

Special Feature

## Breast-feeding: A Commentary by the ESPGHAN Committee on Nutrition

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### ABSTRACT

This medical position article by the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition summarises the current status of breast-feeding practice, the present knowledge on the composition of human milk, advisable duration of exclusive and partial breast-feeding, growth of the breast-fed infant, health benefits associated with breast-feeding, nutritional supplementation for breast-fed infants, and contraindications to breast-feeding. This article emphasises the important role of paediatricians in the implementation of health policies devised to promote breast-feeding. The European Society for Paediatric Gastroenterology, Hepatology, and Nutrition Committee on Nutrition recognises breast-feeding as the natural and advisable way of supporting the healthy growth and development of young children. This article delineates the health benefits of breast-feeding, reduced risk of infectious diarrhoea and acute otitis media being the best documented. Exclusive breast-feeding for around 6 months is a desirable

goal, but partial breast-feeding as well as breast-feeding for shorter periods of time are also valuable. Continuation of breast-feeding after the introduction of complementary feeding is encouraged as long as mutually desired by mother and child. The role of health care workers, including paediatricians, is to protect, promote, and support breast-feeding. Health care workers should be trained in breast-feeding issues and counselling, and they should encourage practices that do not undermine breast-feeding. Societal standards and legal regulations that facilitate breast-feeding should be promoted, such as providing maternity leave for at least 6 months and protecting working mothers. *JPGN* 49:112–125, 2009. **Key Words:** Breast-feeding—Breast milk—Health benefits—Public health. © 2009 by European Society for Pediatric Gastroenterology, Hepatology, and Nutrition and North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition

Breast milk is the natural food for infants. The degree of health benefits derived from breast-feeding is higher in developing countries than in developed countries, and is inversely proportional to the socioeconomic level of the population, which is obviously lower in developing than in developed countries. Evidence from developing

countries demonstrates that under conditions of poor hygiene breast-feeding can be a matter of life or death. It has been estimated that 1.3 to 1.45 million deaths in 42 high-mortality countries could be prevented by increased levels of breast-feeding (1,2). In a recent analysis of the health consequences of child undernutrition, it was estimated that suboptimal breast-feeding was responsible for 1.4 million child deaths and 44 million disability-adjusted life-years, equivalent to 10% of the disability-adjusted life-years in children younger than 5 years (3).

Breast-feeding is also associated with a demonstrable impact on infant morbidity in industrialised countries, for

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example, a reduction of gastrointestinal infection and acute otitis media (4–6). There is, however, no conclusive evidence that breast-feeding affects infant mortality in industrialised countries (7). As described later in this article, there is also some evidence that breast-feeding has positive effects on health in later life. The effects of breast-feeding on the health of the mother are not covered in this article, but a recent analysis found evidence that breast-feeding was associated with a reduced risk of type 2 diabetes mellitus, breast cancer, and ovarian cancer in the mother (5).

Although paediatricians are key people in the field of child health as counselors, educators, and opinion builders, it is regrettable that too many health professionals limit their advocacy of breast-feeding to the oversimplification that “breast is best.” In some European countries, low rates of initiation and short duration of breast-feeding are clearly unsatisfactory. A study performed in the United States showed that when clinicians are positive about the importance of breast-feeding, mothers are more likely to continue exclusive breast-feeding (8). Support from clinicians is also positively associated with breast-feeding duration (9). Paediatricians can and should actively protect, promote, and support breast-feeding, taking into account both public health aspects and the mother’s wishes.

The aim of this position article is to summarise the current situation with regard to breast-feeding, knowledge of the composition of human milk, advisable duration of exclusive and partial breast-feeding, growth of the breast-fed infant, health benefits associated with breast-feeding, supplementation of breast-fed infants and contraindications to breast-feeding, as well as defining the role of paediatricians in the implementation of health policies seeking to promote breast-feeding. This position article focuses on term-born infants living in Europe.

### CURRENT SITUATION

Estimates on the prevalence of breast-feeding in Europe were reported in 2003 (10). The reported situation in 29 European countries in the study is extremely heterogeneous. The rate of initiation of breast-feeding was more than or equal to 90% in 14 countries and ranged from 60% to 80% in 6 other countries. The lowest rates (<60%) were reported in France, Ireland, and Malta. The rate of any breast-feeding at 6 months was more than 50% in only 6 countries. This is a compilation of self-reported data from individual experts in different countries, and caution is needed when interpreting the results because of the lack of a standardised method of data collection. The limited data quality indicates that no standard approach to representative data collection on breast-feeding practices exists, and understanding of definitions (exclusive, full, and partial breast-feeding) differs markedly among

countries. Clearly, a common monitoring system should be a high priority.

The available data show that breast-feeding rates and practices fall short of those considered desirable by many professional organisations and scientific societies. For example, it is regrettable that the International Code of Marketing of Breast milk Substitutes, endorsed in 1981, is not fully applied and submitted to independent monitoring (11). The legislation for working mothers meets on average the International Labour Organization standards, but covers only women with formal employment. In Europe, voluntary mother-to-mother support groups and trained peer counsellors were present, respectively, in 27 and 13 of the 29 countries studied (10). There is room for many countries to improve their policies and practices to better protect, promote, and support breast-feeding, and paediatricians should play an active role in this process.

The implementation of a health policy supporting breast-feeding is important to increase the rate of initiation of breast-feeding as well as the duration of exclusive breast-feeding and partial breast-feeding. The example of Norway illustrates that positive changes can happen. Total breast-feeding rates in Norway increased from <30% at 12 weeks in 1968 to >80% in 1991. Undisturbed and prolonged contact between mother and baby became more common in Norway, as did more respect for the needs of the nursing couple, and more individualised care (12).

