Published in final edited form as:

J Dev Orig Health Dis. 2010 October ; 1(5): 292–299. doi:10.1017/S2040174410000358.

Early infancy – a critical period for development of obesity

M. W. Gillman

Obesity Prevention Program Department of Population Medicine Harvard Medical School Harvard Pilgrim Health Care Institute, Boston MA USA

Abstract

Abundant epidemiologic evidence from the developed world now shows that more rapid weight gain during the first half of infancy predicts later obesity and cardio-metabolic risk. In countries in transition in which stunting is still prevalent, distinguishing the effects of gain in weight from linear growth remains a challenge. Moreover very few studies to date have incorporated body composition measures during infancy, which is key to understanding determinants of infant weight gain that also predict later obesity. In addition to infant feeding type potential determinants include the perinatal endocrine milieu. Animal and emerging human data raise the possibility that ensuring adequate leptin exposure to the growing fetus may regulate energy balance as the infant grows. Understanding these pathways as well as examining the balance between cardiovascular and cognitive effects in both term and preterm infants will point the way toward effective interventions to alter infant growth to prevent later obesity.

Keywords

growth; infancy; leptin; obesity; weight gain

Obesity and its major consequences, diabetes and cardiovascular disease, are highly prevalent among adults in the developed world and are increasingly so in countries undergoing the nutritional/epidemiologic transition. Rates of obesity have mushroomed in children across the world, in whom excess adiposity causes asthma and orthopedic problems, undesirable cardiometabolic risk profiles and psychosocial adversity. Increasing obesity rates have affected all age groups, even infants.¹ Once obesity exists, tenacious physiological processes resist weight loss.² By age 5 years, childhood obesity appears relatively resistant to change.³ For these reasons, early childhood prevention of obesity is crucial.⁴ In this review, I focus on the first few months of life as a potentially critical period for the development of obesity, and therefore a key period for prevention. Most of the emphasis is on studies from the developed world, although I briefly contrast these with studies from low- and middle-income countries.

Address for correspondence: Dr Matthew W. Gillman Obesity, Prevention Program, Department of Population Medicine, Harvard Medical School/Harvard Pilgrim Health Care Institute, 133 Brookline Avenue, 6th floor, Boston MA 02235, USA. matthew_gillman@hms.harvard.edu.

^aPresented in part at the 6th World Congress on Developmental Origins of Health and Disease, Santiago Chile. November 2009 and at the 65th Nestlé Nutrition Institute Workshop. Importance of Growth for Health and Development Kuala Lumpur Malaysia March 2009.

Early infancy is a period of many rapid changes. In the United States, in relative terms weight gain in the first 6 months of life primarily comprises gain in fat, whereas fat-free mass accumulates faster after birth. This phenomenon is depicted in Figure 1: percent fat mass rises in the first half-year before falling gradually in the ensuing year-and-a-half (Fig. 1).^{5,6}

During early infancy, organs and systems are in developmentally plastic stages. In classic experiments from about 50 years ago, reducing energy intake in the first few weeks of life among rat pups produced a lower trajectory of weight gain for the animal's lifespan even if normal energy intake was restored afterward (Fig 2).⁷ In contrast energy reduction during 'adolescence' had only a transient effect on weight gain. In a more recent rat model, administration of leptin in the first two postnatal weeks abolished the otherwise permanent offspring metabolic effects of prenatal maternal energy restriction.⁸ These and other animal experiments raise the possibility that the early postnatal period may be critical to development of healthful energy homeostasis, although one must remember that some aspects of postnatal development in the rat are equivalent to prenatal development in the human.

