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REVIEW ARTICLE

Health Consequences of Nutrition in Childhood and Early Infancy

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Medical and scientific studies have proven that the body's metabolic programming can be influenced by diet and nutrition from early infancy. As a result, the incidence and outcome of several metabolic diseases such as obesity, hypertension and cardiovascular disorders have been found to be associated with birth weight, growth and feeding patterns, and the body composition in early childhood. Exclusive or partial breast feeding for at least 6 months is recommended by the World Health Organization, while the European Society of Pediatric Gastroenterology Hepatology and Nutrition Committee on Nutrition recommends the introduction of complementary foods at 4–6 months of age. The fat content of the diet should not be below 25% of the energy intake in order to maintain ideal growth while dietary proteins above 15% of the energy intake is related to future obesity. Long term benefits of breast feeding include a more ideal serum lipid profile and blood pressure, improved neuro-cognitive scores, and a decreased incidence for atopic dermatitis in children who have family members with atopic diseases. Several studies have also acknowledged the long term benefits for neuro-cognitive development from certain nutrients including long-chain polyunsaturated fatty acids and docosahexaenoic acid. Meat intake has proved to be beneficial to psychomotor development. It is suggested that early introduction for complementary foods before 4 months of age is a risk factor for atopic dermatitis; while no strong evidence showed delaying weaning foods can decrease the risk for allergic diseases.

Nutrition plays a major role in determining a person's health throughout his or her entire lifespan, even as early as the intrauterine period. The nutritional status early in life may alter future metabolic programming and body composition. Feeding habits are the fundamental elements of nutrition, and are influenced by many factors, including personal and familial habits, maternal education, socioeconomic status, and cultural environment.

The source of nutrition for infants and those in early childhood mainly consists of breast milk, infant formula and complementary foods. Over the past few decades, the benefits of breastfeeding during the breastfeeding stage have been well documented for both the baby and the mother. Protection from infectious diseases and a more ideal body weight gain are the most obvious advantages.[1] Recent studies have also demonstrated a relationship between breastfeeding and the development of future health and chronic diseases. Improvements in intelligence, protection against the development of diseases such as allergy, diabetes and celiac

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disease, and an influence on blood pressure later in life have been discussed in the literature, with most of the studies being observational.

The introduction of complementary food in infancy is essential to both developmental and nutritional concerns. It can overcome insufficient supply of macronutrients and micronutrients to ensure optimal health, growth and development of young children during weaning. The World Health Organization recommends exclusive breastfeeding for the first 6 months of age,[2] while the European Society of Pediatric Gastroenterology Hepatology and Nutrition Committee on Nutrition recommends the introduction of complementary foods at 4–6 months of age.[3] Compared with those focusing on breastfeeding, studies on the consequences of different compositions of complementary feeding and the timing of its introduction are scarce. The goal of this review is to sort out and summarize the short and long-term health effects of breastfeeding and the timing and composition of complementary foods.

Growth

Infants who were exclusively breastfed from 0–6 months gained weight, length and adiposity more slowly than formula-fed infants, independent of age at the introduction of solids and maternal factors.[4] Other studies have reported that, compared with formula-fed infants, breastfed infants are slimmer at the age of 12 months, and a longer duration of breastfeeding was associated with a smaller increase in weight for age and weight for length, but not length for age.[5] According to the Boyd-Orr cohort study in 2002,[6] breastfed infants were taller in childhood and adulthood. Leg length was the major component of the height difference and was more obvious in males. The hypothesis of pituitary resetting has been mentioned in some studies. Büyükkayhan et al[7] suggested that insulin-like growth factor-1 (IGF-1) levels during the neonatal period are influenced by gestational age, birth weight and nutrition. Martin et al[8] found that, compared with formula-fed infants, IGF-1 was initially lower in breastfed infants, thus resetting the IGF–pituitary axis due to greater feedback, and resulting in higher IGF-1 levels and growth velocity in later childhood.

