Published in final edited form as:

J Pediatr. 2012 December ; 161(6): 1028–1034. doi:10.1016/j.jpeds.2012.06.001.

Decelerated Early Growth in Infants of Overweight and Obese Mothers

Katie Larson Ode, MD¹, Heather Gray, MPH², Sara Ramel, MD³, Michael Georgieff, MD³, and Ellen W. Demerath, PhD²

¹Department of Pediatrics, University of Iowa, Iowa City, Iowa, United States

²Department of Epidemiology and Community Health, University of Minnesota, Minneapolis, Minnesota, United States

³Department of Pediatrics, University of Minnesota, Minneapolis, Minnesota, United States

Abstract

Objective—To investigate the relationship between maternal pre-pregnancy BMI and early infant growth and body composition.

Study design—Prospective cohort study performed at a University hospital/surrounding community. Ninety-seven non-diabetic mothers with singleton, term, healthy infants completed study visits at 2 weeks and 3 months of age. Pre-pregnancy, 59 mothers were normal weight, 18 were overweight, and 20 were obese. Infant anthropometrics and body composition via air-displacement plethysmography were measured. Infant feeding information and maternal pre-pregnancy weight were self-reported. Additional data were obtained via self-report and the medical record. Main outcome measures: change in weight, length, fat free mass, and fat mass from 2 weeks to 3 months of age. Analysis was by multivariate linear regression.

Results—At 2 weeks, anthropometrics and body composition did not differ across maternal BMI groups. At 3 months infants of overweight or obese mothers had gained less weight ($p=0.02$), grew less in length ($p=0.01$), and gained less fat mass ($p=0.01$). Adjustment for breastfeeding status and regression to the mean via conditional change variables did not alter the results. The results were not altered after adjusting for maternal glucose values from a 50 g glucose challenge and for maternal smoking in a subset including 80% of the women.

Conclusions—Maternal overweight/obesity is associated with early deceleration in linear growth and adipose tissue accrual; replication of these findings is needed.

Keywords

infant growth; body composition; maternal obesity; adiposity

© 2012 Mosby, Inc. All rights reserved.

Corresponding Author: Katie Larson Ode, MD, Pediatric Endocrinology and Diabetes, UI Children's Hospital, 200 Hawkins Dr. 2857 JPP, Iowa City, IA 52242, katie-larsonode@uiowa.edu, Telephone: 319-356-4443, Fax: 319-356-8170.

Presented as a poster at the Pediatric Academic Societies' Meeting in Denver, CO, April 28-May 4, 2011.

The authors declare no conflicts of interest.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

From 1999–2004, 52% of US women of reproductive age were overweight or obese (1). Excess maternal weight prior to pregnancy increases offspring risk of obesity in later life (2, 3). The mechanisms underlying this association have not been fully elucidated, but pregnancy seems to be a critical window for the establishment of future metabolic patterns (4).

Early infancy may also be a sensitive period for later obesity risk, because the patterns of weight gain and growth in infancy have significant relationships to long-term obesity and metabolic risk (5). The rate of weight gain prior to 6 months of age seems to be especially pertinent (6).

In studies to date, some show increased maternal pre-pregnancy BMI to be associated with no effect on early infant growth, and others show an association with either increased or decreased early infant growth (7,8,9). This discrepancy may be explained in that most have focused on infant weight without taking into account linear growth and body composition. Characterizing infants not only by weight, but by body composition, may not only explain the differences found in the literature but may also provide clues as to the pathways from maternal to offspring obesity. However, there is a paucity of data in the literature directly evaluating the effect of maternal pre-pregnancy weight status on the rate of change in body composition of infants soon after birth. In this study, we sought to evaluate the relationship of maternal pre-pregnancy BMI to early infant growth and body composition. These data may add to the understanding of the origins of obesity and provide possible targets for obesity prevention.

Methods

Women were recruited during the third trimester of pregnancy primarily from an ongoing prospective cohort study of the relationship between maternal diet and birth outcomes, and additionally via fliers and word-of-mouth. The University of Minnesota's Institutional Review Board approved the study. All mothers provided verbal and written consent for themselves and their infants to participate in the study. Women were included if they were carrying an uncomplicated, singleton pregnancy and were excluded if they delivered prior to term (<37.0 weeks), were underweight prior to pregnancy (BMI <18.5 kg/m²), or developed gestational diabetes mellitus (GDM). GDM was defined as a 1 hour glucose value ≥130mg/dl (7.22 mmol/l) following a 50g glucose load, and subsequent glucose values during a 3 hour, 100g load, oral glucose tolerance test as follows: fasting plasma glucose ≥95 mg/dl (5.28 mmol/l), 1 hr ≥180mg/dl (10 mmol/l), 2 hr ≥155 mg/dl (8.60 mmol/l), or 3 hr ≥140 mg/dl (7.78 mmol/l) this definition was the standard in use by the obstetric practices in our area at the time of the study (10). Infants were excluded if they were small for gestational age (<10th percentile for weight for gestational age as determined by plotting on the appropriate CDC growth charts) (11). or if they had a health condition that would preclude them from safely being measured in the infant-sized air-displacement plethysmograph.

