Introduction

Early nutrition and growth are important factors in the regulation of both early and long-term health, and many papers on this topic are published every year. For this chapter, we have included 16 papers, which we found of special interest published during the period from July 1, 2018, to June 30, 2019. We have divided them into 8 topics, which are shown in the box below.

In recent years, there has been an increasing interest in breast milk composition with many publications from both low- and middle-income countries and high-income countries. Many of these papers focus on growth and obesity and overall show that breast milk composition has a huge role to play. Furthermore, several papers have examined maternal factors determining breast milk composition. Many different components have been examined including macronutrient content, human milk oligosaccharides, hormones, micronutrients, immune factors, fatty acids, and other bioactive compounds. We have therefore included several papers assessing breast milk composition as well as discussing some of the other papers in the light of the interesting findings on breast milk composition.

The growth patterns in early infancy, including changes in body composition, are increasingly being shown to be influenced by feeding practices and to have long-term health effects. In recent years, multiple studies have examined infants experiencing rapid growth in early infancy, and there is convincing evidence that this is associated with an increased risk of overweight, obesity, and metabolic problems later in life. Recent studies are trying to explain further the details of and the mechanisms behind these associations, including the role of complementary feeding.
We have included a selection of what we find are the most interesting papers on the effects of early nutrition from the last year. Together with the chapters, on the same topics in the Yearbooks from 2016, 2017, 2018, and 2019, this gives a summary of what has happened within this field during recent years.

### Key articles reviewed for this chapter

#### Rapid Early Weight Gain

**Infant formula feeding practices associated with rapid weight gain: a systematic review**  
*Matern Child Nutr* 2018;14:e12602

**Infant feeding and weight gain: separating breast milk from breastfeeding and formula from food**  
Azad MB, Vehling L, Chan D, Klopp A, Nickel NC, McGavock JM, Becker AB, Mandhane PJ, Turvey SE, Moraes TJ, Taylor MS, Lefebvre DL, Sears MR, Subbarao P, on behalf of the CHILD Study Investigators  
*Pediatrics* 2018;142:e20181092

#### Excessive weight gain followed by catch-down in exclusively breastfed infants: an exploratory study

Larsson MW, Lind MV, Larnkjær A, Due AP, Blom IC, Wells J, Lai CT, Mølgaard C, Geddes DT, Michaelsen KF  
*Nutrients* 2018;10:1290

#### Breast Milk Composition and Body Composition

**Carbohydrates in human milk and body composition of term infants during the first 12 months of lactation**  
*Nutrients* 2019;11:1472

**Bioactive components in human milk are differentially associated with rates of lean and fat mass deposition in infants of mothers with normal vs. elevated BMI**  
Young BE, Levek C, Reynolds RM, Rudolph MC, MacLean P, Hernandez TL, Friedman JE, Krebs NF  
*Pediatr Obes* 2018;13:598–606

**Human milk short-chain fatty acid composition is associated with adiposity outcomes in infants**  
Prentice PM, Schoemaker MH, Vervoort J, Hettinga K, Lambers TT, van Tol EAF, Acerini CL, Olga L, Petry CJ, Hughes IA, Koulman A, Ong KK, Dunger DB  
*J Nutr* 2019;149:716–722
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<th>Duration of Breastfeeding and Growth</th>
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<td>Duration of breastfeeding and early growth: a systematic review of current evidence</td>
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<td>Breastfeed Med 2019;14:218–229</td>
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<td>Breastfeeding and growth during infancy among offspring of mothers with gestational diabetes mellitus: a prospective cohort study</td>
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<td>Gunderson EP, Greenspan LC, Faith MS, Hurston SR, Quesenberry CP Jr on behalf of the SWIFT Offspring Study Investigators</td>
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<td>Pediatr Obes 2018;13:492–504</td>
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<th>Mode of infant feeding, eating behaviour and anthropometry in infants at 6-months of age born to obese women: a secondary analysis of the UPBEAT trial</th>
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<td>Patel N, Dalrymple KV, Briley AL, Pasupathy D, Seed PT, Flynn AC, Poston L and on behalf of the UPBEAT Consortium</td>
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<td>BMC Pregnancy Childbirth 2018;18:355</td>
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<th>Formula Feeding: Composition and Growth</th>
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<td>Fleddermann M, Demmelmaier H, Hellmuth C, Grote V, Trisic B, Nikolic T, Koletzko B</td>
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<td>PLoS One 2018;13:e0199859</td>
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<td>Early introduction of complementary foods and childhood overweight in breastfed and formula-fed infants in the Netherlands: the PIAMA birth cohort study</td>
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<td>Pluymen LPM, Wijga AH, Gehring U, Koppelman GH, Smit HA, van Rossem L</td>
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<th>Prospective associations of age at complementary feeding and exclusive breastfeeding duration with body mass index at 5–6 years within different risk groups</th>
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<td>Sirkka O, Vrijkotte T, Halberstadt J, Abrahamse-Berkeveld M, Hoekstra T, Seidell J, Olthof M</td>
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<td>Baby-led complementary feeding: randomized controlled study</td>
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<td>Dogan E, Yilmaz G, Caylan N, Turgut M, Gokcay G, Oguz MM</td>
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<td>Pediatr Int 2018;60:1073–1080</td>
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Rapid Early Weight Gain

Infant formula feeding practices associated with rapid weight gain: A systematic review
Appleton J1,2, Russell CG1, Laws R3, Fowler C1,4,5, Campbell K3, Denny-Wilson E1
1Faculty of Health, University of Technology Sydney, Sydney, Australia; 2Sydney Children’s Hospital, Randwick, New South Wales, Australia; 3Institute for Physical Activity and Nutrition, Deakin University, Geelong, Victoria, Australia; 4Tresillian Chair in Child and Family Health, Faculty of Health, University of Technology Sydney, Sydney, Australia; 5Tresillian Family Care Centres Belmore, Belmore, New South Wales, Australia

Excess or rapid weight gain during the first 2 years of life is associated with an increased risk of later childhood and adult overweight and obesity. When compared with breastfed infants, formula fed infants are more likely to experience excess or rapid weight gain, and this increased risk in formula fed infant populations may be due to a number of different mechanisms. These mechanisms include the nutrient composition of the formula and the way formula is prepared and provided to infants. This systematic literature review examines the association between formula feeding practice and excess or rapid weight gain. This review explores these different mechanisms and provides practical recommendations for best practice formula feeding to reduce rapid weight gain. Eighteen studies are included in this review. The findings are complicated by the challenges in study design and accuracy of measurements. Nevertheless, there are some potential recommendations for best practice formula feeding that
may reduce excess or rapid weight gain, such as providing formula with lower protein content, not adding cereals into bottles, not putting a baby to bed with a bottle, and not overfeeding formula. Although further well-designed studies are required before more firm recommendations can be made.

