Age at Weaning and Infant Growth: Primary Analysis and Systematic Review

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Objective To test whether earlier age at weaning (age 3-6 months) may promote faster growth during infancy.
Study design Weaning at age 3.0-7.0 months was reported by 571 mothers of term singletons in a prospective birth cohort study conducted in Cambridge, UK. Infant weight and length were measured at birth and at age 3 months and 12 months. Anthropometric values were transformed into age- and sex-adjusted *z*-scores. Three linear regression models were performed, including adjustment for confounders in a stepwise manner. Measurements at age 3 months, before weaning, were used to consider reverse causality.
Results Almost three-quarters (72.9%) of infants were weaned before age 6 months. Age at weaning of 3.0-7.0 months was inversely associated with weight and length (but not with body mass index) at 12 months (both $P \leq .01$, adjusted for maternal and demographic factors). These associations were attenuated after adjustment for type of milk feeding and weight or length at age 3 months (before weaning). Rapid weight gain between 0 and 3 months predicted subsequent earlier age at weaning ($P = .01$). Our systematic review identified 2 trials, both reporting null effects of age at weaning on growth, and 15 observational studies, with 10 reporting an inverse association between age at weaning and infant growth and 4 reporting evidence of reverse causality.
Conclusion In high-income countries, weaning between 3 and 6 months appears to have a neutral effect on infant growth. Inverse associations are likely related to reverse causality. *(J Pediatr 2015;167:317-24)*.

The introduction of semisolid or solid foods to an infant, whether breast-fed or formula milk-fed, is an important dietary transition (termed here "weaning"). Smooth foods are typically introduced first, followed by lumpy and finger foods. It should be noted that age at weaning as defined here is not synonymous with the duration of exclusive breastfeeding, because many infants are also given formula milk before being introduced to complementary foods.

Previously, the World Health Organization (WHO) recommended that infants be exclusively breastfed for at least 4 months and subsequently introduced to complementary foods at age 4-6 months.[1] In 2001, the WHO updated this guideline to recommend that infants be exclusively breastfed for the first 6 months of life and then introduced to complementary foods.[2-4] The WHO also currently recommends that formula milk fed infants be introduced to complementary foods beginning at age 6 months.[5]

The appropriateness of the updated WHO recommendation for high-income countries, where concerns about food safety and availability, as well as infectious diseases, are less prevalent, is a matter of current debate.[6] The American Academy of Pediatrics and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition both have expressed general support for the updated WHO recommendations; however, both organizations suggest that complementary foods may be introduced at age 4-6 months, depending on the achievement of developmental milestones and the availability of safe complementary foods.[6-8] The United Kingdom, Australia, and Canada have adopted the updated WHO recommendation,[9-11] but adherence is poor. In the most recent UK Infant Feeding Survey conducted in 2010, 7 years after adoption of the current WHO recommendation, only 30% of mothers had introduced complementary foods by age 4 months, and 75% had done so by age 5 months.[9]

The present study focuses on one aspect of the multifaceted debate over the optimal age at weaning: the impact on growth during infancy. We report a primary analysis of the association between age at weaning and infant growth, as well as a review of the existing literature. Our primary analysis addressed 3 themes highlighted in the literature. First, we investigated the suggestion that earlier weaning is associated with faster infant growth and weight gain.[12-14] Second, we explored the potential role of reverse causality in the relationship between early age at weaning and faster infant growth.[15] Third, we examined the

BMI	Body mass index
CBGS	Cambridge Baby Growth Study
WHO	World Health Organization

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possible interaction between age at weaning and type of pre-weaning milk feeding (breast or formula) on infant growth.[16,17] Our primary analysis and literature review focused largely on the comparison of age at weaning between 3 and 6 months. Studies of very early weaning (age ≤3 months) are discussed only briefly.