Mothers and infants were seen at the outpatient pediatric research center when the infant was two weeks of age and again at three months of age. At the two-week visit, demographic information and maternal and paternal self-reported height and weight were obtained by questionnaire. Maternal pre-pregnancy weight is routinely determined by self-report in the literature (2,3,6,8), and previous studies have shown acceptable agreement between maternal self-report and medical records from pregnancy (12). At both visits, the mother's standing height was obtained by wall-mounted stadiometer (SECA Hanover MD). Maternal pre-pregnancy BMI was calculated from self-reported pre-pregnancy weight and measured height at the first study visit. Infant feeding and sleep behavior were assessed by a second questionnaire (adapted from 13). The infant's recumbent length was obtained in duplicate by

trained staff using an infant recumbent length measuring board (Perspective Enterprises Portage, MI). Head circumference was obtained in duplicate using standard techniques. The infant was weighed nude to the nearest 0.0001 kg using the scale from the air displacement plethysmograph (ADP). Infant weight and length were used to calculate weight-for-age and length-for-age z scores, based on World Health Organization standards (14). Infant body composition was assessed using air-displacement plethysmography (ADP) (PeaPod, COSMED USA, Inc., Concord, CA), using previously described procedures (15). After body weight was obtained, the infant was placed inside the chamber wearing only a wig cap for determination of body volume. Fat mass and fat-free mass were calculated from weight and body volume using the Fomon prediction equation (16). Quality control for the plethysmograph was performed at least once per visit day per manufacturer recommendations.

Prenatal records were extracted to verify infant birth weight, presence of maternal smoking during pregnancy, and glucose levels obtained during 50g glucose load (which had been performed on all participants) and, if performed, 100g oral glucose tolerance tests for gestational diabetes mellitus.

Statistical analyses

Data analysis was performed using the Statistical Analysis Software version 9.2 (SAS institute, Cary NC, USA). All variables were assessed for normality of distribution. Maternal pre-pregnancy BMI was expressed as a categorical variable with normal BMI set at 18.5–24.9 kg/m², overweight at 25.0–29.9 kg/m² and obese as ≥ 30.0 kg/m². The association of maternal BMI category with infant body composition, anthropometrics and infant and parental characteristics was first examined in unadjusted models using ANOVA for continuous variables and chi-square testing for categorical variables. Variables that were associated at $p < 0.10$ in the unadjusted analysis were included as covariates in multiple linear regression models. Maternal height, paternal height, paternal BMI, infant race, maternal gestational weight gain category, parity, gestational age, infant birth weight, infant sex, exclusive breastfeeding and age of formula initiation were initially included in all models. Variables were retained in the multiple linear regression model if $p < 0.05$. Infant sex and gestational age and duration of exclusive breast feeding (never, 2 weeks, 3 months) were included in all models even when not significant by p value. Given that growth increments tend to be negatively correlated with the initial value (the phenomenon of “regression to the mean”) we calculated change variables from 2 weeks to 3 months conditional on the 2 week value (17). That is, conditional length, weight and weight-for-length gain from two weeks to three months of age were calculated from the linear regression of Z-scores at three months on Z-scores at two weeks, and conditional change in body composition variables were calculated from linear regression of the fat mass and fat free mass at 3 months on the same variable at 2 weeks. The resulting conditional variables at 3 months of age can be interpreted as the change in the variables from 2 weeks to 3 months beyond what would be predicted by regression to the mean over the time interval. Additionally, two subgroup analyses were performed, one including the one-hour glucose value from gestational diabetes screening as a continuous covariate, and the other including maternal smoking status during pregnancy as a dichotomous covariate.

