Annales Nestlé

Reprinted with permission from:
Ann Nutr Metab 2013;62(suppl 3):16–25
DOI: 10.1159/000351575

# Feeding Patterns during the First 2 Years and Health Outcome

Ferdinand Haschke[a, c] Nadja Haiden[c] Patrick Detzel[b] Benjamin Yarnoff[e] Benjamin Allaire[e] Elisabeth Haschke-Becher[d]

[a]Nestlé Nutrition Institute, Vevey, and [b]Nestlé Research Centre, Lausanne, Switzerland; [c]Department of Pediatrics, Medical University Vienna, Vienna, and [d]University Institute of Medical and Chemical Laboratory Diagnostics, Paracelsus Medical University, Salzburg, Austria; [e]RTI International, Research Triangle Park, Durham, N.C., USA

## Key Messages

- **All preterm and term infants benefit from breastfeeding.**
- **Low-birth-weight infants have a better health outcome if breast milk is fortified.**
- **Analysis of data from 20 developing countries demonstrates that exclusive breastfeeding until 6 months is associated with a significantly better growth and health outcome.**
- **Nine out of 10 infants in developing countries still receive breast milk between 6 and 12 months. Probability of infection in breastfed infants tends to be lower.**
- **Stunting and wasting rates are high between 12 and 24 months, but no associations exist between feeding patterns and disease outcome.**
- **Long-term follow-up studies in developed countries now indicate that breastfeeding and use of hypoallergenic formula is effective in preventing allergies and atopic disease.**

**Key Words**

Low-birth-weight infants · Term infants · Young children · Nutrition · Breastfeeding · Malnutrition · Health outcome · Allergy prevention

## Abstract

Low-birth-weight infants, in particular those with birth weights <1,500 g, benefit from fortified breast milk. Low protein intake is critical, because it is limiting growth. Long-term health outcomes in small-for-gestational-age infants from developing countries in relation to their early nutrition still need to be evaluated in controlled trials. Term infants both in developing and developed countries also benefit from exclusive breastfeeding: an analysis of a large dataset of surveys from 20 developing countries (168,000 infants and small children from the Demographic Health Survey, United States Agency for International Development) indicates that exclusive breastfeeding until 6 months is associated with significantly higher weight, length, and lower probability of stunting, wasting, and infections. Nine out of 10 infants still receive breast milk between 6 and 12 months and probability of infections tends to be lower if breastfeeding is continued during that age range. Between 12 and 24 months, when stunting and wasting rates are already high, 7 out of 10 infants still receive breast milk. No associations of feeding patterns with disease outcome can be found. Effectiveness trials of complementary feeding strategies in food-insecure countries are urgently needed. Follow-up until 10 years in a developed country now indicates that an infant population at risk for allergic diseases benefits both from breastfeeding and the use of hypoallergenic formula during the first 4 months of life, when compared to cow's milk-based formula: both the cumulative incidences of atopic disease and all allergic diseases are significantly lower.



KARGER

E-Mail karger@karger.com


0250–6807/13/0627–0016$38.00/0

Prof. Ferdinand Haschke, MD
Nestlé Nutrition Institute
Avenue Reller 22
CH–1800 Vevey (Switzerland)
E-Mail ferdinand.haschke@nestle.com

**Table 1.** Required intakes of growing premature infants (per kg body weight) and composition of feedings (per 100 kcal)

| | Required intakes [7] | | | Unfortified human milk | | Fortified human milk, donor milk plus fortifier[1] | Preterm formula | | |
|---|---|---|---|---|---|---|---|---|---|
| | 700–1,000 g | 1,000–1,500 g | 1,500–2,000 g | preterm human milk [2] | term (donor) human milk | | Enfamil Premature High Protein (Mead Johnson) | Similac Special Care High Protein (Abbott) | PreNan RTD (Nestlé) |
| Protein, g | 3.6 | 3.3 | 3 | 2.3 | 1.5 | 2.4–3.5 | 3.5 | 3.3 | 3.6 |
| Na, mEq | 3.3 | 2.7 | 2.4 | 1.7 | 1.1 | 1.7–2.2 | 2.5 | 1.9 | 2.8 |
| Cl, mEq | 2.9 | 2.4 | 2 | 2.3 | 1.8 | 2–2.8 | 2.6 | 2.3 | 2.7 |
| K, mEq | 2.3 | 2 | 1.9 | 2.2 | 2 | 2.6–3.6 | 2.5 | 3.3 | 3.8 |
| Ca, mq | 175 | 154 | 148 | 36 | 41 | 121–177 | 165 | 180 | 145 |
| P, mq | 120 | 107 | 102 | 20 | 19 | 68–99 | 83 | 100 | 96.1 |

[1] Enfamil Liquid, Similac Powder, FM85 Nestlé.

## Introduction

Since 2003, the World Health Organization (WHO) has recommended exclusive breastfeeding until 6 months and continuation of breastfeeding until 2 years of age [1]. For low-birth-weight (LBW) infants, breast milk is the preferred nutrition, but supplementation with breast milk fortifiers is highly recommended [2]. The short- and long-term consequences of adequate early nutrition of LBW infants are now the subject of intensive clinical research, but mainly in developed countries. For term infants, international nutrition committees strongly support exclusive breastfeeding until 6 months. The European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) states that exclusive breastfeeding for around 6 months is a desirable goal, but partial breastfeeding as well as breastfeeding for shorter periods of time is also valuable. Continuation of breastfeeding after the introduction of complementary feeding is encouraged as long as mutually desired by mother and child [3]. Different committees of the American Academy of Pediatrics [4, 5] also provide support for exclusive breastfeeding and focus on nutritional benefits, allergy prevention, and other health aspects. For developing countries, there is a clear breastfeeding recommendation for infants until 2 years, but the implementation of the policy in relation to health outcomes is not always properly monitored. In particular, the global health outcomes in relation to introduction of solids, non-milk-based beverages, formula, and cow's milk between 0 and 24 months are less well documented. Our review focuses therefore on growth and health outcomes of LBW and term infants in relation to their feeding until 2 years of age both in developed and developing countries.

## LBW Infants

The effects of adequate nutrition of LBW (birth weight <2,500 g) and very-low-birth-weight (VLBW) infants (birth weight <1,500 g) are documented in well-designed clinical studies in developed countries and resulted in international recommendations [2]. Most of the infants who participated in those studies were premature infants (i.e. appropriate for gestational age, AGA). In 2010, 32.4 million babies were born small for gestational age (SGA), 27% of all births in low- and middle-income countries [6]. In those countries, >80% of SGA infants are born at term or near term. Well-controlled studies on health outcome of SGA near-term or premature infants in relation to their postnatal nutrition are lacking. In order to further improve feeding of SGA infants during the early period of their life, we need reliable data from clinical trials on long-term health outcome (growth, health, and neurodevelopment) in relation to postnatal nutrition.

