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REGULAR REVIEW

Is breast feeding beneficial in the UK?

Statement of the Standing Committee on Nutrition of the British Paediatric Association

The health benefits of breast feeding in industrialised countries are sometimes questioned on the grounds that modern, hygienically prepared infant formulas are safe and nutritionally complete. Uncertainties increase about this view as more is learnt about the complex composition of breast milk. From a teleological perspective, the complexity of breast milk implies that it possesses numerous functions of biological importance but bridging the gap between observation in vitro and confirmation of function in the human infant presents many challenges. Randomised controlled trials, the ultimate proof of cause and effect, are obviously not feasible and the burden therefore falls upon observational cohort and case-control studies, methodologies which are easily flawed.

Problems specific to infant feeding in the design of such studies have been reviewed with particular reference to the link between artificial feeding and infection[1] but are of equal relevance to other outcomes of infant feeding. They can be summarised as follows:

Definition of feeding method – Some studies fail to inquire adequately as to exclusivity. This could be more relevant to some outcomes than others. For example, could a single feed of formula at a critical period be sufficient to sensitise a baby to cows' milk protein?[2] Detailed information of this type can be difficult to acquire and as 45% of 'breast fed' babies in the UK receive bottles of formula or water in the first week of life,[3] very few are truly breast fed. Errors of this sort are likely to conceal any true difference in outcome by blurring the distinction between feeding methods. Not all studies have sought relationships between the duration of breast feeding and outcome but, in those which have, reductions in the risk of gastrointestinal infection, diabetes mellitus, and breast cancer in young women can be correlated with duration of breast feeding (see below). Such 'dose-response effects' offer some inductive support to the hypothesis that beneficial effects are attributable to, and not simply associated with, breast feeding.

Interindividual variability in the composition of breast milk – Unlike infant formula, human breast milk varies greatly with respect to nutritional composition and the content of other constituents, including contaminants and food antigens. The physiological factors that explain this variation and its significance for infant development are incompletely understood but could potentially explain differences in outcome between apparently similar studies comparing breast and bottle fed infants.

Case detection bias – Some conditions might be more readily assigned to infants fed in a particular way. For example, existing prejudice might cause a rash to be more often labelled eczematous if the infant is formula fed; loose stools may less commonly be described as 'diarrhoea' in a breast fed baby; the threshold for admitting breast fed infants to hospital could be higher, both on account of professional concerns about disrupting lactation and on account of differential usage of the healthcare system. In order to address these problems outcome events need clear definition at the beginning of the study and ideally should be recorded blind to feeding method. Prospective studies tend to be more robust than retrospective ones, both for these reasons and because active interval surveillance reduces the chance of outcome events being missed, a problem with surveys dependent on recall.

Adjustment for confounders – Many socioeconomic factors correlate strongly with feeding method, for example smoking, parental educational attainment, socioeconomic status, family size, and population density. As these generally correlate negatively with both breast feeding and health outcome, adjustment is essential but often difficult. Failure to adjust generally favours an apparent breast feeding benefit.

Breast feeding and infection

About 10% of the protein in mature breast milk is secretory IgA with specificity to antigens, including potential pathogens, in the maternal gastrointestinal and respiratory tract. Lymphocytes, macrophages, proteins with non-specific antibacterial activity, cytokines, and complement are also present. The mechanism by which breast feeding might protect the infant from infection is readily apparent though sceptics argue that the mere presence of these agents is not proof of benefit to the infant; why, for example, is their purpose not simply to protect the lactating breast?

The clearest evidence that breast feeding reduces the risk of infection, particularly gastrointestinal infection, comes from studies conducted in high risk environments. For example, a study in Brazil estimated that infants fed formula were 14·2 times (95% confidence interval (CI) 5·9 to 34·1) more

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likely to die of diarrhoeal disease.[4] Controlled studies among low birthweight infants in India with random allocation to breast milk or formula showed that human milk feeding significantly reduced the risk of systemic, gastrointestinal and superficial infection.[5 6] There is no doubt, therefore, that human milk has a protective effect in a high risk environment; the question is whether this effect is relevant to industrialised societies such as the UK.