Epidemiologic evidence from developed countries

A large number of epidemiologic studies, mostly from the developed world,⁹⁻¹¹ have now addressed the role of weight gain during infancy as a predictor of later adiposity. For example, in a 2005 review of 10 studies, Baird *et al.*⁹ found that relative risks of later obesity ranged from 12 to 57 among infants with more rapid weight gain in the first year of life. Associations were consistent for obesity at different ages and for births from 1927 to 1994. In these studies, most outcomes were limited to body mass index (BMI) rather than more direct measures of adiposity or its physiologic consequences. Furthermore, in these studies the typical predictor was gain in weight during infancy, rather than any measure of weight-for-length or, even better (but not to date), body composition.

Since 2005, more observational studies have appeared, mostly from developed countries, and some with measured adiposity outcomes in addition to BMI. Yli-Harjula *et al.*¹² used a bioimpedance technique to measure body composition among almost 2000 Finnish adult men and women whose weights and heights were available from child records. Gain in BMI from birth to age 1 year, or 1 to 2 years, was associated with later lean, but not fat, mass. The authors did not subdivide the first year of life, but the visual impression from the published figures in Barker *et al.*¹³ from the same cohort suggests that the BMI of Finnish boys who eventually developed coronary heart disease increased in the first 3 months before decreasing (Fig. 3).

Among several hundred French boys and girls, also using a bioimpedance technique, Botton *et al.*¹⁴ showed that weight gain velocity at 3 and 6 months predicted adolescent fat mass better than weight gain velocity at 1 or 2 years. In agreement with that study, among 234 British 4- to 20-year-olds with gold standard body composition measures from a four-compartment model, Chomcho *et al.*¹⁵ showed that weight gain from birth to 3 months predicted both fat mass and fat-free mass; weight gain from 3 to 6 months predicted fat mass

only, and weight gain from 6 to 12 months predicted neither. Weight gain in the early months also predicted centrally deposited fat as indicated by waist circumference and (less so) by dual X-ray absorptiometry (DXA; Fig 4).

Data are emerging on the relationship of infant weight gain with cardiometabolic risk factors. In the US cohort study Project Viva, gain in weight-for-length from 0 to 6 months predicted not only a higher BMI and sum of skinfolds but also blood pressure at age 3 years.^{16,17} In the UK's Barry Caerphilly cohort, a steeper trajectory of weight gain in the first 5 months of life predicted higher blood pressure in adulthood.¹⁸ In the Project Viva cohort, the association of infant weight-for-length gain with 3-year blood pressure was stronger among infants born small for dates (Fig 5) but no similar effect modification by fetal growth was evident for BMI or skinfold outcomes.¹⁷

In the SWEDES study, weight gain from 0 to 6 months predicted both adiposity and a metabolic risk score at age 17 but gain from 3 to 6 years was not associated with this cluster of metabolic risk factors.¹⁹ Similarly, in a small Dutch cohort, Leunissen *et al.*²⁰ reported that weight gain in the first 3 months of life was associated with central obesity, abnormal insulin response and adverse lipid levels in young adulthood.

These studies, which together point to the importance of weight gain in the first half of infancy agree with recent findings from a cohort culled from electronic medical records of well-child visits in a managed care organization. In this group of over 22,000 children 0–5 years old, my colleagues and I observed that upward crossing of two major weight for length percentile lines on the CDC growth charts²¹ in the first 6 months was both common and predicted a high risk of obesity 5 years later.²² Upward crossing from 6 to 12, 12 to 18 or 18 to 24 months was less common and less predictive (Fig 6).

Data presented in abstract form at the 6th World Congress of DOHaD adds to the evidence of long-term effects of early infancy weight gain. In the Dutch ABCD study, more or less rapid weight gain in the first 6 months of life was related to higher fat mass 5 years later.²³ A sib-pair analysis from the US National Collaborative Perinatal Project confirmed the association of early infancy weight gain with BMI at age 7 years,²⁴ although weight gain in later infancy and pre-school years also predicted 7-year BMI.