### COMPOSITION OF HUMAN MILK

The biological characteristics of human milk have been reviewed in detail elsewhere (13–15). Human milk is not a uniform body fluid but a secretion of the mammary gland of changing composition. Foremilk differs from hindmilk, and colostrum is strikingly different from transitional and mature milk. Milk changes with time of day and during the course of lactation. Human milk consists not only of nutrients, such as proteins, lipids, carbohydrates, minerals, vitamins, and trace elements that are of paramount importance to fulfill the nutritional needs of young infants and ensure normal growth and development. Human milk also contains numerous immune-related components such as sIgA, leukocytes, oligosaccharides, lysozyme, lactoferrin, interferon- $\gamma$ , nucleotides, cytokines, and others. Several of these compounds offer passive protection in the gastrointestinal tract and to some extent in the upper respiratory tract, preventing adherence of pathogens to the mucosa and thereby protecting the breast-fed infant against invasive infections. Human milk also contains essential fatty acids, enzymes, hormones, growth factors, polyamines, and other biologically active compounds, which may play an important role in the health benefits associated with breast-feeding.

Maternal diet may have a significant influence on the production and/or composition of human milk when the mother is malnourished or eats an unusually restrictive diet. Malnourished mothers have approximately the same proportion of protein, fat, and carbohydrate as well-nourished mothers, but they produce less milk. The provision of supplemental food is able to improve milk production and the duration of exclusive breast-feeding among undernourished women (16). In contrast, well-nourished women do not show any benefits from energy or protein supplementation. For several nutrients, however, the content in breast milk reflects the diet of the mother. This is the case for several vitamins, for example, vitamin D, vitamin A, and water-soluble vitamins, and for iodine and the composition of fatty acids. Breast-fed infants of mothers following a strict vegan diet are at high risk of severe megaloblastic anemia and neurological abnormalities because of vitamin B<sub>12</sub> deficiency (17). The Committee recommends supplementation of breast-fed infants (or their breast-feeding mothers) with vitamin B<sub>12</sub> if lactating mothers follow a vegan diet.

#### RECOMMENDATIONS FOR DURATION OF BREAST-FEEDING

Before 2001, the World Health Organization (WHO) recommended that infants be exclusively breast-fed for 4 to 6 months with the introduction of complementary foods (any fluid or food other than breast milk) thereafter. The issue of the optimal duration of exclusive breast-feeding, comparing mother and infant outcomes with exclusive breast-feeding for 6 months versus 3 to 4 months, was assessed in a systematic review of the available literature commissioned by WHO in early 2000 (18). Only 2 of the 20 eligible identified studies were randomised trials of different exclusive breast-feeding duration that were both conducted in Honduras, a developing country. All studies performed in industrialised countries were only observational. The review showed that infants who continue to be exclusively breast-fed for 6 months did not experience any deficit in weight or length gain as compared with infants exclusively breast-fed for a shorter period (3–4 months), although larger sample sizes would be required to rule out modest increases in the risk of malnutrition. The data were conflicting with respect to iron status but suggested that, at least in developing countries where iron stores of newborn infants may be suboptimal, exclusive breast-feeding without iron supplementation during the first 6 months of life may compromise haematologic status. The review concluded that “large randomized trials are recommended in both developed and developing countries to ensure that exclusive breast-feeding for 6 months does not increase the risk of undernutrition (growth faltering), to confirm the health benefits reported thus far, and to investigate other potential effects on

health and development, especially over the long-term.” A study on breast-feeding promotion performed in Belarus showed that during the period from 3 to 6 months, morbidity because of gastrointestinal infections was significantly lower in infants who were exclusively breast-fed for 6 months than in those who were mixed breast-fed as of 3 or 4 months of age (19). However, the extent to which conditions and practices in Belarus resemble those in European industrialised countries may be questioned.

At the 54th World Health Assembly on May 18, 2001, the WHO emphasized “exclusive breast-feeding for 6 months on a global public health recommendation, taking into account the findings of the WHO expert consultation on optimal duration of breast-feeding and the provision of safe and appropriate complementary food with continued breast-feeding up to 2 years of age or beyond.” However, it was stated in the expert consultation that the recommendation applies to populations and it was also recognised that some mothers will be unwilling or unable to follow this recommendation, and that these mothers should also be supported to optimise their infant’s nutrition (20). The issue of optimal duration of exclusive breast-feeding has been a matter of intense debate during the past few years, reflecting the limited availability of scientific evidence from industrialised countries to inform the WHO recommendation and the fact that problems encountered in the industrialised countries are different from those in economically developing countries (21). In industrialised countries, there is at present no scientific evidence that introducing complementary foods to breast-fed infants between 4 and 6 months of age is a disadvantage relative to introduction after 6 months (22,23).

On the basis of available data, the Committee recently concluded that full or exclusive breast-feeding for around 6 months is a desirable goal. In exclusively or partially breast-fed infants, complementary feeding, such as any solid or liquid food other than breast milk or infant formula and follow-on formula, should not be introduced to the diet of any infant before 17 weeks or delayed after 26 weeks of age (23).

The WHO recommends continued breast-feeding for at least 2 years, and the American Academy of Pediatrics recommends it for at least 1 year (20,24). For countries with low infectious disease burden, as is typical for Europe, the optimal duration with respect to health outcomes of any breast-feeding after introduction of complementary feeding is uncertain because of lack of data. Breast-feeding should be continued by mother and child for as long as mutually desired, and must be based primarily on considerations other than health outcomes.

#### GROWTH OF BREAST-FED INFANTS

Given the health and nutritional benefits of breast-feeding, the correct interpretation of the growth pattern of

healthy breast-fed infants has great significance in terms of public health.

Infants following the WHO recommendations for prolonged and exclusive breast-feeding, and who lived under conditions favouring the achievement of genetic growth potentials, appeared to show a decrease of growth progression in the first year compared with the National Center for Health Statistics-WHO international growth references, on the basis of predominantly formula-fed infants (25). Observational studies published in the 1990s were consistent in identifying different patterns of growth in breast-fed and formula-fed infants, breast-fed infants showing a reduced rate of accretion, particularly in weight for age, from the third month up to the 12th month of life, with partial catch up by the age of 24 months (26–29). These observations led to the development of new WHO growth standards on the basis of infants following the WHO recommendations on breast-feeding, which were released in 2006 (30–32). Comparing these standards with the previous National Center for Health Statistics-WHO reference confirmed the different growth patterns between breast-fed and formula-fed infants. With the new standards the risk of making an incorrect assessment regarding the adequacy of growth in breast-fed infants, and to mistakenly advise unnecessary supplementation or cessation of breast-feeding is reduced (33).