A methodological review of studies published between 1970 and 1984,[1] which had examined the relationship between feeding method and infection in such circumstances, suggested that only two[7 8] had adequately accounted for the design flaws discussed above. Even these failed to adjust for *all* confounders but a subsequently published prospective cohort study of 750 mother-baby pairs in Dundee, Scotland[9] specifically accommodated the design criteria set out by Bauchner *et al*[1] and showed that breast feeding for 13 weeks or more significantly reduced the risk of gastrointestinal and respiratory illness. Moreover, breast fed babies were less likely to be admitted to hospital with gastrointestinal illness. The protective effect of breast feeding for more than 13 weeks remained evident beyond the period of breast feeding itself.

The anti-infective benefits of breast milk may be particularly relevant to low birthweight infants in the UK. In a study of over 900 babies weighing under 1850 g at birth the risk of necrotising enterocolitis was between six and 10 times greater among those fed formula alone. Although provision of the mother's own milk was a matter of maternal choice, two thirds of those studied were randomly allocated to receive banked breast milk or formula alone or as supplements to the mother's own milk when it was insufficient. Banked breast milk was as effective as maternal milk in preventing necrotising enterocolitis and the risk attributable to formula feeding was greatest among the most mature, growth retarded babies.[10]

Breast feeding and neurological development

Many studies have measured differences in cognitive function between children breast or bottle fed as infants; indeed, Hoefer and Hardy drew attention to the increased incidence of behavioural abnormalities in artificially fed infants over 50 years ago.[11] The obvious difficulty in interpretation is confounding of feeding method by parental educational attainment and socioeconomic status. Moreover breast feeding mothers consume less alcohol and are less likely to smoke.[12] Even when adjustment is made for these factors the criticism has been made that mothers who breast fed self select for other forms of 'positive health behaviour'.[13] Furthermore, maternal social class and educational attainment may not necessarily correlate with maternal IQ.[14]

Children under 5 years who were breast fed have been reported to have fewer speech difficulties than those bottle fed.[15 16] Rodgers, in a cohort study of 5362 children born in the UK during one week in 1946 found a difference of 1·76 points on non-verbal score and 1·55 on mathematics score attributable to breast feeding after adjustment for identifiable confounding factors.[17] This study did not adjust for parental smoking but a subsequent UK birth cohort study did.[18] In this study of over 13 000 5 year old children born in 1970, data about the duration of breast feeding were collected retrospectively and cognitive function measured using the English picture vocabulary test and a design copying test. Children who had been breast fed showed significantly higher scores and those breast fed for longest were at greatest advantage. In contrast to earlier studies, however, no effects on speech[15 16] or behavioural problems[11] were noted. A New Zealand cohort study noted differences of similar magnitude (two points on a test with standard deviation of 10 points) attributable to feeding at the ages of 3, 5, and 7.[19]

A recent study from Cleveland, USA adjusted for maternal race, attitude, smoking, alcohol consumption but also maternal intelligence quotient estimated from a test administered in the postnatal period.[20] Again, this study showed significant advantages in Bayley score attributable to breast feeding. At 2 years of age babies breast fed for four months or less showed a 3·7 point advantage over those artificially fed after adjustment for confounding factors. Those breast fed for more than four months were at a 9·1 point advantage. The variance in Bayley score attributable to method of feeding was 11·7% at 1 year of age and 5·6% at 2 years. Studies like these, which show an effect of duration of breast feeding, suggest that a factor in breast milk is more likely to be responsible rather than the act of suckling itself. Observations in preterm infants gavage fed with breast milk also support this hypothesis[21]; the advantage in intelligence quotient at the age of 7 attributable to feeding maternal breast milk in the neonatal period was 8·3 points, greater than that identified with other perinatal risk factors such as duration of ventilation.

