Adiposity Is Not Altered in Preterm Infants Fed With a Nutrient-Enriched Formula After Hospital Discharge

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ABSTRACT: To determine whether adiposity was altered, body size (weight, length) and composition, determined by dual energy x-ray absorptiometry, were examined in preterm infants fed with a nutrient enriched (A, $n = 56$), a term infant (B, $n = 57$) or the nutrient enriched (discharge and term) plus the term formula (term and 6 mo; C, $n = 26$), and a group of breast-fed preterm infants (D, $n = 25$) at hospital discharge, 3, 6, and 12 mo corrected age. The results were analyzed using standard statistics. One hundred sixty-four infants (birth weight = 1406 ± 248 g, GA = 31 ± 1.7 wk) were studied. All infants underwent “catch-up,” but weight and length were greater in infants in group A compared with groups B, C, or D. More rapid and complete “catch-up” was paralleled by increased total nonfat and fat mass (g) but not percentage of fat mass. Changes in fat mass (g) were primarily explained by increased fat accretion on the legs. More rapid and complete “catch-up” growth, therefore, reflected increased non-fat and peripheral fat mass. These data do not support the hypothesis of increased or central adiposity in infants fed a nutrient-enriched formula after hospital discharge. (*Pediatr Res* 67: 660–664, 2010)

Infants fed with fortified human milk (1) or an enriched preterm formula (2–7) have increased body weight and length than those who are solely breast-fed or fed with a term formula after hospital discharge. Therefore, it is recommended that they can be fed with either fortified human milk or an enriched preterm infant formula for varying periods after hospital discharge (8,9). However, concern exists about “catch-up” growth and the subsequent development of insulin resistance and central adiposity in preterm infants (10).

In growth-retarded term infants, rapid “catch-up” has been related to the development of insulin resistance and metabolic syndrome X (11). In a recent review, Yeung (10) has suggested that this risk may be even greater in preterm infants (12). In effect, better growth may be associated with better development (12,13), but it may also be associated with the development of insulin resistance and visceral adiposity in these high-risk infants (10,14–16).

Several studies have examined body composition in preterm infants fed with nutrient enriched formulas after hospital discharge (17–23), but none have longitudinally assessed the effects of these diets on fat free and fat mass accretion. It is also unclear whether any relationship exists between global fat

mass and central fat mass accretion and how this “tracks” during the first year of life in the preterm infant.

This article focuses on the effects of different infant-formula diets on growth and body composition, how body composition tracks during the first year of life, and the relationship between global and central fat mass accretion in these infants. Changes in growth and body composition are compared with a reference group of breast-fed preterm infants who were studied at the same time. It was hypothesized that differences in body weight would not be associated with increased or altered adiposity in infants fed with the nutrient-enriched formula when compared with those fed with the term formula or those who were breast-fed.

METHODS

This study was a single center, double-masked, controlled, prospective and randomized clinical trial of three parallel treatment groups that began immediately before initial hospital discharge and lasted until 12 mo corrected age (6). Randomization was predetermined centrally, and assignment to a treatment group was done using sealed envelopes. The study was approved by the Ethics Committee of the Newcastle and North Tyneside Health Authority, and informed consent was obtained from the parent(s) or legal guardian.

Preterm infants with a GA ≤ 34 wk and a birth weight of ≤ 1750 g were considered eligible for the study. Those with no evidence of systemic disease, requiring no medication, and growing normally at the time of hospital discharge, i.e. ≥ 25 g/d, were enrolled.

Immediately before hospital discharge, infants were randomized to be fed with a preterm infant formula between discharge and 6 mo corrected age (group A), a standard term infant formula between discharge and 6 mo corrected age (group B), or a preterm formula between discharge and term and then the term formula between term and 6 mo corrected age (group C). A reference group of breast-fed infants were studied at the same time (group D).

The preterm formula differed in several respects from the term formula: e.g. energy (80 versus 66 kcal/100 mL for the preterm and term formulas), protein (2.2 versus 1.4 g/100 mL), protein-to-energy ratio (2.75 versus 2.1 g/100 kcal), calcium (108 versus 54 kcal/100 mL), and phosphorus (54 versus 27 mg/100 mL). Ready-to-feed formula was provided in cartons containing 24×100 mL bottles. Infants were discharged with a 2–3 wk supply of preweighed cartons and instructions to thoroughly shake each bottle before feeding and to feed the formula on demand.