Results

Of the one hundred and eighty-nine women without gestational diabetes who were contacted, 97 women and their infants completed both study visits (33 could not be reached, 28 were excluded, 24 declined, and 7 did not complete both visits). Fifty-nine women had a pre-pregnancy BMI in the normal range, 18 in the overweight range, and 20 in the obese range. There were some differences in maternal and infant characteristics by maternal BMI

group (Table I). More women in the overweight group gained excessive weight during pregnancy, as defined by the Institute of Medicine (18), than either the normal weight or the obese group ($p=0.009$). Infants born to mothers who were overweight but not obese prior to pregnancy had higher birthweights than infants of normal weight mothers ($p=0.005$), but birthweight did not differ between infants of normal weight and obese mothers ($p=0.7$). Infants born to overweight or obese mothers were also less likely to exclusively breastfeed ($p=0.002$).

In unadjusted analyses, there were no significant differences in infant weight, length, or head circumference, across maternal pre-pregnancy BMI categories at 2 weeks of age. By three months of age, infants born to overweight or obese mothers were shorter ($p=0.01$) and weighed less ($p=0.03$) than infants born to normal weight mothers, but head circumference was not different (Table I).

In the fully adjusted model, weight gain from 2 weeks to 3 months of age was significantly lower in infants of overweight ($p=0.0001$) and obese ($p=0.01$) mothers than infants of normal weight mothers (Table II). Infants of overweight and obese mothers also grew significantly less in length than infants of normal weight mothers ($p=0.004$ and $p=0.007$, respectively). Increase in head circumference was significantly lower in infants of obese mothers compared with infants of normal weight mothers ($p=0.02$). Infants born to overweight ($p=0.001$) and obese mothers ($p=0.02$) gained significantly less fat mass from 2 weeks to 3 months of age than did infants born to normal weight mothers. There was no difference in gain of fat free mass between infants of normal weight and obese mothers ($p=0.15$); however, infants of overweight mothers gained less fat free mass than infants of normal weight mothers ($p=0.01$). Although rates of pregnancy weight gain differed across maternal BMI categories, this was not significantly associated with infant growth and body composition in the multivariate models (data not shown). As rates of breastfeeding differed by maternal BMI category, we controlled for duration of exclusive breastfeeding in our models (Table II). The effect of maternal BMI category remained significant in these models and there were no independent differences in the changes in infant growth or body composition in those exclusively breastfed to 3 months compared with those not exclusive breastfed to 3 months ($p>0.09$ for all). We also examined whether the deceleration in infant weight started prior to the 2 week time point. We found, as expected, that weight gain from birth to 2 weeks was lower in infants of overweight and obese mothers than in infants of normal weight mothers, but reached statistical significance only in infants of overweight mothers ($p<0.01$).

The association between maternal BMI category and decreased infant weight and length gain remained significant when we adjusted for regression to the mean using conditional z scores, with infants of overweight and obese mothers showing lower conditional weight gain ($p=0.0001$, 0.02 , respectively) and lower conditional length gain ($p=0.007$, 0.006) than infants born to normal weight mothers (Table III). Conditional weight-for-length gain was not different among maternal BMI categories in the overall model ($p=0.2$), although the p value for infants of overweight mothers as compared with normal weight mothers was significant ($p=0.03$). Using conditional body composition variables, the data continued to indicate that infants of overweight ($p=0.0009$) and obese mothers ($p=0.00095$) had lower conditional fat mass gain compared with infants of normal weight mothers. There was no difference in conditional gain in fat free mass between infants born to normal weight mothers and infants born to obese mothers ($p=0.2$), however, infants of overweight mothers gained less fat free mass than infants of normal weight mothers ($p=0.02$).

We were able to verify from the medical records 1-hour glucose screening results for 78 (80%) of the women included in the study. Fifteen of these women initially had abnormal 1-

hour glucose values, but subsequently had normal values at all points on the 3-hour oral glucose tolerance test. The population who had glucose values available were more likely to feed formula at three months than those without available glucose levels ($p=0.04$). Otherwise, there was no difference in maternal or infant characteristics. There was no difference in proportions of pre-pregnancy BMI categories between the full sample and the subgroup ($p=0.77$). In bivariate analysis, maternal 1-hour glucose value was negatively related to infant length at 3 months ($p=0.02$). When the one-hour glucose value was included in the multivariate models, however, it was not significantly associated with any of the outcomes ($p>0.2$ for all).

We were able to verify maternal smoking status during pregnancy from the medical record for 80 of the women included in the study. Mothers who smoked during pregnancy were more likely to be obese prior to pregnancy ($p=0.0018$), and none of the overweight mothers smoked, but there was no significant association between maternal smoking during pregnancy and any of the outcome variables ($p>0.1$ for all).