A number of studies have found associations between a high growth velocity during the first months of life and an increased risk of noncommunicable diseases later in life (34,35). Such observations are consistent with growth pattern in the breast-fed infant representing the ideal.

#### **METHODOLOGICAL ISSUES FOR ASSESSING HEALTH BENEFITS ASSOCIATED WITH BREAST-FEEDING**

Breast-feeding is associated with many health benefits for both infant and mother. Because the maternal decision to breast-feed is influenced by numerous health-related factors, it is difficult to draw firm conclusions on the causal relationship between breast-feeding and health outcomes (36). For obvious reasons, it is unethical to randomise healthy infants to breast milk or infant formula. However, there is published evidence arising from 2 different intervention studies. The first study was performed in the United Kingdom in the early 1980s, and involved preterm infants (mean gestational age 31 weeks, mean birth weight 1400 g) who were randomised to receive either banked breast milk, preterm or standard formula, with some infants also receiving mother's milk (37). The second study, the Promotion of Breast-feeding Intervention Trial (PROBIT) is a cluster-randomised trial involving 31 Belarusian maternity hospitals and their affiliated clinics that were randomised to either breast-

feeding promotion on the basis of the WHO/UNICEF Baby Friendly Hospital Initiative or standard care (38). The hospitals forming the control group continued with the existing infant feeding practices. All singleton full-term infants with a birth weight of at least 2.5 kg born at the included hospitals were enrolled in the PROBIT study. Because all infants in this study were initially breast-fed, effects of different duration of total and exclusive breast-feeding rather than differences between breast- and formula-feeding can be explored.

Other available information is limited to observational studies, and confounding is, therefore, an important consideration. Educational, socioeconomic, and lifestyle factors such as smoking are strongly associated with the mother's decision to breast-feed. In industrialised countries, mothers who breast-feed have a higher socio-economic status and higher level of education than mothers who choose to formula-feed, whereas the opposite pattern is usually present in developing countries. There is also recall bias on the nature and duration of breast-feeding. Some studies compare infants who were never breast-fed with infants who received any breast-feeding. Other studies compare infants who were exclusively breast-fed with infants who were partially breast-fed. A few studies take into account the influence of the duration of breast-feeding on health benefits. Another relevant issue when interpreting the results from older cohorts is that the composition of infant formula has much improved during the last 30 years.

Three meta-analyses on the health benefits of breast-feeding in developed countries have been published recently, from the Dutch State Institute for Nutrition and Health, the Agency for Healthcare Research and Quality, US Department of Health and Human Services, and the WHO (4,5,39) (Table 1). Even in studies controlling for known confounding variables, residual confounding is still a concern. Caution is therefore needed when interpreting data on the controversial issue of health benefits related to breast-feeding. Because almost all of the data available on breast-feeding and health are gathered from observational studies, association or concomitance should be inferred rather than causality.

#### **HEALTH BENEFITS ASSOCIATED WITH BREAST-FEEDING**

##### **Prevention of Infections**

The preventive effect on infections is by far the most important health benefit in relation to breast-feeding, especially in developing countries. The Dutch and the Agency for Healthcare Research and Quality (AHRQ) meta-analyses concluded that breast-feeding was convincingly associated with a lower risk of gastrointestinal infection and of acute otitis media (AOM), whereas the protective effect on other respiratory tract infections was

**TABLE 1.** Comparison of recent systematic reviews and meta-analyses on health effects of breast-feeding in developed countries

Criteria	WHO, 2007 (39)	US Agency for Healthcare Research and Quality, 2007 (5)	Dutch State Institute for Nutrition and Health, 2005 (4)
Study addressed an appropriate and clearly focused question	Well covered	Well covered	Well covered
Description of the methodology used is included	To assess the long-term effects of BF on blood pressure, diabetes and related indicators, serum cholesterol, overweight and obesity, and intellectual performance	To review the evidence on the effects of breast-feeding on short- and long-term infant and maternal health outcomes in developed countries	To give an overview of the literature on health effects of breast-feeding (taking the beneficial and harmful effects together) for mother and infant
Literature search is sufficiently rigorous to identify all relevant studies	Well covered	Well covered	Well covered
Types of studies included in the review	MEDLINE (1966–March 2006); Scientific Citation Index databases; references lists; authors were contacted if study did not provide sufficient data	SR/MA; RCT; non-RCT comparative trials, prospective cohort, and case-control studies	Observational (nearly all); RCTs
Language Setting	English; French; Portuguese; Spanish	English only	English, Dutch
Study quality is assessed and taken into account	High-income countries and in predominantly white populations	Developed countries only for updates; no difference for earlier studies	Only populations from Western Europe, North America, Australia, New Zealand
There are enough similarities between the studies selected to make combining them reasonable	Graded for methodological quality using a standardised protocol	Graded for methodological quality	Every article tested on its quality; if an article did not fulfill every quality requirement the study was excluded
Risk of bias	Well addressed; heterogeneity assessed	Well addressed; heterogeneity discussed or assessed (if authors performed their own MA)	Not applicable (no formal pooling was performed)
	Almost all data were gathered from observational studies	Almost all data were gathered from observational studies	Almost all data were gathered from observational studies
Main results in infants	WHO, 2007	US Agency for Healthcare Research and Quality, 2007	Dutch State Institute for Nutrition and Health, 2005
Otitis media	—	↓	Convincing evidence ↓
GI infections	—	↓	Convincing evidence ↓
Respiratory infections	—	—	Possible evidence ↓
Severe lower RTI	—	↓	—
Atopy	—	—	Possible evidence ↓
Atopic dermatitis	—	↓	Eczema Probable evidence ↓
Asthma (young children)	—	↓	Probable evidence ↓
Wheezing	—	—	Probable evidence ↓
Obesity	↓ OR 0.78 (0.72 to 0.84)	↓	Convincing evidence ↓
Type 1 diabetes	—	↓	Possible evidence ↓
Type 2 diabetes	↓ OR 0.63 (0.45 to 0.89)	↓	—
Childhood leukaemia	—	↓	Possible evidence ↓
SIDS	—	↓	Insufficient evidence
NEC	—	↓	—
Cardiovascular diseases	—	Not clear	No evidence
Crohn disease	—	—	Possible evidence ↓
Ulcerative colitis	—	—	Insufficient evidence
Infant mortality	—	—	—