Infants were seen at the outpatient clinic every 2 wk between discharge and term and monthly between term and 6 mo. At each visit, intake was determined. Body composition was measured at discharge, term, 12 wk, 6 mo, and 12 mo corrected age. Intake between visits was calculated from the differences in weight between the delivered and returned cartons and averaged for the time interval between visits.

Body composition was measured using DEXA (Hologic QDR 2000, Hologic Inc, Waltham, MA) with a special radiation filter on top of the normal scanning couch, as previously described (24). This filter plate is optimized for a body weight range of 1 to 10 kg. Scan analysis was performed using the Infant Whole Body Software, version 5.56P.

The scan procedure was as follows. Before the arrival of the infant, the scanning couch of the densitometer was moved to the starting position with the radiation filter plate in place. The scanning area was then covered with a

Received September 9, 2009; accepted January 7, 2010.

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Supported by a grant from Cow and Gate Nutricia, United Kingdom.

commercial absorbent paper material and the calibration phantom (the "T" bar) placed at the edge of the scanning area. The phantom was constructed of polymethylmethacrylate (Perspex) and aluminum and designed to simulate three thicknesses of soft tissue and three densities of bone overlying soft tissue.

After arrival, when the baby was settled, she/he was undressed, swaddled in a light cotton sheet, and placed supine on to the scanning surface, parallel to the long axis of the couch with the head ~2 cm from the starting point of the scan as marked on positioning aid. The scan was begun when the infant was quiet and with a research nurse constantly in attendance.

Scan precision was assessed by scanning the torso and arm sections of the pediatric anthropometric phantom seven times. The phantom had been positioned according to the standard protocol for a 1-year-old child. During analysis of each completed baby scan, head, chest, pelvis, legs, and arms were identified as distinct regions of interest, with boundaries drawn using the software provided. All scans were performed by one of the two operators with an intraoperator variability of 1.36 ± 1.0 (mean $\pm$ SD) and $0.92 \pm 0.7\%$ for operators one and two, respectively.

Scans were first inspected to ensure that all four limbs were present and clearly seen. For each scan, DEXA-derived weight was then compared with scale-derived weight. If the paired values agreed ($\pm 15\%$), then data for that scan were included. Scans were also evaluated by comparing weights, as determined by DEXA, between right and left arm and between right and left leg. If paired values agreed ($\pm 10\%$), then the scan was included.

The data were analyzed using ANOVA, with group, age, and sex as blocking variables. Post hoc comparisons were examined using Fishers protected least significant difference test. Stepwise regression analyses were used to compare the relative effects of protein and energy intake on weight and length gain in the study infants. Results were considered significant at $p < 0.05$.

RESULTS

One hundred sixty-four infants (group A = 56, B = 57, C = 26, and D = 25; boys = 75 and girls = 89) were studied. The characteristics of the infants are presented in Table 1. No

Table 1. Characteristics of the study groups (mean $\pm$ 1 SD)

Group	Preterm formula (n = 56)	Term formula (n = 57)	Crossover* (n = 26)	Breast-fed (n = 25)
Birth				
Gestation (w)	31.3 $\pm$ 2.3	30.9 $\pm$ 2.3	30.7 $\pm$ 2.0	30.7 $\pm$ 2.1
Weight	1414 $\pm$ 301	1402 $\pm$ 309	1349 $\pm$ 306	1377 $\pm$ 311
Weight (z)	-0.9 $\pm$ 1.0†	-0.75 $\pm$ 1.0	-0.85 $\pm$ 1.1	-0.42 $\pm$ 0.79†
Male:female	30:26	22:35	13:13	15:10
Entry z-scores				
Weight	-1.36 $\pm$ 0.9	-1.44 $\pm$ 0.8	-1.48 $\pm$ 0.8	-1.59 $\pm$ 0.8
Length	-1.84 $\pm$ 0.9	-1.98 $\pm$ 1.0	-2.06 $\pm$ 1.1	-2.01 $\pm$ 1.0
Head circ	-0.10 $\pm$ 0.8	-0.15 $\pm$ 1.0	-0.05 $\pm$ 1.0	0.47 $\pm$ 1.0

* Infants fed the preterm formula to term, then the term formula to 6 mo.