Although the breastfeeding rate in Taiwan has increased in the last decade, with 13% of infants with exclusive breastfeeding and 20% with breastfeeding supplemented with formula feeding at 6 months (data from Bureau of Health Promotion, Taiwan Department of Health, 2004), progress is far from the ideal goal of exclusive breastfeeding at 4–6 months. Thus, continuing the effort to promote breastfeeding is a crucial health issue.

There is little evidence as to whether the timing of the introduction of complementary foods at 4–6 months of age will affect growth in the short term.[9,10] Some studies have indicated that the baby's weight itself is an important predictive factor for the age of introducing complementary foods, with heavier infants of similar age tending to receive solid foods earlier than lighter infants.[11] The fat content of the complementary food is the major source of energy and is relevant in infant growth. Uauy et al[12] investigated Latin Americans in 19 countries and suggested that diets providing $<$22% of energy from fat and that are low in animal fats may restrict growth. The European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) Committee on Nutrition[3] recommends that the fat content of the diet should provide at least 25% of the energy intake to maintain ideal growth.

According the Nutrition and Health Survey of Taiwan's elementary school children (NAHSIT 2002), suboptimal intake of calcium, iron, zinc, thiamin and niacin are common in this age group; thus, a diet enriched with these key "problem nutrients" should be promoted in our locality.[13]

Obesity

Obesity is a complex disease that is influenced by environmental and genetic factors. Programming of body composition may start as early as the intrauterine period and low birth weight and catch-up growth after malnutrition in early childhood was found to be associated with obesity in adulthood.[14,15] During fetal growth restriction, the development of adipose tissue is altered.[16] Studies found that, despite a similar body mass index (BMI), subjects born small for gestational age had a greater percentage of body fat than subjects born appropriate for gestational age, and the fat distribution difference tended to persist throughout adulthood.[17]

Several recent systematic reviews and studies have demonstrated the protective effect of breastfeeding against childhood obesity,[18] and some even revealed a dose-response effect.[19–21] Other determinants of future obesity, such as socioeconomic status, parental obesity, smoking, birth weight and rapid weight gain in infancy may also play important roles.[22] Although a few studies have shown no significant associations between breastfeeding and obesity,[23] most reports acknowledge that breastfeeding can reduce childhood obesity.[21] It has also been noted in several systematic reviews[24,25] that infants at the highest end of the distribution for weight or body weight mass and those who experience rapid growth are at increased risk for childhood and adulthood obesity. These findings suggest that factors during or before infancy, which are related to infant growth, may contribute to future body weight distribution.

Few published studies have identified the influence of complementary feeding practices on childhood obesity. In the cohort study by Wilson et al,[26] increased fatness at age 7 was noted in children who received weaning foods before 12 weeks of age, which suggests that too-early introduction of complementary foods may be related to childhood obesity. Several studies have discussed the association between the amount of protein intake and risk for obesity. Dietary protein intake approaching 4–5 g/kg weight/day (around 16–20% of total energy intake) at 8–24 months of age was reported to be associated with overweight in later life,[27] while the association with dietary protein levels <14% of energy was not profound.[28] Several studies have tried to find an association between fat intake and weight gain or BMI in infants and toddlers, but failed to establish a significant relationship.[29,30]

In the NAHSIT (2002) study, a total of 2,405 elementary school children (1,290 boys and 1,115 girls) were surveyed. The prevalence rates of being overweight and obese were 15.5% and 14.7% in boys and 14.4% and 9.1% in girls, respectively. Obese children had higher mean levels of blood pressure, triglyceride, low-density lipoprotein (LDL)-cholesterol, uric acid and serum glutamic pyruvic transaminase, but a lower level of high density lipoprotein (HDL)-cholesterol when compared with the normal-weight children. For obese and normal-weight boys, the prevalence was 12.9% and 0.3%, respectively, for high blood pressure, 31.4% and 19.6%, respectively, for dyslipidemia, and 6.4% and 0.8%, respectively, for abnormal serum glutamic pyruvic transaminase level.[31]