(continued)

TABLE 1. Continued

Criteria	WHO, 2007 (39)	US Agency for Healthcare Research and Quality, 2007 (5)	Dutch State Institute for Nutrition and Health, 2005 (4)
High blood pressure	↓systolic MD -1.2 mmHg (-1.7 to -0.7) ↓diastolic MD -0.49 mmHg (-0.87 to -0.11)	—	Convincing evidence ↓
Serum cholesterol	Adulthood ↓ MD -0.18 mmol/l (-0.3 to -0.06) Children and adolescents NS	—	—
Intelligence and schooling	↑ MD 4.9 (2.97 to 6.92)	—	—
Intellectual and motor development	—	—	Probable evidence ↑

BF = breast-feeding, MA = meta-analysis, MD = mean difference, NA = not assessed, NEC = necrotising enterocolitis, NS = not significant, OR = odds ratio, RCT = randomised controlled trial, RTI = respiratory tract infection, SIDS = sudden infant death syndrome, SR = systematic review, WHO = World Health Organization.

The strength of evidence in the Dutch meta-analysis was qualified as convincing, probable, possible, or insufficient.

The criteria used to make this distinction were

1. Convincing evidence: evidence on the basis of epidemiological studies showing consistent associations between exposure and disease, with little or no evidence to the contrary. The available evidence is based on a substantial number of studies, including prospective observational studies. The association should be biologically plausible.

2. Probable evidence: evidence on the basis of epidemiological studies showing fairly consistent associations between exposure and disease, but where there are perceived shortcomings in the available evidence or some evidence to the contrary. Shortcomings in the evidence may be any of the following: insufficient duration of trials (or studies); insufficient trials (or studies) available; inadequate sample sizes; incomplete follow-up. Again, the association should be biologically plausible.

3. Possible evidence: evidence based mainly on findings from case-control and cross-sectional studies. Insufficient randomised controlled trials, observational studies or nonrandomised controlled trials are available. Most trials are required to support the tentative associations, which should also be biologically plausible.

4. Insufficient evidence: evidence on the basis of findings of a few studies that are suggestive, but are insufficient to establish an association between exposure and disease. Better designed research is required to support the tentative associations.

In addition to these 4 categories the following qualifications were used:

1. Conflicting evidence: several studies with sufficient power show opposite effects, so it is impossible to conclude whether breast-feeding has a positive, negative, or no effect on the disease outcome.

2. No evidence: 1 or 2 studies with little power, so no clear statement can be given about the strength of evidence.

more doubtful (4,5). The meta-analysis by AHRQ showed that breast-feeding was always associated with a lower risk of AOM than exclusive bottle-feeding (odds ratio [OR] 0.77, 95% confidence interval [CI] 0.64–0.91) (5). The reduction in the risk of AOM was greater when comparing exclusive breast-feeding with exclusive bottle-feeding, either for more than 3 to 6 months duration (OR 0.50, 95% CI 0.36–0.70). Chien and Howie (40) identified 14 cohort studies and 2 case-control studies from developed countries that qualified for inclusion in their systematic review/meta-analysis on the relation between breast-feeding and the development of gastrointestinal infections in children younger than 1 year of age. The summary crude odds ratio of the 14 cohort studies for the development of gastrointestinal infections in breast-fed infants was 0.36 (95% CI 0.32–0.41), whereas that of the 2 case-control studies was 0.54 (95% CI 0.36–0.80). A recent case-control study of good/adequate methodology from England showed that breast-fed infants had a reduced risk of diarrhoea compared with nonbreast-fed infants (OR 0.36, 95% CI 0.18–0.74) (41). However, the protective effect of breast-feeding did not persist beyond 2 months after cessation of breast-feeding. There is no clear protective effect of breast-feeding on the occurrence of lower respiratory

tract diseases. However, breast-feeding may have a preventive role in the risk of severe lower respiratory tract infections, severe being defined by the need for hospitalisation. A meta-analysis of 7 cohort studies showed a 72% reduction in the risk of hospitalisation secondary to respiratory diseases in healthy full-term infants less than 1 year of age who were exclusively breast-fed for at least 4 months compared with those who were formula-fed (relative risk 0.28, 95% CI 0.14–0.54) (42). The protective effect of breast-feeding against the risk of hospitalisation for lower respiratory infection was recently confirmed in the United Kingdom Millennium Cohort study (6). Collectively the available data indicate an association of breast-feeding with a well-documented reduced risk of infectious diarrhoea as well as AOM, and a possible protection against other infections where level of evidence is less convincing.

## Cardiovascular Health

### Blood Pressure

A randomised trial in the early 1980s comparing the use of banked human milk with preterm formula for feeding premature infants showed that mean diastolic