Fortification of breast milk is necessary for the growing preterm infant because breast milk does not contain energy and nutrients in amounts required for optimal growth (table 1) [7]. Fortified milk has a caloric density of 80–85 kcal/dl, assuming caloric density of native breast milk to be 67 kcal/dl. Expressed breast milk is frequently low in fat content and thus may contain fewer calories than the assumed 67 kcal/dl. Use of calories to quantify breast milk is a convenient practice, but we must always remember that the actual intake of calories is likely to be less than the stated value. Fortifiers provide energy in the form of carbohydrates and lipids because this enables meeting energy needs while keeping feeding volumes low. While the caloric density of the feeding increases with the addition of a breast milk fortifier, the main function of fortification is the increase in protein and mineral con-



Reprinted with permission from:
Ann Nutr Metab 2013;62(suppl 3):16–25

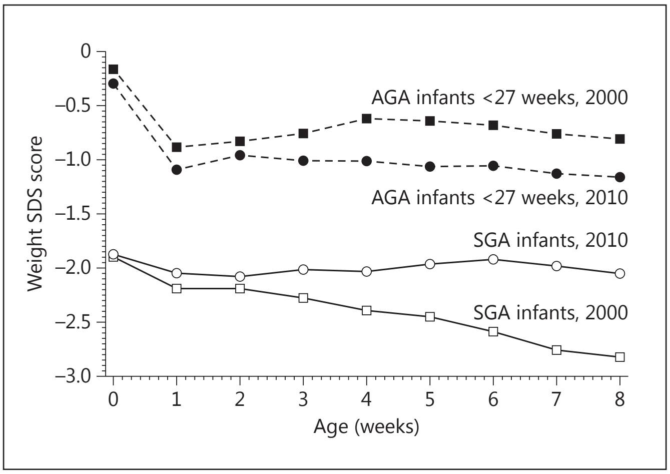


**Fig. 1.** Weight SDS (z) scores in the years 2000 and 2010 of premature AGA (<27 weeks of gestation) and SGA infants. Data from the Department of Pediatrics, University of Iowa, Iowa City, Iowa, USA [12].

tent of the milk. In order to meet those needs, a powdered or liquid breast milk fortifier is added to mother's milk. The addition of a fortifier to breast milk results in a doubling or tripling of the protein content and a fourfold increase in calcium and phosphorus content. The amounts of minerals and vitamins are designed to meet or exceed, together with the nutrients intrinsically present in human milk, the concentrations specified in table 1. The protein provided by fortifiers (1.0–1.1 g/100 ml) is insufficient to meet the needs for protein at all times [7]. Protein intake only meets protein needs if and when the protein content of breast milk is at its highest, i.e. in the first 2 weeks of lactation, but it becomes progressively more inadequate as the protein content of breast milk decreases with the duration of lactation. Inadequate protein intake from fortified breast milk is the main cause of postnatal growth failure. Adequate protein intake can be achieved if the protein content of the fortifier is increased or if, in addition to the standard amount of fortifier, additional protein (e.g. whey protein) is added in a fixed amount, as in many newborn nurseries. There is no question that the amount of protein provided by commercial fortifiers is inadequate and that additional protein must be provided in some form. A fortifier with a protein content of 1.4 g/100 ml was recently found to be safe and resulted in better growth of VLBW infants when compared to 1.0 g/100 ml in a randomized controlled trail [8]. If breast milk is not available, specific formulas designed for premature infants are adequate choices.

Premature infants fed nonsupplemented breast milk grow slowly, which carries the risk of impaired neurocognitive development. In addition, premature infants can develop deficiency states of specific nutrients, such as osteopenia (Ca, P) or zinc deficiency. Improved growth, health, and neurodevelopmental outcomes of premature infants are strongly related to better parenteral and enteral (fortified breast milk) nutritional support [9, 10]. A clinical trial with formula-fed VLBW infants indicated that a protein concentration of 3.6 g/100 kcal is superior to 3.0 g/100 kcal in promoting weight gain [11].

Ziegler [12] has recently shown that postnatal growth of SGA infants can be improved by nutritional intervention. In the year 2000, SGA infants failed to grow parallel to their weight-for-age z-score percentile channel (fig. 1), which was in contrast to the growth of premature AGA infants. Nutritional measures which were introduced at the University Hospital of Iowa, USA, during the last decade [12], among them the increase of the protein:energy ratio of fortified breast milk to 3.2 g/100 kcal, resulted in satisfactory growth in the year 2010 (fig. 1). It is of note that SGA infants receiving the nutritional support in the year 2010 did not show any signs of postnatal 'catch-up growth' which is associated with higher blood pressure, obesity, higher body fat content, waist circumference, and triglycerides as well as lower high-density lipoprotein and insulin sensitivity later in life both in animals [13] and humans [14–16].

*Premature infants fed nonsupplemented breast milk grow slowly, which carries the risk of impaired neurocognitive development.*

### Term Infants 0–6 Months

It is well established that term infants benefit from exclusive breastfeeding during the first 6 months of their life [3–5], but the majority of infants both in developing and developed countries are not fed according to WHO recommendations [1]. To evaluate how nonexclusive or no breastfeeding would affect growth and health outcome in the developing world, one recent study analyzed available datasets from different continents. Past studies have frequently limited their geographic coverage and thus sacrificed generalizability [17]. Data on early feeding patterns in developing countries in relation to growth


Reprinted with permission from:
Ann Nutr Metab 2013;62(suppl 3):16–25

and health outcomes from the Demographic Health Survey (DHS; United States Agency for International Development) are in the public domain. The DHS includes nationally representative surveys of women aged 15–49 years that ask about the health of each woman and her children as well as demographics and socioeconomics. In addition, the DHS asks about all foods that the woman's youngest child received in the past 24 h (recall method). A recent study examined multiple surveys (n = 54) from 20 developing countries (Africa, Asia, and Latin America [18]). The study decided ex-ante to examine 20 countries from the African, Asian, and Latin American regions and selected these countries based on the following criteria: multiple survey years per country and the presence of information on infant feeding and maternal characteristics in each survey. Countries were selected to maximize these two criteria while also maintaining a distribution across the regions. In order to test for the representativeness of the subsample for overall feeding practices, mean feeding indicators from the subsample were compared with mean feeding indicators from the full sample of DHS countries. Mean feeding indicators are virtually identical between this subsample and the full sample of DHS surveys, which suggests that this subsample is representative of overall feeding practices in the full DHS sample. The sample consisted of 168,000 children divided across 3 age groups: 0–6, 6–12, and 12–24 months. Six types of food were of interest: exclusive breastfeeding, nonexclusive breastfeeding, non-milk liquids (e.g. fruit juices, water, and sugar water), solid foods, milk liquids (e.g. powdered or liquid animal's milk), and formula. Health outcome variables of interest were length-for-age z-score, weight-for-height z-score, and whether the child had diarrhea, fever, and a cough in the past 2 weeks.