Data from randomized trials are not only scarcer than from observational studies but also harder to interpret. That is because weight gain can result from many determinants, and existing trials use only variations in infant feeding to effect changes in growth. Nevertheless, the studies of Lucas and Singhai are instructive. Findings from a series of observational follow-up studies of a subset of participants in feeding trials of premature infants suggest that weight gain in the first few weeks is directly associated with adolescent blood pressure and plasma levels of insulin and leptin.²⁵ In their more recent trials, term small-for-gestational age infants randomized to energy-enriched formula had more rapid weight gain from 0 to 9 months and higher fat mass and diastolic blood pressure at age 6–8 years.²⁶ These findings are consistent with those of Stettler *et al.*²⁷ who showed that, weight gain in the first week of life in a formula-only fed population was directly associated with overweight in adulthood.

Evidence from developing countries

In summary, mounting evidence from the developed world suggests that the first few months of life are critical for development of obesity and its related-health conditions. Representation from developing countries, however, where wasting and (especially) stunting are still prevalent, is limited. The same is true for lower-income and racial/ethnic minority populations in western societies. The COHORTS collaboration of five longitudinal studies from low- and middle-income countries is poised to make substantial contributions to this literature. In a pooled analysis from these studies, Adair *et al.*²⁸ reported that weight gains in the first second and third-fourth years of life predict higher adult blood pressure level, through their contribution to adult BMI. Two of the component studies are from Delhi, India and Cebu Philippines. In the Delhi cohort, gain in BMI in the first 6 months was related to BMI, lean mass and (less strongly), to the sum of skinfolds in adulthood.²⁹ In an Indian cohort from Pune however, an abstract from the DOHaD Congress indicated that weight gain during the first 6 months did not appear to predict cardiovascular risk factors at age 12 years.³⁰ In data from the Cebu longitudinal study presented at the DOHaD Congress, weight gain from birth to 4 months predicted a (non-significant) 33% increase in insulin resistance 22 years later, apparently mediated by the association of early infant weight gain with adult BMI.³¹ In other DOHaD abstracts, in a low-income population from Brazil, weight gain from birth to 6 months conferred a greater than 4-fold increase in the prevalence of obesity at age 10 years.³² In addition, in a Chilean cohort, one of the few to incorporate length and weight measures during infancy, gain in BMI from birth to 6 months, as well as gain after 6 months, was associated with higher BMI, fat mass and fat-free mass at age 5 years.³³ Future analyses from the COHORTS group and other studies from developing countries will benefit from evaluating weight-for-length (or BMI), rather than weight alone, during infancy because length faltering in the first 1–2 years of life is often still common in these populations.

Areas for research

A number of research advances are needed to understand more clearly the impact of gain in adiposity in the first few months of life. The first is longitudinal body composition measures during infancy (the exposure period). As weights during infancy are typically available and relatively accurate, most studies have employed only weight measurements. Using weight-for-length is an improvement if length is measured by research standards,³⁴ but even the addition of length is suboptimal. While weight and length are relevant for clinical decision-making, relying on these as exposures in research studies does not provide sufficient information to investigate mechanisms and determinants. Part of the weight (or weight-for-length) gain during infancy comprises lean mass in addition to fat mass. It is not known whether rapid increase in lean mass predicts later obesity and its adverse consequences as strongly as does fat mass. However, this information is key to understanding etiology and thus potential preventive measures. Unfortunately, many body composition techniques are not feasible for large epidemiologic studies. For example, DXA requires babies to be still for a few minutes and emits a small amount of radiation. PEA-POD – a device based on air displacement plethysmography – will not fit babies > 8 kg. MRI is expensive. Skinfold thicknesses are inexpensive and portable but require good training. One technique under

investigation for this age group is bioimpedance, which may represent a good compromise for estimating fat and lean mass over time in infants and children.

