Association of Women's Birth Weight with Their Blood Pressure during Pregnancy and with the Body Size of Their Babies

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The women's own intrauterine environment may influence their own pregnancy and their babies. The aim of our study was to investigate how a woman's birth weight affects the course of her pregnancy later in life as well as the body size of her babies; this study was based on the developmental origins of health and disease (DOHaD) concept. We collected Maternal and Child Health handbooks from 414 women and their biological mothers. They were classified into 3 categories based on the Fetal growth curve of Japan: light-for-date (LFD), which means birth weight is less than the $-1.5SD$; appropriate-for-date (AFD), which means it lies between the $-1.5SD$ and $+1.5SD$; and heavy-for-date (HFD), which means it is in the $+1.5SD$, or higher. In the first trimester, systolic blood pressures (SBPs) were 117.6 (14.4 mmHg), 111.6 (12.4 mmHg), and 105.0 (11.6 mmHg), and diastolic blood pressures (DBP) were 71.0 (8.5 mmHg), 65.7 (9.4 mmHg), and 62.1 (8.7 mmHg) in women born LFD, AFD, and HFD, respectively (SBP: p for trend = 0.018, DBP: p for trend = 0.027). In the second and third trimesters, both SBP and DBP were higher for women born LFD than for those of the other 2 groups. Birth weights of the babies of women born LFD, AFD, and HFD were 2,791.1 (483.0 g), 3,043.4 (361.0 g), and 3,248.0 (431.5 g), respectively (p for trend < 0.01). Our findings support the DOHaD concept and suggest that intrauterine environment in fetal life may be passed down from generation to generation.

Keywords: birth weight of mother; blood pressure during pregnancy; body size of child; developmental origins of disease; intrauterine environment

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Many epidemiological studies have reported that poor fetal growth and small birth size are followed by increased risks of coronary heart disease, stroke, hypertension, and type 2 diabetes (Baker and Osmond 1986; Baker 1995; Eriksson et al. 2002). These findings have led to the hypothesis that the risk of developing some chronic diseases in adulthood is influenced not only by genetic and adult lifestyle factors, but also by environmental factors acting in early life. This "developmental origins of health and disease (DOHaD)" concept is bringing new insights into the pathogenesis of disease (Gluckman and Hanson 2004; Gluckman et al. 2005).

The DOHaD concept, when applied to pregnant women, states that pregnant women who themselves had a low birth weight (which reflects a poor intrauterine environment) would have a different course of pregnancy than pregnant women who were born from a good intrauterine environment and at a good gestational age. Because the genitals of the female fetus develop completely during the

early prenatal period, intrauterine malnutrition during the process of primordial germ cells developing into primordial follicles causes an epigenetic change in the ovum (Reik et al. 2003). It is highly possible that this change will be passed down from generation to generation.

We collected maternal and child health (MCH) handbooks from each pregnant woman in order to determine whether the DOHaD concept could be applied to differences in physiological indices during pregnancy. One was a handbook that was used when the woman herself was a fetus and in which her own gestational age and birth weight were recorded. The other was a handbook that was used when the woman was pregnant, in which data from health checkups during her own pregnancy and information on her baby's body size were recorded. First, we examined the association of the subject's own birth weight with health-checkup data recorded during her own pregnancy, such as blood pressure, urinary proteins, and urinary sugar. Next, we compared her birth weight, which reflected the intra-

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uterine environment during her mother's pregnancy, with her own baby's body size, which was in turn affected by the intrauterine environment during the subject's pregnancy.

Methods

Subjects, design, and study variables

The study involved 414 women who delivered singleton babies at ≥ 36 gestational weeks at 1 of 4 hospitals in Sendai City, Miyagi Prefecture, from April 2008 to March 2009. The MCH handbooks were collected from the subjects and their biological mothers (828 volumes in total).

The birth weights and gestational ages of the subjects were obtained from the MCH handbooks of their biological mothers. On the basis of these data, the subjects were classified into 3 categories: light-for-date (LFD), which corresponded to a birth weight less than the $-1.5SD$; appropriate-for-date (AFD), which corresponded to a birth weight between the $-1.5SD$ and $+1.5SD$; and heavy-for-date (HFD), which corresponded to a birth weight at or higher than the $+1.5SD$. This classification was based on the body-growth values at the time of birth, as designed by the Birth Size Standards by Gestational Age for Japanese Neonates in 1984 (Nishida et al. 1984). Next, the subjects were also classified into 3 groups using only their birth weights: $< 2,500$ g, $2,500 - < 4,000$ g, and $\geq 4,000$ g.

