Table 1 *Maternal and infant characteristics*

	Children and infant growth surveys			Vital statistics reports		
	1980 (n = 5462)	1990 (n = 3490)	2000 (n = 2794)	1980 (n = 1 576 889)	1990 (n = 1 221 585)	2000 (n = 1 190 547)
Infants						
Birth weight (g)	3189 ± 422†	3123 ± 421	3033 ± 429	3190‡	3080	3030
Height at birth (cm)	49.6 ± 2.1†	49.3 ± 2.2	48.9 ± 2.3	–	–	48.9
Gestational length (weeks)	39.5 ± 1.5†	39.1 ± 1.4	38.9 ± 1.7	–	–	–
Birth weight						
Low (<2500 g; %)	4.2	6.1	8.3	5.2	6.3	8.6
Very low (<1500 g; %)	0.1	0.2	0.6	0.4	0.5	0.7
High (≥4000 g; %)	3.2	1.8	1.0	3.0	1.9	1.1
Delivery term						
Preterm (<37 weeks; %)	3.5	3.6	5.8	4.1	4.5	5.4
Early preterm (<32 weeks; %)	0.1	0.3	0.5	0.5	0.6	0.7
Post-term (>41 weeks; %)	4.5	1.7	1.0	4.4	1.7	0.8
Mothers						
Primiparous (%)	40.2	42.9	48.8	41.9	43.2	49.0
Multiple pregnancy (%)	1.3	1.6	2.8	1.2	1.4	2.0
Height (cm)	155.0 ± 5.1†	156.8 ± 5.0	157.9 ± 5.3	–	–	–
Short stature (<150 cm; %)	14.5	6.7	4.6	–	–	–
Age at delivery (years)	–	28.6 ± 4.3†	29.0 ± 4.5	28.1	28.9	29.6
>34 years old (%)	–	9.3	11.4	4.2	8.6	11.9
<20 years old (%)	–	1.0	1.8	0.9	1.4	1.7
Prepregnancy weight (kg)	–	–	51.9 ± 7.6†	–	–	–
Prepregnancy body mass index	–	–	20.8 ± 2.8†	–	–	–
Smoking (%)	–	6.5	10.9	–	–	–
Drinking (%)¶	–	–	1.4	–	–	–

†Mean ± SD. ‡Original data in kilograms. ¶Drinking alcohol three or more times per week. –, Data not available.

Table 2 Univariate logistic regression analysis for low birth weight, according to survey year

Variables	1980			Survey
	No. LBW/total (%)	OR	95%CI	PAF (%)
Infants				
Gestational length				
Preterm	86/190 (45.3)	68.90	43.90–108.00	72.4
Term (37–39 weeks)	107/2511 (4.3)	3.71	2.49–5.52	
Term (40–41 weeks)	27/2454 (1.1)	1.00	Referent	
Sex				
Female	114/2498 (4.8)	1.28	0.98–1.67	
Male	101/2657 (3.8)	1.00	Referent	
Mothers				
Parity				
None	106/2057 (5.2)	1.44	1.10–1.87	1.5
1+	114/3098 (3.7)	1.00	Referent	
Plurality				
Multiple	29/69 (42.0)	19.20	11.70–31.40	40.1
Single	191/5086 (3.8)	1.00	Referent	
Height	–	0.93	0.92–0.95	
Short stature (<150 cm)	55/747 (7.4)	2.04	1.49–2.80	3.7
≥150 cm	165/4403 (3.7)	1.00	Referent	
Age category (years)				
<20	–	–	–	–
20–24	–	–	–	–
25–29	–	–	–	–
30–34	–	–	–	–
≥35	–	–	–	–
Prepregnancy body mass index (kg/m^2)				
–18.98	–	–	–	
18.99–20.30	–	–	–	
20.31–21.93	–	–	–	
≥21.94	–	–	–	
Smoking status				
Smoker	–	–	–	
Non-smoker	–	–	–	
Drinking				
Drinker	–	–	–	
Non-drinker	–	–	–	

Population attributable fractions (PAF) were calculated for variables significantly associated with low birth weight (LBW). –, Data not available; CI, confidence interval; OR, odds ratio.

In order to identify factors that could explain the increase in LBW between the two recent survey periods (1990 and 2000), we applied the multivariate logistic regression analysis using the data set of 1990 and 2000 surveys, as shown in Table 3. For both model 1 (using all variables) and for model 2 (applying the stepwise method), preterm delivery, early term delivery, female sex of the infant, maternal primiparity, multiple gestation, maternal short stature, older maternal age (>24 years), and maternal smoking were independent factors with regard to LBW risk. After adjustment for these factors, the survey period was no longer related to the prevalence of LBW (OR = 1.05, $P = 0.66$ in model 1, whereas OR without adjustment = 1.37, $P < 0.01$) suggesting that these factors sufficiently explained the increase in the LBW rate between the 1990 and 2000 surveys.

The frequency of LBW among the combination groups of multiple gestation and gestational length for 1990 and 2000 is summarized in Table 4. The PAF for

year of children and infant growth surveys							
1990				2000			
No. LBW/total (%)	OR	95%CI	PAF (%)	No. LBW/total (%)	OR	95%CI	PAF (%)
73/127 (57.5)	125	67.5–232	83.5	103/161 (64.0)	172	87.70–339.00	87.0
126/1953 (6.5)	6.39	3.72–10.9		117/1551 (7.5)	7.92	4.25–14.80	
15/1345 (1.1)	1.00	Referent		11/1051 (1.0)	1.00	Referent	
126/1682 (7.5)	1.52	1.15–2.01	2.50	124/1331 (9.3)	1.27	0.97–1.67	
88/1743 (5.0)	1.00	Referent		107/1432 (7.5)	1.00	Referent	
99/1459 (6.8)	1.16	0.88–1.52		106/1341 (7.9)	0.88	0.67–1.15	
115/1966 (5.8)	1.00	Referent		125/1422 (8.8)	1.00	Referent	
30/56 (53.6)	20.4	11.8–35.2	50.9	60/78 (76.9)	49.9	28.80–86.40	75.4
184/3369 (5.5)	1.00	Referent		169/2669 (6.3)	1.00	Referent	
27/230 (11.7)	2.14	1.39–3.28	6.1	20/126 (15.9)	2.17	1.32–3.57	8.4
187/3193 (5.9)	1.00	Referent		211/2636 (8.0)	1.00	Referent	
2/31 (6.5)	0.94	0.22–4.10		8/49 (16.3)	4.37	1.77–10.80	53.7
37/542 (6.8)	1.00	Referent		16/376 (4.3)	1.00	Referent	
85/1482 (5.7)	0.83	0.56–1.24		82/1113 (7.4)	1.78	1.03–3.09	
61/1045 (5.8)	0.85	0.55–1.29		94/907 (10.4)	2.59	1.51–4.46	
29/322 (9.0)	1.35	0.81–2.24		31/314 (9.9)	2.46	1.32–4.58	
–	–	–		67/700 (9.6)	1.70	1.13–2.57	31.4
–	–	–		74/701 (10.6)	1.88	1.26–2.82	
–	–	–		51/702 (7.3)	1.25	0.81–1.92	
–	–	–		39/655 (6.0)	1.00	Referent	
25/222 (11.3)	2.03	1.31–3.16	5.6	32/303 (10.6)	1.36	0.92–2.01	
189/3201 (5.9)	1.00	Referent		199/2457 (8.1)	1.00	Referent	
–	–	–		6/39 (15.4)	2.05	0.85–4.93	
–	–	–		224/2712 (8.3)	1.00	Referent	