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Comments

Comments on this manuscript are incorporated in those on the next manuscript (Azad et al.).

Infant feeding and weight gain: separating breast milk from breastfeeding and formula from food

Azad MB1–3, Vehling L1,2, Chan D1,2, Klopp A1,2, Nickel NC2,4, McGavock JM1,2, Becker AB1,2, Mandhane PJ1, Turvey SE5,7, Moraes TJ8, Taylor MS3,9, Lefebvre DL10, Sears MR10, Subbarao P8, on behalf of the CHILD Study Investigators

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Pediatrics 2018; 142:e20181092

Objectives: Studies addressing breastfeeding and obesity rarely document the method of breast milk feeding, type of supplementation, or feeding in hospital. We investigated these practices in the CHILD birth cohort.

Methods: Feeding was reported by mothers and documented from hospital records. Weight and BMI z scores (BMIzs) were measured at 12 months. Analyses controlled for maternal BMI and other confounders.

Results: Among 2,553 mother-infant dyads, 97% initiated breastfeeding, and the median breastfeeding duration was 11.0 months. Most infants (74%) received solids before 6 months. Among “exclusively breastfed” infants, 55% received some expressed breast milk, and 27% briefly received formula in hospital. Compared with exclusive direct breastfeeding at 3 months, all other feeding styles were associated with higher BMIzs: adjusted β +0.12 (95% CI 0.01–0.23) for some expressed milk, +0.28 (95% CI 0.16–0.39) for partial breastfeeding, and +0.45 (95% CI 0.30–0.59) for exclusive formula feeding. Brief formula supplementation in hospital did not alter these associations so long as exclusive breast-feeding was established and sustained for at least 3 months. Formula supplementation by 6 months was associated with higher BMIzs (adjusted β +0.25; 95% CI 0.13–0.38), whereas supplementation with solid foods was not. Results were similar for weight gain velocity.

Conclusions: Breastfeeding is inversely associated with weight gain velocity and BMI. These associations are dose dependent, partially diminished when breast milk is fed from a bottle, and substantially weakened by formula supplementation after the neonatal period.

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Comments

Many studies have shown that early rapid weight gain is associated with later overweight and obesity. Therefore, it is important to find out how early feeding is associated

with rapid early weight gain, which is the focus of the 2 papers by Appleton et al. [1] and Azad et al. [2] addressed here. Other papers in this chapter cover specific aspects of this topic: the association between duration of breastfeeding and growth and how age at introduction of complementary feeding is associated with growth and overweight. The 2 papers, which are based on a systematic review and a large observational cohort study from Canada, confirm that formula feeding is associated with rapid weight gain. However, what these 2 papers add is how different practices of breastfeeding and formula feeding modify the association with rapid weight gain and thereby provide information that is valuable for guiding parents about optimal early nutrition that may reduce the risk of later overweight and obesity.

In the systematic review by Appleton et al. [1], they included studies focusing on how formula-feeding practices influence growth. The findings are well known, but they strengthen the evidence base behind recommendations on these aspects. The authors have also published an exploratory qualitative study on infant formula-feeding practice based on interviews with mothers from Australia. They concluded that there was a need for additional support for parents feeding their infants with formula [3]. Important aspects are the interpretation of infant cues and the amount of formula given to the infant. In that perspective, it is interesting that a recent paper tested the amount of formula powder parents added when preparing formula and found that 78% added more powder than recommended [4]. This resulted in an energy content 11% above recommendation, which may have an impact on risk of later overweight and obesity.

The cohort study from Canada also provides information, which is valuable when informing parents about optimal early feeding. The duration of breastfeeding was considerably longer in this cohort compared to many other studies. At 12 months, 43.5% were still breastfed, and at 24 months, it was 7.8%. The study confirms that breastfeeding duration was inversely associated with weight gain. The effect of duration of exclusive breastfeeding on weight gain is often analyzed without analyzing if termination of exclusive breastfeeding is due to introduction of formula or due to introduction of complementary feeding. Interestingly, in this study, infants partially breastfed at 6 months had a higher BMI at 12 months compared to exclusively breastfed infants, if the infants got formula, while infants partially breastfed were not different from exclusively breastfed infants, if the infants got complementary feeding and no infant formula. Under future directions, the authors mention that there is a need for studies analyzing body composition. In several of the papers included below, the effect of early nutrition on body composition is explored.
with EWG (HW-group) were examined at 5, 9 and 18 mo and compared to a breastfed group with normal weight gain (NW-group). Anthropometry, body composition, milk and blood samples, and milk intake were measured. Mean body-mass-index-for-age z-scores (BAZ) increased 1.93 from birth to 5 mo in the HW-group (n = 13) while the NW-group (n = 17) was unchanged (–0.01). The HW-group had 70% more fat mass at 5 mo, and then showed marked catch-down in BAZ from 5 to 18 mo (–0.84). Milk intake at 5–6 mo did not differ between the groups. In the HW-group, milk-leptin was lower at 5 mo and serum-leptin was considerably higher at 5 and 9 mo compared to the NW-group. Serum-leptin at 5 mo was positively associated with weight-for-age z-score (WAZ) and fat mass and negatively with WAZ change from 5 to 9 mo. In conclusion, breastfed infants with EWG had catch-down growth when other foods were introduced. Low milk-leptin in the HW-group may have stimulated appetite and milk intake when weight gain was high. High serum-leptin in the HW-group suggests early leptin resistance, which could impact cerebral regulation of energy intake. Larger studies are needed to confirm these results.

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Comments

In this study, we report basic data from a small cohort of infants with excessive weight gain during exclusive breastfeeding [5]. Our findings show a lower milk leptin at 5 months in the HW group, suggesting that this could stimulate appetite and milk intake. At 5 months, the milk intake was 15% higher in the HW group, but the difference was not significant. We find it likely that a key factor in the excessive weight gain was a considerably higher milk intake during the first months after birth. A limitation of the study is that we were not able to measure milk intake before the age of 5 months, when the excessive weight gain had leveled off and when the weight gain possibly was at the same level as in the NW group. We also found significant differences in the HMO pattern between the 2 groups, which was published recently [6]. Several HMOs have been associated with growth velocity in breastfed infants and a suggested mechanism is through a modification of the gut microbiota increasing the energy harvest. Milk and gut microbiota, milk lipid profile, and fecal short-chain fatty acids have been analyzed from this cohort, but data are not yet published.