The following data were collected from the subjects' MCH handbooks: marital age, childbearing age, childbearing history (whether primiparous), body weight, height, body mass index (BMI: body weight [kg]/body height [m]²), occupation, smoking status, alcohol-drinking status, and medical history. We also collected data on systolic blood pressure (SBP), diastolic blood pressure (DBP), urinary proteins, urinary sugar, and body weight that were recorded at a health checkup during pregnancy. The mean SBP and DBP values were calculated in the first, second, and third trimesters. If proteins and sugar were detected in the urine more than twice, by a paper test during pregnancy, the subject was regarded as positive for proteinuria and urinary sugar, respectively. If an SBP of ≥ 140 mmHg and/or a DBP of ≥ 90 mmHg were recorded more than twice during pregnancy, the subject was diagnosed with pregnancy-induced hypertension (PIH). Moreover, data on the gestational age at the time of delivery, delivery mode, duration of delivery, volume of intrapartum hemorrhage, and the baby's body measurements (birth weight, height, and head circumference) were collected.

All subjects in the study gave their informed consent for the use of their personal information for analysis. The present study protocol was approved by the Ethics Committee of Tohoku University.

Statistical analysis

Data were expressed as mean (standard deviation [s.d.]). The significant differences and trends in categorical variables across the LFD, AFD, and HFD groups were assessed with the chi-square test and the chi-square test for trend. One-way analysis of variance with polynomial contrast in an SPSS was used to evaluate the statistical differences and trends in continuous variables across the 3 groups.

All analyses were calculated using PASW version 18.0 for Windows. Values of $p < 0.05$ were considered statistically significant.

Results

Subject characteristics

The subjects were born between 1965 and 1988. The

mean age at which they got married was 27.3 (3.9 years), and the mean age at the time of delivery was 32.7 (4.6) years. The study period marked the first delivery for 241 subjects and at least the second delivery for 173 subjects. The mean (s.d.) height, weight, and BMI were 158.5 (5.1) cm, 52.2 (7.0) kg, and 20.8 (2.6), respectively. Of the subjects, 242 (58.5%) had a job; 5 (1.3%) were smokers; 46 (12.2%) were alcohol drinkers; and 42 (10.6%) had a medical history of diseases, including chronic diseases. The mean birth weight, height, head circumference, and gestational age of the subjects were 3,157.6 (388.0) g, 49.6 (2.4) cm, 33.1 (1.8) cm, and 39.9 (1.4) weeks, respectively.

The number of subjects who had proteinuria, urinary sugar, PIH, and anemia during pregnancy was 52 (12.6%), 39 (9.4%), 23 (5.6%), and 20 (7.3%), respectively. The mean weight change (weight at the time of delivery minus weight before pregnancy) was 10.1 (3.6) kg (range, -3.6 to 26.1 kg). There were 307 (74.2%) vaginal deliveries and 107 (25.8%) cesarian deliveries. The mean duration of delivery was 659.8 (515.2 mins), and the mean volume of intrapartum hemorrhage was 471.9 (401.9 ml). The mean birth weight, height, head circumference, and gestational age of the subjects' babies were 3,051.8 (378.4) g, 48.8 (2.0) cm, 33.6 (1.2) cm, and 39.5 (1.2) weeks, respectively.

The mean birth weight of the subjects (3,157 g) was significantly higher than that of their babies (3,051 g), which is in agreement with the changes observed in recent years throughout Japan. In addition, the mean weight change during pregnancy of the subjects (10.1 kg) was lower than that of their mothers (11.7 kg) according to their MCH handbooks.

Comparison of pre-pregnancy characteristics among the LFD, AFD, and HFD groups.