Another survey in NAHSIT (2002), showed that the prevalence of metabolic syndrome (hyperlipidemia, hypertension and insulin resistance) among high school age adolescents in Taiwan was 14.99% (males 16.9%, females 13.8%), which increased with age. In a mass screening program of schoolchildren aged 6–18 years in Taiwan conducted by Wei at al, obesity was a major risk factor for the development of type 2 diabetes mellitus (T2DM) in children; the odds ratio (95% confidence interval [CI]) of T2DM in children with a BMI in the 95th percentile or higher (obesity) was 18.8 (9.22–38.5) compared with those with a BMI in below the 50th percentile. This study also revealed that the children with T2DM were more obese and had a higher rate of hypercholesterolemia and higher blood pressure.[32]

Other health risks in obese children include asthma, hepatic steatosis, sleep apnea and constipation. The psychosocial risks of social discrimination, stigmatization, low self-esteem, and impaired social functioning among obese children may also persist into adulthood.

Neurocognitive Development

Many studies have suggested a positive association between breastfeeding and cognitive development; however, many experts have implied that confounding factors, including the cultural environment, maternal education and socioeconomic status, may influence the results. In 1999, Anderson et al[33] published a meta-analysis of children aged between 6 months and 15 years old, and tried to exclude the confounding factors. After adjustment for the covariates, the increment in cognitive function was 3.16 (95% CI: 2.35, 3.98) points in breastfed children, and the benefits increased with the duration of breastfeeding. The researchers also noted that the cognitive function of preterm babies, compared with that of term babies, benefits more from breastfeeding. This finding was suggested to be due to long-chain polyunsaturated fatty acid (LCPUFA) and docosahexaenoic acid (DHA). Preterm infants accumulate less LCPUFA and DHA from their mothers due to the shorter gestation, and positive relations were observed between the amount of DHA in umbilical artery phospholipids and birth weight, head circumference and birth length.[34]

Although breast milk already contains LCPUFA, it has been suggest that additional DHA is supplied in complementary foods. Hoffman et al[35] randomly assigned breastfed infants aged 6–12 months into groups to be given baby food containing DHA-enriched egg yolk or a control baby food. After 12 months of age, they found a significant increase of 34% in red blood cell DHA levels and a greater increase in visual-evoked potential acuity in the DHA-fortified group. Other studies[36,37] have reported similar results, but all of these studies focused on children aged less than 1 year of age. Saskia el al[38] performed two 2-by-2 factorial randomized controlled double-blind trials in Australia and Indonesia. Children aged 6–12 years were randomly allocated to receive a drink either a micronutrient mix (iron, zinc, folate and vitamins A, B-6, B-12 and C), a micronutrient mix with DHA and eicosapentaenoic acid (EPA), or with both, or a placebo for 6 days a week for 12 months. The findings showed that only children who received micronutrient-fortified drinks scored better in verbal and memory tests, with or without DHA and EPA supplements. This suggests that the effect of LCPUFA on neurocognitive development may be more significant in younger children, whereas other micronutrients may still have an influence in later childhood. Meat is a rich source of micronutrients and LCPUFA, and has a positive effect on neurodevelopment. In a cohort study by Morgan et al,[39] the red and white meat diet of full-term infants, starting from 4 months, was recorded until 22 months of age. Meat intake at 4–12 and 4–16 months was positively and significantly associated with psychomotor developments at 22 months, with a dose-dependent response.

Cardiovascular Diseases

Intrauterine growth retardation and low birth weight is associated with increased risks of cardiovascular diseases and related disorders, including stroke, hypertension, and T2DM.[40–42] Some studies have proposed that, through fetal programming, nutrition in fetal life, infancy and early childhood can alter the gene expression and influence functional capacity, metabolic competence and responses to the environment in later life.[43] A cohort study by Barker et al[44] revealed that low BMI at 2 years of age and high BMI at 11 years of age were associated with later coronary events ($p<0.001$ and $p<0.05$, respectively). Similarly, other studies[45,46] revealed a high prevalence of T2DM in people who were small at birth but obese later in life. These findings indicate that retarded growth and excessive weight gain in childhood are associated with increased risk for coronary heart disease and glucose intolerance.