The second challenge is identifying modifiable determinants of gain in adiposity in the first few months of life that also predict risk of later obesity. One common assumption is that the mode of infant feeding is the main factor, but this assumption is not necessarily true. First, many but not all studies show that having been breastfed is associated with lower rates of later obesity.³⁵ Second, in Project Viva, while a longer breastfeeding duration was associated with lower prevalence of obesity at age three, this effect did not appear to be mediated by weight gain in the first 6 months (van Rossem *et al.*, unpublished data). In addition, in many studies breastfeeding actually results in faster weight gain than formula feeding in the first few months; only later in infancy do breastfed infants have lower weights (Fig 7).^{36,37} Nevertheless, some dietary components may play a role. In a recent randomized trial, Koletzko *et al.*³⁸ showed that among formula-fed babies, increased protein as a fraction of energy intake resulted in lower gain in weight-for-length over the first 2 years.

It is also plausible that prenatal factors could be involved in entraining postnatal gain in adiposity, especially hormonal adaptations in the maternal-placental-fetal unit.³⁹ A preliminary analysis from Project Viva shows that gestational diabetes, as well as higher umbilical cord blood leptin concentration, is associated with *less* rapid gain in weight-for-length from birth to 6 months.⁴⁰ In abstracts presented at the 6th DOHaD Congress several other putative determinants were presented including FTO genotype AA,^{41,42} lower maternal triglyceride level⁴³ and higher cord blood level of c-peptide.⁴⁴ Additional potential determinants of variation in weight gain during infancy as yet understudied, include exposure to endocrine disruptors such as bisphenol A⁴⁵ and effects of the microbiota.⁴⁶

The actions of leptin may be of particular importance. Leptin, sometimes called the ‘fullness hormone,’ is elaborated by adipocytes and other tissues. In older children and adults leptin levels are associated with subsequent weight gain presumably due to leptin resistance.^{47,48} In younger children, however, the situation appears different. In Project Viva cord blood leptin level – which is derived partly from fetal fat and partly from the placenta – predicted not only slower infant weight gain but also lower BMI at age 3 years.⁴⁹ In the mouse, experiments suggest that the surge of leptin observed in postnatal weeks 1–2 is critical for maturing neural projections in hypothalamic regions responsible for appetite regulation.⁵⁰ Leptin administration to adult leptin-deficient mice does not result in the same maturation. In the rat, paternal leptin administration abolishes the otherwise deleterious metabolic effects of prenatal undernutrition.⁵¹ In addition, oral leptin administration during lactation causes reduced food intake, less weight gain and reduced insulin and leptin resistance in the adult rat.⁵² Taken together, these observations raise the possibility that sufficient leptin during critical hypothalamic developmental periods may have long-lasting beneficial effects on appetite regulation and thus obesity prevention.

Clinical and public health implications

Another challenge is mounting interventions to modify any determinants discovered through observational studies. As the nutritional hormonal or other pathways that lead to harmful

levels of weight gain are likely to be complex, so must any interventions to modify them take these complexities into account. Modifying an infant weight trajectory by any means available may or may not do more metabolic good than harm in the long run.

In addition, interventions that improve some health outcomes may not do the same for others. The amount of weight gain that optimizes both neurocognitive and cardiometabolic risk may differ by gestational age. Among infants born pre-term more rapid weight gain in early infancy predicts better neurocognitive outcomes in childhood,^{53,54} whereas its effects on obesity and cardiovascular risk factors is less clear.^{55,56} In term infants infant weight gain does not appear to be a major factor in predicting later cognition (Fig 8).⁵⁷

Ultimately the need will exist to educate clinicians, policy makers and parents about the findings from these studies. It will not be enough to have pediatric clinicians identify infants who gain rapidly from the usual growth charts, because the proper response is not yet known. Attempting to modify energy intake or expenditure among infants who are entrained by prenatal hormonal or genetic pathways to gain weight on a certain trajectory may be ineffective or harmful.

Researchers need to find the optimal amount of gain in weight and length in early infancy for a variety of populations. Clinicians and the public health community will be interested in those findings, but they will be more informed by research that addresses the challenge of how to achieve the optimal size for each infant. The answers hold great promise for prevention of obesity and its myriad adverse health sequelae.

Acknowledgments

This study is supported by a grant from NIH (K24 HI 068041).