blood pressure at ages 13 to 16 years was higher when assigned preterm formula than banked human milk: 65.0 versus 61.9 mmHg (95% CI for difference  $-5.8$  to  $-0.6$ ;  $P=0.016$ ) (43), which differs considerably in energy and nutrient density. No difference was found for systolic blood pressure. No data were published to compare the outcome of preterm infants fed banked human milk and term formula, which are more similar in energy and nutrient supply. A meta-analysis of Owen et al (44) showed a pooled mean difference in systolic blood pressure of  $-1.10$  mmHg (95% CI  $-1.79$  to  $-0.42$ ) in participants breast-fed as infants. No difference was found for diastolic blood pressure. Another meta-analysis, including an extra approximately 10,000 subjects from 3 studies with more than 1500 participants each, showed that breast-feeding was associated with a  $-1.4$  mmHg (95% CI  $-2.2$  to  $-0.6$ ) difference in systolic blood pressure and a  $-0.5$  mmHg (95% CI  $-0.9$  to  $-0.04$ ) difference in diastolic blood pressure (45). In these 2 meta-analyses, the association weakened after stratification for study size, suggesting the possibility of bias in the smaller studies. A recent meta-analysis included 4 additional studies and other publications identified by 2 independent literature searches at WHO and at the University of Pelotas, Brazil (39). Systolic (mean difference  $-1.21$  mmHg, 95% CI  $-1.72$  to  $-0.70$ ) and diastolic (mean difference  $-0.49$  mmHg, 95% CI  $-0.87$  to  $-0.11$ ) blood pressures were lower among subjects who had been breast-fed as infants. However, in the cluster-randomised PROBIT trial, no effect of breast-feeding on blood pressure was found at age 6.5 years (46).

Although there is no consensus on whether sodium intake during infancy has an influence on blood pressure later in life (47), it is possible that the low sodium content of breast milk may play a role in the reduction of blood pressure. The high content of long-chain polyunsaturated acids (LCPUFA) in breast milk may also be relevant, since LCPUFA are incorporated into cell membranes of the vascular endothelium and supplementation with LCPUFA lowers blood pressure in hypertensive subjects. A randomised controlled trial showed that dietary supplementation with LCPUFA from birth to 6 months was associated with a significant reduction in mean and diastolic blood pressure at 6 years of age (48), and in a randomised intervention study with fish oil supplementation from 9 to 12 months of age, systolic blood pressure at 12 months was 6.3 mmHg lower in infants receiving fish oil (49).

The magnitude of the effect of breast-feeding on blood pressure is similar to the effect of salt restriction ( $-1.3$  mmHg) and weight loss ( $-2.8$  mmHg) in normotensive subjects, and is likely to have substantial public health implications (50). A lowering of population-wide mean blood pressure by 2 mmHg could reduce in adults the prevalence of hypertension by 17%, and the risk of

coronary heart disease, stroke, and transient ischemic attacks by 6% and 15%, respectively.

#### *Lipid Metabolism*

A meta-analysis of 37 studies showed that blood total cholesterol (TC) differed with age. TC concentrations were higher in breast-fed than in formula-fed infants ( $<1$  year), because of the markedly higher content of cholesterol in breast milk than in most commercially available formulae (mean TC difference 0.64, 95% CI 0.50–0.79 mmol/L) (51). Mean TC in childhood or adolescence (1–16 years) was not related to feeding patterns in infancy. However, TC in adults was lower among those breast-fed in infancy (mean TC difference  $-0.18$ , 95% CI  $-0.30$  to  $-0.06$  mmol/L). Patterns for low-density lipoprotein (LDL) cholesterol were similar to those for TC throughout. Whatever the underlying programming stimulus, long-term modifications in cholesterol metabolism are likely to occur, either by regulation of hepatic hydroxymethylglucaryl coenzyme A (HMG-CoA) reductase activity or LDL-receptor activity. The meta-analysis of the WHO confirmed that in adults ( $>19$  years) breast-fed subjects had a mean TC 0.18 mmol/L (95% CI 0.06–0.30 mmol/L) lower than those who were bottle-fed whereas the association was not significant for children and adolescents (39). The association found in adults did not seem to be due to publication bias or confounding. A recent review including data available from 17 studies (17,498 subjects; 12,890 breast-fed, 4608 formula-fed) also confirmed that initial breast-feeding (particularly when exclusive) was associated with lower blood cholesterol concentrations in later life (52).

#### *Cardiovascular Disease*

An important question is whether the potential effects of breast-feeding on later blood pressure and lipid metabolism may lead to a reduction in cardiovascular risk in adulthood. Two studies showed a positive relation of the duration of breast-feeding with arterial distensibility, which is considered a marker of endothelial dysfunction, in 10-year-old children and in adults, respectively (53,54). However, the study performed in adults showed no difference in distensibility between participants who had been bottle-fed and those breast-fed for less than 4 months. A recent Finnish study showed that young adult men who had been breast-fed had better brachial endothelial function compared with men who had been formula-fed. Breast-feeding was not significantly associated with carotid artery intima media thickness (IMT) and carotid artery compliance. No difference was observed between breast-fed and formula-fed women (55).

The follow-up of the British Boyd-Orr cohort showed in 63- to 82-year-old participants that breast-feeding was

associated with lesser ultrasound-measured IMT of common carotid and bifurcation as well as lesser carotid and femoral plaques, compared with bottle-feeding (56). However, there was no evidence of a duration-response relation between breast-feeding and IMT. The study of the same cohort on the basis of a larger number of subjects and a systematic review with meta-analysis of 4 studies failed to show any beneficial effect of breast-feeding on cardiovascular disease mortality (57). The study of the cohort of Caerphilly, Wales, UK, showed a positive association between breast-feeding and coronary heart disease mortality. There was however no duration-response effect (58). In contrast, the study of the participants of the Nurses' Health Study reported an 8% reduced risk of coronary heart disease associated with breast-feeding (59). The Committee concludes that although there are indications for effects of breast-feeding on later blood pressure and blood lipid levels, currently there is no convincing evidence that breast-feeding has an effect on cardiovascular morbidity and mortality.

