Birthweight and Body Mass Index in Young Adulthood: The Swedish Young Male Twins Study

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Many studies have found an inverse association between fetal growth and cardiovascular disease related to the metabolic syndrome in adulthood. Nevertheless, the relative importance of genetics and the intrauterine environment remain unclear. The objective of the study was to test the fetal origins hypothesis and the fetal insulin resistance hypothesis by studying the impact of fetal growth on Body Mass Index (BMI) in young adulthood. In a nationwide cohort study, the Swedish Medical Birth Register for the years 1973–1979 was linked with the Military Service Conscription Register for 1990–1999. In 1998 a questionnaire was mailed to all male twins, included in the two registers, who were alive and still resident in Sweden. The study covers the 923 male twin pairs for which full data were available. Mixed linear models were used to estimate within-pair and between-pair differences in birthweight and their relations to BMI. A weak positive association was found among the monozygotic twins for the within-pair difference in birthweight and BMI. No significant association was found among the monozygotic for the between-pair difference in birthweight and BMI. No significant associations were found for dizygotic twins. These findings do not seem to support either the fetal programming hypothesis or the fetal insulin resistance hypothesis.

The increasing trend in the prevalence of overweight and obesity in many countries in the western world, and also in countries under demographic transition, indicates that environmental factors are important in the etiology of this complex phenotype (Rasmussen et al., 1999). Adoption studies, twin studies and other family studies have shown that genetic factors are important for body mass and obesity. In a review of familial resemblance, genetic factors were found to explain about two thirds of the variance in body mass index (BMI) scores (Maes et al., 1997). A study of twins reared apart has also shown very clearly that genetic factors are important for the occurrence of overweight (Stunkard et al., 1990).

According to the fetal origins hypothesis, intrauterine growth retardation (IUGR) during critical periods of fetal life may alter the programmed development of various metabolic pathways and endocrine regulatory systems. Barker et al. (1993) found that babies with IUGR were at greater risk of non-insulin dependent diabetes mellitus (NIDDM) in adulthood than children without IUGR. Previous Swedish studies have found an inverse association between birthweight and blood pressure among young persons and middle-aged individuals (Leon et al., 2000, Leon et al., 1996).

Using animal models, Gluckman and Harding (1997) reported that IUGR might be related to relative resistance to IGF-1. Verhaeghe et al. (1993) found elevated levels of IGF-1 in serum from the umbilical cord of newborn babies who were small-for-gestational-age, and low levels in large-for-gestational-age babies. In a later paper Verhaeghe et al. (1996) reported a stronger correlation of IGF-1 cord serum levels among monozygotic (MZ) twins than among dizygotic (DZ) twins indicating the likely importance of genetic as well as environmental factors. Long-term intrauterine starvation during pregnancy may give rise to persistent disturbances in the regulation of insulin, IGFs and GH (Barker et al., 1993). Other studies indicate that increased fetal exposure to maternal glucocorticoids might link IUGR and components of the metabolic syndrome in adult life (Benediktsson et al., 1993; Edwards et al., 1993). Mild permanent endocrine abnormalities, involving increased activity of the hypothalamic-pituitary-adrenal axis, have been hypothesized as constituting a pathway for the development of insulin resistance in adulthood among individuals with growth retardation during fetal life (Phillips et al., 1998).

Substantial support for the fetal origins hypothesis has been provided by Ravelli et al. (1976), who studied the occurrence of obesity among the offspring of Amsterdam women who became pregnant during the Dutch famine of 1944-45. The study showed that the risk of developing obesity was highest among young men who were sons of women exposed to severe maternal undernutrition during the first half of pregnancy. In a more recent study, Ravelli et al. (1998) found that prenatal exposure to the famine, during late gestation, was associated with decreased glucose tolerance in adulthood. In accordance with firm evidence from experimental research on animals, observational studies on humans indicate that severe maternal undernutrition in fetal life may lead to permanent changes in insulin-glucose metabolism. Hales et al. (1992) suggest that the high prevalence of NIDDM in some populations, such as native

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Americans, may be partly due to undernutrition in fetal life followed by relative overnutrition in later life, thus supporting the thrifty phenotype hypothesis (Hales, 1997).