Percentages of infants <6 months in the study who were exclusively and nonexclusively breastfed or received no breast milk are indicated in table 2. Corresponding percentages in the overall DHS sample were 34, 62, and 4%, respectively. Of particular interest was the group of nonexclusively breastfed infants, where 91, 37, 25, and 9% received non-milk liquids, solids, milk liquids, and formula, respectively. Exclusive formula feeding was recorded only in 70 out of 47,071 infants (0.15%). In a subsample of 37,750 infants between 0 and 6 months, information on a large set of confounding factors was available: child-specific factors, community resources, geographic factors, household resources, health behavior, and maternal occupation and education. In that subsample, Yarnoff et al. [18] recently analyzed growth and health outcomes in relation to feeding type, correcting for potential confounders. They employed a fixed-effect ordinary least squares regression technique, controlling for potential confounders with community year-fixed effects and control variables such as size at birth, vaccination status, maternal education (no formal education, incomplete primary, complete primary, incomplete secondary, complete secondary, and post-secondary education), maternal weight and height, maternal work status, number of household members, number of children in the household, and whether the family had agricultural land. Associations of the different types of feeding with growth and health were considered. Compared to nonbreastfeeding in the 20 countries, exclusive breastfeeding during the first 6 months was associated with a significantly higher length and weight and lower probability of diarrhea. Nonexclusive breastfeeding was also associated with beneficial effects on growth and health. During the first 6 months, there was no association of maternal education level with exclusive and nonexclusive breastfeeding. Mothers with higher education reported more frequently the use of infant formula and milk liquids. Infants of mothers that were working outside home were less likely to be exclusively breastfed and more likely to be nonex-

**Table 2.** Calculated infant feeding patterns in the age group 0–6 months in 20 developing countries[1] (n = 47,071)

| Feeding | % |
|---|---|
| Exclusive BF | 32 |
| NEBF | 64 |
| NEBF + NML | 26 |
| NEBF + NML/S | 14 |
| NEBF + ML/NML | 6 |
| NEBF + ML/NML/S | 4 |
| NEBF + ML | 3 |
| NEBF + F/NML | 3 |
| NEBF + S | 2 |
| NEBF + F/NML/S | 2 |
| NEBF + ML/S | 1 |
| NEBF + F/NML/ML | 1 |
| NEBF + other | 3 |
| No BF | 4 |

BF = Breastfeeding; NEBF = nonexclusive breastfeeding; NML = non-milk liquids; S = solids; ML = milk liquids; F = formula.

[1] Countries: Bangladesh, Benin, Bolivia, Cameroon, Colombia, Dominican Republic, Egypt, Ghana, India, Indonesia, Kenya, Madagascar, Mali, Nepal, Philippines, Senegal, Tanzania, Turkey, Uganda, and Zambia (database: DHS, USAID).