† Mean difference between A and D = -0.49, $p = 0.05$.

differences were detected between the groups at birth or at entry into the study, with the exception that birth weight z-score was less in infants fed with the preterm formula (group A) than the breast-fed infants (group D; mean difference = -0.49, $p = 0.05$). Mean ($\pm$ 1 SD) age at hospital discharge was 37 ± 1.4 wk corrected age.

Volume and consequently energy and protein intakes decreased in all groups during the study (Fig. 1). Mean daily volume (A = 136 ± 47 < C = 152 ± 43 < B = 164 ± 58 mL/kg/d; $p < 0.001$) and protein (A = 3.0 ± 1.0 > C = 2.4 ± 1.0 > B = 2.3 ± 0.8 g/kg/d; $p < 0.0001$) but not energy (A = 108 ± 37 , B = 105 ± 35 , and C = 108 ± 38 kcal/kg/d) intakes differed between the groups. Intake was not measured in the breast-fed infants.

Weight and length of the study infants are presented in Figure 2. z-Scores for weight increased in group A ($p < 0.001$) and tended to increase in groups B ($p = 0.06$) and D ($p = 0.10$) but not in group C and differed significantly between the groups (A > B, C, D, $p < 0.001$; B > C, $p < 0.05$). In group A, the increase was significant by term ($p < 0.005$), not changing thereafter. In groups B and D, the increase was significant by 12 wk ($p = 0.10$), remaining constant thereafter.

z-Scores for length increased in all groups ($p < 0.0001$) but differed significantly between the groups (A > B, C, D, $p < 0.001$; B > C, $p = 0.08$). In group A, the increase was significant by term ($p < 0.001$), continuing to increase until 6 mo ($p < 0.0001$), not changing thereafter. In group B, the increase was also significant by term ($p < 0.05$) but continuing to increase until 12 mo ($p < 0.0001$). In groups C and D, the increase was significant by 12 wk ($p < 0.001$), not changing thereafter in group C but continuing to increase in group D ($p < 0.05$).

Body weight, fat-free mass, and fat mass data are presented in Table 2. Weight and fat-free mass differed between the groups (A > B, C, D; $p < 0.05$, < 0.0001, < 0.05, respectively). Fat mass was greater in group A than groups B ($p < 0.05$) and C ($p < 0.005$), but no differences were detected in percentage of fat mass between the groups. At 6 and 12 mo, body weight and fat-free mass, but not fat mass (g, %), were greater in group A than in groups B, C, or D ($p < 0.01$).

Increments in weight, fat-free, and fat mass are presented in Table 2. Significant differences were detected in the rate of

Figure 1. Dietary intakes in study infants. A. Volume of intake was less in infants fed the preterm formula (●) than those preterm plus term formula (×) which was less than those fed the term formula (○; * $p < 0.001$). B. Energy intake. **No significant differences were noted in energy intakes between the groups. C. Protein intake was greater in infants fed the preterm formula than those fed the preterm plus term formula which was greater than those fed the term formula († $p < 0.001$).

weight gain ($p < 0.05$) and fat-free mass gain ($p < 0.01$) but not in fat mass gain between the groups. The main differences were noted between discharge and term, with rate of gain being almost identical thereafter. Stepwise regression analyses indicated that variation in protein intake accounted for $\sim 40\%$ of the variation in weight gain ($p < 0.0001$) between the study infants.

A linear relationship was noted between changes in global fat mass and central fat mass and changes in global and leg fat mass (Fig. 3). Changes in central and leg fat mass accounted for 30 and 40% for the variation in global fat mass.

Figure 2. Weight (A) and length (B) scores in study infants at discharge ($\square$), term ($\blacksquare$), 12 wk ($\boxtimes$), 6 mo ($\boxplus$), and 12 mo ($\square$). Groups A, B, C, and D indicate infants fed the preterm formula, term formula, preterm plus term formula, and human milk, respectively. *Z scores greater in group A than in groups B, C, and D ($p < 0.001$).

Figure 3. Relationship between total fat mass and (A) central and (B) leg fat mass. Changes in central ($y = 41.1 + 0.30x$, $r^2 = 90$; $p < 0.0001$) and leg ($y = -34 + 0.40x$, $r^2 = 91$; $p < 0.0001$) fat mass were linearly related to that in central fat mass, with 30 and 40% of the variation in central and leg fat mass accounting for that in central fat mass.