Many studies have tried to find an association between breastfeeding and future cardiovascular diseases. Two meta-analyses from 2003[47] and 2005[48] showed a decrease in systolic blood pressure of 1.10 mmHg and 1.40 mmHg, respectively, later in life. The results were independent of age at measurement of blood pressure and year of birth. Population-wide, a 2-mmHg decrease in diastolic pressure could reduce the prevalence of hypertension by 17% and the risk of coronary heart disease by 6%.[49] However, both studies revealed that selective publication of small studies with positive findings may have exaggerated the claims that breastfeeding in infancy reduces systolic blood pressure in later life. The results of larger studies ($n>1,000$) suggest that feeding in infancy has, at most, a modest effect on blood pressure, which is of limited clinical or public health importance.

Compared with most infant formulas, breast milk contains a higher content of cholesterol, and the blood cholesterol levels of breastfed infants are higher at the age of 4 and 8 weeks.[50] Many studies have tried to establish a relationship between future lipoprotein profiles and early infant feeding practices. According to a meta-analysis by Owen et al,[50] total cholesterol was higher in breastfed infants compared with formula-fed infants before the age of 12 months, but there was no significant difference in older children (1–16 years old). The same meta-analysis also noted a slightly reduced total cholesterol (TC) level in adults who were breastfed during infancy (mean difference in TC: 0.18 mmol/L; 95% CI: 0.30–0.06 mmol/L). Singhal et al[51] noted the LDL:HDL ratio was lower in adolescents who were fed with breast milk during infancy, and the effect was dose-responsive. Whether the effects of breast milk lipoprotein profiles and blood pressure will lead to a reduction in cardiovascular diseases later in life is still under debate. The British Boyd-Orr cohort[52] showed an inverse association between infancy breastfeeding practices and the ultrasound-measured intima-media thickness in 63–82-year-old adults, but failed to establish clear evidence of a duration-response relationship. Surprisingly, according to a cohort study by Martin et al in 2005,[53] breastfeeding was positively associated with cardiovascular disease incidence and mortality, but no dose-response effect was established. By contrast, Rich-Edwards et al[54] reported an 8% decrease in the incidence of coronary heart disease in women aged 30–55 years old who were breastfed. However, there is still no established evidence that early breastfeeding can reduce the risk and mortality of cardiovascular disease later in life.

Whether the diet during the complementary feeding period may affect future cardiovascular outcome is seldom explored. In a randomized trial conducted by Hoffman et al[55] in 1983, infants were randomly assigned to either a low or normal sodium diet. The study showed that sodium intake was positively associated with blood pressure during the first 6 months of life. A 15-year follow-up study of the same participants was conducted in 1997 by Geleijnse et al.[56] Both systolic and diastolic blood pressure were lower (3.6 mmHg and 2.2 mmHg, respectively) in the low-salt diet group, compared with the control group. This indicates that sodium intake during infancy may be a key factor to influence blood pressure later in life. Other nutrients, including protein[57] and LCPUFA,[58] have also been related to reduced levels of blood pressure in randomized studies. However, the cardiovascular effects of complementary food components still require further study and analysis before making specific recommendations.[3]

Allergic Diseases

Previous studies on whether breastfeeding reduces the risk for allergic diseases such as asthma, atopic

Table Health consequences of childhood and early infant nutrition (with references)