Nevertheless, some findings have been reported that are inconsistent with the fetal origins hypothesis. In an Israeli study of 30,000 infants, followed-up at 17 years of age, a positive association was found between birthweight and BMI at 17 years of age (Seidman et al., 1991). And, in a previous study of singletons, there was a weak positive association between birthweight and BMI at 18 years of age (Rasmussen & Johansson, 1998). Further, Sørensen et al. (1997), and also Phillips and Young (2000), have reported a positive association between birthweight and obesity in adulthood.

A fetal insulin resistance hypothesis was proposed by Hattersley and Tooke (1999) as an alternative to the fetal programming hypothesis of Barker and colleagues. According to the former hypothesis, IUGR and insulin resistance syndrome in adulthood are different phenotypic expressions of the same underlying genotype. In such case, studies of MZ and DZ twins may be informative, because twin studies provide partial or complete control for genetic factors. Associations found within MZ pairs of twins should be due to environmental factors since MZ pairs are or are presumed to be genetically identical. Twins have lower birthweight for gestational age than singletons, and most twins catch up with singletons later in childhood with regard to height and weight (Luke et al., 1995; Williams & Poulton, 1999). Thus, the risk of IUGR is higher among twins than among singletons (Barker, 1998). If genetic factors were the main explanation for the association between birthweight and BMI in later life, no association (or a relatively weak association) within MZ pairs would be expected.

Accordingly, the aim of the present Swedish study of young male twins was to test the fetal origins hypothesis and the fetal insulin resistance hypothesis by analyzing the impact of within-pair and between-pair differences in birthweight on BMI among MZ and DZ twin pairs.

Materials and Method

Registry Information

For male twins born 1973–79 data on birthweight, birthlength, gestational age and birth order were obtained from the Swedish Medical Birth Register (MBR). This information source covers more than 99% of all children born in Sweden.

Data on weight and height at age 18 were retrieved from the Military Service Conscription Register (MSCR). Included in this study are the individuals who participated in the conscription examinations of 1991–1999. Such medical examination is compulsory for all males except those with severe chronic diseases or handicaps.

Questionnaire Data

Information about birthweight, birth order, zygosity and physical activity in adulthood was collected by a mailed questionnaire in 1998–99. Twins who had not responded after two reminders were approached by telephone interview. The questions about zygosity have been widely used in twin research (Cederlöf et al., 1961; Pedersen & Lichtenstein, 2000) and were based on self-reports of a) degree of similarity in childhood and b) difficulties teachers may have had in distinguishing between twins in school. Those pairs where both twins reported "as like as two peas in a pod" and that teachers "always or nearly always" had problems in distinguishing between them were categorized as monozygotic (MZ). Those pairs where both twins responded "not more like than siblings in general" to the first question and "seldom" or, "never or almost never" to the second question were categorized as dizygotic (DZ). All remaining pairs were categorized as of uncertain zygosity (XZ). DNA was not available for classification of zygosity in this study. The following question was asked about physical activity. "In general, how would you describe your level of physical activity during leisure time over the last 12 months?"; responses a) "sedentary", b) "light exercise" (without sweating), c) "medium exercise" (regular and sweating), d) "hard exercise" (regular, and sweating and breathing hard).

Data Linkage Errors

In Sweden, when a baby is a few weeks old, the civil registration authorities assign a unique personal identification number to him or her. There is evidence that for some twin pairs this process led to a "cross-over" where the medical birth record for each twin was incorrectly associated with the personal identification number of its co-twin. As the linkage between the MBR and the MSCR was based on the personal identification number, this would lead to an underestimation of the strength of the association between birthweight and BMI within twin pairs, the extent of which would depend on the proportion of cases in which such a cross-over occurred.

We attempted to classify twin pairs according to whether the possibility of cross-over was unlikely, likely or indeterminate. This was done through an examination of the consistency of information on birth order and birthweight obtained from the MBR and by a mailed questionnaire described above in the questionnaire section. Cross-over was considered least likely if the self-reported birth order of each twin in a pair agreed with birth order as given in the MBR. The possibility of cross-over was also assessed by examining self-reported birthweight in relation to birthweight reported in the MBR. For the majority of twin pairs the consistency of information suggested that cross-over had not occurred and these were thus included in further analyses. However, in 59 twin pairs there was good evidence of cross-over, with the self-reported information for each twin matching the MBR information for their co-twin. For these 118 individuals the assumed cross-over was corrected by reassignment of the birth registry information of each twin to their co-twin, after which these individuals were also included. However, 671 twin pairs were excluded from further analysis because of other inconsistencies between self-reported information and that from the MBR. Copies of the algorithm used to determine which twin pairs to include in the full analyses are available from the corresponding author on request.