each survey period were calculated by applying the OR shown in Table 3 to these frequency data. The PAF for LBW in multiple gestations and under-term delivery was 85.1% in 1990 and 89.3% in 2000, clearly indicating that the majority of LBW were attributable to multiple gestations and under-term delivery. In the same manner, we also examined the effect of smoking and maternal age distribution by using the data shown in Tables 3 and 4. The PAF for smoking alone was 6.4% in 1990, and 7.6% in 2000. The PAF for smoking and maternal age distribution was 37.5% in 1990 and 41.6% in 2000.

Discussion

The data from the CIG survey from 1980 to 2000 were used to identify the underlying factors influencing the recent rise in LBW Japanese infants, and to investigate the current risk factors for LBW. The increase in the number of preterm deliveries and multiple gestations

Table 3 Multivariate logistic regression analysis for low birth weight in the 1990 and 2000 surveys

Variables	Model 1			Model 2		
	OR	95%CI	*P*-value	OR	95%CI	*P*-value
Survey period (2000 *vs* 1990)	1.05	0.83–1.33	0.66	–	–	–
Infants						
Gestational length (weeks)						
Preterm	128.00	79.50–207.00	<0.01	129.00	79.80–207.00	<0.01
Term (37–39)	6.66	4.37–101.00	<0.01	6.66	4.38–10.20	<0.01
Term (40–41)	1.00	Referent		1.00	Referent	
Female (*vs* male)	1.79	1.41–2.26	<0.01	1.78	1.41–2.26	<0.01
Mothers						
Primiparity (*vs* multiparity)	1.62	1.26–2.07	<0.01	1.62	1.27–2.08	<0.01
Multiple gestation (*vs* single)	19.20	12.30–30.20	<0.01	19.30	12.30–30.30	<0.01
Short stature (*vs* normal stature)	1.84	1.22–2.26	<0.01	1.83	1.21–2.76	<0.01
Age category (years)						
<20	2.23	0.95–5.22	0.07	2.26	0.97–5.28	0.06
20–24	1.00	Referent		1.00	Referent	
25–29	1.57	1.07–2.03	0.02	1.57	1.07–2.31	0.02
30–34	1.75	1.16–2.64	0.01	1.77	1.18–2.66	0.01
≥35	1.73	1.06–2.81	0.03	1.74	1.07–2.83	0.02
Smoker (*vs* non-smoker)	2.19	1.55–3.09	<0.01	2.20	1.56–3.11	<0.01

Model 1: All variables were forced to enter into the model. Model 2: Significant variables were selected using the stepwise method. CI, confidence interval; OR, odds ratio.

Table 4 Prevalence of low-birth-weight (LBW) infants according to selected factors

Combination of variables		1990		2000	
		No. LBW/total	(%)	No. LBW/total	(%)
Plurality	Gestational length (weeks)				
Multiple	Preterm	12/14	85.7	36/38	94.7
	Term (37–39)	18/42	42.9	24/38	63.2
	Term (40–41)	0/0	–	0/2	0.0
Single	Preterm	61/113	54.0	66/122	54.1
	Term (37–39)	108/1911	5.7	93/1505	6.2
	Term (40–41)	15/1345	1.1	10/1042	1.0
Smoking	Age at delivery (years)				
Smokers	<20	0/9	0.0	4/15	26.7
	20–24	10/62	16.1	3/79	3.8
	25–29	7/79	8.9	14/130	10.8
	30–34	6/48	12.5	8/59	13.6
	≥35	2/24	8.3	3/19	15.8
Non-smokers	Under 20	2/22	9.1	4/34	11.8
	20–24	27/480	5.6	13/297	4.4
	25–29	78/1403	5.6	68/982	6.9
	30–34	55/997	5.5	86/848	10.1
	≥35	27/297	9.1	28/294	9.5

was found to be an important factor with regard to the increase in the LBW rate. The increased prevalence of maternal smoking and changes in maternal age distribution did not substantially explain the increase in LBW infants in Japan.

The present study showed a consistency with prior investigations[15–17] regarding the relationship between LBW and its risk factors. All of the factors shown in Table 3, such as shorter gestational length, female sex of the infant, maternal primiparity, both young and advanced maternal age, and smoking, have been demonstrated as risk factors for LBW.[15–17] However, the temporary trend for an increased rate of LBW as a result of increased preterm deliveries and multiple

gestations is uniquely observed in Japan, while other industrialized countries[2–4] have experienced a decrease in LBW despite increased preterm deliveries and multiple gestations.[18] In these countries, an increase in fetal growth, particularly of term infants, has been observed over time, which is attributed to increased maternal size and decreased maternal smoking.

Why then, are Japanese infants born lighter despite a decrease in short-statured mothers? The mean maternal height has also been increasing during the study period, as shown in Table 1. This suggests that nutritional status was adequate in these mothers during their period of physical growth, but that it somehow deteriorated in adulthood. Through the analysis of 25 years of anthropometric data in young women (aged 15–29 years), we observed an increase in the proportion of underweight women (BMI <18.5 kg/m^2) to nearly one-quarter of the survey population.[19] Also, our previous study on pregnant women showed that dietary intake was low, with a mean energy intake of 7827 ± 2080 kJ/day.[20] We speculate that the increase in nutritionally deprived underweight women with insufficient diet while pregnant has led to poor maternal weight gain and is affecting optimal fetal growth.

An increase in both young (<20 years) and advanced-aged mothers (>34 years) was observed during the survey period, together with a rise in smoking prevalence. Although not statistically significant ($P = 0.06$), the OR for LBW in young mothers was 2.26 (95% CI = 0.97–5.28) compared with the reference age group of 20–24 years. We could not demonstrate a strong effect of smoking and maternal age on LBW increase, but the present trend, as shown in Figure 1 and Table 4, might affect maternal and child health in the near future. Attention by government officials and health professionals is needed to encourage smoking cessation among young women to prevent LBW infants.

Our present analyses have several limitations due to the data collection methods used in the CIG survey. First, as already mentioned, participants in this survey were limited to live infants who were able to attend infant health examinations at local public health centers. This is most likely to be the reason for the decrease in the survey participation rate between 1990 and 2000. Non-participants in the 2000 survey might have been mostly LBW, who were either hospitalized, or were currently ill, although information on non-participants was not assessed in this survey. Our LBW sample might have been limited to low-risk infants, as shown in the low percentage of VLBW infants and early preterm infants compared with the vital statistics data (Table 1).

