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Editorial Comment

Breast-feeding and cancer prevention

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For the new mother, the benefits of breast-feeding begin immediately. Suckling provokes strong contractions in the uterus, facilitating its involution and reducing the risk of post-partum haemorrhage. Ovulation is inhibited during lactation and so breast-feeding acts as a natural contraceptive [1]. The practical advantages of breast feeding are also obvious — feeding during the night is convenient and since it can readily be done with one hand it leaves a spare arm for cuddling older siblings or performing more mundane tasks. The emotional satisfaction is perhaps more variable between women, but for many, breast-feeding is a deeply rewarding experience.

For the nursing infant, the benefits, both short- and long-term, are even more substantial. Breast milk provides immediate protection against microbial assault via both the specific activity of antibodies and the non-specific action of proteins, glycoproteins and lipids [2]. As a direct consequence, the breast-fed infant is at reduced risk of acute infective illnesses including gastroenteritis, septicaemia, urinary tract infection, encephalitis, pneumonia and otitis media. The morbidity and mortality of breast-fed infants is lower that that of their bottle-fed contemporaries [3].

Breast milk contains a wide range of biologically active compounds including hormones, cytokines and enzymes which are important not only for maturation of the immune system, but also for neurological development, especially in premature infants [4]. The benefits of breast-feeding are not restricted to the period of lactation for either mother or child. For the mother there is some evidence that breast-feeding may confer protection against ovarian cancer — although the advantage is small with a reduction in risk of around 6% for every 6 months breast-feeding [5]. Similarly breast feeding probably reduces the risk of breast cancer — especially that diagnosed before the menopause which may be reduced by approximately 20–35%, suggesting that the onset of the disease may be at least postponed in women who have breast fed their children for a reasonable length of time [6].

For the child, the protection against infective illness is prolonged and there is evidence for protection against diarrhoea, respiratory tract infection, otitis media and influenza remaining for several years after weaning [7]. Some of these protective effects display a dose-dependency in that they are greater in those children who are breast fed the longest [8]. It is also probable that breast milk contributes to tolerance of environmental antigens thus reducing the risk of the common allergic conditions such as asthma and eczema [2]. There is also evidence that the breast-fed child is protected against type I diabetes and inflammatory bowel disease, again presumably by modulation of the immune response [4]. The influence of breast-feeding lasts even into adult life with those who were breast fed being, on average, leaner, with lower blood pressure and a more favourable circulating lipid profile than those who were bottle-fed. Their cardiovascular disease risk is correspondingly lower and they may, in addition, be less likely to develop type II diabetes [9].

The latest report on the protection against childhood leukaemia afforded by breast-feeding by Bener and colleagues appears in this issue of the *European Journal of Cancer* (pp. 234–238) [10]. In a case–control study of 117 children diagnosed with acute lymphoblastic leukaemia (ALL), Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL) between 2 and 14 years of age, Bener and colleagues report an overall odds ratio (OR) of 2.8 (95% confidence interval (CI): 1.5–5.1) for those who were breast fed for 0–6 months compared with those who were breast fed for longer than 6 months. This is equivalent to a 70% reduction in risk for the babies who were breast fed for over 6 months. The reduction in risk was similar for children with ALL,

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NHL and HD, though only for the 69 children with ALL did the association reach statistical significance, presumably because of the small number of cases and hence low statistical power in the other diagnostic groups. Within the study, which was conducted in the United Arab Emirates, it was not possible to estimate the risk in children who were not breast fed at all since all infants received breast milk.

In 1998 Davis reviewed the evidence for an association between breast-feeding and risk of childhood leukaemia and lymphoma from the nine relevant case–control studies published up to that time [11]. Davis concluded that there was evidence of a decreased risk for HD in those who were breast-fed. All five studies which investigated the risk of all lymphoma or HD in particular reported increased risk in those who were not breast fed at all, or who were breast fed for less than 6 months in comparison with those who were breast fed for a longer period of time. In two of these studies the risk of HD was found to be significantly lower in children who were breast fed for longer than 6 months compared with those who were not breast fed, and in one study the duration of breast feeding was significantly shorter in cases than controls. The risk in those breast-fed for over 6 months being over 60% lower than those who were not breast fed and the reported magnitude of the effect is consistent with that reported by Bener and colleagues (Table 1).

However, Davis found little support for a protective effect of breast-feeding against ALL or NHL. More recently, however, findings from one of the largest case–control studies yet to address the hypothesis that breast-feeding protects against childhood leukaemia are supportive of an effect. Shu and colleagues performed a case–control study of 1744 children with ALL and 456 with acute myeloid leukaemia (AML) in the USA. They found that the risk of leukaemia was around 30% lower in those children who were breast fed for longer than 6 months of age (OR not breast fed versus breast fed >6 months 0.70 (95% CI: 0.59–0.82)) and that results for ALL and AML were similar [12]. The risk decreased progressively as duration of breast-feeding increased over the first year of life (P for trend $=0.0002$). The protective effect for ALL reported by Bener and colleagues is greater than that reported by Shu and colleagues, but not significantly so. The higher point estimate reported by Bener and colleagues probably reflects the relatively small sample size and possible differences in patterns of antigenic exposure between the two populations and the possibility, as with all these studies, of uncontrolled confounding. Differences in the patterns of antigenic exposure of the mother before and during pregnancy, and of the infant during its first months of life between different populations may also explain, at least in part, why many previous studies have failed to find an effect of breast feeding on risk of ALL and NHL.

