clinic by means of a fast of one to three days. If test results are negative hypoglycaemia is not recognised. On an empirical basis, however, a diet low in refined sugars and rich in fibre is recommended.[5] The five hour oral glucose tolerance test has, in our opinion, no diagnostic value in these subjects.[6-9]

The uniformity of the symptoms at presentation in different countries[6] and the general recognition of "postprandial" or "reactive" hypoglycaemia as a possible diagnosis by European diabetologists,[10] however, made us study the persistence of hypoglycaemic symptoms in a group of patients with functional hypoglycaemia. In addition, we tested whether chemical hypoglycaemia could be shown during everyday life and in relation to hypoglycaemic symptoms with the technique of monitoring blood glucose concentrations at home.