Table 2. Body weight, fat-free and fat mass in the study groups (mean $\pm$ 1 SD)

Group	Term (n = 148)*	12 wk (n = 141)*	6 mo (n = 145)*	12 mo (n = 138)*	
Weight (g)					A > B ($p < 0.05$), C ($p < 0.001$), D ($p < 0.05$)
Preterm (A)	3315 $\pm$ 627	5725 $\pm$ 858	7242 $\pm$ 1124	9203 $\pm$ 1213	
Term (B)	2904 $\pm$ 416	5390 $\pm$ 661	7078 $\pm$ 935	8649 $\pm$ 943	
Crossover (C)	3073 $\pm$ 428	5137 $\pm$ 736	6793 $\pm$ 1003	8476 $\pm$ 1337	
Breast-fed (D)	2502 $\pm$ 414	5127 $\pm$ 1466	6998 $\pm$ 871	8604 $\pm$ 1209	
Fat-free mass					A > B ($p < 0.05$), C ($p < 0.001$) D ($p < 0.005$)
Preterm (A)	2745 $\pm$ 445	4270 $\pm$ 452	5208 $\pm$ 638	6872 $\pm$ 806	
Term (B)	2393 $\pm$ 276	4022 $\pm$ 411	5139 $\pm$ 515	6592 $\pm$ 738	
Crossover (C)	2507 $\pm$ 244	3948 $\pm$ 431	4978 $\pm$ 541	6399 $\pm$ 881	
Breast-fed (D)	2171 $\pm$ 296	3762 $\pm$ 1051	5063 $\pm$ 568	6451 $\pm$ 746	
Fat mass (g)					A > B ($p < 0.05$), C ($p < 0.005$)
Preterm (A)	570 $\pm$ 256	1455 $\pm$ 461	2033 $\pm$ 686	2332 $\pm$ 679	
Term (B)	511 $\pm$ 222	1367 $\pm$ 419	1940 $\pm$ 586	2058 $\pm$ 477	
Crossover (C)	566 $\pm$ 204	1188 $\pm$ 366	1815 $\pm$ 632	2077 $\pm$ 623	
Breast-fed (D)	331 $\pm$ 128	1365 $\pm$ 527	1934 $\pm$ 658	2153 $\pm$ 645	
Fat mass (%)					p = ns
Preterm (A)	17 $\pm$ 5.5	25 $\pm$ 4.7	28 $\pm$ 5.9	25 $\pm$ 5.3	
Term (B)	17 $\pm$ 6.0	25 $\pm$ 5.5	27 $\pm$ 5.1	24 $\pm$ 4.4	
Crossover (C)	18 $\pm$ 4.7	23 $\pm$ 4.1	26 $\pm$ 5.8	24 $\pm$ 4.5	
Breast-fed (D)	13 $\pm$ 3.2	25 $\pm$ 8.2	27 $\pm$ 6.8	25 $\pm$ 4.8	

* Body composition determinations.

Table 3. Regional fat distribution in study infants (mean $\pm$ 1 SD)