Breast Milk Composition and Body Composition

Carbohydrates in Human Milk and Body Composition of Term Infants during the First 12 Months of Lactation

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Nutrients 2019;11:1472

Human milk (HM) carbohydrates may affect infant appetite regulation, breastfeeding patterns, and body composition (BC). We investigated relationships between concentrations/calculated daily intakes (CDI) of HM carbohydrates in first year postpartum and maternal/term infant BC, as well as breastfeeding parameters. BC of dyads (n = 20) was determined at 2, 5, 9, and/or 12 months post-
partum using ultrasound skinfolds (infants) and bioelectrical impedance spectroscopy (infants/mothers). Breastfeeding frequency, 24-h milk intake and total carbohydrates (TCH) and lactose were measured to calculate HM oligosaccharides (HMO) concentration and CDI of carbohydrates. Statistical analysis used linear regression/mixed effects models; results were adjusted for multiple comparisons. Higher TCH concentrations were associated with greater infant length, weight, fat-free mass (FFM), and FFMI index, and decreased fat mass (FM), FM index (FMI), %FM and FM/FFM ratio. Higher HMO concentrations were associated with greater infant FFM and FFMI, and decreased FMI, %FM, and FM/FFM ratio. Higher TCH CDI were associated with greater FM, FMI, %FM, and FM/FFM ratio, and decreased infant FFMI. Higher lactose CDI were associated with greater FM, FMI, %FM, and FM/FFM ratio and decreased FFMI. Concentrations and intakes of HM carbohydrates differentially influence development of infant BC in the first 12 months post-partum, and may potentially influence risk of later obesity via modulation of BC.

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Comments

This paper is one of 3 recent publications based on a small study analyzing the association between composition of human milk and growth and body composition [7]. The other 2 publications focus on protein (casein and whey) and on adipokines (leptin and adiponectin) [8, 9]. Strengths of the studies are detailed measurements of infant growth and body composition during the first 12 months, and that 24-h milk intake was measured so that calculated daily intakes (CDI) of the nutrients were included in the analysis. In addition to the findings in the paper analyzing carbohydrate content, they found that HMO concentrations were positively associated with fat-free mass. It is interesting that CDI of lactose was positively associated with fat mass and negatively with fat-free mass. It has been suggested that a high content of lactose in breast milk will increase milk intake [10]. However, this is partly based on studies of weanling piglets where a higher lactose content in feeds increase both feed intake and weight gain [11]. In addition to providing more energy, a hypothesis is that lactose might provide a prebiotic effect on the microbiota that could increase energy utilization [11].

Bioactive components in human milk are differentially associated with rates of lean and fat mass deposition in infants of mothers with normal versus elevated BMI

Young BE1, Levek C2, Reynolds RM3, Rudolph MC4, MacLean P4, Hernandez TL4,5, Friedman JE3,4, Krebs NF1

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Pediatr Obes 2018;13:598–606

This manuscript is also discussed in Chapter 2 by Shalitin et al, page 29. 

Objective: To model breastfed infant growth and body composition patterns over the first 4 months with multiple bioactive components of human milk (HM) and clinical factors (including maternal BMI status), which are related to growth.
**Methods:** Longitudinal observation of infant growth and body composition from 0 to 4 months among 41 predominantly breastfed infants (25 mothers of Normal-weight and 16 mothers with overweight/obesity). Fasted morning HM samples were collected at 5 time-points. Macronutrients, leptin, adiponectin, ghrelin, insulin, cytokines and \( n-6:n-3 \) esterified fatty acid ratio were measured. Infant weight-for-length Z-score (WLZ) trajectory, fat-free mass (FFM) gain, fat mass gain and %fat gain were modelled controlling for clinical covariates.

**Results:** HM insulin negatively associated with WLZ trajectory among infants of NW mothers \((p = 0.028)\), but not associated with WLZ trajectory among infants of OW/Ob mothers. HM glucose \((p < 0.001)\) was associated with slower rates of infant FFM gain. Infants of mothers with OW/Ob exhibited slower rates of FFM gain. HM protein, adiponectin and insulin concentrations, and \( n-6:n-3 \) ratio were all significant predictors in the model of infant fat mass gain \((p < 0.03)\). Any amount of formula supplementation was associated with faster fat gain \((p = 0.002)\). The model of %fat gain was similar to that of fat mass gain, excepting HM adiponectin was not a significant covariate, and a trend for maternal OW/Ob to correlate with faster %fat gain \((p = 0.056)\).

**Conclusion:** Bioactive components in HM may contribute to regulation of partitioning of body composition, and these contributions may differ between mothers of normal-weight vs. with OW/Ob.

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**Comments**

Comments on this manuscript are incorporated in those on the next manuscript (Prentice et al.).

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**Human milk short-chain fatty acid composition is associated with adiposity outcomes in infants**

Prentice PM\(^1\), Schoemaker MH\(^2\), Vervoort J\(^5\), Hettinga K\(^5\), Lambers TT\(^4\), van Tol EAF\(^4\), Acerini CL\(^1\), Olga L\(^1\), Petry C\(^1\), Hughes IA\(^3\), Koulman A\(^3\), Ong K\(^1\)\(^2\), Dunger DB\(^1\).\(^2\)

\(^1\)Department of Paediatrics, University of Cambridge, Cambridge, UK; \(^2\)Wellcome Trust-MRC Institute of Metabolic Science, NIHR Cambridge Comprehensive Biomedical Research Centre, University of Cambridge, Cambridge, UK; \(^3\)MRC Epidemiology Unit, Wellcome Trust-MRC Institute of Metabolic Science, NIHR Cambridge Comprehensive Biomedical Research Centre, Cambridge Biomedical Campus, University of Cambridge, Cambridge, UK; \(^4\)Mead Johnson Pediatric Nutrition Institute, Nijmegen, The Netherlands; \(^5\)Department of Agrotechnology and Food Sciences, Wageningen University, The Netherlands

*J Nutr* 2019;149:716–722

**Background:** Presumed benefits of human milk (HM) in avoiding rapid infancy weight gain and later obesity could relate to its nutrient composition. However, data on breast milk composition and its relation with growth are sparse.

**Objective:** We investigated whether short-chain fatty acids (SCFAs), known to be present in HM and linked to energy metabolism, are associated with infancy anthropometrics.