Discussion

A pattern of early growth deceleration in infancy followed by growth acceleration in later infancy and childhood has been seen in infants of diabetic mothers, with Touger et al showing marked decline in weight z scores of infants of diabetic mothers from birth to 2 years of age with acceleration thereafter (19). In Regnault et al, who did not exclude mothers with gestational diabetes, infants of obese mothers were heavier and longer at birth, but had decreased weight and length-gain velocity such that by 3 months of age there was no difference in infant weight or length between infants of obese and normal weight mothers (7). Knight et al, who excluded maternal diabetes and controlled for maternal glycemia, had similar findings, showing a decline in weight and length standard deviation scores in infants of mothers in the highest weight tertile from birth to 3 months of age (9). The main difference between our study and those of Regnault and Knight is that in our study, the infants of obese mothers still experienced growth deceleration in the absence of GDM or elevated birthweights. This suggests that early infant growth deceleration in offspring of obese mothers may be at least partially independent of birth size.

Neither Regnault nor Knight studied body composition in their populations, making it difficult to determine whether the decreased velocity of weight gain in their study can be attributed to decreased gain of fat mass, as in our population. Eriksson et al found that maternal BMI correlated with infant birthweight and infant weight at 10 days, but did not correlate with body composition findings or to any anthropomorphic measurements at 3 months of age (20). However, their population, had a much lower rate of maternal obesity (5% vs 21%), which may have resulted in reduced power to detect differences in growth in offspring of obese and non-obese mothers. They also did not comment on maternal diabetes status (20). The HAPO study (21) obtained neonatal size and body composition in relationship to maternal BMI and gestational diabetes. The authors found that increased maternal BMI and gestational diabetes had independent, additive effects on the risk of elevated birthweight and percent body fat at 72 hours of life. However, subsequent body composition changes in these infants are unknown (21).

By what mechanism might maternal overweight/obesity lead to slower growth in early infancy? In early life, leptin has neurotrophic effects and is thought to be involved in the maturation of neural projections within the hypothalamus controlling appetite (22). Increased cord blood leptin has been associated with decreased weight gain for length from birth to 6 months of age in the Project Viva study (23). Leptin does not cross the placenta, therefore cord blood levels are due to production of leptin in fetal adipocytes, and not from

maternal levels (24). Elevated maternal leptin levels could, however, increase transfer of free fatty acids to the fetus, which could increase fetal fat mass and hence fetal leptin. However, this is not a likely mechanism in our population, as our infants had no difference in fat mass at two weeks of age and no difference in weight for length between the groups.

Traditionally, pituitary growth hormone was thought to have no effect on growth in early infancy. Growth *in utero* is dependent on insulin-like-growth factor one (IGF-1) which is driven primarily by fetal insulin secretion in response to fetal nutrition (glucose, free fatty acids and amino acids (25). However, it is now recognized that pituitary secretion of growth hormone does play a role in growth prior to birth and in early infancy (26). How the change from nutrition-dependent growth to growth hormone dependent growth is orchestrated in the fetus and young infant is not known, but it is possible that elevated *in utero* nutrition and the resultant increase in IGF-1 may cause feedback-inhibition of the pituitary growth hormone secretion and delay the onset of growth hormone driven growth. This could result in a growth pattern very similar to that observed in the infants of overweight and obese mothers in our study.

The obese pregnancy is also a chronic inflammatory state, which has been shown to induce increased free fatty acids, reactive oxygen species, inflammatory cells, and markers of endothelial dysfunction (27). Increased transfer of free fatty acids may promote fetal growth and gain of fat mass (28). One could hypothesize that while in utero, the deleterious effects of the inflammatory state are counterbalanced by excess nutrition, and in the early post-natal period, when excess energy from the mother is no longer available, growth would be relatively slower in these infants.

It has been shown that obese and overweight mothers who breastfeed produce less milk than normal weight mothers (29) and likewise in the present study, obese mothers were more likely to have fed their infants formula. Formula feeding is known to result in slower post-natal weight gain until approximately 3–6 months of age, when formula fed infants then begin to grow more rapidly, developing a greater risk for later obesity (30). We controlled for infant feeding type (exclusive breast milk feeding at 2 weeks and/or at 3 months) in our multivariate model, but this did not appear to mediate the relationship between maternal obesity and infant growth. It is possible, however, that a more quantitative measure of breast milk and formula intake might have explained our findings. In this regard, the observed growth deceleration in infants of overweight and obese mothers, if replicated, has significant clinical implications. If offspring of obese and overweight mothers tend to show a slower rate of linear growth in the early postnatal period, it may suggest to pediatricians and mothers that the infant is not receiving adequate nutrition, and thereby encourage mothers to cease exclusive breast feeding and initiate formula supplementation, or to augment milk feeds with cereals and other complementary foods earlier than is recommended. Further work delineating the bidirectional relationships between infant feeding behaviors, maternal obesity, and infant growth trajectories has been recently called for, and may help to identify causal mechanisms underlying our findings.