**Table 3.** Feeding patterns, growth, and health at 0–6 months: counterfactual regression analysis[1]

| Feeding groups | | | Length z-score[2] | Weight z-score[2] | Stunting[3] | Wasting[3] | Diarrhea[4] | Fever[4] | Cough[4] |
|---|---|---|---|---|---|---|---|---|---|
| *Age 0–6 months (n = 37,214); stunting 10%; wasting 6%* | | | | | | | | | |
| EBF | vs. | no BF | **0.314 (0.088 to 0.541)** | **0.432 (0.244 to 0.621)** | **–9.2 (–14.9 to –3.8)** | –4.1 (–8.7 to 0.5) | **–10.5 (–16.7 to –4.3)** | **–12.3 (–19.9 to –4.7)** | **–7.3 (–14.6 to 0.0)** |
| EBF | vs. | NEBF | **0.129 (0.072 to 0.185)** | **0.140 (0.078 to 0.202)** | **–2.6 (–3.9 to –1.3)** | 0.1 (–1.0 to 1.1) | **–6.1 (–7.5 to –4.7)** | **–9.3 (–10.9 to –7.7)** | **–7.0 (–8.8 to –5.3)** |
| NEBF | vs. | no BF | 0.194 (–0.036 to 0.423) | **0.298 (0.109 to 0.487)** | **–6.7 (–12.2 to –1.2)** | –4.5 (–9.2 to 0.1) | –4.6 (–10.9 to 1.7) | –2.0 (–9.6 to 5.7) | 0.0 (–7.4 to 7.4) |
| EBF | vs. | NEBF + NML | **0.119 (0.056 to 0.182)** | 0.058 (–0.018 to 0.135) | **–1.5 (–3.0 to 0.0)** | –0.8 (–3.2 to 1.7) | **–4.6 (–6.2 to –3.0)** | **–6.2 (–8.0 to –4.3)** | **–4.0 (–6.0 to –2.0)** |
| EBF | vs. | NEBF + NML /S | **0.104 (0.029 to 0.180)** | **0.218 (0.134 to 0.303)** | **–3.8 (–5.6 to –1.9)** | 0.7 (–1.2 to 2.6) | **–10.6 (–12.6 to –8.6)** | **–13.8 (–16.1 to –11.4)** | **–10.7 (–13.3 to –8.1)** |
| EBF | vs. | NEBF + S | **0.138 (0.022 to 0.255)** | **0.174 (0.060 to 0.288)** | **–3.9 (–7.0 to –0.9)** | –4.6 (–9.5 to 0.2) | **–8.3 (–11.5 to –5.0)** | **–12.4 (–16.4 to –8.4)** | **–10.7 (–15.0 to –6.4)** |
| EBF | vs. | NEBF + ML | **0.160 (0.055 to 0.266)** | **0.115 (0.012 to 0.218)** | –2.3 (–5.0 to 0.4) | **–4.8 (–9.5 to –0.1)** | –0.6 (–3.3 to 2.2) | **–6.8 (–10.0 to –3.6)** | **–5.9 (–9.7 to –2.2)** |
| EBF | vs. | NEBF + NML/F | **0.216 (0.088 to 0.343)** | 0.109 (–0.019 to 0.236) | –2.7 (–5.6 to 0.3) | 1.2 (–1.1 to 3.4) | **–5.1 (–8.7 to –1.5)** | **–6.6 (–10.9 to –2.3)** | **–5.0 (–9.7 to –0.4)** |
| EBF | vs. | NEBF + F | **0.249 (0.098 to 0.401)** | 0.064 (–0.083 to 0.212) | –2.8 (–6.5 to 0.8) | –0.9 (–2.6 to 0.7) | –2.8 (–6.9 to 1.3) | **–5.2 (–10.1 to –0.3)** | –5.0 (–10.4 to 0.4) |
| EBF | vs. | NEBF + NML/ML | **0.127 (0.042 to 0.211)** | **0.159 (0.077 to 0.241)** | **–2.1 (–4.2 to 0.0)** | –0.2 (–2.0 to 1.7) | **–2.9 (–5.1 to –0.6)** | **–8.2 (–10.9 to –5.5)** | **–6.0 (–8.8 to –3.1)** |
| EBF | vs. | NEBF + ML /F | **0.257 (0.108 to 0.406)** | **0.165 (0.020 to 0.310)** | –3.4 (–7.2 to 0.4) | 0.4 (–0.9 to 1.6) | –1.1 (–5.0 to 2.9) | **–7.3 (–12.1 to –2.5)** | **–7.0 (–12.3 to –1.6)** |
| EBF | vs. | NEBF + ML/S | **0.146 (0.034 to 0.258)** | **0.275 (0.167 to 0.382)** | **–4.5 (–7.4 to –1.6)** | 0.0 (–2.0 to 2.0) | **–6.5 (–9.5 to –3.5)** | **–14.4 (–18.1 to –10.8)** | **–12.7 (–16.8 to –8.6)** |
| EBF | vs. | NEBF + ML/NML/S | **0.112 (0.018 to 0.206)** | **0.319 (0.229 to 0.409)** | **–4.4 (–6.6 to –2.1)** | –0.3 (–2.3 to 1.7) | **–8.8 (–11.3 to –6.3)** | **–15.8 (–18.8 to –12.9)** | **–12.7 (–15.8 to –9.5)** |
| *Age 4–6 months (n = 18,531); stunting 13%; wasting 7%* | | | | | | | | | |
| EBF | vs. | no BF | 0.026 (–0.346 to 0.398) | **0.397 (0.097 to 0.696)** | –3.5 (–12.7 to 5.7) | –3.9 (–10.9 to 3.0) | –6.7 (–16.4 to 3.1) | –12.2 (–24.9 to 0.6) | –1.7 (–12.9 to 9.6) |
| EBF | vs. | NEBF | –0.110 (–0.226 to 0.006) | 0.080 (–0.027 to 0.187) | **3.4 (0.3 to 6.4)** | 0.7 (–1.6 to 3.0) | –2.7 (–5.8 to 0.4) | **–4.9 (–8.6 to –1.1)** | –2.8 (–6.7 to 1.0) |
| NEBF | vs. | no BF | 0.135 (–0.231 to 0.502) | **0.312 (0.017 to 0.607)** | –7.3 (–16.5 to 1.8) | –4.4 (–11.2 to 2.4) | –4.2 (–13.8 to 5.5) | –6.5 (–19.0 to 6.1) | –0.2 (–11.3 to 10.9) |
| EBF | vs. | NEBF + NML | –0.044 (–0.170 to 0.081) | –0.019 (–0.139 to 0.101) | **3.6 (0.2 to 6.9)** | 0.9 (–3.5 to 5.4) | –2.3 (–5.7 to 1.1) | –3.1 (–7.2 to 0.9) | –1.2 (–5.4 to 3.0) |
| EBF | vs. | NEBF + NML/S | **–0.217 (–0.357 to –0.078)** | 0.111 (–0.019 to 0.240) | 3.6 (–0.1 to 7.3) | 1.7 (–1.9 to 5.3) | **–4.8 (–8.7 to –1.0)** | **–6.4 (–11.1 to –1.7)** | –2.7 (–7.5 to 2.0) |
| EBF | vs. | NEBF + S | –0.036 (–0.227 to 0.154) | 0.040 (–0.157 to 0.238) | 1.4 (–4.4 to 7.1) | –3.6 (–11.1 to 3.9) | –3.8 (–9.5 to 2.0) | **–8.5 (–15.5 to –1.5)** | **–8.2 (–15.5 to –0.9)** |
| EBF | vs. | NEBF + ML | 0.081 (–0.101 to 0.263) | 0.071 (–0.101 to 0.243) | 2.4 (–2.9 to 7.7) | –5.2 (–12.4 to 2.1) | 1.6 (–3.8 to 6.9) | –5.7 (–11.6 to 0.2) | **–7.4 (–13.9 to –0.9)** |
| EBF | vs. | NEBF + NML/F | 0.132 (–0.097 to 0.361) | –0.040 (–0.268 to 0.188) | 0.3 (–5.5 to 6.1) | 3.4 (–1.0 to 7.8) | –2.8 (–9.8 to 4.1) | –1.0 (–9.2 to 7.3) | –2.4 (–11.1 to 6.3) |
| EBF | vs. | NEBF + F | **–0.313 (0.057 to 0.569)** | –0.110 (–0.367 to 0.146) | –1.9 (–8.8 to 4.9) | –0.7 (–3.8 to 2.5) | –1.8 (–9.9 to 6.3) | –3.1 (–12.9 to 6.7) | –7.9 (–17.7 to 1.9) |
| EBF | vs. | NEBF + NML/ML | –0.100 (–0.245 to 0.045) | **0.141 (0.000 to 0.282)** | **4.6 (0.5 to 8.7)** | –1.6 (–5.0 to 1.8) | 0.5 (–3.6 to 4.7) | –3.6 (–8.2 to 1.1) | –1.9 (–6.8 to 3.1) |
| EBF | vs. | NEBF + ML/F | 0.257 (–0.004 to 0.519) | 0.050 (–0.199 to 0.300) | –0.9 (–8.0 to 6.2) | 0.9 (–1.6 to 3.4) | 1.0 (–7.1 to 9.1) | –3.5 (–12.8 to 5.8) | –8.5 (–18.1 to 1.0) |
| EBF | vs. | NEBF + ML/S | –0.092 (–0.286 to 0.102) | **0.201 (0.019 to 0.382)** | 2.4 (–3.3 to 8.0) | 0.4 (–3.2 to 4.1) | –0.9 (–6.4 to 4.6) | **–8.9 (–15.2 to –2.6)** | **–8.9 (–15.9 to –1.9)** |

EBF = Exclusive breastfeeding; BF = breastfeeding; NEBF = nonexclusive breastfeeding; NML = non-milk liquids; S = solids; ML = milk liquids; F = formula. [1] For countries, see table 2. [2] Differences in z-scores between feeding groups (95% CI). [3] Percentage differences between feeding groups (95% CI). [4] Probability of disease. Percentage differences between feeding groups (95% CI).

clusively breastfed and to receive milk liquids, non-milk liquids, and solid foods.