**Methods:** In a prospective birth cohort, HM hindmilk samples were collected from 619 lactating mothers at 4–8 week postnatally (median [IQR] age: 33.9 [31.3–36.5] years, body mass index [BMI; kg/m\(^2\)]: 22.8 [20.9–25.2]). Their offspring, born at 40.1 (39.1–41.0) week gestation with weight 3.56 (3.22–3.87) kg and 51% male, were assessed with measurement of weight, length, and skinfold thickness at ages 3, 12, and 24 months, and transformed to age- and sex-adjusted z scores. HM SCFAs were measured by 1H-nuclear magnetic resonance spectroscopy (NMR) and GC-MS. Multivariable linear regression models were conducted to analyze the relations between NMR HM SCFAs and infancy growth parameters with adjustment for potential confounders.
**Results:** NMR peaks for HM butyrate, acetate, and formic acid, but not propionate, were detected. Butyrate peaks were 17.8% higher in HM from exclusively breastfeeding mothers than mixed-feeding mothers ($p = 0.003$). HM butyrate peak values were negatively associated with changes in infant weight (standardized $B = -0.10, p = 0.019$) and BMI ($B = -0.10, p = 0.018$) between 3 and 12 months, and negatively associated with BMI ($B = -0.10, p = 0.018$) and mean skinfold thickness ($B = -0.10, p = 0.049$) at age 12 months. HM formic acid peak values showed a consistent negative association with infant BMI at all time points ($B \leq -0.10, p \leq 0.014$), whereas HM acetate was negatively associated with skinfold thickness at 3 months ($B = -0.10, p = 0.028$) and 24 months ($B = -0.10, p = 0.036$).

**Conclusions:** These results suggest that HM SCFAs play a beneficial role in weight gain and adiposity during infancy. Further knowledge of HM SCFA function may inform future strategies to support healthy growth.

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**Comments**

Human breast milk contains multiple compounds that are associated with the growth and health of the infant [10]. Potentially, the composition of breast milk can have long-lasting programming effects for the infants. When examining breast milk composition, there are several methodological considerations to take into account. One of the major difficulties is getting comparable determinations of breast milk composition across studies, as there are large differences in sampling methods. For example, the fat content differs considerably between fore- and hindmilk, and there can be differences in the content of many substances in a small sample taken by hand expression and a sample from a full emptying of a breast with a milk pump. The content of milk components might also change during the day, as well as with the feeding state of the mother. Thus, standardized study protocols for measuring breast milk composition are needed in order to get comparable results. The 2 studies above examine many different compounds and associations with growth and adiposity [12, 13]. Both studies have quite complex findings regarding the association of bioactive compounds and growth.

The study by Young et al. [12] provides interesting insights into multiple interesting bioactive compounds in human milk. One of these compounds is insulin, which has been shown to be potentially important for infant growth [14]. However, the results are somewhat inconsistent across studies, but the authors provide an interesting hypothesis about the human milk insulin levels and growth. As they found that insulin levels are only associated with WLZ trajectories in infants of normal weight mothers (during pregnancy) and not in infants of overweight or obese mothers – there might be a fetal programming of the infants of overweight or obese mothers to be less responsive to human milk insulin. This would explain why insulin seems to be associated with growth in some populations and not in others. This is a very interesting aspect, which highlights that we need both large cohorts and experimental studies in order to get a good understanding of the biology behind these effects.

The study by Prentice et al. [13] examined short-chain fatty acids (SCFAs) as bioactive compounds in breast milk. This study is an expansion of the study the group published previously where they presented interesting results of the association between breast milk macronutrients and infant growth [15]. SCFAs are synthesized by the gut microbiota and can both act as an energy substrate for the microbiota or enter circulation where they may play a role in energy metabolism. This study showed that the SCFAs butyrate was associated with lower BMI and mean skinfold thickness at 12 months. Butyrate has been shown to be important in appetite regulation [16], and thus, the relationship with BMI and mean skinfold thickness at 12 months is intriguing. Furthermore, the authors show that butyrate concentrations were higher in the breast
milk of exclusively breastfeeding mothers compared to milk of mothers both breast-
feeding and giving formula. Thus, future studies could investigate whether the link
between butyrate, slower growth, and breastfeeding might be mediated by satiety
cues in the infant. Furthermore, it should be explored how much the breast milk SC-
FAs contribute on top of the endogenously produced SCFAs, and whether or not
breast milk is a prominent source of SCFAs for the infant. These 2 studies also highlight that our understanding of the determinants of breast
milk composition is thus far limited. However, we know that some substances in breast
milk seem to be influenced by maternal factors. These include genes, maternal BMI,
infant sex, parity, mode of delivery, and lifestyle factors such as nutrition, including the
time of the last meal before sampling, and smoking [10]. However, some of these ma-
ternal factors are also related to infant growth, which can render it difficult to conclude
about causality. Future large-scale studies are needed in order to get an overview of
potential determinants of later overweight and obesity, both modifiable and nonmod-
ifiable, as well as to establish reference levels for nutrients and bioactive compounds.

Duration of Breastfeeding and Growth

Duration of breastfeeding and early growth: a systematic review of current
evidence
Patro-Gołąb B, Zalewski BM, Polaczek A, Szajewska H
Department of Paediatrics, Medical University of Warsaw, Warsaw, Poland
Breastfeed Med 2019;14:218–229

Introduction: Growth patterns of breastfed and formula-fed infants differ, but the influence of
breastfeeding duration on early growth remains unclear. The objective of this study is to evaluate
current evidence on the association of exclusive and partial breastfeeding duration with different
growth parameters during infancy.

Materials and Methods: In this systematic review, we searched MEDLINE, EMBASE, and addi-
tional sources from January 2011 until March 2018 to identify relevant cohort studies and random-
ized controlled trials (RCTs).

Results: Twenty studies that recruited infants from the general population were included. In the
developed setting, exclusive breastfeeding duration was inversely associated with weight and length
gain during infancy in observational studies. Longer duration of exclusive breastfeeding was also
associated with an earlier peak in infant body mass index (BMI). Inconsistent results were observed
for the associations of exclusive breastfeeding duration with other infant BMI characteristics. In an
RCT conducted in Iceland, exclusive breastfeeding for 4 versus 6 months did not affect infant
growth patterns. In the developing setting, conflicting findings on the associations of exclusive
breastfeeding duration with infant weight and length parameters were shown in observational stud-
ies. Shorter partial breastfeeding duration was associated with higher weight gain during infancy,
with limited or inconclusive data regarding other growth parameters.

Conclusions: Longer duration of exclusive and partial breastfeeding tended to be associated with
slower growth rates during infancy in the developed setting only. These associations seem to be
dose dependent and more pronounced in exclusively versus partially breastfed infants.