Second, the information on maternal smoking and drinking habits was only obtained from self-report. This might have led to under-reporting, as suggested in former validation studies in pregnant women.[21–23] Third, important factors influencing pregnancy outcomes, such as prior obstetric history,[24] weight gain during pregnancy,[25] maternal anemia,[26] pregnancy complications,[27] and use of assisted reproductive technologies,[28] were not assessed in this survey. Lastly, there was no information on whether the surveyed infants were delivered spontaneously or not. Scheduled cesarean deliveries, labor induction, and indicated preterm deliveries[29] are known to affect gestational length, and therefore, birth weight.

However, our study has illustrated the emergent need to identify the etiology of preterm deliveries in Japan, which is the major factor for the LBW increase. There are interactions between the increase in preterm deliveries and multiple gestations, because multiple gestations are reported to be at an increased risk for preterm delivery, compared with singletons.[30] They are also at an increased risk of LBW even at term, as shown in Table 4. Moreover, women delivering preterm infants are at a higher risk of a subsequent preterm delivery.[18]

In order to develop effective prevention strategies to decrease LBW, further research should be conducted to: (i) identify factors influencing preterm deliveries, including the use of assisted reproductive technologies; (ii) collect accurate information on smoking and drinking prevalence in pregnancy; and (iii) monitor weight gain in pregnancy according to maternal prepregnancy body size to develop appropriate weight gain goals. A public health approach to educate adolescents to prevent teenage child birth might also be necessary.

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Reference birth-length range for multiple-birth neonates in Japan

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Abstract

Aim: To clarify the birth length of twins according to gestational age.

Methods: We studied a total of 51 910 live-birth–live-birth pairs of twins, 4561 triplet live births and 256 quadruplet live births, using data obtained from corresponding birth certificates. The birth length of twins was analyzed according to gestational age.

Results: Compared to singleton neonates, the median birth length of twins was approximately 0.5 cm smaller after the gestational age of 34 weeks, increasing to approximately 2.0 cm at 42 weeks of gestation. The median birth length according to gestational age was found to be the greatest in twins, lower in triplets and the lowest in quadruplets, in which the difference was <2.0 cm.

Conclusion: The birth length of twins was smaller than that of singletons, but the difference was smaller than the difference in birthweight between twins and singletons.

Key words: asymmetrical growth, birth length, gestational age, twins.

Background

Since the introduction of assisted reproductive technology, the rate of multiple births has increased rapidly in Japan.[1] Required promptly in the clinical setting, studies on the birthweight of twins have been conducted in many countries.[2–5] Kato has previously analyzed the birthweight of multiple-birth neonates according to gestational age, using data from corresponding birth certificates.[6]

For the assessment of fetal intrauterine growth, it is not adequate to use only the birthweight according to gestational weeks. The intrauterine growth of multiple-birth neonates is often reported to be asymmetrical.[7,8] To determine if fetal growth is symmetrical or not, other measurements such as birth length and head circumference should be taken into account.[7,8]

Since 1995, the birth-length has been included in the birth certificate, so the authors were able to analyze birth length according to gestational week for neonates born in Japan.

Materials and Methods

In Japan, birth, death, and stillbirth certificates are currently stored in data files on magnetic tapes. This database contains information about the neonate, including the sex, birthweight, birth length, gestational age, the

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parity of the mother, and the ages of the father and mother. From this database, we identified 105 382 twins, 4561 triplets and 256 quadruplets born in Japan between 1995 and 1999. The data related to multiple births were not linked to each other.

In order to determine whether both twins of each pair were still alive, the twins were arranged into pairs, based on both births occurring in the same municipality, within 10 days of each other, and to parents of the same age. Using this method, 51 910 live-birth–live-birth pairs of twins were selected for analysis in this study.

Birthweight was recorded to 1 g, birth length was rounded to 1 cm, and gestational age to 1 day.

The means and standard deviations of gestational age were calculated for twins, triplets and quadruplets according to sex and parity. The means and standard deviations of birthweight and birth length were calculated for twins, triplets and quadruplets according to sex, parity and birth order. The significance of differences between mean values was tested using Student's *t*-test where the comparison was between two groups, and using one-way ANOVA where the comparison was between more than three groups.

A reference birth-length curve was calculated using Altman's method.[9] The normality of the distribution for birth length in each gestational week was tested and the null hypothesis was not rejected.

The smoothed standard deviation for each gestational age was calculated using linear regression weighted by the number of cases for each gestational week.

The number of subjects at each gestational age is shown in Table 1.

Results

The mean gestational age, birthweight, and birth length were analyzed according to sex, birth order and parity, with statistical significance shown in Table 2. Female, and multiparous neonates had a longer gestational age and the difference was significant among twins. Male, multiparous and lower birth order neonates were found to have a greater birthweight and longer birth lengths. These differences were statistically significant, except for the difference between parity in triplets and between sex in quadruplets.

For multiple-birth neonates, the median birth length according to gestational age was shown to be the longest in twins, followed by triplets and quadruplets (Figs 1,2). The difference in the median birth length for each gestational age between singletons and quadruplets was <2.0 cm in both male and female neonates.

Birth length according to the gestational age in twins, as calculated in our study, and according to the results among Japanese singletons as reported by

Table 1 Number of subjects used in the analysis for each gestational week

Gestational age	Twins		Triplets		Quadruplets	
(weeks)	Male	Female	Male	Female	Male	Female
24	154	108	25	19	2	2
25	200	161	28	27	3	1
26	220	180	45	43	10	9
27	322	219	54	43	8	7
28	397	358	63	46	18	9
29	448	371	74	82	14	6
30	522	485	151	155	32	35
31	774	700	181	164	15	25
32	1 094	1 009	240	248	11	13
33	1 660	1 476	31	310	14	6
34	2 701	2 710	405	405	8	3
35	4 824	4 604	336	314		
36	9 859	9 360	208	216		
37	14 915	14 925	92	130		
38	8 160	8 496	12	13		
39	3 781	3 962				
40	1 488	1 643				
41	247	328				
42	24	44				

Table 2 Gestational age, birthweight and birth length of twins, triplets and quadruplets according to variables