The pre-pregnancy characteristics in the 3 subject groups are shown in Table 1. The mean height in the LFD, AFD, and HFD groups was 154.9 (4.9) cm, 158.4 (5.1) cm, and 161.0 (5.0) cm, respectively, showing significant differences and trends across the groups (p for difference = 0.001; p for trend < 0.01). No significant differences were seen in body weight or BMI. There were no significant differences in marital age, age at delivery, the proportion of women for whom this was the first delivery, and the proportion of women with a job.

Comparison of data from health checkups during pregnancy among the 3 groups

Data from health checkups of the subjects during pregnancy are shown in Table 2. The proportion of women with proteinuria, urinary sugar, and anemia was not significantly different across the groups. The mean values for weight gain during pregnancy were 9.6 (2.5) kg, 10.0 (3.6) kg, and 11.2 (3.1) kg in the LFD, AFD, and HFD groups, respectively, showing no significant differences and no significant trends across the groups (p for difference = 0.160; p for trend = 0.205). In the first trimester, the mean SBP was

Table 1. Comparison of characteristics before pregnancy among the three groups of women born with LFD, AFD, and HFD.

	Women born with LFD <i>n</i> = 12	Women born with AFD <i>n</i> = 365	Women born with HFD <i>n</i> = 37	<i>p</i> value for difference	<i>p</i> value for trend
Age (years)	30.3 ± 4.5	32.7 ± 4.5	32.9 ± 4.8	0.179	0.086
Subject's own birth weight (g)	<i>n</i> = 12 2,503.5 ± 139.8	<i>n</i> = 365 3,109.0 ± 326.2	<i>n</i> = 37 3,826.0 ± 185.1	< 0.001	< 0.001
Marital age (years)	<i>n</i> = 12 25.4 ± 3.8	<i>n</i> = 334 27.3 ± 4.0	<i>n</i> = 32 27.4 ± 3.5	0.253	0.137
Height before pregnancy (cm)	<i>n</i> = 12 154.9 ± 4.9	<i>n</i> = 339 158.4 ± 5.1	<i>n</i> = 33 161.0 ± 5.0	0.001	< 0.001
Weight before pregnancy (kg)	<i>n</i> = 12 49.6 ± 5.8	<i>n</i> = 326 52.2 ± 7.0	<i>n</i> = 31 53.4 ± 6.8	0.281	0.113
Body mass index before pregnancy (kg/m ²)	<i>n</i> = 12 20.7 ± 2.1	<i>n</i> = 323 20.8 ± 2.7	<i>n</i> = 31 20.5 ± 2.2	0.865	0.886
First delivery/ Second or over delivery	8/4	217/148	22/15	0.882	0.237
Age at delivery (years)	30.3 ± 4.5	32.7 ± 4.5	32.9 ± 4.8	0.179	0.086
Having a job (%)	8/12 (66.7)	212/331 (64.0)	22/34 (64.7)	0.981	0.890

Number of cases do not add up to the total due to missing information.

LFD; Light-for-dates, AFD; Appropriate-for-dates, HFD; Heavy-for-dates (Birth Size Standards by Gestational Age for Japanese Neonates designed in 1984).

Table 2. Comparison of data at health check-up during the subject's pregnancy among the three groups of women born with LFD, AFD, and HFD.

	Women born with LFD <i>n</i> = 12	Women born with AFD <i>n</i> = 365	Women born with HFD <i>n</i> = 37	<i>p</i> value for difference	<i>p</i> value for trend
Proteinuria (%)	1/12 (8.3)	47/365 (12.9)	4/37 (10.8)	0.847	0.735
Urinary sugar (%)	1/12 (8.3)	38/364 (10.4)	0/37 (0.0)	0.117	0.703
Anemia (%)	0/10 (0.0) <i>n</i> = 10	20/241 (8.4) <i>n</i> = 315	0/25 (0.0) <i>n</i> = 30	0.209	0.651
Weight change (kg)	9.6 ± 2.5	10.0 ± 3.6	11.2 ± 3.1	0.160	0.205
In the first trimester	<i>n</i> = 7	<i>n</i> = 287	<i>n</i> = 24		
SBP (mmHg)	117.6 ± 14.4	111.6 ± 12.4	105.0 ± 11.6	0.018	0.018
DBP (mmHg)	71.0 ± 8.5	65.7 ± 9.4	62.1 ± 8.7	0.059	0.027
In the second trimester	<i>n</i> = 12	<i>n</i> = 363	<i>n</i> = 36		
SBP (mmHg)	108.6 ± 9.4	109.7 ± 10.5	107.7 ± 10.5	0.509	0.788
DBP (mmHg)	62.8 ± 7.8	63.8 ± 7.8	62.5 ± 7.1	0.583	0.931
In the third trimester	<i>n</i> = 12	<i>n</i> = 365	<i>n</i> = 37		
SBP (mmHg)	114.5 ± 9.7	114.0 ± 9.9	112.7 ± 8.0	0.723	0.583
DBP (mmHg)	68.0 ± 7.0	68.5 ± 6.7	68.0 ± 5.4	0.884	0.998
PIH (%)	1/12 (8.3)	21/365 (5.8)	1/37 (2.7)	0.678	0.552