References

1. Kim J, Peterson KE, Scanlon KS, et al. Trends in overweight from 1980 through 2001 among preschool-aged children enrolled in a health maintenance organization. *Obesity* (Silver Spring). 2006; 14:1107–1112. [PubMed: 16899790]
2. Leibel RL. Molecular physiology of weight regulation in mice and humans. *Int J Obes (Lond)*. 2008; 32(Suppl 1):S98–S108. [PubMed: 19136999]
3. Gardner DS, Hosking J, Metcalf BS, et al. Contribution of early weight gain to childhood overweight and metabolic health: a longitudinal study (Early Bird 36). *Pediatrics*. 2009; 123:e67–e73. [PubMed: 19117849]
4. Gillman MW. Early infancy as a critical period for development of obesity and related conditions. *Nestlé Nutr Workshop*. 2010; 65:13–24.
5. Veldhuis JD, Roemmich JN, Richmond EJ, Bowers CY. Somatotrophic and gonadotrophic axes linkages in infancy childhood and the puberty-adult transition. *Endocr Rev*. 2006; 27:101–140. [PubMed: 16434512]
6. Butte NF, Hopkinson JM, Wong WW, Smith EO, Ellis KJ. Body composition during the first 2 years of life: an updated reference. *Pediatr Res*. 2000; 47:578–585. [PubMed: 10813580]
7. Widdowson EM, McCance RA. The effect of finite periods of undernutrition at different ages on the composition and subsequent development of the rat. *Proc R Soc Lond [Biol]*. 1965; 158:329–342.
8. Vickers MH. Developmental programming and adult obesity: the role of leptin. *Curr Opin Endocrinol Diabetes Obes*. 2007; 14:17–22. [PubMed: 17940414]