	Twins			Triplets			Quadruplets		
	No. of cases	Mean	Standard deviation	No. of cases	Mean	Standard deviation	No. of cases	Mean	Standard deviation
Gestational age (weeks)									
Total	102 755	36.6	2.6	4521	33.2	3.0	256	30.1	2.4
Male	51 965	36.6	2.6 ***	2297	33.1	3.0	135	30.2	2.4
Female	51 060	36.7	2.5	2224	33.2	2.9	121	30.1	2.5
Primipara	57 997	36.6	2.6 ***	3529	33.2	2.9	216	30	2.5
Multipara	44 758	36.7	2.5	984	33.2	2.9	39	31.3	1.6
Birthweight (kg)									
Total	103 264	2.30	0.49	4534	165	0.46	265	1.19	0.35
Male	51 974	2.33	0.50 ***	2299	1.68	0.47 ***	135	1.23	0.38 *
Female	51 290	2.26	0.47	2235	1.62	0.45	121	1.15	0.32
Primipara	58 285	2.24	0.48 ***	3542	1.64	0.45 **	216	1.15	0.35 ***
Multipara	44 979	2.36	0.49	984	1.69	0.48	39	1.45	0.27
First born	51 634	2.33	0.48 ***	1521	1.71	0.46	65	1.24	0.34 *
Second born	51 630	2.26	0.49	1522	1.65	0.46 ***	65	1.23	0.34
Third born				1491	1.58	0.44	63	1.22	0.36
Fourth born							63	1.07	0.36
Birth length (cm)									
Total	100 621	45.3	3.4	4192	41.2	4.1	240	37.2	4.2
Male	50 603	45.6	3.5 ***	2133	41.4	4.1 **	127	37.5	4.5
Female	50 018	45.1	3.3	2059	40.9	3.9	113	36.8	3.8
Primipara	56 673	45.1	3.4 ***	3263	41.2	4.0	200	36.7	4.2 ***
Multipara	43 948	45.6	3.3	923	41.3	4.1	39	40.0	2.5
First born	50 335	45.4	3.3 ***	1408	41.5	4.0	61	37.4	4.5 *
Second born	50 286	45.2	3.5	1406	41.2	4.0 ***	61	37.5	3.8
Third born				1378	40.8	4.2	59	37.6	4.0
Fourth born							59	36.2	4.2

*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Ogawa *et al.*,[10] are shown in Figures 3 and 4 and in Table 3. At a gestational age of <36 weeks, the mean birth length of twins was 0.5 cm shorter than that of singletons. This difference increased to 2.0 cm after 40 weeks of gestation. Male neonates were longer than female, and the average difference over all gestational ages was 0.5 cm.

Twins were classified into four groups according to birthweight and birth length whether they were larger or smaller than the 10th percentile value of the singleton standard of the corresponding gestational week[10] (Table 4).

While the rate of twins with birthweights that were less than the 10th percentile of singletons was 31.6%, that of twins with birth lengths that were less than the 10th percentile of singletons was 16.0%. The rate of twins with birthweights that were less than the 10th percentile of singletons and also with birth lengths that were greater than the 10th percentile of singletons was 19.6%.

In triplets, the median birth length was 0.4 cm longer in male neonates than in female (Fig. 5; Table 5). In quadruplets, male neonates were 1.5 cm longer than female after 34 weeks of gestation (Fig. 6; Table 5).

Discussion

We found that the birth length of twins that were born after 34 weeks of gestation was longer than that calculated by Fukuda.[11] This discrepancy is thought to be because Fukuda obtained data from a hospital that specialized in high-risk pregnancies.

The gestational age of multiple-birth neonates was shorter than that of singletons, and this difference increased with an increasing number of fetuses. The difference in birth length according to sex and parity was comparable with previous studies.[12–14]

Karn reported that twins exhibited greater weight deficits than singletons after 30 weeks of gestation.[14] According to a report by Naeye *et al.*, after 33 weeks of

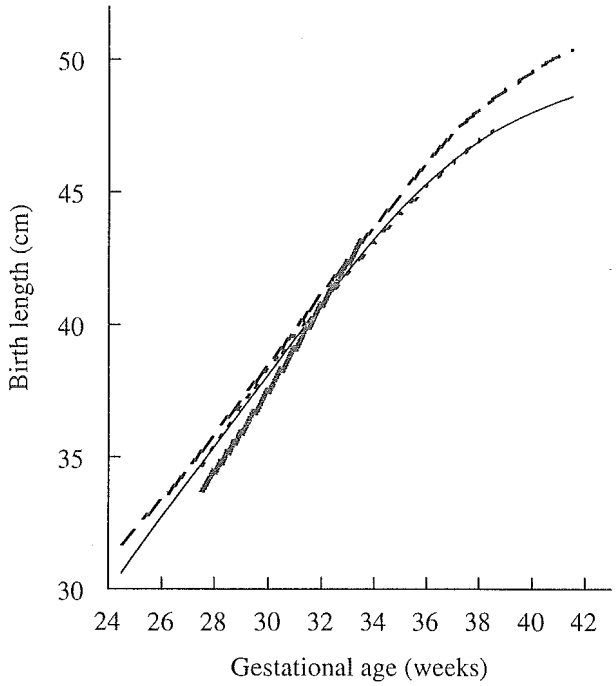

Figure 1 Median birth length of multiple-birth neonates (male). (– –) Singletons, (—) twins, (- - -) triplets, (▬) quadruplets.

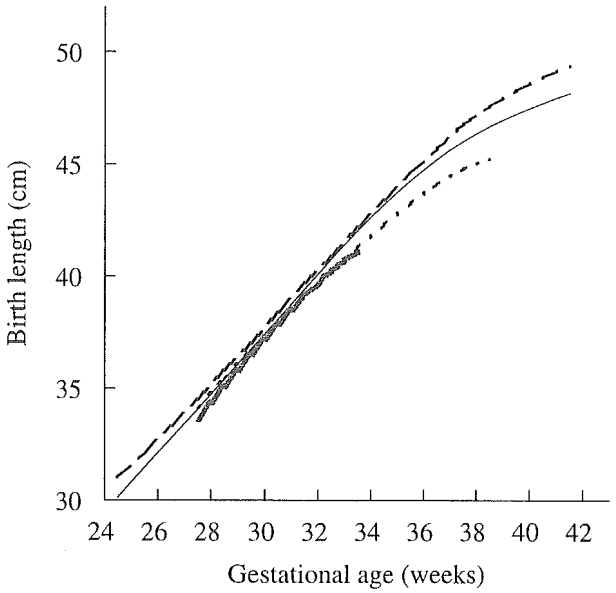

Figure 2 Median birth length of multiple-birth neonates (female). (– –) Singletons, (—) twins, (- - -) triplets, (▬) quadruplets.

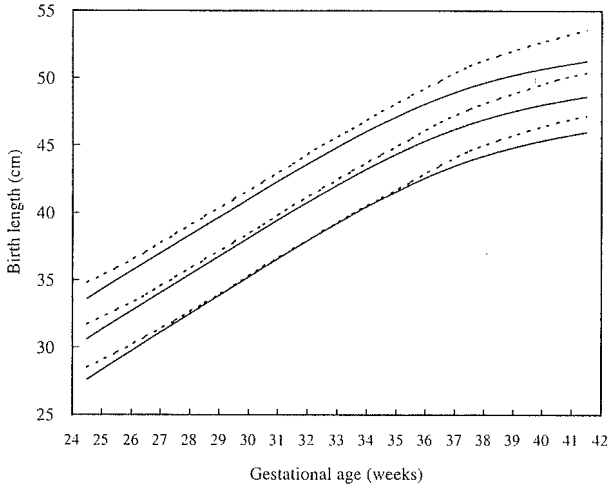

Figure 3 Birth-length percentile curves of twins (male). (- - -) Singletons, (—) twins. The three lines of each category correspond to the 10th, 50th and 90th percentiles.