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Study Population

Initially eligible for the study were 3,566 male twins born 1973–1979 who were alive and resident in Sweden during the spring of 1998. Of these 3,566 subjects, 80 decided not to participate in the study. Data were available on key variables in the MBR for 3,418 (98%) of all the remaining 3,486 male twins. Information about weight and height could be retrieved from the MSCR for 3,052 (88%) of the 3,486. Twin pairs who were 20 years or older at conscription examination and pairs where one twin underwent conscription examination more than 6 months before his twin brother were excluded from the analyses. Twin pairs who had undergone conscription examination at different centers were also excluded. As described above, 1,342 twins had been excluded because it was impossible to establish whether the ID number of Twin 1 had been erroneously given to Twin 2 in the MBR or vice-versa. Following exclusions 1,846 twins (53% of the original set) remained available for statistical analysis.

Statistics

Mixed linear models were used for analyzing within-pair and between-pair differences in birthweight in relation to BMI (outcome variable) at 18 years of age. The Mixed Procedure in SAS was utilized (SAS Institute Inc., 1997).

Table 1

Anthropometrical Data, by Zygosity, at Birth and at Conscription Among 1,846 Swedish Male Twins

	MZ twins (n = 800)			DZ twins (n = 568)			XZ twins (n = 478)			All twins (n = 1,846)		
	Mean	*SD*	Range	Mean	*SD*	Range	Mean	*SD*	Range	Mean	*SD*	Range
Anthropometrical data at birth												
Gestational age (weeks)	37.2	2.5	28,44	37.2	2.3	30,44	37.3	2.5	29,43	37.2	2.4	28,44
Birthweight (grams)	2644	511	910,4250	2733	527	1230,4360	2649	541	1050,4380	2673	525	910,4380
Birthlength (cm)	47.2	2.7	35,57	47.7	2.7	38,54	47.2	2.9	35,55	47.4	2.8	35,57
Anthropometrical data at conscription												
Weight (kg)	68.7	9.5	46,108	70.2	9.1	50,118	68.5	9.1	46,106	69.1	9.3	46,118
Height (cm)	178.7	6.8	157,199	179.4	6.0	160,198	178.5	6.7	162,198	178.9	6.6	157,199
BMI (kg/m^2)	21.49	2.6	16,34	21.81	2.6	17,36	21.50	2.6	16,33	21.59	2.6	16,36

Table 2

Means and Standard Deviations of BMI by Characteristics at Birth and at Military Conscription Examination, by Zygosity, Among 1,846 Swedish Male Twins

	MZ twins (n = 800)			DZ twins (n = 568)			XZ twins (n = 478)			All twins (n = 1,846)		
	N	Mean	*SD*	*N*	Mean	*SD*	*N*	Mean	*SD*	*N*	Mean	*SD*
Birthweight (grams)												
800–1499	18	20.42	1.92	9	20.23	1.85	10	21.32	2.21	37	20.62	1.98
1500–1999	64	21.79	2.82	30	22.35	2.74	46	20.97	2.49	140	21.64	2.73
2000–2499	202	21.27	2.45	136	21.89	2.76	119	21.25	2.43	457	21.45	2.55
2500–2999	313	21.69	2.72	221	21.61	2.66	185	21.81	2.71	719	21.70	2.70
3000–3499	176	21.33	2.32	131	21.99	2.50	91	21.54	2.65	398	21.59	2.47
3500–4400	27	21.78	2.71	41	21.96	2.36	27	21.27	2.24	95	21.71	2.42
Gestational age (weeks)												
28–34	106	21.48	2.50	76	21.66	2.38	66	21.57	2.68	248	21.55	2.50
35–36	134	21.40	2.65	96	22.54	2.99	106	21.50	2.66	336	21.76	2.79
37–39	460	21.41	2.51	324	21.67	2.58	206	21.81	2.64	990	21.58	2.56
40–44	100	21.95	2.80	72	21.59	2.46	100	20.80	2.18	272	21.43	2.54
Age at examination (years)												
17	237	21.32	2.46	154	21.44	2.43	182	21.42	2.70	573	21.38	2.53
18	538	21.56	2.65	407	21.94	2.69	287	21.54	2.53	1232	21.68	2.64
19	25	21.56	1.69	7	22.03	2.93	9	21.63	2.01	41	21.66	1.96