9. Baird J, Fisher D, Lucas P, et al. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *BMJ*. 2005; 331:929–934. [PubMed: 16227306]
10. Ong KK, Loos RJ. Rapid infancy weight gain and subsequent obesity: systematic reviews and hopeful suggestions. *Acta Paediatr*. 2006; 95:904–908. [PubMed: 16882560]
11. Monteiro PO, Victora CG. Rapid growth in infancy and childhood and obesity in later life – a systematic review. *Obes Rev*. 2005; 6:143–154. [PubMed: 15836465]
12. Yliharsila H, Kajantie E, Osmond C, et al. Body mass index during childhood and adult body composition in men and women aged 56 to 70 years. *Am J Clin Nutr*. 2008; 87:1769–1775.
13. Barker DJP, Osmond C, Forsen TJ, Kajantie E, Eriksson JG. Trajectories of growth among children who later have coronary events. *N Engl J Med*. 2005; 353:1802–1809. [PubMed: 16251536]
14. Botton J, Heude B, Maccario J, et al. Postnatal weight and height growth velocities at different ages between birth and 5 years and body composition in adolescent boys and girls. *Am J Clin Nutr*. 2008; 87:1760–1768. [PubMed: 18541566]
15. Chomtho S, Wells JC, Williams JE, et al. Infant growth and later body composition: evidence from the 4-component model. *Am J Clin Nutr*. 2008; 87:1776–1784. [PubMed: 18541568]
16. Belfort MB, Rifas-Shiman SI, Rich-Edwards J, Kleinman KP, Gillman MW. Size at birth infant growth, and blood pressure at three years of age. *J Pediatr*. 2007; 151:670–674. [PubMed: 18035150]
17. Taveras EM, Rifas-Shiman SI, Belfort MB, et al. Weight status in the first 6 months of life and obesity at 3 years of age. *Pediatrics*. 2009; 123:1177–1183. [PubMed: 19336378]
18. Ben Shlomo Y, McCarthy A, Hughes R, et al. Immediate postnatal growth is associated with blood pressure in young adulthood; the Barry Caerphilly growth study. *Hypertension*. 2008; 52:638–644. [PubMed: 18768401]
19. Ekelund U, Ong KK, Linne Y, et al. Association of weight gain in infancy and early childhood with metabolic risk in young adults. *J Clin Endocrinol Metab*. 2007; 1:98–103. [PubMed: 17032722]
20. Leunissen RW, Kerkhof GF, Stijnen T, Hokken-Koelega A. Timing and tempo or first-year rapid growth in relation to cardiovascular and metabolic risk profile in early adulthood. *JAMA*. 2009; 301:2234–2242. [PubMed: 19491185]
21. Centers for Disease Control and Prevention. Retrieved December 8 2009 from <http://www.cdc.gov.GrowthCharts/>
22. Taveras, EM.; Rifas-Shiman, SI.; Oken, E., et al. Crossing growth percentiles in infancy and risk of obesity at age 5; 2008 Pediatric academic Societies Annual Meeting; Honolulu HT. May 2–6; 2008.
23. deBeer M, van Eijdsen M, Vrijkotte TGM, Gemke RBJ. Relation of early weight gain with body size body composition and fat distribution at the age of 5 in a prospective birth cohort: the ABCD study. *J Dev Orig Health Dis*. 2009; 1(Suppl 1):s18–s19.
24. Terry MB, Wei Y, Esserman D, McKeague I, Susser E. Pre- and postnatal determinants of childhood body size. *J Dev Orig Health Dis*. 2009; 1(Suppl 1):s31.
25. Singhal A, Lucas A. Early Origins of cardiovascular disease: is there a unifying hypothesis? *Lancet*. 2004; 363:1642–1645. [PubMed: 15145640]
26. Singhal A, Cole TJ, Fewtrell M, et al. Promotion of faster weight gain in infants born small for gestational age is there an adverse effect on later blood pressure? *Circulation*. 2007; 115:213–220. [PubMed: 17179023]
27. Stettler N, Stallings VA, Troxel AB, et al. Weight gain in the first week of life and overweight in adulthood: a cohort study of European American subjects fed infant formula. *Circulation*. 2005; 111:1897–1903. [PubMed: 15837942]
28. Adair IS, Martorell R, Stein AD, et al. Size at birth weight gain in infancy and childhood and adult blood pressure in 5 low- and middle income-country cohorts: when does weight gain matter? *Am J Clin Nutr*. 2009; 89:1383–1392. [PubMed: 19297457]
29. Sachdev HS, Fall CH, Osmond C, et al. Anthropometric indicators of body composition in young adults: relation to size at birth and serial measurements of body mass index in childhood in the New Delhi birth cohort. *Am J Clin Nutr*. 2005; 82:456–466. [PubMed: 16087993]