### Overweight, Obesity, and Type 2 Diabetes

In a recent meta-analysis including 33 studies, breast-fed individuals were less likely to be considered overweight and/or obese in childhood and adolescence (OR 0.78, 95% CI 0.72–0.84) (39). The effect was no longer evident in adulthood. Control for confounding, age at assessment, year of birth, and study design did not modify the protective effect of breast-feeding. Because a statistically significant protective effect was observed among those studies that controlled for socioeconomic status and parental anthropometry, as well as with more than or equal to 1500 participants, the effect of breast-feeding was not likely to be due to publication bias or confounding (39). Some but not all studies show a dose-response effect, with a more marked effect associated with a longer duration of breast-feeding (60). In the cluster-randomised PROBIT trial, no protective effect of longer breast-feeding on weight and adiposity was found in the group of breast-fed infants at age 6.5 years (46). The mechanisms by which breast-feeding may protect against later obesity have been reviewed in detail (61). A behavioural explanation could be that because breast-fed babies control the amount of milk consumed they may learn to better self-regulate their energy intake later in life. Lower protein and energy content of breast milk compared with infant formula may also influence later body composition. A lower protein intake may also contribute to a diminished insulin release and thereby fat storage and obesity. The preventive effect of breast-feeding on overweight and obesity may also be related to the slower growth during the first year of life in breast-fed infants as compared with formula-fed infants (62). Two systematic reviews clearly showed that upward

percentile crossing for weight and length in infancy was associated with late obesity (odds ratios for obesity risk ranging from 1.2 to 5.7 in infants with rapid growth) (34,35).

Little information is available on the long-term development of body composition of previously breast-fed infants. Butte et al (63) have looked at the development of lean and fat mass and observed that, although weight velocity was lower in breast-fed infants in the 3- to 6-month period, fat mass and fat mass percentage were higher in breast-fed compared with formula-fed infants in the same interval. These issues deserve further attention.

A review of 7 studies including 76,744 subjects suggested that breast-feeding may provide a degree of long-term protection against the development of type 2 diabetes (OR 0.61, 95% CI 0.41–0.85), with lower blood glucose and serum insulin concentrations in infancy and marginally lower insulin concentrations in later life (64). This risk reduction for type 2 diabetes was also reported in the WHO meta-analysis (39).

In conclusion, the potential for breast-feeding to contribute to reduction of later obesity development, and its possible effects on type 2 diabetes should be explored in more detail.

### Disorders of the Immune System

#### *Allergy*

In the 1930s, a large 9-month follow-up study involving more than 20,000 infants found an impressive 7-fold reduction in the incidence of eczema comparing breast-feeding with cow's milk (65). Although the impact of breast-feeding on the development of allergies has been investigated continuously ever since, the issue remains controversial today. The potential for reverse causation should also be considered as an additional methodological drawback for assessing the impact of breast-feeding on the risk for allergy. Indeed, mothers who know that their infants are at risk for allergy may be more likely to breast-feed but also to breast-feed for a longer time than mothers of infants with no family risk for allergy. Moreover, strong genetic and environmental factors interact with breast-feeding.

Some breast-fed infants with atopic eczema may benefit from elimination of cow's milk, egg, or other antigens from their mother's diet. Maternal dietary antigens also have the ability to cross the placenta. However, prescription of an antigen avoidance diet during pregnancy is unlikely to reduce substantially the child's risk of atopic disease, and such a diet may adversely affect maternal or fetal nutrition, or both (66). There is also no convincing evidence for a long-term preventive effect of maternal diet during lactation on atopic disease in childhood (67). The benefits of breast-feeding seem to be limited to at-risk infants, that is, those with a first-degree



relative (father, mother, sibling) presenting with confirmed atopic disease. The AHRQ and Dutch meta-analyses pointed to a transient, protective effect of exclusive breast-feeding for at least 4 months on atopic dermatitis, wheezing, and asthma in infancy and early childhood (4,5). It is unlikely that a policy of exclusive breast-feeding would prevent allergy, especially its respiratory manifestations. Whatever this protective effect, women with a family history of allergy should breast-feed their infants like everyone else, and, in this targeted population, exclusive breast-feeding is recommended until the age of 6 months.

#### *Type 1 Diabetes*

Two meta-analyses suggest that breast-feeding for at least 3 months reduced the risk of childhood type 1 diabetes compared with breast-feeding for less than 3 months, with a 19% (95% CI 11%–26%) reduction and a 27% (95% CI 18%–35%) reduction, respectively (4,5). In addition, 5 of 6 studies published since the meta-analyses reported similar results (5). The Dutch and the AHRQ meta-analyses also suggest a possible protective effect of breast-feeding on the occurrence of diabetes type 1 later in life (4,5). Early introduction of cow's milk protein into the infant diet may be the main contributory factor. More information will come from the TRIGR (Trial to Reduce IDDM in the Genetically At-Risk) study, randomising high-risk infants to different supplemental formulae, either a hydrolysed feed or a regular cow's milk-based formula, after breast-feeding for 6 to 8 months of life (68).

#### *Celiac Disease*

A recent review of 6 observational studies suggested that breast-feeding may protect against the development of coeliac disease (CD) (69). With the exception of a small study, an association was found between increasing duration of breast-feeding and reduced risk of developing CD. The meta-analysis showed that the risk of CD was markedly reduced in infants who were breast-feeding at the time of gluten introduction as compared with nonbreast-fed infants (OR 0.48, 95% CI 0.40–0.59). However, breast-feeding may not provide a permanent protection against CD but may only delay the onset of symptoms.

Morris et al (70) recently reported that both early (less than or equal to 3 months) and late (more than or equal to 7 months) introduction of gluten-containing cereals were associated with an increased risk of CD. This study was based on a cohort at risk for the development of CD or diabetes mellitus, based on human leukocyte antigen typing, or having a first-degree relative with type 1 diabetes mellitus. On the basis of current data the Committee considers it prudent to avoid both early (below 4 months)

and late (7 or more months) introduction of gluten and to introduce gluten while the infant is still breast-fed (23).

#### *Inflammatory Bowel Disease*

A meta-analysis showed a protective effect of breast-feeding on the risk of inflammatory bowel disease (IBD): the risk for Crohn disease (CD) and for ulcerative colitis (UC) decreased by 33% and 23%, respectively (71). However, out of a total of 17 studies, only 4 studies of CD and 4 studies of UC were of high methodological quality. The Dutch meta-analysis pointed to evidence of a protective effect of breast-feeding against CD and to insufficient evidence for UC (4). A paediatric, population-based, case-control study was performed in northern France to examine the environmental risk factors associated with IBD (72). In a multivariate model adjusted for mother's education level, breast-feeding (partial or exclusive) was a risk factor for the development of CD (OR 2.1, 95% CI 1.3–3.4;  $P = 0.003$ ), but not for UC. Further studies are needed to fully understand the relation between breast-feeding and IBD.