Methods

The primary analysis was based on participants from the Cambridge Baby Growth Study (CBGS), a prospective longitudinal birth cohort study. Mothers were recruited from ultrasound clinics at Rosie Maternity Hospital in Cambridge, UK, between August 2001 and August 2009. Mothers aged <16 years and mothers unable to give informed consent were excluded from the study. Mother–infant pairs were included in this analysis if they met the following inclusion criteria: (1) full-term birth (≥36 weeks); (2) singleton birth; (3) recorded age at weaning between 3.0 and 7.0 months; and (4) recorded anthropometric measurements at birth, 3 months, and 12 months. A total of 571 mother–infant pairs met these inclusion criteria out of the 1121 CBGS pairs asked to record age at weaning at age 12 months (from August 2005 onward). The study was approved by the local Cambridge Research Ethics Committee, and all mothers gave written informed consent.

Anthropometry

Infant weight and length were measured at birth, 3 months, and 12 months by trained pediatric research nurses. Weight was measured with electronic scales to the nearest 1 g. Supine length was measured with a Kiddimeter (Holtain Ltd, Crymych, UK) to the nearest 0.1 cm. Body mass index (BMI) was calculated using the formula weight (kg)/height (m^2). Following the current national recommendations, weight, length, and BMI at birth were transformed into age and sex-adjusted *z*-scores by comparison with the British 1990 Growth Reference,[18] and weight, length, and BMI at age 3 months and 12 months were transformed into age- and sex-adjusted *z*-scores by comparison with the 2006 WHO growth standard.[19]

Dietary Assessment

Type of milk feeding at the infant's 3-month research clinic visit was assessed by questionnaire. Infants were categorized into 3 groups: exclusively breastfed, exclusively formula fed, or mixed fed at 3 months. At 12 months, mothers retrospectively reported when their infant had first been introduced to smooth, lumpy, and finger foods. For each infant, the earliest of these 3 ages was defined as the age at weaning, which was then classified as 3.00-3.99, 4.0-4.9, 5.0-5.9, and 6.0-6.9 months.

Statistical Analyses

The Pearson χ^2 test and ANOVA were used to compare maternal and infant characteristics across the 4 age at weaning groups. ANOVA also was used to compare mean weight, length, and BMI z-scores at birth and at age 3 months and 12 months across the age at weaning groups. Multiple linear regression models were applied to assess the linear association between age at weaning and anthropometric *z*-scores at birth and at age 3 months and 12 months. Three models were performed. Model 1 adjusted only for potential demographic confounders: infant age and sex (*z*-scores used) and maternal age, parity, and deprivation score. Maternal smoking status, marital status, education level, and prepregnancy BMI were not included in the model, because the number of mothers in 1 or more categories was insufficient. Model 2 was also adjusted for type of milk feeding at age 3 months. Model 3 was also adjusted for the same growth outcome measurement (weight, length, or BMI), but at the preceding time point (birth or 3 months). To test the interaction between age at weaning and type of milk feeding at 3 months (breast vs formula), the product of these variables was entered as an additional variable into model 2. All statistical analyses were performed using SPSS version 22 (IBM, Armonk, New York).

Literature Review

A systematic search was carried out in PubMed and Web of Science for the following terms: infant* AND (growth OR length OR height OR weight OR BMI) AND (time OR timing) AND (complementary OR wean*) AND (food* OR feed*).

Articles were reviewed from database inception through June 30, 2014. Additional studies were retrieved via hand searches of publication lists of selected studies and review articles. Studies had to meet the following inclusion criteria: (1) conducted in a high-income country in North America, Europe, or Australia; (2) participants full-term, single births not selected by disease or risk group; (3) exposure defined as age at introduction of solids, not duration of exclusive breastfeeding or introduction of specific solids; (4) anthropometric outcomes measured at or before age 24 months; (5) papers written in English; and (6) nonduplication of reported results. A formal meta-analysis was not possible owing to heterogeneity in the categorization of age at weaning and in the timing of growth outcome measures among included studies. Instead, results were summarized in table format.

Results

Of the 571 infants included, 44 (7.7%) were weaned at age 3.0-3.9 months, 146 (25.6%) at age 4.0-4.9 months, 226 (39.6%) at age 5.0-5.9 months, and 155 (27.1%) at age 6.0-6.9 months. Earlier age at weaning was associated with male sex, formula milk feeding, and younger maternal age (all $P < .01$; **Table I**). Similar trends were observed with lower maternal education level and higher prepregnancy BMI, but the numbers in some of these categories were insufficient to meet the assumptions of the Pearson χ^2 test.