The effects of maternal obesity and overweight must always be separated from the effects of gestational diabetes mellitus, which often co-occurs with obesity. Our study is strengthened by the exclusion of women with any form of diabetes, but is nonetheless limited by the fact that glucose tolerance was determined from the medical chart, relying on diagnosis of GDM via standard screening, and that we were only able to obtain the glucose screening results on 80% of women. Given that there are effects on infant outcomes of maternal glycemia in the absence of clinical diagnosis of GDM (8, 19), and also that the HAPO study has demonstrated independent additive effects of maternal weight status and glycemia on infant birth weight and other outcomes (21), we cannot rule out that some of the effects found in

our study derive from subclinical hyperglycemia. However, the lack of effect when controlling for glycemia in our subgroup analysis suggests that growth deceleration in infants of obese mothers is at least partially independent of maternal glycemia.

Our study is also limited by the fact that we did not have complete smoking data on our sample, as smoking during pregnancy is well known to restrict infant linear growth. It is reassuring, however, that our subgroup analysis did not find evidence for a significant effect, and that similar decrements in growth were found in overweight mothers, none of whom reported smoking, and the obese mothers, who had a higher rate of smoking.

The complex interplay of maternal overweight/obesity, infant growth, and infant feeding has important clinical implications, and the somewhat counterintuitive findings of slower early fat mass gain in infants of overweight and obese mothers in this small exploratory study requires replication in larger prospective studies beginning in pregnancy.

Acknowledgments

Antoinette Moran, MD, professor and Division Chief of Pediatric Endocrinology at the University of Minnesota provided mentorship to K.O. and made significant contributions to the writing of the manuscript. Logan Spector, PhD, from the Division of Epidemiology and Clinical research in the Department of Pediatrics at the University of Minnesota provided access to his database and permission to contact his subjects for inclusion in our study. William Johnson, PhD, from the Division of Epidemiology and Community Health in the School of Public Health, assisted with analysis. Jan Reimer at the University of Minnesota Cancer Center, Megan Slater, MPH, in the Department of Pediatrics, and Laura Hauff, MA, in the Department of Anthropology all made critical contributions to subject recruitment, enrollment, data collection, and data entry. The Center for Neurobehavioral Development at the University of Minnesota provided material support for study visits.

Supported by the National Institutes of Health (U54 CA116849 to E.W.), NIH training grant (NIDDK T32 DK065519 to K.O. [PI: Antoinette Moran]), and University of Minnesota Academic Health Center Faculty Research Development (grant to E.D.).

Abbreviations

BMI	body mass index
GDM	gestational diabetes mellitus
IGF-1	insulin like growth factor 1

References

1. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999–2004. *JAMA*. 2006; 295:15849–15855.
2. Lake JK, Power C, Cole TJ. Child to adult body mass index in the 1958 British birth cohort: associations with parental obesity. *Arch Dis Child*. 1997; 77:376–81. [PubMed: 9487953]
3. Li L, Law C, Lo Conte R, Power C. Intergenerational influences on childhood body mass index: the effect of parental body mass index trajectories. *Am J Clin Nutr*. 2009; 89:551–7. [PubMed: 19106237]
4. Botton J, Heude B, Maccario J, Ducimetiere P, Charles M-A. FLVS study group. Postnatal weight and height growth velocities at different ages between birth and 5 y and body composition in adolescent boys and girls. *Am J Clin Nutr*. 2008; 87:1760–8. [PubMed: 18541566]
5. Ong KK, Ahmed ML, Emmett PM, Preece MA, Dunger DB. the Avon Longitudinal Study of Pregnancy and Childhood Study Team. Association between postnatal catch-up growth and obesity in childhood: prospective cohort study. *BMJ*. 2000; 320:967–971. [PubMed: 10753147]
6. Ay L, Van Houten VAA, Steegers EAP, Hofman A, Witteman JCM, Jaddoe VWV, et al. Fetal and Postnatal growth and body composition at 6 months of age. *J Clin Endocrinol Metab*. 2009; 94:2023–2030. [PubMed: 19293269]