To have a more detailed view, we employed counterfactual analysis using results from the regression analysis [18] to compare growth and health outcomes of exclusively breastfed infants in the DHS with infants on other feeding schemes (table 3). Z-scores for length and weight were calculated based on the WHO 2006 Child Growth Standards [19]. In addition, percentages of infants with stunting and wasting were calculated. The cutoffs for stunting and wasting were 2 z-scores below the median of the WHO z-scores (2.3rd percentile). Exclusively breastfed infants had significantly higher height and weight z-scores than nonbreastfed infants and a lower probability of stunting and wasting (table 3). In addition, probability of different diseases was significantly lower. The differences were also significant when exclusively breastfed infants were compared with the whole cohort of nonexclusively breastfed infants including the subgroups who received different types of weaning foods, milk liquids, and formula. Exclusive breastfeeding could not be compared with exclusive formula feeding, because most individual country surveys had identified only <3 infants who were exclusively fed formula. Counterfactual analysis in the subgroup of infants between 4 and 6 months of age indicated trends of lower disease probability in exclusively breastfed infants (table 3). Breastfed infants had higher weight z-scores than nonbreastfed infants. The analysis confirmed that in infants below 6 months of age, both exclusive and nonexclusive breastfeeding was associated with beneficial effects on growth and health when compared to nonbreastfeeding. The limitations of all DHS data are that they are cross-sectional, and dietary intake and morbidity are self-reported by the parents. Therefore, only associations can be presented here but no causal relationship. This DHS data review and analysis, like many other studies, strongly supports the importance of the WHO feeding recommendations for infants between 0 and 6 months [1]. Suboptimal breastfeeding results in >800,000 child deaths annually [20]. A systematic review of 110 randomized clinical trials and quasi-experimental studies recently indicated that educational or counseling interventions may increase exclusive breastfeeding by 90% from 1 to 6 months [20]. If such interventions will work, the exclusive breastfeeding rate could go up from 32 to 60% in the 20 countries in this analysis.

***The analysis confirmed that in infants below 6 months of age, both exclusive and nonexclusive breastfeeding was associated with beneficial effects on growth and health when compared to nonbreastfeeding.***

**Table 4.** Effect of PHF and EHF on prevention of allergic disease

| | Intention-to-treat analysis (n = 2,252) RR (95% CI) | Per protocol analysis (n = 988) RR (95% CI) |
|---|---|---|
| PHF-W | | |
| Any allergy | 0.87 (0.77; 0.99) | 0.82 (0.70; 0.96) |
| AD | 0.82 (0.68; 1.00) | 0.77 (0.55; 0.91) |
| EHF-C | | |
| Any allergy | 0.83 (0.72; 0.95) | 0.83 (0.70; 0.97) |
| AD | 0.72 (0.58; 0.88) | 0.69 (0.53; 0.88) |

German Infant Nutrition Intervention (GINI) study [23] RR for cumulative incidence at 10 years (95% CI) compared to cow's milk formula. PHF-W formula had no significant effect [22].

PHF-W = Partially hydrolyzed whey-based formula; EHF-C = extensively hydrolyzed casein-based formula; AD = atopic dermatitis; RR = relative risk.

For infants who cannot be exclusively breastfed or when breastfeeding stops before 6 months, the best choice is the use of modern infant formulas. Feeding low-protein formulas (1.8–1.9 g protein/100 kcal) now enables infants to grow according to the WHO growth standards, which are based on predominantly and exclusively breastfed infants [21]. In particular, the 'accelerated' weight gain which was reported when high-protein formulas were fed was no longer observed. Infants at risk of allergic diseases (i.e. as having at least 1 parent or biological sibling with a history of allergic disease) benefit from exclusive breastfeeding or feeding of a whey-based partially hydrolyzed formula (PHF-W; hypoallergenic formula). In a meta-analysis, the risk for allergy and atopic disease was compared in infants at risk of allergy who received either PHF or cow's milk-based formula at least until 4 months of age. Until 36 months of age, there was a significant risk reduction (incidence, cumulative incidence, and period prevalence) for both atopic disease and allergic diseases during most analyzed periods [22]. Recently, the German GINI study group published the 10-year follow-up results of infants at risk who had received PHF-W, extensively hydrolyzed casein formula (EHF-C), or

**Table 5.** Calculated infant feeding patterns in the age groups 6–12 and 12–24 months in 20 developing countries (see table 2)

| Feeding | Infants aged 6–12 months % (n = 43,147) | Infants aged 12–24 months % (n = 78,170) |
|---|---|---|
| Exclusive BF | 3 | 2 |
| NEBF | 88 | 72 |
| NEBF + S/NML | 42 | 38 |
| NEBF + S/NML/ML | 18 | 19 |
| NEBF + F/ML/NML/S | 10 | 6 |
| NEBF + other | 18 | 9 |
| No BF, other food | 9 | 26 |
| No BF, other food/F | 3 | 5 |

Database: DHS, USAID. BF = Breastfeeding; NEBF = nonexclusive breastfeeding; NML = non-milk liquids; S = solids; ML = milk liquids; F = formula.

cow's milk-based formula during the first 4 months of their life [23]. The relative risk for the cumulative incidence of any allergic disease (table 4; intention-to-treat analysis) was 13 and 17% lower for PHF-W and EHF-C, respectively, compared with standard cow's milk formula. The corresponding figures for atopic eczema and dermatitis were –18 and –28%, respectively. In the per-protocol analysis (n = 988) effects were even stronger. The authors of the biggest well-controlled study so far concluded that the significant preventive effect persisted until 10 years of age. They also pointed out that the preventive effect was similar, but not better, than in breastfed infants. From a health-economic point of view, there is no doubt that the cheapest and best way to prevent atopic disease in a child at risk is exclusive breastfeeding. If breastfeeding is not possible, it has recently been shown that the hypoallergenic formula studied (i.e. PHF-W) was cost effective and even cost saving until 6 years of age when compared to cow's milk-based formula both for health insurances and the societal perspective [24].