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Comments

This systematic review adds to and updates the existing literature showing that the longer an infant is exclusively and partially breastfed the slower they are growing [17]. The conclusion is that duration of breastfeeding “tended” to be associated with slower growth in high-income countries. The few studies from low- or middle-income countries found no association. It is of special interest that the only RCT in the review, where infants were randomized to start complementary feeding at 4 or 6 months, did not show an effect on growth [18]. Another approach to examine the association between breastfeeding and growth was used in a systematic review and meta-analysis by Giugliani et al. [19], where they looked at the effect of breastfeeding promotion interventions. Sixteen studies were included, of which 11 were from middle-income countries and only 2 from high-income countries, and 15 of the studies only followed growth until the age of 6 months or less. The overall conclusion of this review was that there were no effects of the interventions on weight and length and a small but significant negative effect on BMI or weight-for-height.

Breastfeeding and Growth: Mothers with Obesity or Gestational Diabetes Mellitus

Breastfeeding and growth during infancy among offspring of mothers with gestational diabetes mellitus: a prospective cohort study

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BACKGROUND: Breastfeeding (BF) may protect against obesity and type 2 diabetes mellitus in children exposed to maternal diabetes in utero, but its effects on infant growth among this high-risk group have rarely been evaluated.

OBJECTIVES: The objective of this study was to evaluate BF intensity and duration in relation to infant growth from birth through 12 months among offspring of mothers with gestational diabetes mellitus (GDM).

METHODS: Prospective cohort of 464 GDM mother-infant dyads (28% White, 36% Hispanic, 26% Asian, 8% Black, 2% other). Weight and length measured at birth, 6–9 weeks, 6 months and 12 months. Categorized as intensive BF or formula feeding (FF) groups at 6–9 weeks (study baseline), and intensity from birth through 12 months as Group 1: consistent exclusive/mostly FF, Group 2: transition from BF to FF within 3–9 months and Group 3: consistent exclusive/mostly BF. Multivariable mixed linear regression models estimated adjusted mean (95% confidence interval) change in z-scores; weight-for-length (WLZ), weight-for-age and length-for-age.

RESULTS: Compared with intensive BF at 6–9 weeks, FF showed greater increases in WLZ-scores from 6 to 9 weeks to 6 months (+0.38 [0.13 to 0.62] vs. +0.02 [−0.15 to 0.19]; p = 0.02) and birth to 12 months (+1.11 [0.87 to 1.34] vs. +0.53 [0.37 to 0.69]; p < 0.001). For 12-month intensity and duration, Groups 2 and 3 had smaller WLZ-score increases than Group 1 from 6 to 9 weeks to 6 months.
(-0.05 [-0.27 to 0.18] and +0.07 [-0.19 to 0.23] vs. +0.40 [0.15 to 0.64]; p = 0.01 and 0.07), and birth to 12 months (+0.60 [0.39 to 0.82] and +0.59 [0.33 to 0.85] vs. +0.97 [0.75 to 1.19]; p < 0.05).

Conclusions: Among offspring of mothers with GDM, high intensity BF from birth through 1 year is associated with slower infant ponderal growth and lower weight gain.

Comments
Comments on this manuscript are incorporated in those on the next manuscript (Patel et al.).

Mode of infant feeding, eating behaviour and anthropometry in infants at 6-months of age born to obese women – a secondary analysis of the UPBEAT trial
Patel N, Dalrymple KV, Briley AL, Pasupathy D, Seed PT, Flynn AC, Poston L and on behalf of the UPBEAT Consortium
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BMC Pregnancy Childbirth 2018; 18:355

Background: Maternal obesity and rapid infant weight gain have been associated with increased risk of obesity in childhood. Breastfeeding is suggested to be protective against childhood obesity, but no previous study has addressed the potential benefit of breastfeeding as a preventive method of childhood obesity amongst obese women. The primary aim of this study was to assess the relationship between mode of feeding and body composition, growth and eating behaviours in 6-month-old infants of obese women who participated in UPBEAT; a multi-centre randomised controlled trial comparing a lifestyle intervention of diet and physical activity to standard care during pregnancy.

Methods: Three hundred and fifty-three mother and infant pairs attended a 6-months postpartum follow-up visit, during which they completed the Baby-Eating Behaviour Questionnaire, a parent-reported psychometric measure of appetite traits. Measures of infant body composition were also undertaken. As there was no effect of the antenatal intervention on infant feeding and appetite the study was treated as a cohort. Using regression analyses, we examined relationships between: (1) mode of feeding and body composition and growth; (2) mode of feeding and eating behaviour and (3) eating behaviour and body composition.

Results: Formula fed infants of obese women in comparison to those exclusively breastfed, demonstrated higher weight z-scores (mean difference 0.26; 95% CI 0.01–0.52), higher rate of weight gain (0.04; 0.00–0.07) and greater catch-up growth (2.48; 1.31–4.71). There was also a lower enjoyment of food (p = 0.002) amongst formula fed infants, following adjustment for confounders. Independent of the mode of feeding, a measure of infant appetite was associated with sum of skinfold thicknesses (β 0.66; 95% CI 0.12–1.21), calculated body fat percentage (0.83; 0.15–1.52), weight z-scores (0.21; 0.06–0.36) and catch-up growth (OR 1.98; 1.21–3.21).

Conclusion: In obese women, exclusive breastfeeding was protective against increasing weight z-scores and trajectories of weight gain in their 6-month old infants. Measures of general appetite in early infancy were associated with measures of adiposity, weight and catch up growth independent of cord blood leptin concentrations and mode of early feeding.

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Comments
Infants born to mothers with obesity or gestational diabetes mellitus (GDM) are considered to be a high-risk group for later development of obesity and type 2 diabetes. Therefore, preventive strategies in these groups are of high interest. The 2 studies mentioned
above show that breastfeeding is associated with a slower growth in the first 6–12 months of life and thus could be protective of later development of obesity and type 2 diabetes [20, 21]. This is in accordance with other studies in general populations where breastfeeding has also shown to be associated with slower growth and lower long-term obesity risk [17, 22].

However, some studies have shown that breast milk from mothers with obesity or GDM might be different in composition compared to breast milk from healthy normal weight mothers [23, 24]. This includes multiple differences, for example, in energy and micronutrient content [24], branched-chain amino acids [25], leptin [23], and immune factors [26]. Alterations in breast milk composition such as higher content of branched-chain amino acids might lead to an increase in growth stimuli. Thus, it has been speculated that breast milk from mothers with obesity/GDM could be composed in such a way that these infants have more rapid growth [27]. However, others have shown that higher values of immune factors associated with obesity, such as IL-6 and TNF-α, are associated with lower lean mass and weight gain [28]. However, the 2 published studies show that breastfeeding compared to formula feeding is still associated with lower growth rates.

In future studies, it would be interesting to also include a normal weight/normoglycemic control group as a comparator and to include analysis of breast milk composition. Interestingly, despite the higher growth rate in one of the studies, the formula-fed infants of obese mothers showed a lower enjoyment of food according to the Baby-Eating Behaviour Questionnaire, a finding requiring further exploration in how appetite and early feeding mode are related to weight gain.