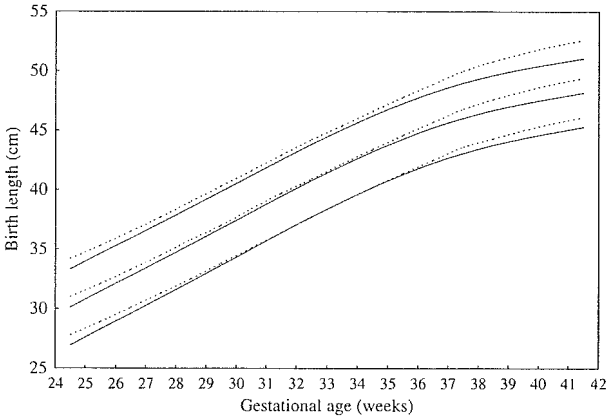

Figure 4 Birth-length percentile curves of twins (female). (- - -) Singletons, (—) twins. The three lines of each category correspond to the 10th, 50th and 90th percentiles.

gestation, the mean weight of twins was markedly less than that of singletons.[15] Birth-length curves are said to show few differences, with a significant fall beginning from 39 weeks of gestation.[16] In the present study, the birth length showed deficits after 37 weeks of gestation. Compared with birthweight, birth length showed less deficit,[8-10] with normal twins said to show 'asymmetrical' hypotrophy.[7] The median birthweight curves of the subjects in this study, which are similar to those of McKeown and Record,[16] suggest that growth

Table 3 Birth-length percentiles of twins (cm)

Gestational age (weeks)	Male percentile			Female percentile		
	10th	50th	90th	10th	50th	90th
24	27.6	30.6	33.6	26.9	30.1	33.3
25	29.0	32.0	35.0	28.3	31.5	34.6
26	30.4	33.4	36.3	29.6	32.8	35.9
27	31.8	34.7	37.7	30.9	34.1	37.2
28	33.2	36.1	39.0	32.3	35.4	38.5
29	34.5	37.4	40.3	33.6	36.7	39.8
30	35.9	38.8	41.7	35.0	38.1	41.2
31	37.3	40.1	43.0	36.4	39.4	42.5
32	38.6	41.4	44.2	37.7	40.8	43.8
33	39.8	42.6	45.5	39.0	42.0	45.1
34	41.0	43.8	46.6	40.2	43.2	46.2
35	42.1	44.8	47.6	41.3	44.3	47.3
36	43.0	45.8	48.5	42.2	45.2	48.2
37	43.9	46.6	49.3	43.1	46.0	49.0
38	44.5	47.2	50.0	43.7	46.7	49.6
39	45.1	47.8	50.5	44.3	47.2	50.2
40	45.6	48.2	50.9	44.8	47.7	50.6
41	46.0	48.6	51.3	45.3	48.2	51.0

Table 4 Number of twins above or below the 10th percentile for birthweight and birth length

	Birth length		Total (%)
	>10th percentile (%)	<10th percentile (%)	
Birthweight			
>10th percentile	66 675 (64.2)	4 375 (4.2)	71 050 (68.4)
<10th percentile	20 591 (19.8)	12 279 (11.8)	32 870 (31.6)
Total	87 266 (84.0)	16 654 (16.0)	103 920 (100.0)

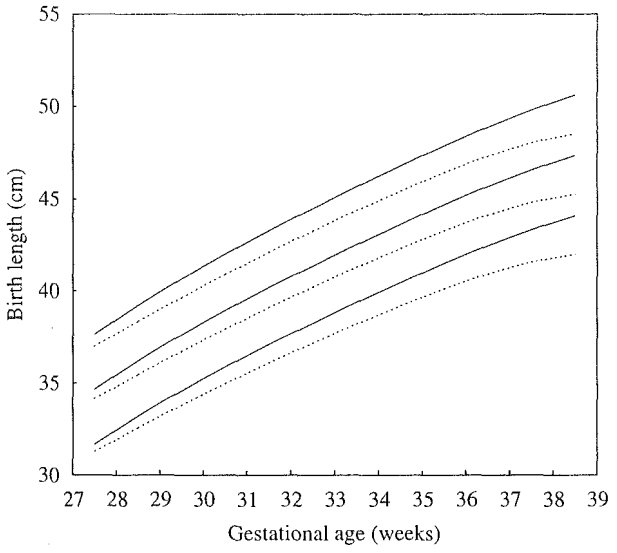

Figure 5 Birth-length percentile curves of triplets. (- - -) Female, (—) male. The three lines of each category correspond to the 10th, 50th and 90th percentiles.

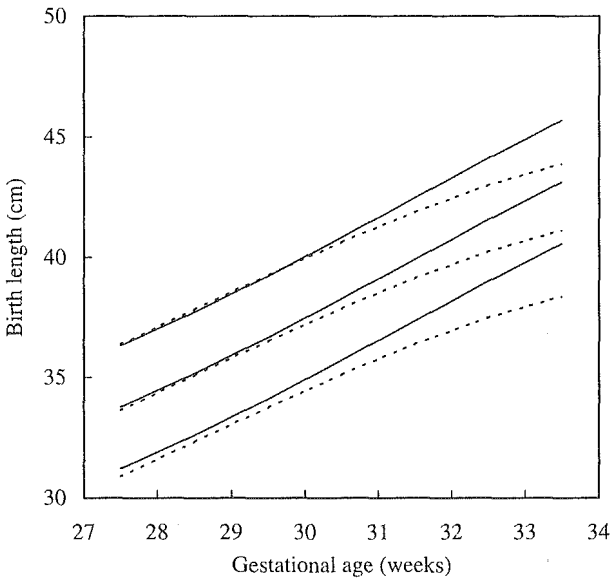

Figure 6 Birth-length percentile curves of quadruplets. (- - -) Female, (—) male. The three lines of each category correspond to the 10th, 50th and 90th percentiles.

Table 5 Birth-length percentiles of triplets and quadruplets (cm)

Gestational age (weeks)	Triplets						Quadruplets					
	Male percentile			Female percentile			Male percentile			Female percentile		
	10th	50th	90th	10th	50th	90th	10th	50th	90th	10th	50th	90th
27	31.7	34.7	37.6	31.3	34.1	37.0	31.2	33.8	36.3	30.9	33.6	36.4
28	33.2	36.2	39.2	32.6	35.5	38.3	32.6	35.2	37.7	32.3	35.1	37.8
29	34.6	37.6	40.7	33.8	36.7	39.6	34.1	36.7	39.2	33.8	36.5	39.3
30	35.9	38.9	42.0	35.0	37.9	40.9	35.7	38.3	40.8	35.1	37.9	40.6
31	37.1	40.2	43.3	36.1	39.1	42.1	37.4	39.9	42.5	36.4	39.1	41.9
32	38.3	41.4	44.5	37.2	40.2	43.3	39.0	41.5	44.1	37.5	40.2	43.0
33	39.4	42.5	45.7	38.2	41.3	44.4	40.6	43.1	45.7	38.4	41.1	43.9
34	40.5	43.6	46.8	39.2	42.3	45.4						
35	41.5	44.7	47.9	40.1	43.3	46.4						
36	42.5	45.7	48.9	40.9	44.1	47.3						
37	43.3	46.6	49.8	41.6	44.8	48.0						
38	44.1	47.3	50.6	42.0	45.3	48.5						

limitations within the uterus become more marked with increasing numbers of fetuses.