Infants at risk of vertical transmission or HIV infected at an early age in developing countries should be exclusively breastfed and receive antiretroviral medication [25, 26]. Those recommendations are valid in the community setting even though the quality of HIV clinical trials has recently been challenged [27]. There has been significant progress towards the goal of eliminating vertical transmission of HIV. Guidelines published by the WHO in 2010 place strong emphasis on exclusive breastfeeding until 6 months and continuation of breastfeeding until 12 months, in some developing countries overturning a prior emphasis on formula feeding. However, merely changing guidelines is not sufficient to change practice, particularly with regard to culturally sanctioned forms of feeding, such as mixed feeding [26]. Structural, social, and contextual barriers to effective implementation of the guidelines still exist and need to be addressed. If exclusive breastfeeding in developing countries is not possible or its duration is too short, a study in South Africa showed that the use of acidified infant formulas under the supervision of health care professionals can be considered [28].

## Infants and Young Children 6–24 Months

Continuation of breastfeeding is recommended during the age period 6–24 months [1, 3–5]. Data from the DHS in 20 developing countries (table 5) indicated that almost 9 out of 10 infants were still breastfed between 6 and 12 months, but only 3% were exclusively breastfed. Fifty percent of nonexclusively breastfed infants received milk-based weaning food. Formulas played a minor role during that age period, because only 14% of the infants were exposed. Higher maternal education was associated with use of milk liquids, formula, non-milk liquids, and solid foods but not with breastfeeding. Maternal work status was associated with use of formula, but no association with other food types was found. Between 6 and 12 months, breastfeeding was associated with lower trends of disease probability. Weight z-scores and percentages of stunting and wasting were similar in breastfed and non-breastfed infants (table 6). Breastfed infants who were fed milk-based weaning foods had significantly higher weight z-scores than breastfed infants who received only solids and non-milk liquids.

Seven out of 10 young children were still breastfed between 12 and 24 months. The survey did not allow analysis of data from mothers with short birth intervals. In the case of short birth intervals, percentages of young children who are still breastfed during the second year of their life are probably much lower. Less than 50% of breastfed infants received milk-based weaning foods. Only 12% of all infants were exposed to formula. Higher maternal education was associated with lower breastfeeding rates and more frequent use of formula and milk liquids. Maternal work status was not associated with any specific feeding pattern. Stunting and wasting rates were high and corresponded to international estimates [6, 29]. Continuation of breastfeeding during the second year of life was associated with slightly lower length and weight z-scores and no difference in disease prevalence. Higher weaning food diversity between 12 and 24 months was not associated with better growth outcome and lower disease probability. Interventions to improve length and weight z-scores and lower the high stunting rates include nutrition education and provision of complementary foods. However, evidence for the effectiveness of complementary feeding strategies at present is insufficient. Bhutta et al. [20] indicate that further effectiveness trials are needed in food-insecure populations with standardized foods (prefortified or nonfortified), duration of intervention, outcome definition, and cost effectiveness.

In developed countries and higher socioeconomic population segments in developing countries [6], an important focus of early nutrition is on the prevention of

**Feeding of formulas with a high protein content led to higher weight and body mass index at 1 and 2 years of age.**

later obesity. It is well documented that maternal overweight and obesity are risk factors, even in breastfed infants [21, 30, 31]. Protein intakes of breastfed infants are lower than those of formula-fed infants, and this is believed to be the reason why breastfed infants are at lower risk of obesity later in life than formula-fed infants [32, 33]. Protein requirements between 9 and 12 months are about 1 mg/kg/day [3, 34], which corresponds to about 1.3 g protein per 100 kcal consumed. The recommended protein content of follow-up formulas (www.codexalimentarius.org/) exceeds these levels by considerable margins, especially in the case of growing-up milks, which are offered to young children from 12 months onwards. Direct evidence of the growth-stimulating effect of high-protein feedings has been provided by the prospective, randomized trial conducted in the European Obesity Project [35]. The feeding of formulas with a high protein content (2.2 g/100 kcal from 0 to 4 months; 4.60 g/100 kcal from 4 to 12 months) led to increased weight and body mass index at 1 and 2 years of age. It is worth noting that the lower-protein formula used in that trial between 4 and 12 months still had a protein content of 2.20 g/100 kcal, which was greater than the required level by a considerable margin. There should, therefore, be room for reducing the protein content of formulas without compromising protein intakes necessary for normal growth. Such a formula could have a protein concentra-

**Table 6.** Feeding patterns, growth, and health at 6–24 months: counterfactual regression analysis[1]

| Feeding groups | Length z-score[2] | Weight z-score[2] | Stunting[3] | Wasting[3] | Diarrhea[4] | Fever[4] | Cough[4] |
|---|---|---|---|---|---|---|---|
| *Age 6–12 months (n = 33,723); stunting 24%; wasting 11%* | | | | | | | |
| EBF vs. no BF | −0.076 (−0.217 to 0.064) | 0.068 (−0.066 to 0.203) | −0.4 (−5.0 to 4.2) | 0.0 (−3.7 to 3.6) | −2.7 (−7.2 to 1.8) | −0.1 (−4.8 to 4.5) | −0.5 (−5.2 to 4.2) |
| EBF vs. NEBF | **−0.315 (−0.531 to −0.099)** | 0.110 (−0.073 to 0.292) | 0.5 (−5.8 to 6.8) | −1.3 (−6.3 to 3.7) | −4.3 (−10.4 to 1.7) | −3.0 (−9.3 to 3.3) | −4.6 (−11.2 to 2.0) |
| NEBF vs. no BF | **−0.244 (−0.402 to −0.086)** | 0.048 (−0.078 to 0.174) | 1.2 (−3.0 to 5.5) | −1.7 (−5.1 to 1.7) | −1.7 (−6.0 to 2.7) | −3.0 (−7.6 to 1.6) | −4.5 (−9.3 to 0.3) |
| NEBF + NML/ML/S vs. NEBF + NML/S | −0.026 (−0.091 to 0.039) | 0.036 (−0.023 to 0.095) | −0.3 (−2.5 to 1.9) | −0.9 (−2.5 to 0.7) | 0.7 (−1.4 to 2.7) | 0.6 (−1.7 to 2.8) | −0.1 (−2.3 to 2.0) |
| NEBF + NML/ML/S/F vs. NEBF + NML/S | −0.070 (−0.202 to 0.062) | **0.134 (0.009 to 0.259)** | 0.2 (−3.8 to 4.1) | −1.8 (−4.9 to 1.4) | 2.2 (−1.9 to 6.3) | 1.7 (−3.0 to 6.4) | −2.6 (−7.3 to 2.0) |
| *Age 12–24 months (n = 62,496); stunting 45%; wasting 14%* | | | | | | | |
| EBF vs. no BF | **−0.156 (−0.306 to −0.005)** | **−0.132 (−0.244 to −0.021)** | 3.3 (−1.5 to 8.2) | 3.3 (−0.5 to 7.1) | −2.0 (−5.9 to 2.0) | **−4.5 (−8.9 to −0.2)** | −3.5 (−7.8 to 0.9) |
| EBF vs. NEBF | −0.022 (−0.169 to 0.126) | −0.050 (−0.158 to 0.057) | 1.6 (−3.0 to 6.3) | 1.7 (−1.9 to 5.3) | −2.8 (−6.6 to 1.1) | **−5.5 (−9.7 to −1.3)** | −4.0 (−8.3 to 0.2) |
| NEBF vs. no BF | **−0.141 (−0.188 to −0.094)** | **−0.087 (−0.124 to −0.050)** | **2.0 (0.5 to 3.6)** | **1.8 (0.6 to 2.9)** | 0.8 (−0.4 to 2.1) | 0.9 (−0.5 to 2.4) | 0.6 (−0.9 to 2.1) |