### Formula Feeding: Composition and Growth

**Association of infant formula composition and anthropometry at 4 years: Follow-up of a randomized controlled trial (BeMIM study)**

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*PLoS One 2018; 13:e0199859*

The relationships between nutrition, metabolic response, early growth and later body weight have been investigated in human studies. The aim of this follow-up study was to assess the long-term effect of infant feeding on growth and to study whether the infant metabolome at the age of 4 months might predict anthropometry at 4 years of age. The Belgrade-Munich infant milk trial (BeMIM) was a randomized controlled trial in which healthy term infants received either a protein-reduced infant formula (1.89 g protein/100 kcal) containing alpha-lactalbumin enriched whey and long-chain polyunsaturated fatty acids (LC-PUFA), or a standard formula (2.2 g protein/100 kcal) without LC-PUFA, focusing on safety and suitability. Non-randomized breastfed infants were used as a reference group.

Of the 259 infants that completed the BeMIM study at the age of 4 months (anthropometry assessment and blood sampling), 187 children participated in a follow-up visit at 4 years of age. Anthropometry including weight, standing height, head circumference, and percent body fat was determined using skinfolds (triceps, subscapular) and bioelectrical impedance analysis. Plasma metabolite con-
centration, collected in samples at the age of 4 months, was measured using flow-injection tandem mass spectrometry. A linear regression model was applied to estimate the associations between each metabolite and growth with metabolites as an independent variable. At 4 years of age, there were no significant group differences in anthropometry and body composition between formula groups. Six metabolites (Asn, Lys, Met, Phe, Trp, Tyr) measured at 4 months of age were significantly associated with changes in weight-for-age z-score between 1 to 4 months of age and BMI-for-age z-score (Tyr only), after adjustment for feeding group. No correlation was found between measured metabolites and long-term growth (up to 4 years of age). No long-term effects of early growth patterns were shown on anthropometry at 4 years of age. The composition of infant formula influences the metabolic profile and early growth, while long-term programming effects were not observed in this study.

Comments

This is a 4-year follow-up of the BeMIM study published in 2014 [29]. The findings are a little surprising suggesting that the intake of the high-protein formula was not associated with higher BMI at age 4 years, as this has been reported in other controlled intervention studies like the CHOP study [30]. In the CHOP study, the high-protein formula group induced a higher weight gain already after 3 months [31], which was not the case in the BeMIM study, where there was a tendency to a higher weight gain (p = 0.06) and a significant higher length gain (p = 0.02) in the protein-reduced formula group [29]. One reason for these findings may be that the protein-reduced formula was enriched with both alpha-lactalbumin and LC-PUFA. In the original paper by Fleddermann et al. [32], these enrichments were mentioned as a possible reason for higher energetic efficiency (growth per energy intake). This study underlines that not only protein quantity but also quality may be important for growth stimulation and programming effects. Future studies should thus focus not only on the amount of protein but also on quality and content of functional proteins and peptides.
Methods: We included 2,611 participants that were born at term from a Dutch population-based birth cohort (n = 3,963) designed to investigate the development of asthma and allergies. Parents kept records of their infant’s age when CF were first introduced. Weight and height were parent reported yearly from age 1 to 8 years, and at ages 11, 14 and 17 years. We used multivariate generalized estimating equations analysis to investigate the association between timing of CF introduction (before 4 months versus at or after 4 months of age) and overweight at ages 1–17 years.

Results: Children with CF introduction before 4 months had higher odds of being overweight during childhood than children with CF introduction at or after 4 months (OR 1.32, 95% CI 1.19–1.47). This association was observed in formula-fed infants (OR 1.51, 95% CI 1.17–1.94) and breastfed infants (OR 1.32, 95% CI 1.19–1.47). The duration of breastfeeding modified the association between CF introduction and overweight: children breastfed for shorter than 4 months, but not children breastfed for 4 months or longer with CF introduction before 4 months had higher odds of being overweight (OR 1.37, 95% CI 1.19–1.57 and 1.07, 95% CI 0.87–1.32, respectively), compared to those with CF introduction at or after 4 months.

Conclusions: In children born at term, formula-fed infants and infants who were breastfed for shorter than 4 months, but not infants who were breastfed for 4 months or longer, had a higher risk of being overweight during childhood when being introduced to CF before 4 months of age.

Prospective associations of age at complementary feeding and exclusive breastfeeding duration with body mass index at 5–6 years within different risk groups

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Pediatr Obes 2018;13:522–529

Background: Children with overweight or obesity are at risk for developing obesity in adulthood. Certain maternal characteristics, such as ethnicity, education, body mass index (BMI) or neighbourhood, are determinants for childhood overweight risk. There are large variations in how mothers differing in these characteristics feed their infants. Therefore, associations of age at complementary feeding, exclusive breastfeeding duration with childhood overweight may differ in these groups. Understanding these associations would be essential to develop overweight prevention strategies.

Objectives: The objective of this study is to study the associations of age at complementary feeding, exclusive breastfeeding duration with BMI-standard deviation score (SDS) at 5–6 years within risk groups.

Methods: Using data from the Amsterdam Born Children and their Development study, a population-based birth cohort (n = 4,495), we formed groups of children at varying risk of overweight according to maternal characteristics of ethnicity, education, pre-pregnancy BMI and neighbourhood. Linear and logistic regression analyses were conducted.
**Results:** Complementary feeding after 5 months of age was associated with lower BMI-SDS in children of mothers of Dutch ethnicity (B –0.12; 95% CI –0.21 to –0.04), medium-level education (–0.19; –0.30 to –0.08), normal BMI (–0.08; –0.16 to –0.01) and high-risk neighbourhood (–0.16; –0.29 to –0.02). Compared with exclusive breastfeeding for <3 months, exclusive breastfeeding for ≥6 months was associated with lower BMI-SDS in groups of medium-level education (–0.28; 0.44 to –0.11), normal BMI (–0.18; –0.29 to –0.08) and medium-risk (–0.18; –0.33 to –0.04) and high-risk (–0.22; –0.42 to –0.02) neighbourhoods.

**Conclusions:** Associations between infant feeding practices and childhood BMI may differ between risk groups, implying that overweight prevention strategies should be group-specific.

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**Comments**

It is well known that overweight and obesity in childhood may track into adulthood. As obesity in adulthood is difficult to reverse and is associated with risk of noncommunicable diseases such as hypertension, diabetes mellitus type II, and cardiovascular diseases, it is important to have strategies for the prevention of overweight already in childhood. The 2 Dutch studies investigate how timing of introduction of complementary feeding and duration of breastfeeding may affect later BMI and identify potential modifying factors [33, 34].