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Results

Table 1 shows anthropometrical data at birth and at conscription by type of twin pair. The DZ twins had slightly higher birthweight, and also greater height and weight at 18 years of age than the MZ twins. Table 2 presents means of BMI by birthweight, gestational age, age at conscription examination, and type of twin. DZ twins had higher mean values of BMI at age 18 than MZ and XZ twins in most birthweight categories. No association was found between birthweight and BMI.

Table 3 presents correlations between BMI at conscription and birthweight, birthlength and gestational age according to type of twin. No clear-cut association was found between BMI and any of the birth characteristics.

Table 4 shows mixed linear regression models for associations between the outcome variable (BMI), and the within-pair mean of birthweight (between-pair effect) *and* the deviation from the within-pair mean of birthweight (within-pair effect), after controlling for age, conscription-examination center, year of conscription examination, and gestational age. The relationship between birthweight and BMI was modeled for all twin pairs (n = 1,846), and also separately for MZ twins, DZ twins and XZ twins. For the MZ twins there was a positive association between BMI and the within-pair effect of birthweight. Adjustments for covariates did not affect the size of the estimate (Table 4). For MZ twins no association was found between BMI and the between-pair effect of birthweight. For the DZ twins no statistically significant association was found for either between-pair or within-pair effects on BMI. Among XZ twins a weak positive association was found between BMI and the within-pair effect of birthweight. A model including control for level of physical activity as a covariate, in addition to all the covariates described above, did not influence the within-pair effect for either MZ twins (β = 0.58; 95% CI:0.21,0.94) or DZ twins (β = 0.40; 95% CI: –0.33,1.14).

Discussion

The main finding of the present study was a positive association between BMI and within-pair difference in birthweight among MZ twins. No significant association was found among the MZ twins for the between-pair difference in birthweight and BMI. No significant associations were found for DZ twins. These findings do not seem to support either the fetal programming hypothesis or the fetal insulin resistance hypothesis. According to the fetal origins hypothesis one would have expected an inverse association within MZ pairs of twins' birthweight in relation to BMI in young adulthood as an indication of environmental factors operat-

Table 3

Correlations with 95% Confidence Interval Between Characteristics at Birth and BMI (kg/m²) at Conscription Examination, by Zygosity, Among 1,846 Swedish Male Twins

	MZ twins (n = 800)	DZ twins (n = 568)	XZ twins (n = 478)	All twins (n = 1,846)
Gestational age (weeks)	0.01 (–0.06,0.08)	–0.04 (–0.12,0.04)	–0.07 (–0.16,0.01)	–0.03 (–0.07,0.02)
Birthweight (kg)	0.03 (–0.04,0.10)	0.02 (–0.07,0.10)	0.07 (–0.02,0.16)	0.04 (–0.01,0.08)
Birthlength (m)	0.01 (–0.06,0.08)	–0.06 (–0.14,0.02)	0.02 (–0.07,0.11)	–0.01 (–0.05,0.04)

Table 4

Within-pair and Between-pair Effects of Birthweight on BMI, by Zygosity, Among 1,846 Swedish Male Twins (Analyses Conducted by Mixed Linear Regression)