7. Regnault N, Botton J, Forhan A, Hankard R, Thiebugeorges O, Hillier TA, et al. Determinants of early ponderal and statural growth in full-term infants in the EDEN mother-child cohort study. *Am J Clin Nutr.* 2010; 92:594–602. [PubMed: 20592134]
8. Ong KK, Diderholm B, Salzano G, Wingate D, Hughes IA, MacDougall J, et al. Pregnancy insulin, glucose and BMI contribute to birth outcomes in nondiabetic mothers. *Diabetes Care.* 2008; 31:2193–2197. [PubMed: 18697902]
9. Knight B, Shields BM, Hill A, Powell RJ, Wright D, Hattersly AT. The impact of maternal glycemia and obesity on early postnatal growth in a nondiabetic Caucasian population. *Diabetes Care.* 2007; 30:777–83. [PubMed: 17251277]
10. Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. *Am J Obstet Gynecol.* 1982; 144:768–73. [PubMed: 7148898]
11. Centers for Disease Control. [black and white growth charts set 1]. Washington DC: National Center for Health Statistics in collaboration with the national Center for Chronic Disease Prevention and Health Promotion; published May 30, 2000[updated May 30, 2000; cited March 10, 2011] Available from→<http://www.cdc.gov/growthcharts/data/set1clinical/set1b&w.pdf>
12. Lederman SA, Paxton A. Maternal reporting of prepregnancy weight and birth outcome: consistency and completeness compared with the clinical record. *Maternal Child Health J.* 1998; 2:123–126.
13. Wright CM, Parkinson KM, Drewett RF. How does maternal and child feeding behavior relate to weight gain and failure to thrive? Data from a prospective birth cohort. *Pediatrics.* 2006; 117:1262–1269. [PubMed: 16585323]
14. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards: Length/height-for-age, weight-for-age, weight-for-length, weight-for-height and body mass index-for-age: Methods and development. Geneva: World Health Organization; 2006. [Cited March 10, 2011] Available from→<http://www.who.int/childgrowth/standards/en/>
15. Orlando A, Dempster P, Aitkens S. A new air displacement plethysmograph for the measurement of body composition in infants. *Pediatr Res.* 2003; 53:486–92. [PubMed: 12595599]
16. Fomon SJ, Haschke F, Ziegler EE, Nelson SE. Body composition of reference children from birth to age 10 years. *Am J Clin Nutr.* 1982; 35:1169–75. [PubMed: 7081099]
17. Cameron N, Preece MA, Cole TJ. Catch-up Growth or Regression to the Mean? Recovery from stunting revisited. *Am J Hum Biol.* 2005; 17:412–417. [PubMed: 15981181]
18. Institute of Medicine (US) and National Research Council (US) Committee to reexamine IOM Pregnancy Weight Guidelines. Weight Gain during pregnancy: examining the guidelines. In: Rasmussen, KM.; Yaktine, AL., editors. *Weight gain during pregnancy: examining the guidelines.* Washington (DC): National Academies Press (US); 2009.
19. Touger L, Looker H, Krakoff J, Lindsay RS, Cook V, Knowler WC. Early growth in offspring of diabetic mothers. *Diabetes Care.* 2005; 28:585–589. [PubMed: 15735192]
20. Eriksson B, Lof M, Forsum E. Body composition in full-term healthy infants measured with air displacement plethysmography at 1 and 12 weeks of age. *Acta Paediatrica.* 2010; 99:563–568. [PubMed: 20064135]
21. Catalano PM, McIntyre HD, Cruickshank JK, McCance DR, Dyer AR, Metzger BE, et al. for the HAPO Study Cooperative Research Group. The Hyperglycemia and Adverse Pregnancy Outcome Study: Associations of GDM and obesity with pregnancy outcomes. *Diabetes Care.* 2012; 35:780–786. [PubMed: 22357187]
22. Bouret SG, Simerly RB. Development of leptin-sensitive circuits. *J Neuroendocrinol.* 2007 Aug 19.:575–82. [PubMed: 17620099]
23. Parker M, Rifas-Shiman SL, Belfort MB, Taveras EM, Oken E, Mantzoros C, et al. Gestational glucose tolerance and cord blood leptin levels predict slower weight gain in early infancy. *J Pediatr.* 2011; 158:227–33. [PubMed: 20855080]
24. Laivuori H, Gallaher MJ, Collura L, Crombleholme WR, Markovic N, Rajakumar A, et al. Relationships between maternal plasma leptin, placental leptin mRNA and protein in normal pregnancy, pre-eclampsia and intrauterine growth retardation without pre-eclampsia. *Mol Hum Reprod.* 2006; 12:551–556. [PubMed: 16870954]