Health consequence	Breastfeeding	Complementary foods
Child growth	1. Exclusively breastfed infants are slimmer before the age of 12 months[4,5] 2. Breastfed infants are taller in child hood and adulthood[6]	1. Heavier infants receive solid foods earlier than lighter infants[11] 2. Fat content of diet should be at least 25% of the energy intake for ideal growth[3]
Obesity	1. Breastfeeding may prevent future obesity with a dose-responsive effect[20,21] 2. Low birth weight and catch-up growth are related to future obesity[14,15]	1. Too early feeding of weaning foods may increase future risk of obesity[26] 2. Protein content should be less than 16% of diet to prevent obesity[27]
Neuro-cognitive development	1. Breastfed children have better neurocognitive functions[33] 2. Preterm infants benefit even more from breastfeeding[34]	1. Additional DHA supplement in complementary food is suggested[35–37] 2. Meat intake is positively related to psychomotor development[39]
Cardiovascular diseases	1. Breastfeeding reduces future blood pressure[47,48] 2. Lower LDL/HDL ratio in adolescents who were breastfed[51] 3. No consistent evidence that breastfeeding may reduce the risk and mortality of cardiovascular diseases[52–54]	3. Salt intake in infancy is a factor to future blood pressure[55,56] 4. No established recommendations of complementary feeding on future cardiovascular outcomes[3]
Allergic diseases	1. Breastfeeding for at least 4 months may prevent future atopic dermatitis and early childhood wheezing with high risk families[60,61]	1. Early introduction of complementary foods before 4 months of age increases the risk for atopic dermatitis[62] 2. No established protective effect by delaying complementary foods[63,64]

DHA = docosahexaenoic acid; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

dermatitis and hay fever in the general population have demonstrated inconclusive and conflicting results.[59,60] However, breastfeeding for at least 4 months is still recommended in children from families at high-risk for allergies, because many studies have shown findings that support the protective effect of breastfeeding against future atopic dermatitis and early childhood wheezing.[60,61] A cohort study by Benn et al[60] found no overall effect of breastfeeding on atopic dermatitis; however the effect of exclusive breastfeeding for 4 months depended on the parental history of allergic diseases, and the tendency toward protection increased when more family members were diagnosed with atopic diseases.

There is evidence from observational studies that the introduction of complementary foods before 4 months of age may increase the risk for atopic dermatitis, both in short-term and long-term follow-up.[62] Although it is thought that delaying the introduction of solid foods could decrease the risk of atopic diseases, many studies have shown controversial results. No association was established between the timing of the introduction of solid foods and the occurrence of eczema or wheezing during the 1st year of life in a birth cohort study in Dundee.[63] Some studies even suggested that delaying the introduction of solid foods actually increases the risk of allergic sensitization.[64,65] A cohort study in Australia consisting of 516 children with family history of asthma showed no significant association between the duration of breastfeeding or the timing of the introduction of solid foods and protection against allergic disease at the age of 5 years, and noted an increased risk of atopy in children breastfed for 6 months or more and who were introduced to solid foods after 3 months.[66] The potential nutritional consequences of delaying or avoiding specific foods must also be considered. Therefore, with the currently available data, there is no evidence that delaying or avoiding allergic foods can reduce allergic diseases, irrespective of whether the infants are at high risk or not.

Conclusions

Breastfed infants have been observed to grow more slowly before 12 months of age, but tend to be taller after late childhood, compared with formula-fed infants. The fat content of the diet of infants should be at least 25% of the energy intake to maintain ideal growth, and the protein content of the diet should be 16% or less to reduce future obesity risk. Breastfeeding has a long-term positive impact on neurocognitive development, and the effect is more noticeable in children born prematurely. Meat is a rich source of several micronutrients and enhances psychomotor development. Although breastfeeding has varying effects on blood pressure and lipid profiles, there is no established association between breastfeeding and the risk and outcome of cardiovascular diseases. Dietary components in infancy, including sodium, protein, and LCPUFA, were found to have an influence on future metabolic profiles, but more studies are needed to establish their association with metabolic diseases. Primary prevention against allergic diseases by breastfeeding for the first 4–6 months in high-risk infants is recommended; however, the protective effect in the general population is still controversial. Delaying the introduction of complementary foods has no effect on reducing the risk of allergen sensitization, but the introduction of weaning foods before 4 months of age may increase the risk of atopic dermatitis, and should be avoided. Infants born small for gestation age and children who experience a rapid increase in body weight are at risk for developing future metabolic diseases, including obesity, cardiovascular disease and T2DM.

Nutrition in infancy and early childhood is a cornerstone in the development of life-long health. Table shows the summary and references of this review. We should pay more attention to its importance and acknowledge its long-term influence on and relationship with adult disease. As Professor Lawrence T. Weaver in Glasgow has said, “Pediatricians should be more interested in adult disease because the child is the father of the man”.[67]

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