	MZ pairs (n = 400)			DZ pairs (n = 284)			XZ pairs (n = 239)			All pairs (n = 923)		
	β	95% CI[c]	P value	β	95% CI[c]	P value	β	95% CI[c]	P value	β	95% CI[c]	P value
Crude												
Within	0.58	0.22,0.94	0.002	0.43	–0.28,1.15	0.236	0.58	0.04,1.12	0.035	0.53	0.22,0.84	0.001
Between	0.06	–0.45,0.58	0.815	–0.01	–0.55,0.54	0.984	0.26	–0.36,0.88	0.414	0.12	–0.20,0.44	0.466
Adjusted[a]												
Within	0.58	0.22,0.95	0.002	0.44	–0.29,1.16	0.236	0.58	0.04,1.12	0.036	0.53	0.22,0.84	0.001
Between	0.04	–0.48,0.56	0.888	0.003	–0.56,0.57	0.992	0.24	–0.40,0.88	0.461	0.14	–0.18,0.46	0.394
Adjusted[b]												
Within	0.58	0.22,0.95	0.002	0.44	–0.29,1.16	0.234	0.58	0.04,1.12	0.036	0.53	0.22,0.84	0.001
Between	0.02	–0.63,0.67	0.951	0.35	–0.47,1.17	0.404	0.87	0.02,1.72	0.044	0.41	–0.02,0.83	0.061

Notes: [a]Regression adjusted for conscription examination center, age at conscription examination, and year of conscription examination.

[b]Regression adjusted for conscription examination center, age at conscription examination, year of conscription examination, and gestational age.

[c]CI=Confidence Interval.

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ing in utero. Neither do the present results support the fetal insulin resistance hypothesis. According to this hypothesis fetal growth retardation and components of the metabolic syndrome are phenotypic expressions explained by the same underlying genotypes (Hattersley & Tooke, 1999).

In a recent paper, Lucas et al. (1999) discussed controlling for body size when studying the association between fetal growth and the risk of chronic disease in adulthood. For the present study no information was available about BMI during childhood. But, in two studies of growth in childhood, the authors have described possible links between catch-up growth and chronic diseases in adulthood (Eriksson et al., 1999; Ong et al., 2000). Babies who are thin at birth seem to have higher death rates from coronary heart disease even when catch-up growth from birth to young childhood is taken into account (Eriksson et al., 1999).

It would have been of great interest to adjust for BMI at some point during childhood, for example at late preschool age if information had been accessible. Data on BMI in childhood, however, are available in a study by Forsén et al. (1999), in which associations were found between risk of coronary heart disease and birthlength for women, and between risk of coronary heart disease and thinness for men.

In an earlier mentioned twin study from New Zealand, Williams and Poulton (1999) found that twins at ages 9 and 18 had both lower birthweight and lower systolic blood pressure than singletons. This finding challenges the fetal origins hypothesis. By contrast, the effect of maternal smoking was found to be consistent with the fetal origins hypothesis, since the infants of smokers had lower birthweight and higher blood pressure. If the fetal origins hypothesis were confirmed, a higher mortality rate from myocardial infarction would be expected for twins than singletons due to lower birthweight among twins (Barker, 1995). But, in a previous Swedish twin study, Vågerö and Leon (1994) did not find a higher mortality rate from myocardial infarction among twins than singletons. This finding is out of line with that of Forsén et al. (1999), who found that catch-up growth was a risk factor for cardiovascular disease. Nevertheless, twins tend to show a higher rate of catch-up than singletons in early childhood, and the risk of coronary heart disease was not found to be higher for twins in the Vågerö and Leon study (1994).

Twin pregnancies are to some extent different from singleton pregnancies, and the results of twin studies may not necessarily be applicable to singletons. Some MZ twins share the same placenta, whereas other pairs of MZ twins have separate placenta (like singletons). It has been suggested that type of placentation was of importance for survival, and speculated that placentation type might be related to risk of high blood pressure, obesity, etc. In the present study the authors were unable to categorize MZ twins by type of placentation. Pairs of twins are also quite heterogeneous with regard to degree of fetal growth retardation.

The current study has the strengths that it is population-based and has nationwide coverage. The fact that birthweight and birthlength were measured by midwives, and height and weight at age 18 by trained medical personnel also contribute to the validity of the study. The twins were matched for many environmental factors during pregnancy (such as smoking), childhood and adolescence. This made it possible to disentangle the impacts of genetic factors and the effects of environmental factors in fetal life.

This study solely employs information on BMI, obtained from measures of weight and height. More advanced measures of percentage body fat would have been useful. However, many studies have shown a strong correlation between BMI and fat mass as measured by DXA scanning (Ellis et al., 1999). Although BMI is strongly related to fat mass, high muscle mass would also contribute to the BMI score.