Pluymen et al. [33] examine if age when starting complementary feeding is associated with overweight throughout childhood (1–17 years) and if this is different between breastfed and formula-fed infants. Previous studies have shown conflicting results regarding the impact of infant feeding mode on how age of introduction of complementary feeding influence the risk of later overweight. Whereas Huh et al. [35] observed a protective effect of breastfeeding beyond 4 months, Moss et al. [36] and Sun et al. [37] found no difference between breastfed and formula-fed infants. In the study by Pluymen et al. [33], they observe the expected association between early introduction of complementary feeding (before 4 months) and overweight during childhood for both breastfed and formula-fed infants. However, breastfeeding beyond 4 months eliminated this unfavorable relation. Hence, it seems important to support breastfeeding also in respect to introducing complementary feeding, and the recommendation for the timing of introducing complementary feeding may differ between groups depending on infant-feeding mode. Future studies should investigate this further, and according to the study by Sirkka et al. [34], the impact of maternal factors should be investigated as well.

In the other Dutch study by Sirkka et al. [34], the associations between age of complementary feeding introduction and duration of exclusive breastfeeding on BMI at 5–6 years were examined according to different risk groups, that is, ethnicity, educational level, pre-pregnancy BMI, and neighborhoods [34]. Associations with BMI at 5–6 years differed between the different risk groups. For example, analyses between introduction of complementary feeding at ≥5 months of age and BMI at the age of 5–6 years showed a significant inverse association and a reduced risk for Dutch ethnicity but not for the other ethnicities. The authors conclude that interventions should be group specific. However, this will be difficult to address, as there was no overall clear pattern. However, they direct attention to an important challenge as complementary feeding is influenced by culture and traditions and therefore may differ between groups and be difficult to change. As discussed above, adherence to recommendations could be improved with special focus on relevant risk groups. Future studies may help to identify relevant risk groups and methods for targeting these groups.
Baby-led complementary feeding: Randomized controlled study

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Pediatr Int 2018;60:1073–1080

Background: Baby-led weaning (BLW) is an approach to introducing solid foods to infants that gives control of the feeding process to the infant. Anecdotal evidence suggests that BLW is becoming popular with parents, but scientific research is limited to a few publications. This study assessed growth, hematological parameters and iron intake in 6–12-month-old infants fed by traditional or baby-led complementary feeding.

Methods: We recruited 280 healthy 5–6-month-old infants allocated to a control (traditional spoon feeding [TSF]) group or an intervention (BLW) group in a randomized controlled trial. Infant growth, hematologic parameters and iron intake were evaluated at age 12 months.

Results: Infants in the TSF were significantly heavier than those in the BLW group. Mean weight in the BLW group was 10.4 ± 0.9 kg compared with 11.1 ± 0.5 kg in the TSF group. There was no statistically significant difference in the iron intake from complementary foods between the BLW (7.97 ± 1.37 mg/day) and TSF (7.90 ± 1.68 mg/day) participants who completed the diet records. Hematologic parameters were similar at 12 months. The incidence of choking reported in the weekly interviews was not different between the groups.

Conclusion: To the best of our knowledge, this is the first randomized-controlled study to have examined the impact of weaning method on iron intake, hematological parameters and growth in breast-fed infants. BLW can be an alternative complementary feeding type without increasing the risk of iron deficiency, choking or growth impairment.

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Comments: Baby-led weaning (BLW) is a relatively recent method used for the transition from infant feeding to family foods. The idea of the concept is that the infant is exposed to a range of foods and decides what and how much to eat, which might reduce overeating and strengthen self-regulation. Though BLW is becoming more popular, only a few studies have examined the effect on growth, nutrient intake, and safety compared to traditional complementary feeding. This randomized study shows that after about 6 months of intervention, the weight was significantly lower for BLW group compared to infants using traditional weaning practices at the age of 12 months [38]. However, there were no differences in length, head circumference, choking, or iron intake between the groups. This is in accordance with other recent studies [39, 40] indicating that BLW is a safe approach enabling the infant to get sufficient nutrients to obtain normal growth in stature. An interesting aspect of BLW approach is the role of the self-regulation. The complementary feeding approach may have an impact on the development of satiety regulation, and BLW seems to regulate the food intake differently from the traditional weaning approach [41]. Analogous breastfeeding also enables the infant to self-regulate food intake and has
in some meta-analyses shown to have a protective, although small effect, against later obesity [22]. In future studies, it would therefore be interesting to examine the potential effect of BWL on later weight development to establish the long-term consequences of BLW.

**Early Nutrition and Growth Faltering in Low-Income Countries**

**Association between breast milk intake at 9–10 months of age and growth and development among Malawian young children**

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*Matern Child Nutr* 2018;14:e12582

World Health Organization recommends exclusive breastfeeding for infants for the first 6 months of life, followed by introduction of nutritious complementary foods alongside breastfeeding. Breast milk remains a significant source of nourishment in the second half of infancy and beyond; however, it is not clear whether more breast milk is always better. The present study was designed to determine the association between amount of breast milk intake at 9–10 months of age and infant growth and development by 12–28 month of age. The study was nested in a randomized controlled trial conducted in Malawi. Regression analysis was used to determine associations between breast milk intake and growth and development. Mean (SD) breast milk intake at 9–10 months of age was 752 (244) g/day. Mean (SD) length-for-age z-score at 12 months and change in length-for-age z-score between 12 and 18 months were –1.69 (1.0) and –0.17 (0.6), respectively. At 18 months, mean (SD) expressive vocabulary score was 32 (24) words and median (interquartile range) skills successfully performed for fine, gross, and overall motor skills were 21 (19–22), 18 (16–19), and 38 (26–40), respectively. Breast milk intake (g/day) was not associated with either growth or development. Proportion of total energy intake from breast milk was negatively associated with fine motor (β = –0.18, p = 0.015) but not other developmental scores in models adjusted for potential confounders. Among Malawian infants, neither breast milk intake nor percent of total energy intake from breast milk at 9–10 months was positively associated with subsequent growth between 12 and 18 months, or development at 18 months.