The difference between the median birthweight curve of singletons and that of twins was approximately 0.5 kg at 40 weeks of gestation, which is similar to the interval between the 10th and 50th percentile lines of birthweight according to Kato.[6] The interval between the corresponding median birth-length curve was approximately 2.0 cm, approximately half of the interval between the 10th and 50th percentile lines of birth length. Therefore, the differences were relatively small for birth length.

As for triplets, Yokoyama *et al.* demonstrated that the birthweight of triplets was associated with sex, sex combination and birth order, and that birth length was associated only with sex.[17] The mean birth length that Yokoyama *et al.* showed indicated a larger value than this study, which is caused by the difference in study population.

After birth, catch-up growth has been shown to occur in multiple births. Ooki and Asaka showed that the size deficit at birth was recovered over the first 6 years of life, and no size deficit was observed in school-age children.[18] According to Wilson, body length is less depressed than weight at birth, and recovery also occurs during the first year of life.[19]

Buckler and Buckler studied the growth of multiple birth children at various ages throughout childhood.[20] The height of twins was comparable with the overall population of singletons, but that of higher multiples was slightly below average.

Intrauterine growth standards are referred to in the assessment of birth length according to gestational age. The present research indicates that the same standard can be used to estimate birth length with gestational age <35 weeks, although the standard for multiple births is necessary after 36 weeks of gestation. This report shows a birth-length reference range for exclusive use in the assessment of multiple births.

In conclusion, the mean birth length of multiple-birth neonates is shorter than that of singletons. Moreover, the mean birth length of higher order multiple births is shorter than that of twins, but intrauterine growth of length was less depressed than growth of weight. Our results can be used in the assessment of birth lengths of multiple births in Japan.

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Young Investigator Award Winner's Special Article

Strategies for Prevention and Management of Hypertension throughout Life

Katsuyuki Miura[1]

Hypertension has been acknowledged as one of the greatest and established risk factors for cardiovascular diseases. In this special article, strategies for the prevention and management of hypertension throughout human's life were discussed. Studies showing the relationship of birth weight and height increase in childhood to future blood pressure suggest that both environments during pregnancy and during childhood and adolescence are important to prevent hypertension. The promotion of a DASH (Dietary Approach to Stop Hypertension) dietary pattern, rich in fruits and vegetables, is important not only for treatment of high blood pressure but also for long-term prevention of blood pressure rise as well. Blood pressure measured in young adulthood can effectively predict long-term risks of cardiovascular and all-cause mortality, so population-wide primary prevention of high blood pressure for young adults is important. Recent large scale cohort studies confirmed that detection and evaluation of hypertension based mainly on systolic blood pressure remains the most practical and easy approach in the general population for young adult, middle-aged, and older men and women. Researchers in Asia are desired to establish high-quality epidemiologic evidences for Asian for the prevention and management of hypertension.
J Epidemiol 2004;14:112-117.

Key words: blood pressure, hypertension, prevention, epidemiology

Introduction

Hypertension has been acknowledged as one of the greatest and established risk factors for cardiovascular diseases (heart diseases and stroke). Particularly in Asian countries, where the mortality and morbidity of stroke are higher than in western countries, measures against hypertension are considered very important in the prevention of stroke.[1-3] Hypertension affects a majority of the elderly, and drug therapies for hypertension have greatly added to medical costs in most developed countries. The conquest of hypertension is now a major challenge.[4]

This special article is written on the occasion that I was given the Young Investigator's Award of the Japan Epidemiological Association in January 2004. I have been involved mainly in epidemiologic researches on the prevention and management of hypertension, and the award was given for these researches. In this article, I would attempt to discuss strategies for the prevention and management of hypertension throughout human's life, showing results from my related research papers.

Birth weight, childhood growth, and future blood pressure

Recent epidemiologic studies have demonstrated that birth weight and other measures of prenatal growth are associated with adult blood pressure (BP)[5-7] and with cardiovascular disease mortality in later life.[8-11] On the other hand, it has also been suggested in Western populations that short stature is an important risk factor for cardiovascular diseases.[12-16] Although Barker et al hypothesized that malnutrition during pregnancy is responsible for the development of short stature and overweight as well as of several risk factors in adult life, including hypertension,[17] socioeconomic conditions that persist throughout life can cause both lower birth weight and slower increase in height during adolescence.[18] Some cross-sectional within-population studies, especially in children and adolescents, have shown a positive relationship between

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height and BP,[19-21] and another inter-population study showed inverse relation between height and BP.[16] Thus, the underlying mechanism of the association of height with cardiovascular disease is not yet clear. However, findings on the effect of height increase during childhood, independent of birth weight, on cardiovascular disease and its major risk factors are limited.

To determine whether birth weight and childhood growth, especially height increase rate, independently relate to BP in adult life, we conducted a 20-year follow-up study, using the record-linkage method, in a Japanese population.[22] In this study, both birth weight and rate of height increase in childhood and adolescence were inversely and independently associated with BP at age 20 years (Table 1). These results suggest that both environments during pregnancy and during childhood and adolescence independently affect subsequent BP level.

Food intake and long-term BP increase

By the early 1990's, based on scientific evidence available at the time, nutritional guidelines for prevention and control of high blood pressure recommended weight control, reduced intake of sodium chloride (salt), avoidance of heavy alcohol consumption, and increased dietary potassium intake.[23, 24] The DASH (Dietary Approach to Stop Hypertension) study recently added further dietary approaches to reduce BP in both nonhypertensive and hypertensive individuals using a "combination" dietary pattern during an 8-week intervention.[25-27] This dietary pattern emphasizes higher than usual intakes of fruit and vegetables and low-fat dairy products. It also includes selection of whole grains, poultry, fish, and nuts, and reduced intake of total fats, saturated fats, cholesterol, red meats, sweets, and sugar-containing beverages. This diet is high in potassium, magnesium, phosphorus, calcium, fiber, and protein. The DASH-Sodium trial also showed that the combination diet plus reduced salt intake (at about 50 mmol/day) yielded substantial combined reductions in BP of both nonhypertensive and hypertensive persons. The DASH dietary concept, emphasizing a healthy pattern based on food rather than nutrient intake, has been incorporated into recent dietary guidelines by the American Heart Association[28] and by JNC7 (the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure).[29] While the DASH combination diet is effective in lowering blood pressure, influences of specific foods and food groups (e.g., vegetables, fruits, fish, red meats) on BP have not been well studied long-term. Information is especially sparse on relationships of food groups to BP change in populations followed prospectively for years.