It was surprising that a substantial number of the twin pairs were hard to classify with regard to zygosity on the basis of the classical questionnaire items extensively used in previous Swedish twin studies. The authors made a deliberate choice to have a rather large group of "unclassified" (XZ) pairs. These XZ twins will be easy to allocate to the MZ and DZ groups when DNA information becomes available within a few years.

In conclusion, the present findings do not support either the fetal origins hypothesis or the insulin resistance hypothesis concerning an inverse association between fetal growth and BMI in adulthood. The findings are, however, in accordance with a previous Swedish and a further Danish study showing a positive association between birthweight and BMI in adulthood (Rasmussen & Johansson, 1998; Sørensen et al., 1997).

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References

Barker, J. P., Gluckman, P. D., Godfrey, K. M., Harding, J. E., Owens, J. A., & Robinson, J. S. (1993). Fetal nutrition and cardiovascular disease in adult life. *Lancet, 341,* 938–941.

Barker, D. J. P. (1995). Fetal origins of coronary heart disease. *British Medical Journal, 311,* 171–174.

Barker, D. J. P. (1998). *Mothers, babies and health in later life.* Edinburgh: Churchill Livingstone.

Benediktsson, R., Lindsay, R. S., Noble, J., Seckl, J. R., & Edwards, C. R. W. (1993). Glucocorticoid exposure in utero: New model for adult hypertension. *Lancet, 341,* 339–341.

Cederlöf, R., Friberg, L., & Jonsson, E. K. L. (1961). Studies on similarity diagnosis on twins with the aid of mailed questionnaires. *Acta Geneticae Medicae et Gemellologiae, 11,* 338–362.

Edwards, C. R. W., Benediktsson, R., Lindsay, R. S., & Seckl, J. R. (1993). Dysfunction of placental glucocorticoid barrier: Link between fetal environment and adult hypertension? *Lancet, 341,* 355–357.

Ellis, K. J., Abrams, S. A., & Wong, W. W. (1999). Monitoring childhood obesity: Assessment of the weight/height^2 index. *American Journal of Epidemiology,150,* 939–946.

Eriksson, J. G., Forsén, T., Tuomilehto, J., Winter, P. D., Osmond, C., & Barker, D. J. P. (1999). Catch-up growth in childhood and death from coronary heart disease: Longitudinal study. *British Medical Journal, 318,* 427–431.

Forsén, T., Eriksson, J. G., Tuomilehto, J., Osmond, C., & Barker, D. J. P. (1999). Growth in utero and during childhood among women who develop coronary heart disease: Longitudinal study. *British Medical Journal, 319,* 1403–1407.

Gluckman, P. D., & Harding, J. E. (1997). Fetal growth retardation: Underlying endocrine mechanisms and postnatal consequences. *Acta Paediatrica, Suppl. 422,* S69–S72.

Hales, C. N., & Barker, D. J. P. (1992). Type 2 (non-insulin-dependent diabetes mellitus) — the thrifty phenotype hypothesis. *Diabetologia, 35,* 595–601.

Hales, C. N. (1997). Fetal and infant growth and impaired glucose tolerance in adulthood: The "thrifty phenotype" hypothesis revisited. *Acta paediatrica, Suppl 422,* S73–S77.

Hattersley, A. T., & Tooke, J. E. (1999). The fetal insulin hypothesis: An alternative explanation of the association of low birthweight with diabetes and vascular disease. *Lancet, 353,* 1789–1792.

Leon, D. A., Koupilova, I., Lithell, H-O., Berglund, L., Mohsen, R., Vågerö, D., Lithell, U-B., & McKeigue, P. M. (1996). Failure to realise growth potential in utero and adult obesity in relation to blood pressure in 50 year old Swedish men. *British Medical Journal, 312,* 401–406.

Leon, D. A., Johansson, M., & Rasmussen, F. (2000). Gestational age and growth rate of fetal mass associated with systolic blood pressure in 18-year-old Swedish men. *American Journal of Epidemiology, 152,* 597–604.

Lucas, A., Fewtrell, M. S., & Cole, T. J. (1999). Fetal origins of adult disease – the hypothesis revisited. *British Medical Journal, 319,* 245–249.