Group	Term	12 wk	6 mo	12 mo	
Torso (g)					C < A ($p < 0.001$), B ($p < 0.01$), D ($p < 0.01$)
Preterm (A)	113 $\pm$ 50	354 $\pm$ 129	427 $\pm$ 161	424 $\pm$ 158	
Term (B)	129 $\pm$ 53	333 $\pm$ 110	431 $\pm$ 128	373 $\pm$ 100	
Crossover (C)	127 $\pm$ 46	266 $\pm$ 99	383 $\pm$ 168	351 $\pm$ 79	
Breast-fed (D)	87 $\pm$ 28	340 $\pm$ 131	454 $\pm$ 170	416 $\pm$ 143	
Pelvis					C < A ($p < 0.01$), B ($p < 0.01$), D ($p < 0.01$)
Preterm (A)	59 $\pm$ 20	179 $\pm$ 50	223 $\pm$ 73	275 $\pm$ 102	
Term (B)	53 $\pm$ 22	162 $\pm$ 50	205 $\pm$ 57	240 $\pm$ 86	
Crossover (C)	59 $\pm$ 24	125 $\pm$ 50	196 $\pm$ 76	221 $\pm$ 101	
Breast-fed (D)	61 $\pm$ 34	163 $\pm$ 63	234 $\pm$ 82	242 $\pm$ 92	
Trunk					C < A ($p < 0.01$), B ($p < 0.01$), D ($p < 0.01$)
Preterm (A)	172 $\pm$ 65	532 $\pm$ 168	651 $\pm$ 218	699 $\pm$ 249	
Term (B)	182 $\pm$ 71	485 $\pm$ 154	635 $\pm$ 170	613 $\pm$ 160	
Crossover (C)	186 $\pm$ 67	394 $\pm$ 136	579 $\pm$ 221	573 $\pm$ 162	
Breast-fed (D)	147 $\pm$ 54	503 $\pm$ 183	688 $\pm$ 229	657 $\pm$ 230	
Arms					
Preterm (A)	59 $\pm$ 28	171 $\pm$ 59	254 $\pm$ 138	244 $\pm$ 133	
Term (B)	56 $\pm$ 37	163 $\pm$ 61	239 $\pm$ 117	213 $\pm$ 82	
Crossover (C)	60 $\pm$ 29	137 $\pm$ 60	187 $\pm$ 97	195 $\pm$ 124	
Breast-fed (D)	28 $\pm$ 12	145 $\pm$ 58	206 $\pm$ 98	246 $\pm$ 75	
Legs					A > B ($p < 0.005$), C ($p < 0.001$), D ($p < 0.10$)
Preterm (A)	159 $\pm$ 58	500 $\pm$ 155	736 $\pm$ 270	975 $\pm$ 354	
Term (B)	133 $\pm$ 73	451 $\pm$ 168	652 $\pm$ 300	830 $\pm$ 271	
Crossover (C)	129 $\pm$ 75	458 $\pm$ 133	602 $\pm$ 247	822 $\pm$ 409	
Breast-fed (D)	98 $\pm$ 58	454 $\pm$ 183	654 $\pm$ 289	897 $\pm$ 254	
Head					
Preterm (A)	138 $\pm$ 103	171 $\pm$ 114	273 $\pm$ 180	281 $\pm$ 150	
Term (B)	100 $\pm$ 96	181 $\pm$ 92	245 $\pm$ 157	273 $\pm$ 146	
Crossover (C)	109 $\pm$ 96	114 $\pm$ 61	276 $\pm$ 193	249 $\pm$ 117	
Breast-fed (D)	143 $\pm$ 25	204 $\pm$ 147	236 $\pm$ 160	264 $\pm$ 159	

DISCUSSION

This is the first study to longitudinally evaluate total and regional body composition in preterm infants during the first year of life and to suggest that percentage of body fat is not altered at 12 wk, 6 mo, or 12 mo of age in these high-risk infants. This study is the first to suggest that more rapid and more complete “catch-up,” as was noted in infants fed with the nutrient-enriched formula, is not associated with altered adiposity but is paralleled by an increase in fat free and peripheral fat mass. These data have important implications for feeding preterm infants after hospital discharge.

Yeung (10) has suggested that because of recurrent “stress” and protein, under-nutrition preterm infants are at an increased risk for the development of an insulin-resistant state. This, in turn, leads to hyper-insulinemia, a down regulation of visceral β_3 -adrenoreceptors and increased intraabdominal adiposity, which may or may not be associated with general adiposity (25).

At the same time, Ong (11) has suggested that there are two types of rapid catch-up growth in infants. One is paralleled by an increase in “predominantly fat mass, central in location and associated with insulin resistance,” and the second by “predominantly lean mass and height gain.” This author then goes on to suggest that the former is much more likely in growth-retarded term infants and, therefore, the development of metabolic syndrome X in later life (11).

Data from this study do not support this suggestion in the preterm postnatally growth-retarded infant. Although all infants demonstrated “catch-up” growth, in terms of weight

and/or height gain, in no instance did percentage of fat mass or central fat mass differ between the formula-fed and the breast-fed infants. These data suggest that “catch-up” was largely “healthy catch-up growth” as defined by Ong (11) and, therefore, perhaps desirable.

The rate of “catch-back” also varied between the groups. In infants fed with the nutrient-enriched formula, z -score for body weight peaked at term compared with 12 wk in infants fed with the term formula or the breast-fed infants. In infants fed with the nutrient-enriched formula, z -score for length peaked at 12 wk compared with 6 or 12 mo in the other groups. This suggests that needs for “catch-back” were more rapidly recouped with the nutrient-enriched formula.

The extent of “catch-back” also differed between the formula-fed infants. z -Scores for body weight and length were greater in infants fed with the nutrient-enriched formula, increased weight and length reflecting increased nonfat mass and fat mass deposition on the legs, *i.e.* peripheral fat. This not only suggests “healthy” but also more complete catch-up growth in infants fed with the nutrient-enriched formula.