The mechanisms that explain differences in neurodevelopmental outcome between breast and bottle fed infants are not currently understood but differences in long chain ω-3 fatty acid intake, particularly docosohexaenoic acid (C22:6ω-3), may be important. The ratio of ω-6:ω-3 fatty acids in breast milk is conserved independently of maternal dietary intake, supplementation of infant formulas with the ω-3 long chain fatty acid docosohexaenoic acid beneficially modifies maturation of visual function in preterm infants,[22] and the composition of lipids in the infant brain is sensitive to dietary intake.[23] However, differences in the biochemical composition of brain lipids have not yet been correlated with differences in cognitive function. The role of other milk constituents is also unclear. For example growth factors might exert the primary influence and differences in fatty

acid intake merely fuel the process. Preterm infants are able to absorb a molecule as large as lactoferrin (molecular weight 78 000),[24] only one of many growth factors present in human milk.

Breast feeding and allergic disease

The belief that breast feeding protects against the later development of allergic disease is widespread among both professionals and public, though evidence for such an effect is debatable. Problems specific to this area include the presence of food antigens in breast milk, the definition of 'exclusive' breast feeding and diagnostic bias. Moreover, there is a heritable element to allergic disease which almost certainly leads allergic families to self select for breast feeding. This was cited as a possible explanation for the finding of a *positive* association between breast feeding and eczema in one study.[25]

The potential protective effect of breast feeding in allergic disease has been reviewed repeatedly over the years and is still debated.[26–28] A study in preterm infants randomly allocated to receive preterm formula or banked human milk, alone or as supplements to the mother's own, suggested that use of human milk significantly reduced the incidence of allergic disease, particularly eczema, at 18 months in those with a family history. In those without there was no significant protective effect.[29] Although preterm infants might be expected to differ from term infants in the immunological response to diet it seems unlikely that similar evidence from a randomised controlled study will ever become available in the latter group.

Breast feeding and disease in later life

INSULIN DEPENDENT DIABETES MELLITUS

Avoidance of cows' milk during early life prevents onset of diabetes in rats genetically at risk.[30] Recently acquired evidence in humans similarly suggests that exposure to bovine serum albumin through infant feeding could trigger the autoimmune process leading to juvenile onset diabetes. There is structural homology between bovine serum albumin and the pancreatic islet β cell surface antigen p69. Furthermore, the serum of newly diagnosed diabetic children contains antibodies to a 17 amino acid sequence, known as ABBOS, of bovine serum albumin. Anti-ABBOS antibodies react with p69 antigen and represent the predominant form of antibovine serum albumin IgG found in the serum of diabetic children but not of controls.[31]

Epidemiological association between cows' milk formula feeding and diabetes has also been found in humans; an American study found that children who were breast fed for more than 12 months were at half the risk of developing diabetes mellitus (odds ratio 0·54, 95% CI 0·27 to 1·08).[32] A significant but less marked effect was also apparent in those breast fed for shorter periods. Overall, the odds ratio in babies breast fed was 0·7 (95% CI 0·5 to 0·97) and the authors estimated that the proportion of juvenile onset diabetes mellitus attributable to method of feeding was between 2 and 26%, depending on the prevalence of breast feeding in the community. Scott noted an inverse association between the risk of juvenile onset diabetes mellitus and prevalence of breast feeding in various countries but the correlation was weak (r −0·53) and the plot showed considerable heteroscedasticity*.[33] A recent Finnish case-control study estimated the risk (odds ratio) of babies breast fed for seven months developing diabetes before the age of 7 as 0·45 (95% CI 0·24 to 0·84) that of children who were formula fed.[34] As in the previous study cited,[33] risk was lowest in babies breast fed longest. The dose dependent reduction in diabetes risk associated with breast feeding and demonstration of a plausible molecular mechanism strongly suggest that formula feeding in infancy plays a part in the pathogenesis of juvenile onset diabetes mellitus.