Luke, B., Leurgans, S., Keith, L., & Keith, D. (1995). The childhood growth of twin children. *Acta Geneticae Medicae et Gemellologiae, 44,* 169–178.

Maes, H. H., Neale, M. C., & Eaves, L. J. (1997). Genetic and environmental factors in relative body weight and human adiposity. *Behavior Genetics, 27,* 325–351.

Ong, K. K. L, Ahmed, M. L., Emmett, P. M., Preece, M. A., Dunger, D. B. et al., (2000). Association between postnatal catch-up growth and obesity in childhood: Prospective cohort study. *British Medical Journal, 320,* 967–971.

Pedersen, N., & Lichtenstein, P. (2000). The Swedish twin registry. A presentation. In B. Smedby, I. Lundberg, T. I. A. Sørensen, (Eds.), *Scientific evaluation of the Swedish twin registry.* Stockholm: Gotab.

Phillips, D. I. W., Barker, D. J. P., Fall, C. H. D., Seckl, J. R., Whorwood, C. B., Wood, P. J., & Walker, B. R. (1998). Elevated plasma cortisol concentrations: A link between low birth weight and the insulin resistance syndrome? *Journal of Clinical Endocrinology and Metabolism, 83,* 757–760.

Phillips, D. I. W., & Young, J. B. (2000). Birth weight, climate at birth and the risk of obesity in adult life. *International Journal of Obesity, 24,* 281–287.

Rasmussen, F., & Johansson, M. (1998). The relation of weight, length and ponderal index at birth to body mass index and overweight among 18-year-old males in Sweden. *European Journal of Epidemology, 14,* 373–380.

Rasmussen, F., Johansson, M., & Hansen, H. O. (1999). Trends in overweight and obesity among 18-year-old males in Sweden between 1971 and 1995. *Acta Paediatrica, 88,* 431–437.

Ravelli, G. P., Stein, Z. A., & Susser, M. W. (1976). Obesity in young men after famine exposure in utero and early infancy. *New England Journal of Medicine , 295,* 349–353.

Ravelli, A. C. J., van der Meulen, J. H. P., Michels, R. P. J., Osmond, C., Barker, D. J. P., Hales, C. N., & Bleker, O. P. (1998). Glucose tolerance in adults after prenatal exposure to famine. *Lancet, 351,* 173–177.

SAS Institute Inc. (1997). *SAS/STAT Software: Changes and enhancements through Release 6.12.* Cary, NC: SAS Institute Inc.

Seidman, D. S., Laor, A., Gale, R., Stevenson, D. K., & Danon, Y. L. (1991). A longitudinal study of birth weight and being overweight in late adolescence. *American Journal of Diseases of Children, 145,* 782–785.

Stunkard, A. J., Harris, J. R., Pedersen, N. L., & McClearn, G. E. (1990). The body mass index of twins who have been reared apart. *New England Journal of Medicine, 322,* 1483–1487.

Sørensen, H. T., Sabroe, S., Rothman, K. J., Gillman, M., Fischer, P., & Sørensen, T. I. A. (1997). Relation between weight and length at birth and body mass index in young adulthood: Cohort study. *British Medical Journal, 315,* 1137.

Verhaeghe, J., Van Bree, R., Van Herck, E., Laureys, J., Boullion, R., & Van Assche, F. A. (1993). C-peptide, insulin-like growth factors I and II, and insulin-like growth factor binding protein-1 in umbilical cord serum: Correlations with birth weight. *American Journal of Obstetrics and Gynecology, 169,* 89–97.

Verhaeghe, J., Loos, R., Vlietinck, R., Herck, E. V., van Bree, R., & Schutter, A. M. (1996). C-peptide, insulin-like growth factors I and II, and insulin-like growth factor binding protein-1 in cord serum of twins: Genetic versus environmental regulation. *American Journal of Obstetrics & Gynecology, 175,* 1180–1188.

Vågerö, D., & Leon, D. (1994). Ischemic heart disease and low birth weight: A test of the fetal-origins hypothesis from the Swedish twin registry. *Lancet, 343,* 260–263.

Williams, S., & Poulton, R. (1999). Twins and maternal smoking: Ordeals for the fetal origins hypothesis? A cohort study. *British Medical Journal, 318,* 897–900.

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