Number of cases do not add up to the total due to missing information.

LFD; Light-for-dates, AFD; Appropriate-for-dates, HFD; Heavy-for-dates (Birth Size Standards by Gestational Age for Japanese Neonates designed in 1984).

117.6 (14.4) mmHg, 111.6 (12.4) mmHg, and 105.0 (11.6) mmHg, respectively, and the mean DBP was 71.0 (8.5) mmHg, 65.7 (9.4) mmHg, and 62.1 (8.7) mmHg, respectively, in the LFD, AFD, and HFD, groups. There were significant trends in both SBP and DBP across the groups

(SBP: *p* for difference = 0.018, *p* for trend = 0.018; DBP: *p* for difference = 0.059, *p* for trend = 0.027). In both the second and third trimesters, the mean SBP and DBP were higher in the LFD group than in the other 2 groups, although there was no significant difference and trend. The

Table 3. Comparison of data at the subject's delivery and anthropometric data of the subject's babies among the three groups of women born with LFD, AFD, and HFD.

	Women born with LFD ^a <i>n</i> = 12	Women born with AFD ^a <i>n</i> = 365	Women born with HFD ^a <i>n</i> = 37	<i>p</i> value for difference	<i>p</i> value for trend
Caesarian section (%)	4/12 (33.3)	94/365 (25.8)	9/37 (24.3)	0.833	0.237
Gestational age at delivery (week)	<i>n</i> = 12 40.0 ± 1.4	<i>n</i> = 365 39.5 ± 1.2	<i>n</i> = 37 39.7 ± 1.2	0.168	0.471
Duration of delivery (min)	<i>n</i> = 8 430.0 ± 335.3	<i>n</i> = 269 667.4 ± 525.0	<i>n</i> = 28 652.3 ± 455.5	0.438	0.283
Volume of intrapartum hemorrhage (ml)	<i>n</i> = 10 548.5 ± 492.6	<i>n</i> = 312 470.5 ± 409.1	<i>n</i> = 35 481.3 ± 314.8	0.829	0.642
Subject's baby					
Birth weight (g)	<i>n</i> = 12 2,791.1 ± 483.0	<i>n</i> = 365 3,043.4 ± 361.0	<i>n</i> = 37 3,248.0 ± 431.5	< 0.001	< 0.001
Birth Height (cm)	<i>n</i> = 12 48.1 ± 2.6	<i>n</i> = 365 48.7 ± 1.9	<i>n</i> = 37 49.4 ± 2.3	0.059	0.036
Head circumference (cm)	<i>n</i> = 12 32.6 ± 1.3	<i>n</i> = 365 33.6 ± 1.2	<i>n</i> = 37 34.2 ± 1.1	< 0.001	< 0.001
LFD (%) ^b	4/12 (33.3)	20/365 (5.5)	1/37 (2.7)	< 0.001	< 0.001

Number of cases do not add up to the total due to missing information.

^aLFD; Light-for-dates, AFD; Appropriate-for-dates, HFD; Heavy-for-dates (Birth Size Standards by Gestational Age for Japanese Neonates designed in 1984).

^bLFD; Light-for-dates (Birth Size Standards by Gestational Age for Japanese Neonates designed in 1998).

proportion of women with PIH was not significantly different among the groups.