25. Gluckman PD, Butler JH, Comline R, Fowden A. The effects of pancreatectomy on the plasma concentrations of insulin like growth factors 1 and 2 in the sheep fetus. *J Dev Physiol.* 1987; 9:79–88. [PubMed: 3549860]
26. Ranke MB, Lindberg A. Early-Onset idiopathic growth hormone deficiency within KIGS. *Horm Res.* 2003; 60(suppl1):18–21. [PubMed: 12955013]
27. Ramsay JE, Ferrell WR, Crawford L, Wallace AM, Greer IA, Sattar N. Maternal obesity is associated with dysregulation of metabolic, vascular, and inflammatory pathways. *J Clin Endocrinol Metab.* 2002; 87:4231–4237. [PubMed: 12213876]
28. Yoshikawa K, Okada T, Munakata S, Okahashi A, Yonezawa K, Makimoto M, et al. Association between serum lipoprotein lipase mass concentration and subcutaneous fat accumulation during neonatal period. *Eur J Clin Nutr.* 2010; 64:447–453. [PubMed: 20197787]
29. Rasmussen KM, Kjolhede CL. Prepregnant overweight and obesity diminish the prolactin response to suckling in the first week postpartum. *Pediatrics.* 2004; 113:e465–e471. [PubMed: 15121990]
30. Haschke F, van Hof MA. Euro-Growth references for breast-fed boys and girls: influence of breast-feeding and solids on growth until 36 months of age. Euro-Growth Study Group. *J Pediatr Gastroenterol Nutr.* 2000; 31(Suppl 1):S60–71. [PubMed: 10896090]

Table 1

Characteristics of parents and infants by maternal pre-pregnancy BMI category.

	Maternal BMI Category			
	N	Normal N=59	Overweight N=18	Obese N=20
Parental Characteristics				
Maternal pre-pregnancy BMI (kg/m ²)	97	21.8± 0.37	27.2± 0.67	36.7± 0.64
Maternal educational level (% with high school diploma or less)	97	17%	11%	15%
Maternal race (% white)	97	89.83%	83.33%	60%
Maternal ethnicity (%Hispanic)	97	3.39%	11.11%	0%
Maternal pre-pregnancy weight (kg)	97	60.41± 1.17	75.17± 2.12	96.18± 2.00
Maternal height (m)	97	1.66± 0.009	1.66± 0.017	1.62± 0.016
Maternal age (years)	97	30.73± 0.62	30.94± 1.14	32.45± 1.08
Maternal age at menarche (years)	96	13.1± 0.2	12.3± 0.3	12± 0.3
Maternal gestational weight gain (kg)	95	15.86± 0.75	16.38± 1.34	12.72± 1.27
Maternal gestational weight gain by IOM category**	95			
%inadequate		20.3%	0%	15%
%adequate		40%	11.1%	25%
%excessive		40.7%	88.9%	60%
Parity (% primiparous)		63%	50%	25%
Paternal BMI (kg/m ²)	96	26.37± 0.68	26.43± 1.22	31.54± 1.16
Paternal height (m)	97	1.80± 0.008	1.79± 0.02	1.79± 0.01
Maternal 1 hour glucose values	78	107±22	114± 19	128±27
% mothers smoking during pregnancy	80	4%	0%	29%
Infant characteristics				
Gestational age (weeks)	97	39.77± 0.14	39.69± 0.25	39.79± 0.24
Birth weight (g)	93	3467.21±57.29	3812.24±104.9	3510.92±99.22
Infant sex (% female)	97	45.8%	77.8%	35.0%
Infant race (% white)	97	91.5%	77.8%	60.0%
Infant ethnicity (%Hispanic)	97	8.5%	22.2%	5.0%
2 week visit				
Infant age (months)	97	0.55± 0.01	0.59± 0.02	0.58± 0.02