#### **Malignant Disease**

Breast milk may have a role in the prevention of malignant disease by stimulating or modulating the immune response and promoting its development in early life. A recent meta-analysis showed that long-term (>6 months) breast-feeding was associated with a small but significant reduction in the risk of acute lymphocytic leukaemia (OR 0.80, 95% CI 0.71–0.91) (5). The Dutch meta-analysis concluded that there is a possible reduced risk for childhood leukaemia in breast-fed infants (4). Kwan et al (73) reported a reduction in the risk of acute myelogenous leukaemia for long-term breast-feeding (OR 0.85, 95% CI 0.73–0.98) but not for short-term breast-feeding (less than or equal to 6 months) (OR 0.90, 95% CI 0.80–1.02). A meta-analysis of 11 studies showed that breast-fed women have a slightly reduced risk of premenopausal breast cancer (relative risk 0.88, 95% CI 0.79–0.98) but not of postmenopausal breast cancer (74). The evidence for a causal relation between breast-feeding and protection against malignant disease must be considered weak.

#### **NEURODEVELOPMENT**

Many studies have shown that breast-feeding is associated with an enhanced neurodevelopment, but causal relation is difficult to establish because of many confounding factors. The meta-analysis of Anderson et al (75) showed an increment in cognitive function of 3.2 points after adjustment for maternal intelligence in breast-fed infants compared with formula-fed infants. Better cognitive development was present as early as

6 months of age and was sustained throughout childhood and adolescence. Low-birth-weight infants derived larger benefits (5.2 points) than did normal-weight infants (2.7 points). Increasing duration of breast-feeding was accompanied by an increase in cognitive development. The most important residual confounding factor is the influence of maternal socioeconomic status on the child's cognitive development. However, a study from the Philippines evaluated the relation between breast-feeding and cognitive development in a population in which socioeconomic advantage was inversely correlated with rate of breast-feeding, the opposite of industrialised countries (76). Scores at 8.5 and 11.5 years were higher for infants breast-fed longer (1.6 points and 9.8 points higher among normal birth weight and low birth weight infants, respectively, breast-fed infants for 12 to 18 months versus <6 months). The large cluster randomisation study from Belarus showed that breast-feeding promotion resulted in a significant increase in verbal IQ (7.5 points; 95% CI 0.8–14.3) (77). Teachers' academic ratings were significantly higher in the experimental group for both reading and writing.

Little is known about the effects of breast-feeding on adult cognition. A positive association between duration of breast-feeding and cognitive functions was observed in 2 samples of young Danish adults, assessed with 2 different IQ tests (78). In men ages 60 to 74 years from the Caerphilly cohort, having been artificially fed was associated with a lower cognitive function only in those with a birth weight below the median (79). However, differences in age-related decline in cognitive function may weaken the association, so that it was only significant among those with low birth weight.

The use of sibling comparisons weakens the effect of familial confounding variables. Evenhouse and Reilly examined the relation between breast-feeding history and cognitive ability in 2734 sibling pairs from the US National Longitudinal Study of Adolescent Health. The benefit of the effects of being ever breast-fed on intelligence score (Peabody Picture Vocabulary Test) assessed during adolescence was 1.7 and 2.4 points within and between families, respectively, and the difference was statistically significant (80). Another recent study involving >5000 US children also used sibling comparison analysis. Any confounding factor that was the same for both members of a pair of siblings was automatically controlled for (81). The mother's IQ was more highly predictive of breast-feeding status than were her race, education, age, poverty status, smoking, the home environment, or the child's birth weight or birth order. One standard deviation advantage in maternal IQ more than doubled the odds of breast-feeding. Breast-feeding was associated with an increase of around 4 points in mental ability that was mostly accounted for by maternal intelligence. When fully adjusted for relevant confounders, the benefit in breast-fed infants

was small and not significant (0.52, 95% CI –0.19 to 1.23). However, sibling comparisons cannot completely eliminate bias because of unobserved factors that lead a mother to feed 2 infants differently and that also drive children's later outcomes.

The benefits of breast milk may be related to its content of docosahexaenoic acid (DHA, 22: 6 $\omega$ 3), that plays an important role in brain and retina development. Breast-fed infants undergoing postmortem examination because of sudden death had a greater proportion of DHA in their brain cortex relative to those fed formula (82). The role of DHA is also suggested by the effect of DHA supplementation of breast-feeding mothers from delivery to 4 months postpartum. There was no effect on visual function at 4 and 8 months or on neurodevelopmental indices at 1 year. In contrast, the Bayley Psychomotor Development Index, but not the Mental Development Index was significantly higher in the supplemented group at 30 months of age (83). It has been recently shown that the association between breast-feeding and better cognitive development was moderated by a genetic variant in *FADS2*, a gene encoding the delta-6 desaturase that is the rate-limiting step on the metabolic pathway leading to arachidonic and DHA production (84). Brain sialic acid may play a beneficial role in brain development and cognition (85); concentrations have been reported to be different between breast-fed and formula-fed infants.

The available evidence suggests that breast-feeding may be associated with a small but measurable advantage in cognitive development that persists into adulthood. Although the effect size of cognitive benefits may not be of major importance for an individual, it could provide a significant advantage on a population basis.

## SUPPLEMENTATION OF BREAST-FED INFANTS

The vitamin D status of European women of child-bearing age and thereby the vitamin D content of breast milk is often inadequate because of the limited use of vitamin D supplemented cows' milk and dairy products, lack of sunshine, and ethnic tradition of covering of the body. Moreover, the risk of sunburn (short-term) and skin cancer (long-term) attributable to sunlight exposure makes it prudent to counsel against sun exposure and to support the use of sunscreen in infancy (24). Breast-fed infants should receive daily vitamin D supplementation regardless of maternal vitamin D status. The breast-fed infant has limited sources of vitamin K, usually present only in low concentrations in human milk. Generally, European paediatric societies recommend a vitamin K supplementation during the first weeks or months of life, either only to breast-fed infants or to all infants (86). There are different practices of fluoride supplementation in Europe, which take into account the fluoride content in drinking water. Premature and low birth weight infants as well as infants with iron deficiency require early iron

supplementation that can be administered while continuing exclusive breast-feeding. During the complementary feeding period, >90% of the iron requirements of a breast-fed infant must be met by complementary foods, which should provide sufficient bioavailable iron (23).