EBF = Exclusive breastfeeding; BF = breastfeeding; NEBF = nonexclusive breastfeeding; NML = non-milk liquids; S = solids; ML = milk liquids; F = formula. [1] For countries, see table 2. [2] Differences in z-scores between feeding groups (95% CI). [3] Percentage differences between feeding groups (95% CI). [4] Probability of disease. Percentage differences between feeding groups (95% CI).

tion of <2.20 g/100 kcal but >1.30 g/100 kcal. Indeed, recent studies indicate that feeding low-protein formulas (1.61–1.65 g/100 kcal) between 3 and 12 months is safe and resulted in lower weight gain and body mass index in infants of obese [36] and nonobese mothers [37]. Lower IGF-1 levels in plasma were observed in infants of obese mothers who received the low-protein formula [36]. Low-protein formulas could be the next formula generation for infants older than 3 months and young children.

## Conclusions

Nutrition during the first 2 years of life has short- and long-term effects on health. Both LBW and term infants benefit from breastfeeding. Breastfed LBW infants need protein and mineral supplements to achieve their growth potential. The DHS survey in developing countries confirms the growth- and health-promoting effect of exclusive breastfeeding from 0 to 6 months in 20 developing countries. Stunting and wasting rates between 6 and 24 months are high, but no clear associations exist between feeding patterns and disease outcome. In developed countries, randomized clinical trials show the health-promoting effects of hypoallergenic and low-protein formulas in nonbreastfed infants.

## Disclosure Statement

F.H. is the chairman of the Nestlé Nutrition Institute, a Swiss Association and separate legal entity, which receives funding from Nestec Ltd., Switzerland. P.D. works at the Nestlé Research Centre, Lausanne, Switzerland. All other authors have no conflicts of interest. The study was supported by an educational grant of the Nestlé Nutrition Institute.

## References


1 World Health Organization: Global strategy for infant and young child feeding. 2003. http://whqlibdoc.who.int/publications/2003/9241562218.pdf (accessed September 25, 2012).

2 Agostoni C, Buonocore G, Carnielli VP, De Curtis M, Darmaun D, Decsi T, Domellöf M, Embleton ND, Fusch C, Genzel-Boroviczeny O, Goulet O, Kalhan SC, Kolacek S, Koletzko B, Lapillonne A, Mihatsch W, Moreno L, Neu J, Poindexter B, Puntis J, Putet G, Rigo J, Riskin A, Salle B, Sauer P, Shamir R, Szajewska H, Thureen P, Turck D, van Goudoever JB, Ziegler EE; ESPGHAN Committee on Nutrition: Enteral nutrient supply for preterm infants: commentary from the European Society of Paediatric Gastroenterology, Hepatology and Nutrition Committee on Nutrition. J Pediatr Gastroenterol Nutr 2010;50:85–91.

3 ESPGHAN Committee on Nutrition, Agostoni C, Braegger C, Decsi T, Kolacek S, Koletzko B, Michaelsen KF, Mihatsch W, Moreno LA, Puntis J, Shamir R, Szajewska H, Turck D, van Goudoever J: Breast-feeding: a commentary by the ESPGHAN Committee on Nutrition. J Pediatr Gastroenterol Nutr 2009;49:112–125.

4 Greer FR, Sicherer SH, Burks AW; American Academy of Pediatrics Committee on Nutrition; American Academy of Pediatrics Section on Allergy and Immunology: Effects of early nutritional interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, timing of introduction of complementary foods, and hydrolyzed formulas. Pediatrics 2008;121:183–191.

5 Section on Breastfeeding; Johnston M, Landers S, Noble L, Szucs K, Viehmann L: Breastfeeding and the use of human milk. Pediatrics 2012;129:e827–e841.

6 Black RE, Victora CG, Walker SP, Bhutta ZA, Christian P, de Onis M, Ezzati M, Grantham-McGregor S, Katz J, Martorell R, Uauy R; the Maternal and Child Nutrition Study Group: Maternal and child undernutrition and overweight in low-income and middle-income countries. Lancet 2013, DOI: 10.1016/S0140-6736(13)60937-X.

7 Ziegler EE: Meeting the nutritional needs of the low-birth-weight infant. Ann Nutr Metab 2011;58(suppl 1):8–18.

8 Miller J, Makrides M, Gibson RA, McPhee AJ, Stanford TE, Morris S, Ryan P, Collins CT: Effect of increasing protein content of human milk fortifier on growth in preterm infants born at <31 wk gestation: a randomized controlled trial. Am J Clin Nutr 2012;95:648–655.

9 Ehrenkranz RA, Dusick AM, Vohr BR, Wright LL, Wrage LA, Poole WK: Growth in the neonatal intensive care unit influences neurodevelopmental and growth outcomes of extremely low birth weight infants. Pediatrics 2006;117:1253–1261.

10 Ehrenkranz RA, Das A, Wrage LA, Poindexter BB, Higgins RD, Stoll BJ, Oh W; Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network: Early nutrition mediates the influence of severity of illness on extremely LBW infants. Pediatr Res 2011;69:522–529.

11 Cooke R, Embleton N, Rigo J, Carrie A, Haschke F, Ziegler E: High protein pre-term infant formula: effect on nutrient balance, metabolic status and growth. Pediatr Res 2006;59:265–270.