The mechanism by which breast-feeding protects against leukaemia needs to be fully elucidated. The cause of most acute leukaemias and lymphomas is unknown. This is particularly true for children since the opportunity for exposure to agents known to be leukaemogenic in adults, for example, ionising radiation and solvents is limited. The aetiological pathways in childhood leukaemia and lymphoma are undoubtedly complex and multifactorial, though there is increasing evidence that in childhood leukaemia, the initiating event occurs very early in life — most probably *in utero*. A subsequent event (possibly an exposure to an unusual pattern of infection) may then lead to acute leukaemia in children, perhaps by means of an inappropriate lymphoproliferative response to an otherwise innocuous infection [13,14].

Breast milk provides both short- and long-term protection against infection by a variety of mechanisms, including passive antibody protection and modulation of the immune system. It has also been suggested that breast feeding leads to increased antigen exposure of the infant, for example, by ingestion of maternal skin born bacteria and viruses. It is entirely plausible that the

Table 1
Summary of published results reporting associations between Hodgkin's disease and breast feeding [18]

Author [Ref.]	Country of study	Cancers studied (n)	OR (95% CI or P value)	
			No breast feeding versus any breast feeding	No breast feeding versus breast feeding >6 months
McKinney [17]	UK	Lymphoma (63 cases, 126 controls)	<2 ($P>0.05$)	
Davis [18]	USA	Lymphoma (26 cases, 181 controls)	1.45 (0.59–3.55)	5.62 (1.41–22.42)
		Hodgkin's disease (13 cases, 181 controls)	2.31 (0.64– 9.32)	[a](1.8–infinity)($P=<0.01$)
Schwartzbaum [19]	USA	Hodgkin's disease (133 cases, 72 controls)		2.55 ($P=0.02$)
Mathur [20]	India	Lymphoma (19 cases, 90 controls)		Duration of breast feeding, cases versus control $P<0.05$
Shu [12]	China	Hodgkin's disease (14 cases, 14 controls)	5.26 (0.25– infinity)	6.67 (0.48– infinity)
Bener [10]	United Arab Emirates	Hodgkin's disease (22 cases, 22 controls)		3.75 (0.80–18.69)[a]

OR, odds ratio; CI, confidence interval.

[a] Comparison between breast fed for less that 6 months with longer than 6 months

immunomodulating activity of breast milk could modify the response to postnatal antigenic exposures and thereby reduce the susceptibility of individuals to a potentially leukaemogenic exposure. An understanding of the mechanisms by which exposure to breast milk reduces leukaemia and lymphoma risk will undoubtedly greatly facilitate the understanding of the process of leukaemogenesis and advance the possibility of disease prevention.

It is equally important that breast-feeding should be strongly promoted; the benefits are astonishing. For the mother, death from at least three causes is reduced — post partum haemorrhage, ovarian and breast cancer. For the child, death and morbidity from a wide range of serious and debilitating infective and allergic conditions are reduced throughout life and once adult, cardiovascular disease risk is lower in those who were breast fed as children. In addition the evidence now supports a substantial protective effect against childhood leukaemia and lymphoma. A commercial pharmaceutical preparation with the properties of breast milk would be worth a fortune — if people could believe its omnipotence! Despite the World Health Organisation recommendations, only a small minority of infants in many parts of the world, including most of Europe and North America, are breast fed for longer than 6 months. Indeed in some countries, such as the UK, only a minority of infants are breast fed at all. In many countries throughout the world the majority of women and their children are failing to reap the very real and tangible rewards of breast-feeding. There are 650 000 babies born in the UK each year. Approximately 500 of these will develop leukaemia or lymphoma by the age of 15 years. Currently only 50% of these children will be breast fed for longer than 2 weeks and very few breast fed for longer than 6 months. If the effect estimates of breast feeding on leukaemia and lymphoma are correct and the reduction in risk is approximately 30–50%, it is possible that if all babies were breast fed, as many as 25% of the cases of leukaemia and lymphoma in children could be prevented — indeed worldwide there is the possibility of avoiding at least one child developing leukaemia or lymphoma for every additional 3000 babies breast fed. Together with all its other benefits, this must make the promotion of breast-feeding an even more imperative public health option.

Breast-feeding promotion, even in inner cities can be successful and inexpensive [15]. Since its nadir in the 1970s the proportion of infants breast fed at birth has increased in most European countries and North America, reflecting the success of the various promotional campaigns. However, despite apparently high initial rates of breast-feeding, the majority of women switch to artificial feeding very quickly. In Europe only a small minority of children are still breast fed at 6 months of age, for example, rates of 4% have been reported in Spain, 20% in the UK and Italy. Women must be strongly encouraged not only to initiate breast feeding but also to maintain it for as long as possible during the first year of their babies' lives. Women must make informed decisions about whether to breast feed their babies or not. However, it would not seem even remotely possible that the 80–90% of European and North American women who are currently not choosing to breast feed their babies for a minimum of 6 months are in full possession of the facts about the benefits of breast-feeding. Women respond well to information about the benefits of breast-feeding and the continued benefits of prolonged breast-feeding need to be strongly emphasised [16]. Flexible working hours, adequate maternity leave and local childcare provision obviously have a role to play in enabling women to continue breast-feeding their babies.

Culturally, societally and individually, the decision must be that breast is best.

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