### CONTRAINDICATIONS TO BREAST-FEEDING

There are a few conditions under which breast-feeding may not be in the best interest of the infant. The main contraindication to breast-feeding is maternal human immunodeficiency virus (HIV) infection. Transmission of HIV during breast-feeding is a multifactorial process. The risk factors are maternal viral load, maternal immune status, breast health, pattern and duration of breast-feeding. To minimise the risk of HIV-transmission, WHO recommends "when replacement feeding is acceptable, feasible, affordable, sustainable and safe, avoidance of all breast-feeding by HIV-infected mothers is recommended, otherwise, exclusive breast-feeding is recommended during the first months of life" (87). Indeed, a study performed in South Africa showed that exclusive breast-feeding was associated with a lower risk of post-natal transmission at 6, 12 and 18 months than predominant breast-feeding and mixed breast-feeding (88). An intervention cohort study in South Africa also showed that breast-fed infants who received solids during the first 6 months were nearly 11 times more likely to acquire HIV infection than those exclusively breast-fed, and that infants who at 14 weeks of age were fed both breast milk and formula milk were nearly twice as likely to be infected as those exclusively breast-fed (89). In Europe, HIV-positive women should be counselled not to breast-feed.

Breast-feeding is also contraindicated in mothers who are human T-cell lymphotropic virus (HTLV) type I- or II-positive, and in mothers who have herpes simplex lesions on a breast (90). Breast-feeding is not contraindicated for infants born to mothers who are hepatitis B surface antigen-positive and those who are infected with hepatitis C virus (90). Cytomegalovirus (CMV) infection transmitted via breast milk is usually asymptomatic in term infants, whereas preterm infants are at greater risk of symptomatic CMV infection, such as sepsis-like symptoms (91). In very low birth weight infants (<1500 g or gestational age <32 weeks) born to CMV-seropositive mothers, the benefit of breast-feeding should be weighed against the risk of CMV transmission. Milk pasteurisation prevents CMV infection. Freezing significantly reduces the CMV viral load in breast milk and may also reduce the risk of infection.

In the classic variant of galactosaemia, in which no erythrocyte galactose-1-phosphate uridyl transferase (gal-1-put) activity occurs, the infants are unable to metabolise galactose, so that breast-feeding should be avoided. In the milder variant of the disease, with partial

reduction in the amount of gal-1-put, the infants may be breast-fed or at least partially breast-fed because of a higher tolerance to galactose (90). There are few other inborn errors of metabolism representing absolute contraindications to breast-feeding, for example, disorders of long-chain fatty acid oxidation and related disorders, as well as congenital lactase deficiency, whereas some amounts of breast milk may be tolerated in other disorders such as hyperchylomicronaemia (type 1 hyperlipidaemia) and abetalipoproteinaemia. Although there is no definite evidence that breast-feeding improves the outcome of phenylketonuria from randomised trials, observational studies have shown some developmental advantages, suggesting that breast-feeding should be encouraged to the extent permitted by the individual phenylalanine tolerance (92,93). Further work is needed in developing guidelines for feeding and for clinical and biochemical monitoring for breast-fed infants with inherited metabolic disorders (94).

Breast-feeding is contraindicated in mothers who are receiving diagnostic or therapeutic radioactive isotopes or have had exposure to radioactive materials, and in those who are receiving specific medications (95).

Most drugs transfer into human milk, but most do so in subclinical amounts and it is often safe to breast-feed while using a medication. However, the choice of medication is extremely important. Health professionals and parents are advised to carefully choose those with limited adverse effect profiles. Almost always, with the adequate choice of medication, breast-feeding can be continued while the mother undergoes drug therapy (14).

Human milk may be compromised by unwelcome chemicals from the environment, especially persistent organic pollutants, which accumulate in the food chain, as a result of eating, drinking, and living in a technologically advanced world. However, the presence of an environmental chemical in human milk does not necessarily indicate that a serious health risk exists for breast-fed infants. No adverse effect has been clinically or epidemiologically demonstrated as being associated solely with consumption of human milk containing background levels of environmental chemicals (96). In Europe the general downward trend in the level of persistent organic pollutants, such as dioxins, dibenzofurans, and dioxin-like polychlorobiphenyls, indicates a continuing decline in exposure as measures to reduce emissions have been implemented. The health benefits of breast-feeding still far outweigh the potential harmful effects related to the presence of environmental contaminants in breast milk.

### CONCLUSIONS

Breast-feeding is the natural and advisable way of supporting the healthy growth and development of young children. There are numerous indicators of benefits of breast-feeding on child health, both during infancy and

later in life; a reduced risk of infectious diarrhoea and acute otitis media are the best documented effects.

Exclusive breast-feeding for around 6 months is a desirable goal, but partial breast-feeding as well as breast-feeding for shorter periods of time are also valuable. Continuation of breast-feeding after the introduction of complementary feeding is to be encouraged as long as mutually desired by mother and child.

Although it is acknowledged that parents are responsible for decisions on breast-feeding of their infants, the role of health care workers, including paediatricians, is to protect, promote, and support breast-feeding.

Health care workers should be trained in breast-feeding issues and counselling, and they should encourage practices that are in line with the International Code for Breast Milk Substitutes. Societal standards and legal regulations that facilitate breast-feeding should be promoted, such as providing maternity leave for at least 6 months and protecting working mothers.

Breast-feeding practices should be regularly monitored, applying agreed-upon definitions of breast-feeding, and strategies for improving practice should be scientifically evaluated.

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