In young children with protein-energy malnutrition, visceral tissue is conserved at the expense of muscle and fat. In the initial stages of refeeding with high energy intakes (26), rapid weight gain reflects an increase in body fat (27,28), which is followed later by an increase in muscle mass (29). In our study, initial weight gain was primarily paralleled by an increase in fat-free mass, with protein not energy accounting for a significant amount of the variation in weight and length gain.

All preterm infants are protein malnourished at hospital discharge; the more immature the infant, the greater the degree of malnutrition (30). Protein malnutrition seems to play an important role in the development of insulin resistance (11). Therefore, correction of the protein deficit may be critical in minimizing the risk of developing insulin resistance and promoting normal growth in these infants. Data from this study tend to support this hypothesis, in that protein rather than energy intake played a more critical role in determining weight gain and linear growth in these infants.

Growth in infants fed with the preterm formula to term, then the term formula to 6 mo (group C) is disconcerting. Between discharge and term, when infants are fed with the preterm formula, *z*-scores for weight and length improved (Fig. 2). After term, when infants are fed with the term formula, *z*-score for weight “falters,” that for length no longer continues to “catch-back.” This can be directly related to changes in nutrient intake during this time. Changed to the term formula, it took 8 wk for infants to up regulate volume to ensure an isocaloric intake when compared with the other formula groups (Fig. 1). In the interim, infants were underfed and growth “falters.” The functional implications of this rapid acceleration followed by a significant deceleration during this critical epoch of growth remain to be determined.

Our observations have some shortcomings. Body composition was measured using DEXA, which does not differentiate s.c. and visceral fat. At the same time, trunk and pelvis fat were summed to estimate central fat mass and subtle differences in visceral fat mass may have gone undetected. Measures of insulin sensitivity/resistance were not determined and it remains unclear whether any relationship exists between dietary protein intake and the development of insulin resistance and visceral adiposity in these high-risk infants.