12 Ziegler EE, Carlson SJ, Nelson SE: Interventional strategies to promote appropriate growth; in Bhatia J, Bhutta ZA, Kalhan SC (eds): Maternal and Child Nutrition: The First 1,000 Days. Nestle Nutr Inst Workshop Ser vol 74. Basel, Karger, 2013, pp 183–194.

13 Ozanne SE, Hales CN: Lifespan: catch-up growth and obesity in male mice. Nature 2004;427:411–412.

14 Leunissen RW, Kerkhof GF, Stijnen T, Hokken-Koelega A: Timing and tempo of first-year rapid growth in relation to cardiovascular and metabolic risk profile in early adulthood. JAMA 2009;301:2234–2242.

15 Singhal A, Cole TJ, Fewtrell M, Kennedy K, Stephenson T, Elias-Jones A, Lucas A: Promotion of faster weight gain in infants born small for gestational age: is there an adverse effect on later blood pressure? Circulation 2007;115:213–220.

16 Singhal A, Kennedy K, Lanigan J, Fewtrell M, Cole TJ, Stephenson T, Elias-Jones A, Weaver LT, Ibhanesebhor S, MacDonald PD, Bindels J, Lucas A: Nutrition in infancy and long-term risk of obesity: evidence from 2 randomized controlled trials. Am J Clin Nutr 2010;92:1133–1144.

17 Ruel MT, Menon P. Child feeding practices are associated with child nutritional status in Latin America: innovative uses of the demographic and health surveys. J Nutr. 2002; 132: 1180-7.

18 Yarnoff BO, Allaire BT, Detzel P: Predicting the health effects of switching infant feeding practices for use in decision-making; in Singhal A, Uauy R, Black R (eds): International Nutrition: Achieving Millennium Goals and Beyond. Nestle Nutr Workshop Ser, vol 78. Basel, Karger, in press.
19 WHO Child Growth Standards. 2006. www.who.int/childgrowth/en (accessed June 12, 2013).
20 Bhutta ZA, Das JK, Rizvi A, Gaffey MF, Walker N, Horton S, Webb P, Lartey A, Black RE; The Lancet Nutrition Interventions Review Group; Maternal and Child Nutrition Study Group: Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? Lancet 2013, DOI: 10.1016/S0140-6736(13)60996-4.
21 Haschke F, Steenhout P, Grathwohl D, Haschke-Becher E: Evaluation of growth and early infant feeding: a challenge for scientists, industry and regulatory bodies. World Rev Nutr Diet 2013;106:33–38.
22 Szajewska H, Horvath A: Meta-analysis of the evidence for a partially hydrolyzed 100% whey formula for the prevention of allergic diseases. Curr Med Res Opin 2010;26:423–437.
23 von Berg A, Filipiak-Pittroff B, Krämer U, Hoffmann B, Link E, Beckmann C, Hoffmann U, Reinhardt D, Grübl A, Heinrich J, Wichmann HE, Bauer CP, Koletzko S, Berdel D; GINIplus study group: Allergies in high-risk schoolchildren after early intervention with cow's milk protein hydrolysates: 10-year results from the German Infant Nutritional Intervention (GINI) study. J Allergy Clin Immunol 2013, E-pub ahead of print.
24 Mertens J, Stock S, Lüngen M, von Berg A, Krämer U, Filipiak-Pittroff B, Heinrich J, Koletzko S, Grübl A, Wichmann HE, Bauer CP, Reinhardt D, Berdel D, Gerber A: Is prevention of atopic eczema with hydrolyzed formulas cost-effective? A health economic evaluation from Germany. Pediatr Allergy Immunol 2012;23:597–604.
25 Penazzato M, Prendergast A, Tierney J, Cotton M, Gibb D: Effectiveness of antiretroviral therapy in HIV-infected children under 2 years of age. Cochrane Database Syst Rev 2012;7:CD004772.
26 Lazarus R, Struthers H, Violari A: Promoting safe infant feeding practices – the importance of structural, social and contextual factors in Southern Africa. J Int AIDS Soc 2013;16:18037.
27 Wadman M: HIV trial under scrutiny. Nature 2013;493:279–280.
28 Velaphi SC, Cooper PA, Bolton KD, Mokhachane M, Mphahlele RM, Beckh-Arnold E, Monaheng L, Haschke-Becher E: Nutrition. Growth and metabolism of infants born to women infected with human immunodeficiency virus and fed acidified whey-adapted starter formulas. Nutrition 2008;24: 203–211.
29 Unicef: Improving child nutrition. The achievable imperative for global progress. 2013. http://www.unicef.org/publications/files/Nutrition_Report_final_lo_res_8_April.pdf (accessed June 22, 2013).
30 Agras WS, Hammer LD, McNicholas F, Kraemer HC: Risk factors for childhood overweight: a prospective study from birth to 9.5 years. J Pediatr 2004;145:20–25, erratum in J Pediatr 2004;145:424.
31 Steyn NP, Labadarios D, Nel J, Kruger HS, Maunder EM: What is the nutritional status of children of obese mothers in South Africa? Nutrition 2011;27:904–911.
32 Harder T, Bergmann R, Kallischnigg G, Plagemann A: Duration of breastfeeding and risk of overweight: a meta-analysis. Am J Epidemiol 2005;162:397–403.
33 Weng SF, Redsell SA, Swift JA, Yang M, Glazebrook CP: Systematic review and meta-analyses of risk factors for childhood overweight identifiable during infancy. Arch Dis Child 2012;97:1019–1026.
34 Dewey KG, Beaton G, Fjeld C, Lönnerdal B, Reeds P: Protein requirements of infants and children. Eur J Clin Nutr 1996;50(suppl 1):S119–S147; discussion S147–S150.
35 Koletzko B, von Kries R, Closa R, Escribano J, Scaglioni S, Giovannini M, Beyer J, Demmelmair H, Gruszfeld D, Dobrzanska A, Sengier A, Langhendries JP, Rolland Cachera MF, Grote V; European Childhood Obesity Trial Study Group: Lower protein in infant formula is associated with lower weight up to age 2 years: a randomized clinical trial. Am J Clin Nutr 2009;89:1836–1845.
36 Inostroza J, Steenhout P, Prieto R, Grathwohl D, Ziegler EE, Haschke F: Lower weight gain in infants of obese mothers who receive a low protein formula. E-PAS 2012:2820.2.
37 Fields DA, Chernausek S, Haschke F, Steenhout P, Gratwohl D, Ziegler EE: Low-protein formula: effect on infant growth from 3 to 6 months. PAS May 2013, in press.