30. Joglekar C, Yajnik CS, Osmond C, Fall C. Newborn size postnatal growth and cardiovascular risk factors and body composition at 12 years (Pune Maternal Nutrition Study). *J Dev Orig Health Dis.* 2009; 1(Suppl 1):s19–s20.
31. Slining MM, Adair LS. Early rapid weight gain and insulin resistance in young adulthood: evidence from the Cebu Longitudinal Health and Nutrition Study. *J Dev Orig Health Dis.* 2009; 1(Suppl 1):s30–s31.
32. Fernandes MTB, Ferraro AA, Bassotto AP, Santos E, Schwartzman C. Association between catch-up in the first years of life and overweight/obesity at 10 years of age, in a low-income community in Sao Paulo Brazil. *J Dev Orig Health Dis.* 2009; 1(Suppl 1):s201–s205.
33. Corvalan C, Uauy R, Lera I, Galvan M, Kain J. Body mass index and height growth from birth to 4 y and body composition at 5 y in Chilean children with normal birthweight. *J Dev Orig Health Dis.* 2009; 1(Suppl 1):s204.
34. Rifas-Shiman SI, Rich-Edwards JW, Scanlon KS, Kleinman K, Gillman MW. Misdiagnosis of overweight and underweight children younger than 2 years of age due to length measurement bias. *MedGenMed.* 2005; 7:56. [PubMed: 16614678]
35. Owen CG, Martin RM, Whincup P, Davey Smith G, Cook DG. Effect of infant feeding on the risk of obesity across the life course: a quantitative review of published evidence. *Pediatrics.* 2005; 115:1367–1377. [PubMed: 15867049]
36. Kramer MS, Guo T, Platt RW, et al. Breastfeeding and infant growth: biology or bias? *Pediatrics.* 2002; 110:343–347. [PubMed: 12165588]
37. Kramer MS, Guo T, Plarr RW, et al. Feeding effects on growth during infancy. *J Pediatr.* 2004; 145:600–605. [PubMed: 15520757]
38. Koletzko B, von Kries R, Closa R, et al. Lower protein in infant formula is associated with lower weight up to age 2 y: a randomized clinical trial. *Am J Clin Nutr.* 2009; 89:1836–1845. [PubMed: 19386747]
39. Gillman MW, Rifas-Shiman S, Kleinman K, et al. Developmental origins of childhood overweight: potential public health impact. *Obesity (Silver Spring).* 2008; 16:1651–1656. [PubMed: 18451768]
40. Parker, M.; Rifas-Shiman, SI.; Belfort, MB., et al. Pre- and perinatal predictors of weight gain in early infancy; 2009 Pediatric Academic Societies Annual Meeting; Baltimore, MD.
41. Pennell CE, Ang QW, Marsh JA, et al. Gene environment interactions between the fat mass and obesity-associated (fmo) gene and nutrition modify the association between fmo and obesity in childhood and adolescence. *J Dev Orig Health Dis.* 2009; 1(Suppl 1):s34–s35.
42. deBeer M, Vrijkotte TGM, van der Wal MF, van Weissenbruch MM, Gemke RBJ. Relation of maternal hypertension with infant growth: the ABCD study. *J Dev Orig Health Dis.* 2009; 1(Suppl 1):s66–s67.
43. Algera SJ, Twickler ThB, van Eijdsden M, Vrijkotte TGM. Maternal lipid profile in early pregnancy in relation to prenatal and postnatal growth. *J Dev Orig Health Dis.* 2009; 1(Suppl 1):s125.
44. Regnault N, Dargent-Molina P, Botton J, et al. Higher serum C-peptide concentrations are associated with slower growth rare in the first year of life in girls. *J Dev Orig Health Dis.* 2009; 1(Suppl 1):s169–s170.
45. Lang IA, Galloway TS, Scarlett A, et al. Association of urinary bisphenol A concentration with medical disorders and laboratory abnormalities in adults. *JAMA.* 2008; 300:1303–1310. [PubMed: 18799442]
46. Turnbaugh PJ, Ley RE, Mahowald MA, et al. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature.* 2006; 444:1027–1031. [PubMed: 17183312]
47. Fleisch AF, Agarwal N, Roberts MD, et al. Influence of serum leptin on weight and body fat growth in children at high risk for adult obesity. *J Clin Endocrinol Metab.* 2007; 92:948–954. [PubMed: 17179198]
48. Johnson MS, Huang II, Figueroa-Colon R, Dwyer JH, Goran MI. Influence of leptin on changes in body fat during growth in African American and white children. *Obes Res.* 2001; 9:593–598. [PubMed: 11595775]
49. Mantzoros CS, Rifas-Shiman SI, Williams CJ, et al. Cord blood leptin and adiponectin as predictors of adiposity in children at 3 years of age: a prospective cohort study. 2009; 123:682–689.