We reported relationships of food intake to BP change in a prospective cohort study of 1,710 middle-aged men, the Chicago Western Electric Study.[30] The Generalized Estimating Equation method was used to analyze relationships of food group intakes to average annual BP change, adjusting for age, weight at each year, alcohol, calories, and other foods. Men who consumed 0.5-1.5 cups vegetables/day were estimated to have 2.8 mmHg less systolic BP (SBP) rise in 7 years than men who consumed <0.5 cups/day. Men who consumed 0.5-1.5 cups fruit/day were estimated to have 2.2 mmHg less SBP increase in 7 years than men who consumed <0.5 cups/day. Beef-veal-lamb intake and poultry intake were related directly to greater BP rise. These findings lend further support to the promotion of a DASH-style dietary pattern not only for treatment of high blood pressure but also for long-term prevention of BP rise as well.

BP in young adults can predict future cardiovascular mortality

For middle-aged and older populations worldwide, BP has repeatedly been shown to be a significant risk factor for coronary heart disease (CHD), stroke, and the major cardiovascular diseases (CVD).[1-3] These relationships, for both SBP and diastolic BP

Table 1. Predicted differences in systolic blood pressure (mmHg) at age 20 for 1 standard deviation higher values of birth weight, % increase in height, and weight at age 20 estimated by multiple linear regression analysis, among 2,198 men and 2,428 women born in 1965-1974, Ishikawa, Japan.

	Men			Women		
	1 standard deviation	Predicted difference	95% confidence interval	1 standard deviation	Predicted difference	95% confidence interval
Model 1						
Birth weight	0.44 kg	-1.5	-2.0 , -1.0	0.41 kg	-1.0	-1.4 , -0.5
Weight at age 20	9.4 kg	4.4	4.0 , 4.9	7.3 kg	3.3	2.9 , 3.7
Model 2						
Birth weight	0.44 kg	-1.6	-2.1 , -1.1	0.41 kg	-1.0	-1.4 , -0.5
% increase in height (age 3 to 20)	5.4 %	-0.7	-1.1 , -0.2	4.9 %	-0.5	-0.9 , -0.1
Weight at age 20	9.4 kg	4.5	4.0 , 5.0	7.3 kg	3.4	3.0 , 3.8

Both models are also adjusted for gestational age.
Modified from reference 22.

(DBP), are continuous, graded, strong, independent of other risk factors, consistent, predictive, and generally assessed as etiologically significant. In contrast, long-term observations on blood pressure and CHD-CVD mortality in young adults are limited. Because major CVD events are rare before age 50 years in men and 60 in women, studies on risk factors measured at an average age of about 30 years require long-term follow-up or large sample sizes to accrue adequate numbers of events. The few reports of prospective population-based studies are from nested case-control investigations in former college students.[31-33] Other evidence comes from autopsy studies showing that coronary risk factors relate to early atherosclerotic lesions in young adults.[34-36] Although hypertension treatment guidelines are usually considered applicable for persons ages 18 and older,[23,24,29] there is limited documentation supporting screening and treatment of young adults.

The Chicago Heart Association Detection Project in Industry Study is one of the largest and longest prospective studies providing CVD mortality data. Approximately 11,000 men ages 18-39 at baseline (30 years on average) were followed for 25 years, and we reported the relationship of baseline BP to 25-year CHD, CVD, and all-cause mortality.[37] The main findings on this cohort of young adult men are: (1) BP measured in young adulthood predicted long-term risks of CHD, CVD, and all-cause mortality. As in middle-aged and older persons,[1-3] relationships of SBP, DBP, and SBP/DBP (JNC-VI strata[23]) to mortality were generally graded, strong, and independent. (2) Multivariate-adjusted HRs tended to be greater for SBP than DBP, and similar in size to those for middle-aged men. And (3) for the two large strata with high-normal BP and with stage 1 hypertension, 25-year absolute risks and absolute excess risks of mortality were substantial, e.g., all causes death rates of 63 and 72 per 1,000, absolute excess rates of 10 and 20 per 1,000, translating into estimated shorter life expectancy of 2.2 and 4.1 years. These two strata accounted for 59% of all excess deaths attributable to SBP/DBP above normal (Figure 1).

These data lend strong support to two strategic concepts: First, the importance of population-wide primary prevention by safe nutritional-hygienic means of adverse BP levels, so that a substantial increase is achieved in the proportion of people in the population who, throughout life, have favorable levels of BP (and other risk factors). Second, population-wide efforts for early detection of children, teenagers, and young adults – as well as others – with unfavorable BP levels, so that therapeutic efforts can be instituted early, first and foremost to improve lifestyles.

Importance of SBP and DBP in various age groups

Some recent epidemiologic studies reported that pulse pressure (PP), the difference between SBP and DBP, is a useful predictor for CHD or total CVD especially in middle-aged or older people.[38-41] These reports emphasized the importance of PP as a CHD or CVD risk factor, especially because PP is often higher after age 50, apparently due to increased arterial stiffness.[42,43] In regard to prior reports on PP, many did not compare the significance of PP with that of SBP or DBP, and some others were studies on hypertensive persons only. Therefore, it was uncertain whether PP is superior to SBP or DBP in predicting future CHD, CVD, and all-cause deaths in various age-sex groups of the general (i.e., apparently healthy) population. Moreover, because recent discussions have emphasized the importance of SBP compared to DBP,[44-46] and these are strongly correlated, it is also important to assess whether DBP has any additional role in predicting risks independently from SBP.