0.1

	Maternal BMI Category				P value*
	N	Normal N=59	Overweight N=18	Obese N=20	
Infant weight (kg)	97	3.82± 0.05	4.03± 0.09	3.87± 0.09	0.15
Infant weight Z score	97	0.05± 0.09	0.44± 0.17	0.009± 0.16	0.09
Infant length (cm)	97	52.95± 0.23	53.41± 0.42	52.69± 0.4	0.42
Infant length Z score	97	0.3± 0.11	0.59± 0.2	0.04± 0.19	0.14
Infant head circumference (cm)	97	11.49± 0.1	11.91± 0.19	11.72± 0.18	0.33
Infant fat mass (kg)	97	0.53± 0.02	0.64± 0.04	0.58± 0.04	0.17
Infant fat free mass (kg)	97	3.29± 0.04	3.39± 0.08	3.29± 0.07	0.42
Infant % body fat	97	13.8± 0.5	15.7± 0.9	14.9± 0.9	0.29
Average nighttime sleep (hours)	97	8.0± 0.22	7.86± 0.4	7.38± 0.39	0.008
3 month visit					
Infant age (months)	97	3.04± 0.02	3.06± 0.04	3.03± 0.03	0.35
Infant weight (kg)	97	6.29± 0.09	5.85± 0.16	5.97± 0.15	0.03
Infant weight Z score	97	0.12± 0.11	-0.27± 0.21	-0.36± 0.2	0.06
Infant length (cm)	97	61.94± 0.27	61.23± 0.49	60.36± 0.46	0.01
Infant length Z score	97	0.54± 0.12	0.43± 0.22	-0.29± 0.21	0.0009
Infant head circumference (cm)	97	14.4± 0.15	14.26± 0.26	13.98± 0.25	0.8
Infant fat mass (kg)	97	1.64± 0.06	1.37± 0.1	1.41± 0.1	0.02
Infant fat free mass (kg)	97	4.65± 0.06	4.47± 0.1	4.56± 0.1	0.34
Infant % body fat	97	25.7± 0.7	23.1± 1.2	23.5± 1.1	0.06
Average nighttime sleep (hours)	97	9.44± 0.25	8.66± 0.45	8.39± 0.42	0.03
Breastfeeding	97				0.01
Exclusive to 3 mo		69.5%	38.9%	30.0%	
Exclusive to 2 wks		11.9%	16.7%	20.0%	
Never exclusive		18.6%	44.4%	50.0%	

* from ANOVA for continuous variables, from chi square for categorical variables, continuous variables expressed as mean ± standard error

** Women with normal BMI should gain 11.5–16 kg total during pregnancy, women who are overweight by BMI should gain 7–11.5 kg, and women who are obese by BMI should gain 5–9 kg (19).

Table 2

Infant outcomes from multivariate model by maternal BMI category. Mean change from 2 weeks to 3 months of age, comparing infants of overweight and obese mothers to infants of normal weight mothers.

Maternal BMI Category	Normal N=59	Overweight N=18	Obese N=20
Change in weight (kg)	2.50±0.10	1.91±0.14 ^{***}	2.12±0.15 ^{**}
Change in length (cm)	9.11±0.26	8.05±0.35 ^{**}	8.09±0.37 ^{**}
Change in head circumference (cm)	4.36±0.11	4.13±0.17	3.99±0.17 ^{**}
Change in fat mass (kg)	1.12±0.07	0.76±0.10 ^{***}	0.86±0.11 [*]
Change in fat free mass (kg)	1.38±0.06	1.15±0.08 ^{**}	1.26±0.09
Change in percent body fat (%)	12.35±0.93	7.76±1.30 ^{***}	9.40±1.36 [*]

Values expressed as least squared means ± standard error. All models controlled for formula versus breast feeding, infant sex, gestational age, and exact age between visits; model for change in length additionally controlled for maternal parity, model for change in infant head circumference additionally controlled for birthweight.

*
p 0.05

**
p 0.01,

p 0.001 for the comparison to infants of normal weight mothers.

Table 3

Values for conditional variables by maternal pre-pregnancy BMI category*

Maternal BMI Category	Normal N=59	Overweight N=18	p**	Obese N=20	p**
Conditional weight for age z score [†]	0.23±0.09	-0.54±0.17	0.0001	-0.20±0.15	0.02
Conditional length for age z score [†]	0.18±0.08	-0.29±0.15	0.007	-0.29±0.14	0.006
Conditional weight for length z score ^{††}	0.09±0.12	-0.46±0.22	0.03	0.14±0.21	0.8
Conditional fat mass	0.13±0.05	-0.25±0.1	0.0009	-0.14±0.09	0.0095
Conditional fat free mass	0.06±0.04	-0.14±0.07	0.02	-0.05±0.07	0.17

* Conditional variables represent the change in the variable from 2 weeks to 3 months beyond what would be predicted by regression to the mean over that time interval

** p value for comparison to mothers with normal pre-pregnancy weight, all models controlled for infant sex, gestational age and the appropriate 2 week variable. Model for conditional length z score additionally controlled for parity, model for conditional fat mass additionally controlled for infant length.

[†] Z scores derived from WHO standards (15).

^{††} although the comparison between normal and overweight mothers was significant at p= 0.03, the p value for the overall model for conditional weight for length z-score was non-significant at p=0.2