50. Bouret SG, Draper SJ, Simerly R. Trophic action of leptin on hypothalamic neurons that regulate feeding. *Science*. 2004; 304:108–110. [PubMed: 15064420]
51. Vickers MH, Gluckman PD, Coveny AH, et al. Neonatal leptin treatment reverses developmental programming. *Endocrinology*. 2005; 146:4211–4216. [PubMed: 16020474]
52. Sanchez J, Priego I, Palou M, et al. Oral supplementation with physiological doses of leptin during lactation in rats improves insulin sensitivity and affects food preferences later in life. *Endocrinology*. 2008; 149:733–740. [PubMed: 17991728]
53. Ehrenkranz RA, Dusick AM, Vohr BR, et al. Growth in neonatal intensive care unit influences neurodevelopmental and growth outcomes of extremely low birth weight infants. 2006; 117:1253–1261.
54. Casey PH, Whiteside-Mansell I, Barrett K, Bradley RH, Gargus R. Impact of prenatal and/or postnatal growth problems in low birth weight preterm infants on school-age outcomes: an 8-year longitudinal evaluation. 2006; 118:1078–1086. [PubMed: 16951001]
55. Belfort, MR.; Martin, CR.; Gillman, MW.; McCormick, MC. Does more rapid infant weight gain lead to higher blood pressure or better neurodevelopment in former preterm infants?; 2009 Pediatric Academic Societies Annual Meeting; Baltimore MD. May 2–5; 2009.
56. Washburn IK, Nixon PA, Snively BM, O'Shea TM. Early weight gain and outcomes at 9 years in very low birth weight children. *J Dev Orig Health Dis*. 2009; 1(Suppl 1):s223–s224.
57. Belfort MB, Rifas-Shiman SI, Rich-Edwards JW, et al. Infant growth and child cognition at 3 years or age. *Pediatrics*. 2008; 122:e689–e695. [PubMed: 18762504]

Fig. 1.
Changes in percent fat mass (%FM) during the first 2 years of life Adapted from Butre *et al.*⁶.

Fig 2.
Lifelong lower trajectory of weight gain programmed by a reduction in energy reduction during the lactation period in the rat. Adapted from Widdowson and McCance.⁷

Fig 3.

Mean z (SD) scores for height, weight and body mass index (BMI) in the first 11 years after birth among boys who had coronary heart disease as adults. The mean values for all boys are set at zero, with deviations from the mean expressed as standard deviations (z -scores).

Reproduced with permission from Barker *et al.*¹³

Fig. 4.

Adjusted mean SD (z) scores for later body mass index (BMI), fat mass index (FMI), fat-free mass index (FFMI) and waist circumference (WC), stratified according to change in weight SDS scores quartiles from 0 to 3 months and 3 to 6 months of age. Error bars indicate 95% CIs. Data from general linear models adjusted for birth weight SDS, sex, puberty physical activity, socioeconomic class, ethnicity and parental BMI. Reproduced with permission from Chomtho *et al.*¹⁵

Fig. 5.

Predicted difference in systolic blood pressure (BP) at age 3 years according to quartile of weight-for-length z-score at birth and age 6 months adjusted for child age, sex, height and blood pressure measurement conditions, and maternal income, education, race ethnicity and smoking status. Reproduced with permission from Belfort *et al.*¹⁶

Fig. 6.

Prevalence of obesity at age 5 years (body mass index greater than 95th percentile) predicted by crossing upwards two major percentile lines on the CDC growth charts 21 from 1 to 6, 6 to 12, 12 to 18 and 18 to 24 months of age Taveras *et al.* unpublished data.

Fig 7.

Weight-for-age z-score in the first year of life in experimental v control trial groups and three observational groups Data from a PROBIT randomized controlled trial of breastfeeding promotion in the Republic of Belarus. Reproduced with permission from Kramer *et al.*³⁶

Fig 8.

Peabody Picture Vocabulary Test III (PPVT-III) score (standard error) within deciles of infant weight z-score at 6 months. Estimates adjusted for child birth weight z-score sex, age at cognitive assessment, gestational age, breastfeeding duration race/ethnicity and English as second language status; maternal age, parity, smoking status and PPVT-III score; parental educational levels; and annual household income. Reproduced with permission from Belfort *et al.*⁵²