We reported relations of four BP indices — PP, SBP, DBP, and

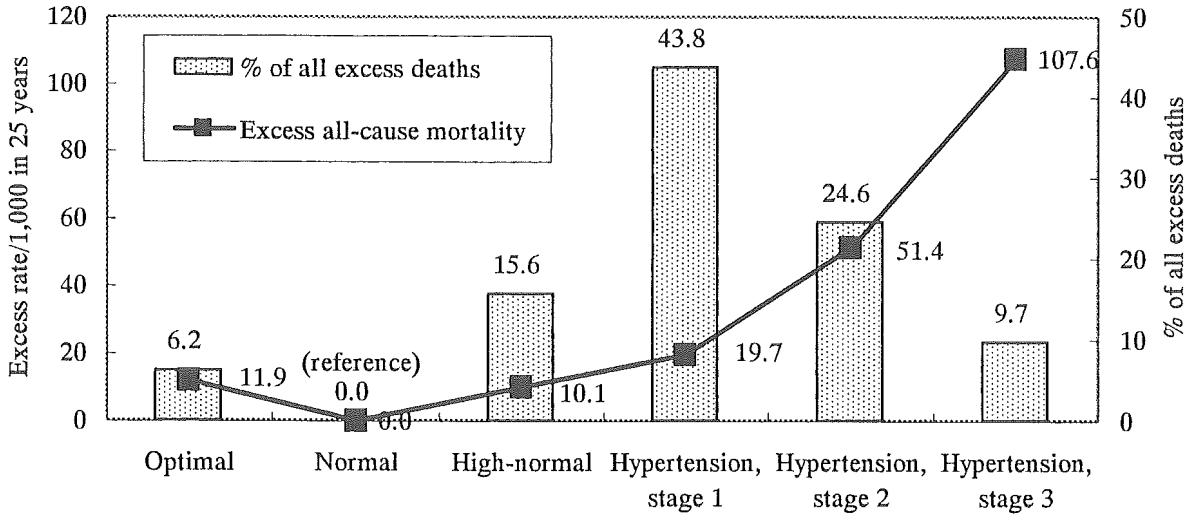

Figure 1. Absolute excess risk per 1,000 in 25 years and percentage of all excess deaths from all causes in strata of JNC-VI classification[23] in 10,874 men aged 18-39 years at baseline, the Chicago Heart Association Detection Project in Industry. Percentage of all excess deaths was calculated from estimated number of excess deaths compared with the normal blood pressure stratum by JNC-VI criteria during 25 years of follow-up. Modified from reference 37.

mean arterial pressure (MAP) — to 25-year mortality risks from CHD, CVD, and all causes in five population cohorts (total 28,360 men and women) classified by age and sex from the Chicago Heart Association Detection Project in Industry Study.[47] The main findings from this study were: (1) Relationships of PP were less strong than those of SBP for all endpoints in all age-sex groups studied. (2) Relationships of PP were less strong than those of DBP for all endpoints in middle-aged men and women and in older women. (3) Among the four BP indices, the strongest relationship was observed either for SBP or MAP in all age-sex groups. (4) Relationships of SBP to mortality tended to be stronger than or similar to those of DBP. And (5) with control for SBP, DBP was positively and significantly related to mortality in middle-age men and women, but not in younger men and older men and women.

As to implications of these results for public health policy and clinical practice: (1) They affirm continued emphasis on SBP,[44-46] particularly for younger men and older people. For middle-aged people ages 40-59, DBP should be given concomitant careful consideration because of its strong independent relationship to mortality. (2) In younger and middle-aged people, emphasis on PP should be avoided. There is no evidence, in a general population less than age 60, showing that PP is superior to SBP in predicting CVD or total mortality. Emphasizing risks associated with PP is likely to underestimate true risks. And (3) relationships of MAP to risk were generally as strong as or slightly stronger than those of SBP. However, use of this index may not be practical in daily clinical and public health practice, because there are no guidelines for hypertension diagnosis and management using MAP. Detection and evaluation of hypertension based mainly on SBP remains the most practical and easy approach in the general population for young adult, middle-aged, and older men and women (at least up to about age 63 years). After this report, several cohort studies including older people did the same kind of analysis and showed that the relationship of PP to mortality from total cardiovascular diseases and coronary heart disease was less strong than those of other BP indexes.[48-50]

Making evidences for Asian people

Very fortunately, I was able to contribute to long-term, large-scale cohort studies in Chicago. However, most study participants in these studies were Caucasian, and, as it is commonly true for many other major hypotheses in preventive cardiology, epidemiologic evidences for Asian people tend to be sparse. Recently I have had a good opportunity to participate in the INTERnational cooperative study of MAcro- and micro-nutrients and blood Pressure (the INTERMAP) and found that there are big differences in body mass, fat intake, cigarette smoking, etc., between Asian and Western people.[51, 52] Strategies for the prevention and management of hypertension and cardiovascular diseases for Asian would be different from those for Western people. Researchers in Asia should establish high-quality epidemiologic evidences for Asian and accomplish the prevention of hypertension and cardiovascular diseases throughout life.

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学際領域の診療

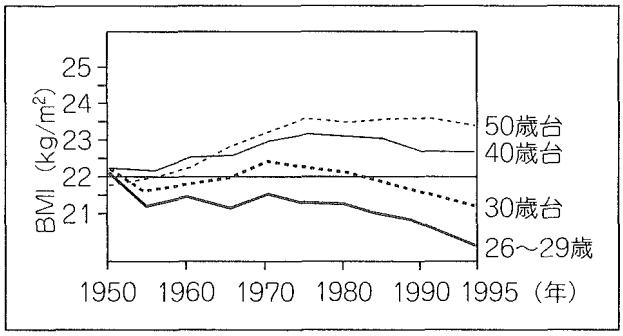
Interdisciplinary Practice

妊産婦と栄養

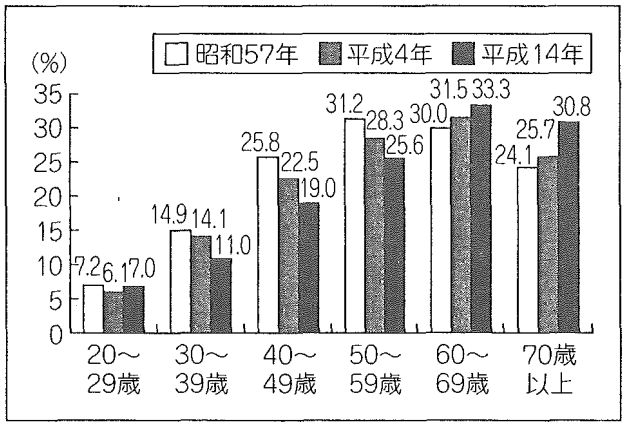
Nutrition during Pregnancy

はじめに

近年のわが国における生活習慣の変化に伴い，肥満症の頻度は激増しており，肥満に起因する種々の疾患や合併症の罹患率が増加している．体格指数(Body mass index：BMI)は，個人の栄養状態をみる簡易な指標である．肥満学会では，女性の場合，BMIが22において疾患罹患度の最も低い指数であると設定し，これに基づき，標準体重(身長(m)×身長(m)×22)を算出するように提唱している[1]．興味深いことに，50年前のわが国では，いずれの年代層もBMIは健康的と考えられる22前後でほぼ一定であるのに対し，時代の推移とともに年代間のBMIの解離が認められる(図１)．一方，最近肥満の頻度が高くなっていることは周知の事実であるが，女性に限ってみると，年代によって肥満の頻度が異なっていることに留意すべきである．すなわち図２に示すように，肥満(BMI：25以上)頻度の経時的推移として30～50歳代まではむしろ減少しており，その後増加していることがわかる．さらにやせの頻度をみると，40歳代まで増加していることがわかる(図３)．これらの現象はわが国の女性においても白人と同様，若いときにやせているにもかかわらず，その後，agingとともに脂肪蓄積が増加することを示すデータであり，これは近年の女性における生活習慣病の原因を示す重要な現象である．また産婦人科領域では，肥満ややせの妊婦がハイリスク妊娠であることや，肥満が多嚢胞性卵巣症候群や子宮体癌と関連することが知られており，産婦人科医



(図１)　日本人女性の年代別BMIの推移(厚生労働省)



(図２)　わが国の年代別肥満女性の推移(厚生労働省)
(肥満　BMI：25以上)