INFLAMMATORY BOWEL DISEASE

The presence of cows' milk antibodies in serum of patients with ulcerative colitis prompted Whorwell *et al* to examine feeding history in 57 patients with Crohn's disease, 51 with ulcerative colitis, and 216 age/sex matched controls.[35] Feeding history was sought by questionnaire, average age of patients being 33 and 37 respectively. Crohn's disease was significantly associated with early gastroenteritis (11% of patients *v* 1% of controls) but not mode of feeding whereas significantly more patients with ulcerative colitis had never been breast fed (30% patients *v* 12% of controls). However, differences were not statistically significant in those breast fed for more than two weeks. In contrast, a further study of Crohn's disease patients <18 years of age which also used retrospective case-control methodology indicated that patients were less likely to have been breast fed.[36] Relative risk for those formula fed as babies was 3·6 (95% CI 1·4 to 9·0) but duration of breast feeding had no apparent effect. Current evidence that breast feeding affects the incidence of later inflammatory bowel disease therefore seems equivocal.

NEOPLASTIC DISEASE

A study from Denver, Colorado of 201 children with cancer matched for age, sex, and area of residence with 181 controls showed the odds risk increased for those artificially fed as infants, particularly in the case of 26 children with lymphoma (odds ratio 5·6, 95% CI 1·4 to 22·4).[37] It appeared that the reduction in risk correlated with duration of breast feeding, though no convincing mechanism for such an effect has yet been proposed. A larger UK study failed to find any association but the precise questions asked about infant feeding were not clear.[38]

*Variance in y changes with x.

Sudden infant death syndrome (SIDS)

The New Zealand case-control study of SIDS found that 66% of cases but 85% of controls were breast fed on discharge from hospital. This difference was statistically significant after adjustment for other identifiable risk factors including parental smoking and sleeping position. Recommendation to breast feed was included in medical advice designed to reduce the very high incidence of SIDS in New Zealand[39] and in Australia. Studies in Avon in the UK have not demonstrated any protective effect associated with breast feeding and a review of the relationship between breast feeding and SIDS concluded that some studies failed to adjust for confounders, the most important being smoking, and others were difficult to interpret.[40] The UK chief medical officer's expert group concluded that published studies have not clearly identified a relationship between bottle feeding and SIDS but recommended that breast feeding be encouraged.

The mechanism of any protective effect of breast feeding on SIDS is unclear. It is often assumed, without direct evidence, to operate through reduction in the incidence of viral infection but recent indications that the sleep patterns of bottle and breast fed infants differ raise the speculation that differences in neurological maturation attributable to dietary composition could be relevant.

Breast feeding and maternal health

Recently further evidence has emerged that breast feeding reduces the risk of breast cancer in young women.[41 42] A case-control study of women living in 11 UK health districts who developed breast cancer before the age of 36 showed that risk was negatively correlated with both the duration of breast feeding and the number of babies breast fed. Adjustment was made for use of oral contraceptives, nulliparity, age at first birth, family history, and age at menarche. Cases and controls were similar in respect of marital status, age at leaving school, and alcohol consumption; no adjustment was made for these.

Generally studies have revealed a trend towards reduced incidence of premenopausal breast cancer in women who breast fed, though in some individual studies it has not been statistically significant (reviewed by Byers *et al*[43]). There is no evidence of a protective effect in postmenopausal breast cancer.

Conclusions

Important differences exist between the composition of breast milk and artificial formulas. Epidemiological evidence convincingly indicates that breast fed infants are at significantly reduced risk of infection, particularly gastrointestinal infection, even in industrialised societies. Breast feeding is particularly important for low birthweight infants in whom both reduced mortality associated with necrotising enterocolitis and advantages in cognitive function have been associated with provision of breast milk. Significant advantages in cognitive function have also been associated with breast feeding of healthy term infants. Whereas these have previously been attributed to events which confound choice of feeding method, new evidence about breast milk lipid composition and brain maturation suggests a plausible biological mechanism. Long term benefits of breast feeding may also include reduction in the risk of juvenile onset diabetes and maternal breast cancer. Debate continues about the relationship between feeding method and allergic disease but there are some grounds to indicate that it is important in those genetically at risk.

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