In addition, we compared blood pressures among the 3 groups classified according to birth weight: < 2,500 g, 2,500 - < 4,000 g, and ≥ 4,000 g (Table 4). No significant differences were noted in SBPs and DBPs during pregnancy among the 3 groups. Women born weighing < 2,500 g were likely to have higher BPs than those born weighing ≥ 4,000 g, but lower BPs than those born weighing 2,500 - < 4,000 g, although few women were born weighing < 2,500 g or ≥ 4,000 g.

Comparison of data at the time of delivery and anthropometric data of babies born among the 3 groups

Table 3 shows data at the subjects' delivery and anthropometric data of their babies. No significant differences in the proportion of caesarian section, gestational age at delivery, duration of delivery, and volume of intrapartum hemorrhage were observed among the 3 groups. Birth weights of the babies of women born LFD, AFD, and HFD were 2,791.1 (483.0 g), 3,043.4 (361.0 g), and 3,248.0 (431.5 g), respectively, showing a significant difference and trend across the groups (*p* for difference < 0.01, *p* for trend < 0.01). As for height and head circumference, a significant trend was observed. The proportions of the babies who were diagnosed as LFD were 33.3% (4/12), 5.5% (20/365), and 2.7% (1/37) among women born LFD, AFD, and HFD, respectively (*p* for difference < 0.01). The 3 categories are LFD that corresponds to a birth weight less than the 10th percentile, AFD that corresponds to a birth weight between

the 10th and 90th percentiles, and HFD that corresponds to a birth weight at or higher than the 90th percentile (Ogawa et al. 1998).

Moreover, we compared anthropometric data from the subjects' babies among the 3 groups based on the subjects' own birth weights of < 2,500 g, 2,500 - < 4,000 g, and ≥ 4,000 g (Table 4). Birth weight, birth height, and head circumference in the babies who were born to women weighing < 2,500 g at birth were likely to be lower than in those of the other 2 groups.

Discussion

This is the first study to investigate differences in the course of pregnancy between women born under different intrauterine environments. We found that women born as LFD babies had higher mean values of SBP and DBP at the first trimester when they themselves were pregnant, as compared to those born AFD. Both the SBP and DBP of women born AFD were higher than those of women born HFD. A significant linear trend was observed across the 3 groups.

There are many previous studies reporting that birth weight is inversely associated with subsequent blood pressure in adulthood (Eriksson et al. 2000; Miura et al. 2001; Tamakoshi et al. 2006). In particular, infants with development disorders resulting in disproportionately small, thin, and short figures have been reported to subsequently have a high risk of lifestyle-related disease (Barker and Osmond 1986; Eriksson et al. 2001). Huxley et al. (2000) reviewed 80 papers (444,000 subjects aged 0-84 years), published

Table 4. Comparison of blood pressure during the subject's pregnancy and their babies' size among the three groups of birth weight.

	Birth weight category (g)			<i>p</i> value for difference	<i>p</i> value for trend
	<2,500 <i>n</i> = 12	2,500 - < 4,000 <i>n</i> = 395	4000- <i>n</i> = 7		
Blood pressure during pregnancy					
In the first trimester	<i>n</i> = 9	<i>n</i> = 304	<i>n</i> = 5		
SBP (mmHg)	107.7 ± 12.8	111.5 ± 12.4	101.0 ± 14.4	0.120	0.335
DBP (mmHg)	62.4 ± 10.2	65.8 ± 9.4	57.8 ± 8.8	0.101	0.384
In the second trimester	<i>n</i> = 12	<i>n</i> = 392	<i>n</i> = 7		
SBP (mmHg)	108.2 ± 14.2	109.6 ± 10.4	105.2 ± 8.9	0.489	0.545
DBP (mmHg)	61.3 ± 9.7	63.8 ± 7.7	60.7 ± 6.9	0.324	0.865
In the third trimester	<i>n</i> = 12	<i>n</i> = 395	<i>n</i> = 7		
SBP (mmHg)	113.6 ± 13.3	113.9 ± 9.6	111.8 ± 8.0	0.854	0.693
DBP (mmHg)	66.8 ± 8.6	68.4 ± 6.5	67.0 ± 5.3	0.590	0.958
Subject's baby					
Birth weight (g)	<i>n</i> = 12	<i>n</i> = 395	<i>n</i> = 7		
	2815.5 ± 304.3	3061.6 ± 380.4	2909.1 ± 199.6	0.051	0.601
Birth Height (cm)	<i>n</i> = 12	<i>n</i> = 395	<i>n</i> = 7		
	47.5 ± 1.4	48.8 ± 2.0	48.1 ± 1.5	0.045	0.496
Head circumference	<i>n</i> = 12	<i>n</i> = 395	<i>n</i> = 7		
	33.2 ± 1.4	33.6 ± 1.2	34.3 ± 0.4	0.161	0.056
<2,500 g (%)	1/12(8.3)	27/395(6.8)	0/7(0%)	0.944	0.550