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**Comments**

Comments on this manuscript are incorporated in those on the next 2 manuscripts (Skau et al. and Cheng et al.).
**Stunting, wasting and breast-feeding as correlates of body composition in Cambodian children at 6 and 15 months of age**

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*Br J Nutr* 2019; 121: 688–698  

The study aimed at assessing stunting, wasting and breast-feeding as correlates of body composition in Cambodian children. As part of a nutrition trial (ISRCTN19918531), fat mass (FM) and fat-free mass (FFM) were measured using 2H dilution at 6 and 15 months of age. Of 419 infants enrolled, 98% were breastfed, 15% stunted and 4% wasted at 6 months. At 15 months, 78% were breastfed, 24% stunted and 11% wasted. Those not breastfed had lower FMI at 6 months but not at 15 months. Stunted children had lower FM at 6 months and lower FFM at 6 and 15 months compared with children with length-for-age z ≥0. Stunting was not associated with height-adjusted indexes fat mass index (FMI) or fat-free mass index (FFMI). Wasted children had lower FM, FFM and FFMI at 6 and 15 months compared with children with weight-for-length z (WLZ) ≥0. Generally, FFM and FFMI deficits increased with age, whereas FM and FMI deficits decreased, reflecting interactions between age and WLZ. For example, the FFM deficits were −0.99 (95% CI −1.26 to −0.72) kg at 6 months and −1.44 (95% CI −1.69 to −1.19) kg at 15 months (interaction, <0.05), while the FMI deficits were −2.12 (95% CI −2.53 to −1.72) kg/m<sup>2</sup> at 6 months and −1.32 (95% CI −1.77 to −0.87) kg/m<sup>2</sup> at 15 months (interaction, <0.05). This indicates that undernourished children preserve body fat at the detriment of fat-free tissue, which may have long-term consequences for health and working capacity.

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**Comments**  Comments on this manuscript are incorporated with those on the manuscripts above and below (Kumwenda et al. and Cheng et al.).

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**Supplementation with lactoferrin and lysozyme ameliorates environmental enteric dysfunction: A double-blind, randomized, placebo-controlled trial**

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*Am J Gastroenterol* 2019; 114: 671–678  

**Introduction:** Environmental enteric dysfunction (EED) predisposes children throughout the developing world to high rates of systemic exposure to enteric pathogens and stunting. Effective i-
Interventions that treat or prevent EED may help children achieve their full physical and cognitive potential. The objective of this study is to test whether 2 components of breast milk would improve a biomarker of EED and linear growth during the second year of life.

**Methods:** A prospective, randomized, double-blind, placebo-controlled clinical trial among children aged 12–23 months was conducted in rural Malawi. The experimental group received a daily supplement of 1.5 g of lactoferrin and 0.2 g of lysozyme for 16 weeks. The primary outcome was an improvement in EED, as measured by the change in the percentage of ingested lactulose excreted into the urine (Δ%L).

**Results:** Among 214 children who completed the study, there was a significant difference in Δ%L between the control and experimental groups over 8 weeks (an increase of 0.23 vs. 0.14%, respectively; \( p = 0.04 \)). However, this relative improvement was not as strongly sustained over the full 16 weeks of the study (an increase of 0.16 vs. 0.11%, respectively; \( p = 0.17 \)). No difference in linear growth over this short period was observed. The experimental intervention group had significantly lower rates of hospitalization and the development of acute malnutrition during the course of the study (2.5 vs. 10.3%, relative risk 0.25; \( p < 0.02 \)).

**Discussion:** Supplementation with lactoferrin and lysozyme in a population of agrarian children during the second year of life has a beneficial effect on gut health. This intervention also protected against hospitalization and the development of acute malnutrition, a finding with a significant clinical and public health importance. This finding should be pursued in larger studies with longer follow-up and optimized dosing.

**Comments**

Growth faltering during the first 2 years of life is widespread in low-income countries [42], and attempts to reverse the decline in height-for-age through breastfeeding promotion or nutrition interventions have only had no or small effects [19, 43]. The studies by Kumwenda et al. [44] and Cheng et al. [45] examined the effects of breastfeeding and nutrition interventions during the second half of infancy on growth and body composition.

Kumwenda et al. [44] investigated the associations between intake of breast milk at 9–10 months of age and growth at 12–18 months in children from rural Malawi. They found that breast milk intake, measured in g/day or calculated as percentage of total energy intake per day, was not associated with length-for-age Z (LAZ) at 12 months or change in LAZ from 12 to 18 months of age. The mean LAZ declined between 12 and 18 months of age despite high breastfeeding rate and the fact that mean energy intake was higher than the mean requirements of children at this age. The results are discussed and are in line with cited studies in both younger children and older children where no evidence of breastfeeding and growth was found in low-income countries. However, some breastfeeding studies mentioned in the paper did find positive associations between breastfeeding practices and growth. The strength of the current study is the quantitative measurement of breast milk intake using stable isotope technique and the relatively large sample size (\( n = 358 \)).

In rural Cambodia, Skau et al. [46] found that although breastfeeding rates were high and all children received a daily dietary supplement, the stunting rate increased from 15 to 24% and wasting increased from 4 to 11% in young children from 6 to 15 months of age. Non-breastfed infants at 6 months had a lower fat mass index (FMI) than breastfed infants, suggesting that breastfeeding supports accretion of fat mass. However, the number of non-breastfed children at 6 months was very low, and the results should be interpreted with caution. Stunting was not associated with FMI or fat-free mass index (FFMI). This means that stunted children gained fat and fat-free tissue “in the same proportion to their length” as nonstunted children. However, there was a
differential effect of wasting on FMI and FFMI at 6 and 15 months of age. Deficits in FFMI increased with age, whereas FMI deficits decreased with age. This suggests that body fat is preserved at the expense of accretion of fat-free tissue during wasting (acute malnutrition). This could have long-term consequences, including reduced working capacity and higher risk of noncommunicable diseases. This study also used stable isotope technique to measure body composition.

Environmental enteric dysfunction (EED), a condition involving villus atrophy, intestinal inflammation, and increased gut permeability has been found to contribute to stunting [47]. Cheng et al. [45] investigated if EED could be reduced by giving lactoferrin and lysozyme to 12- to 23-month-old children. Human milk contains both lactoferrin and lysozyme, and the level used in the supplement was based on the estimated amounts a 12-month-old child would receive from breast milk. The supplement was given during the hunger season when EED was expected to increase. One biomarker, Δ%L (change in lactulose excreted into urine), was used to measure EED. There was a modest effect of the intervention on Δ%L after 8 weeks (p = 0.04), which was not maintained after 16 weeks (p = 0.17). As expected, there was no effect on linear growth during the short intervention period. The number of children being hospitalized or developing moderate acute malnutrition during the intervention was lower in the experimental group compared to the control group.

In conclusion, stunting is still a challenge with approximately 25% of children below 5 years being stunted [48]. Research investigating the underlying mechanisms of stunting is needed in order to develop interventions aiming at the prevention of stunting. Interventions focusing on improvements of gut health may be one of the ways forward.

References


Early Nutrition and Its Effect on Growth, Body Composition, and Later Obesity


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