REFERENCES

- O'Connor DL, Khan S, Weishuhn K, Vaughan J, Jefferies A, Campbell DM, Asztalos E, Feldman M, Rovet J, Westall C, Whyte H 2008 Growth and nutrient intakes of human milk-fed preterm infants provided with extra energy and nutrients after hospital discharge. *Pediatrics* 121:766–776
- Carver JD, Wu PY, Hall RT, Ziegler EE, Sosa R, Jacobs J, Baggs G, Auestad N, Lloyd B 2001 Growth of preterm infants fed nutrient-enriched or term formula after hospital discharge. *Pediatrics* 107:683–689
- Bishop NJ, King FJ, Lucas A 1993 Increased bone mineral content of preterm infants fed with a nutrient enriched formula after discharge from hospital. *Arch Dis Child* 68:573–578
- Lucas A, Fewtrell MS, Morley R, Singhal A, Abbott RA, Isaacs E, Stephenson T, MacFadyen UM, Clements H 2001 Randomized trial of nutrient-enriched formula versus standard formula for postdischarge preterm infants. *Pediatrics* 108:703–711
- Cooke RJ, Griffin IJ, McCormick K, Wells JC, Smith JS, Robinson SJ, Leighton M 1998 Feeding preterm infants after hospital discharge: effect of dietary manipulation on nutrient intake and growth. *Pediatr Res* 43:355–360
- Cooke RJ, McCormick K, Griffin IJ, Embleton N, Faulkner K, Wells JC, Rawlings DC 1999 Feeding preterm infants after hospital discharge: effect of diet on body composition. *Pediatr Res* 46:461–464
- Cooke RJ, Embleton ND, Griffin IJ, Wells JC, McCormick KP 2001 Feeding preterm infants after hospital discharge: growth and development at 18 months of age. *Pediatr Res* 49:719–722
- Carlson SE 2005 Feeding after discharge: growth, development and long-term effects. In: Tsang RC, Uauy R, Koletzko B, Zlotkin S (eds) *Nutrition of the Preterm Infant*. Digital Educational Publishing Inc, Cincinnati, OH, pp 357–382
- Aggett PJ, Agostoni C, Axelsson I, De Curtis M, Goulet O, Hernell O, Koletzko B, Lafeber HN, Michaelsen KF, Puntis JW, Rigo J, Shamir R, Szajewska H, Turck D, Weaver LT 2006 Feeding preterm infants after hospital discharge: a commentary by the ESPGHAN Committee on Nutrition. *J Pediatr Gastroenterol Nutr* 42:596–603
- Yeung MY 2006 Postnatal growth, neurodevelopment and altered adiposity after preterm birth—from a clinical nutrition perspective. *Acta Paediatr* 95:909–917
- Ong KK 2007 Catch-up growth in small for gestational age babies: good or bad? *Curr Opin Endocrinol Diabetes Obes* 14:30–34
- Latal-Hajnal B, von Siebenthal K, Kovari H, Bucher HU, Largo RH 2003 Postnatal growth in VLBW infants: significant association with neurodevelopmental outcome. *J Pediatr* 143:163–170
- Ehrenkranz RA, Dusick AM, Vohr BR, Wright LL, Wrage LA, Poole WK 2006 Growth in the neonatal intensive care unit influences neurodevelopmental and growth outcomes of extremely low birth weight infants. *Pediatrics* 117:1253–1261
- Uthaya S, Thomas EL, Hamilton G, Dore CJ, Bell J, Modi N 2005 Altered adiposity after extremely preterm birth. *Pediatr Res* 57:211–215
- Hofman PL, Regan F, Jackson WE, Jefferies C, Knight DB, Robinson EM, Cutfield WS 2004 Premature birth and later insulin resistance. *N Engl J Med* 351:2179–2186
- Regan FM, Cutfield WS, Jefferies C, Robinson E, Hofman PL 2006 The impact of early nutrition in premature infants on later childhood insulin sensitivity and growth. *Pediatrics* 118:1943–1949
- Brunton JA, Saigal S, Atkinson SA 1998 Growth and body composition in infants with bronchopulmonary dysplasia up to 3 months corrected age: a randomized trial of a high-energy nutrient-enriched formula fed after hospital discharge. *J Pediatr* 133:340–345
- Wauben IP, Atkinson SA, Shah JK, Paes B 1998 Growth and body composition of preterm infants: influence of nutrient fortification of mother's milk in hospital and breastfeeding post-hospital discharge. *Acta Paediatr* 87:780–785
- Yadav M, Thomas AG 2000 Feeding preterm infants after hospital discharge: effect of diet on body composition. *J Pediatr Gastroenterol Nutr* 31:462–463
- De Curtis M, Pieltain C, Studzinski F, Moureau V, Gerard P, Rigo J 2001 Evaluation of weight gain composition during the first 2 months of life in breast- and formula-fed term infants using dual energy X-ray absorptiometry. *Eur J Pediatr* 160:319–320
- De Curtis M, Pieltain C, Rigo J 2002 Body composition in preterm infants fed standard term or enriched formula after hospital discharge. *Eur J Nutr* 41:177–182
- Pieltain C, De Curtis M, Gerard P, Rigo J 2001 Weight gain composition in preterm infants with dual energy X-ray absorptiometry. *Pediatr Res* 49:120–124
- Koo WW, Hockman EM 2006 Posthospital discharge feeding for preterm infants: effects of standard compared with enriched milk formula on growth, bone mass, and body composition. *Am J Clin Nutr* 84:1357–1364
- Cooke RJ, Rawlings DJ, McCormick K, Griffin IJ, Faulkner K, Wells JC, Smith JS, Robinson SJ 1999 Body composition of preterm infants during infancy. *Arch Dis Child Fetal Neonatal Ed* 80:F188–F191
- Ong KK, Loos RJ 2006 Rapid infancy weight gain and subsequent obesity: systematic reviews and hopeful suggestions. *Acta Paediatr* 95:904–908
- Ashworth A 1969 Growth rates in children recovering from protein-calorie malnutrition. *Br J Nutr* 23:835–845
- MacLean WC Jr, Graham GG 1980 The effect of energy intake on nitrogen content of weight gained by recovering malnourished infants. *Am J Clin Nutr* 33:903–909
- Jackson AA 1990 Protein requirements for catch-up growth. *Proc Nutr Soc* 49:507–516
- Jackson AA, Golden MH, Jahoor PF, Landman JP 1980 The isolation of urea nitrogen and ammonia nitrogen from biological samples for mass spectrometry. *Anal Biochem* 105:14–17
- Embleton NE, Pang N, Cooke RJ 2001 Postnatal malnutrition and growth retardation: an inevitable consequence of current recommendations in preterm infants? *Pediatrics* 107:270–273