Number of cases do not add up to the total due to missing information.

from 1996 to March 2000, examining the association between birth weight and blood pressure. This association is smaller during puberty, adolescence, and young adulthood than in childhood and after middle age, and has previously been reported to be inconsistent. It is noteworthy that a significant linear trend in blood pressure during pregnancy was observed across 3 groups of women born with LFD, AFD, and HFD weights.

Blood pressure during pregnancy is controlled by several mechanisms (Furuhashi et al. 1991). Despite the increases in circulating blood volume and cardiac output, arterial blood pressure decreases during pregnancy (Conningham 2005). This phenomenon is due to increased progesterone, which has a peripheral vasodilator effect. The production of both nitric monoxide (NO) and prostaglandin I₂ (PGI₂), which have peripheral vasodilator effects, is also activated in the vascular endothelium during pregnancy (Sladek et al. 1993). In our study, blood pressure in the second trimester was lower than that in the first trimester, which is consistent with the above-mentioned facts. However, the blood pressure of women born LFD was higher than that of women born AFD and HFD. As mentioned above, if a fetus is exposed to a low-nutrition environment for some reason, irreversible anatomical metabolic changes occur in some organs.

We also found that the infants of women born LFD were lighter in weight and smaller in head circumference than those of women born AFD and HFD. As for factors affecting the weight of the infant, various factors can be

considered, such as natural, social, maternal, and the intra-uterine environment itself. It has been reported that the increase in maternal body weight during pregnancy is positively associated with birth weight of the child (Abrams and Laros 1986). In order to prevent the birth of infants with low birth weights, the American College of Obstetricians and Gynecologists (ACOG) and the American Academy of Pediatrics (AAP) advocate an ideal increase in maternal body weight during pregnancy, based upon the mother's BMI during non-pregnant periods. In our study, women born LFD were short and their weight gain during pregnancy was small. Consequently, their children were light at birth. Assuming that birth weight is an indicator of the intrauterine environment, our finding suggests that the intrauterine environment may be passed down from generation to generation.

The strength of the present study lies in the use of MCH handbooks of mothers and daughters. To our knowledge, there is no previous study comparing the obstetric data of 2 generations. In Japan, the MCH Handbook, which is provided to all pregnant women by their local government, contains important information relevant to pregnancy, including birth weight data recorded by midwives and obstetricians. Therefore, our data are reliable. We were also able to decide upon the 3 categories of LFD, AFD, and HFD, according to gestation. The limitations of this study deserve mention. First, our study subjects were recruited over a limited area of Japan. Further studies are needed in other areas where environment and lifestyle are different.

Second, we are aware that a cross-sectional study design is susceptible to selection bias. Low-birth-weight babies who survived and became pregnant as adults were probably healthier than those who did not survive or, if they did, could not get pregnant. If the number of women born LFD who become pregnant increases in the future because of the development of assisted reproductive technology, we expect that further studies of these women will support our findings. Third, we could not avoid using the body-growth curve designed in 1984 because, to our knowledge, no data on the distribution of birth weight by gestational age were officially published in the 1970s. Fourth, unfortunately, data on pre-pregnancy blood pressure were not available in our study. Our findings may only reflect the difference in blood pressure prior to pregnancy. Further prospective longitudinal studies on female babies that examine the effect of birth weight on their health, including the course of their subsequent pregnancies, should be conducted to overcome the problems noted above.

In conclusion, women born LFD were likely to have higher blood pressure during pregnancy (but within the normal range) compared with those born AFD and HFD. This phenomenon may be explained by the DOHaD concept. However, there was no positive proof that pregnancy itself was responsible for this phenomenon. Moreover, their children were light in birth weight and small in head circumference. This finding suggests that the intrauterine environment in fetal life may be passed down from generation to generation.

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Conflict of Interest

We declare no conflict of interest.

References

- Abrams, B.F. & Laros, R.K. Jr. (1986) Pregnancy weight, weight gain, and birth-weight. *Am. J. Obstet. Gynecol.*, **154**, 503–509.
- Barker, D.J.P. (1995) Fetal origins of coronary heart disease. *BMJ*, **311**, 171–174.
- Barker, D.J.P. & Osmond, C. (1986) Infant mortality, childhood nutrition, and ischaemic heart disease in England and Wales. *Lancet*, **1**, 1077–1081.
- Conningham, F.G. (2005) Maternal physiology. *Williams Obstetrics*, 22nd ed. New York: McGraw-Hill., 129–137.
- Eriksson, J.G., Forsen, T., Tuomilehto, J., Jaddoe, V.W.V., Osmond, C. & Barker, D.J.P. (2002) Effects of size at birth and childhood growth on the insulin resistance syndrome in elderly individuals. *Diabetologia*, **45**, 342–348.
- Eriksson, J.G., Forsen, T., Tuomilehto, J., Osmond, C. & Barker, D.J.P. (2000) Fetal and childhood growth and hypertension in adult life. *Hypertension*, **36**, 790–794.
- Eriksson, J.G., Forsen, T., Tuomilehto, J., Osmond, C. & Barker, D.J.P. (2001) Early growth and coronary heart disease in later life: longitudinal study. *BMJ*, **322**, 949–953.
- Furuhashi, N., Tsujiei, M., Kimura, H., Yajima, A., Nagae, H. & Kimura, C. (1991) Maternal and fetal atrial natriuretic peptide levels, maternal plasma renin activity, angiotensin II, prostacyclin and thromboxane A2 levels in normal and preeclamptic pregnancies. *Tohoku J. Exp. Med.*, **165**, 79–86.
- Gluckman, P.D. & Hanson, M.A. (2004) Living with the past: evolution, development, and patterns of disease. *Science*, **305**, 1733–1736.
- Gluckman, P.D., Hanson, M.A., Spencer, H.G. & Bateson, P. (2005) Environmental influences during development and their later consequences for health and disease: implications for the interpretation of empirical studies. *Proc. Biol. Sci.*, **272**, 671–677.
- Huxley, R.R., Shiell, A.W. & Law, C.M. (2000) The role of size at birth and postnatal catch-up growth in determining systolic pressure: a systematic review of the literature. *J. Hypertens.*, **18**, 815–831.
- Miura, K., Nakagawa, H., Tobata, M., Morikawa, Y., Nishijio, M. & Kagamimori, S. (2001) Birth weight, childhood growth, and cardiovascular disease risk factors in Japanese aged 20 years. *Am. J. Epidemiol.*, **153**, 783–789.
- Nishida, H., Sakanoue, M., Kurachi, K., Asada, A., Kubo, S. & Funakawa, H. (1984) Fetal growth curve of Japanese. *Journal of Japan Society of Neonatal Medicine*, **20**, 90–97 (in Japanese).
- Ogawa, Y., Iwamura, T., Kuriya, N., Nishida, H., Takeuchi, H., Takada, M., Itabashi, K., Imura, S. & Isobe, K. (1998) Birth size standards by gestational age for Japanese neonates. *Journal of Japan Society of Neonatal Medicine*, **34**, 624–632 (in Japanese).
- Reik, W., Santos, F. & Dean, W. (2003) Mammalian epigenomics: reprogramming the genome for development and therapy. *Theriogenology*, **59**, 21–32.
- Sladek, S.M., Regenstein, A.C., Lykins, D. & Roberts, J.M. (1993) Nitric oxide synthase activity in pregnant rabbit uterus decreases on the last day of pregnancy. *Am. J. Obstet. Gynecol.*, **169**, 1285–1291.
- Tamakoshi, K., Yatsuya, H., Wada, K., Matsushita, K., Otsuka, R., Yang, P.O., Sugiura, K., Hotta, Y., Mitsuhashi, H., Kondo, T. & Toyoshima, H. (2006) Birth weight and adult hypertension: cross-sectional study in a Japanese workplace population. *Circ. J.*, **70**, 262–267.