

Original Article

Physical Growth Charts from Birth to Six Years of Age in Japanese Twins

Syuichi Ooki,¹ and Yoshie Yokoyama.²

BACKGROUND: The purpose of this study was to analyze the characteristics of the physical growth of twins in childhood and to present growth charts of Japanese twins.

METHODS: The subjects consisted of 2029 pairs of normally developed Japanese twins. Growth data were obtained by mailed or hand-distributed questionnaires. Factors that affect body weight and height/length at selected ages were analyzed by stepwise regression analysis. Selected percentiles of body weight, height/length, and body mass index were calculated according to sex, and growth curves were drawn using a spline function. The size deficit of the twins compared to the standards for the general population of Japan was calculated.

RESULTS: Gestational age, parity, zygosity, and birth order affected physical growth in varying degrees, although the overall effects themselves were small and mostly disappeared by one year of age. Growth charts of the twins present growth at selected percentiles from birth to 6 years of age according to sex. The size deficit of the twins was largest at birth: more than 20% for weight and approximately 6% for length compared to the 50th percentile of the standard for the general population of Japan. These deficits decreased rapidly in the first 6 to 12 months, and were found to be as low as 0-2% at 4 to 6 years of age.

CONCLUSION: Growth charts specifically for twins are needed, at least for the first 1 to 3 years of age but not beyond the age of 6 years.

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Key words: Twins, Growth, Weight Gain, Japan.

In Japan, as in other developed countries, the rate of multiple births has been increasing since 1975. The higher twinning rates in Japan since 1987 have been attributed to both the higher proportion of mothers treated with ovulation-inducing hormones and to the increasing use of in vitro fertilization.¹ Currently about 1% of all births are multiples.² Therefore, there is an increasing need to provide appropriate information to parents and nursing staff on the biological characteristics of twins, such as their intrauterine growth, physical growth after birth, and motor and language development.³ However, little information is available, in part because the lack of a population-based twin registry makes it difficult to collect growth data on twins, especially after birth. There have been many studies on the physical growth of twins in child-

hood in Western countries,⁴⁻¹⁰ including Wilson's detailed summary of the features of twin growth.¹¹

It is well known that the growth patterns of twins in utero and in childhood are very different from those of singletons.^{3,12-14} Because there are no growth standards for twins in Japan, the physical growth of twins in childhood must be evaluated using the standards for the general population¹⁵ — that is, standards for singletons. As a result, many twins are regarded as having poor growth, especially when they are very young, and this causes both the twins and their parents much embarrassment and concern. In general in Japan, pediatricians and public health nurses, the professional advisors for the growth of children, do not have adequate information to answer questions that the parents of twins

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ask about their children's growth. Moreover, many factors that affect body size after birth, such as the perinatal medical system, body size at birth, and the body size of the mother, differ significantly between Japan and Western countries. To resolve these shortcomings in appropriate data, it is essential to obtain objective growth data based on a large sample of Japanese twins.

There are two dimensions to estimating the growth of twins: comparing individual twins versus singletons,^{6,9} and comparing the similarity of the twins within a pair by zygosity.^{5,8,10} The present study deals with twins as individuals. The purpose of this study is to analyze the characteristics of twins' physical growth from birth to 6 years of age and to present growth charts of normally developed Japanese twins in comparison with those of the general population. This comparison between twin and singleton standards may also be useful in growth studies of Caucasians.

METHODS

Subjects

In Japan only two main sources of data about multiple births have been established, and the gap between them is wide. First, vital statistics may be available without access to information on specific individuals. Second, data from hospitals have been used in the field of obstetrics, mainly in managing high-risk pregnancies. Although this method is relatively easy to use, it may allow large selection biases to occur.³ To cover the gap between vital statistics and hospital data, the authors have been constructing a twin database that would contribute to overall health care for families with multiples. The database is larger and less biased than hospital data and its information is more detailed than the vital statistics, especially as to zygosity. In addition, the authors made much of after-birth data, which neither vital statistics nor hospital data adequately supply. The basic characteristics of this database are described in detail elsewhere (Ooki et al: Construction of Japanese database on child twins and their families; submitted to the journal *Twin Research*). The present data were drawn from this database and were obtained by questionnaire.

The subjects of this study were 2029 mothers and their 4058 twin children, who were recruited from among two different groups. The first group of subjects consisted of 937 mothers and their 1874 twins who belonged to various associations for parents of multiples throughout Japan (maternal associations group). The second group of subjects consisted of 1092 mothers and their 2184 twins living in the Tokyo metropolitan area; all of the twins in this group had applied to (though not necessarily enrolled in) the secondary education school attached to the faculty of education of the University of Tokyo between 1982 and 2003 (school applicants group). In the maternal associations group the twins were born between 1986 and 2002, and in the school applicants group the twins were born between 1968 and 1991. At the time data were collected, in 2002-2003, the twins in the maternal associations group ranged in age from 0 to 15 years (mean 6.0 years, standard deviation 3.8 years, median age 5.0 years), and the twins

in the school applicants group were all 11 or 12 years old.

Data collection

Data were collected through mailed or hand-delivered questionnaires, which had nearly the same format between the two groups. The questions asked about family structure; obstetrical findings on the mothers; the twins' physical growth, zygosity, motor, language, and mental development; the twins' and parents' medical histories; and any behavioral problems the twins had had. In the school applicants group, one parent of each twin, usually the mother, participated in a medical interview by two or three interviewers, including, from 1988 on, one of the present authors (Ooki), in which their responses to the questionnaire were checked carefully.

Detailed obstetrical records on the mothers in the school applicants group were also obtained from the "Maternal and Child Health Handbook", which the Ministry of Health, Labor and Welfare of Japan provide to all pregnant women. No complete information on chorionicity was obtained.

In Japan, the health examination system after birth differs according to life stage. This has made it difficult to obtain continuous growth data on children before and after 6 years of age. Until 6 years of age, children receive a health examination administered by the Ministry of Health, Labor and Welfare based on age, which is counted as real weeks, months, or years after birth. The "Maternal and Child Health Handbook" presents the growth standards of weight and height/recumbent length and developmental milestones every 10 years, e.g., 1980, 1990,¹⁵ and 2000. The growth data of children based on mass examinations are usually recorded in this Handbook. The authors of the present study advised the mothers to refer to these records when completing the questionnaire. Growth data were assigned to the appropriate age groups on the basis of days since birth, which was calculated as the date at mass examination minus the child's birthday. For example, if the subject's age was 73 days, his or her data were assigned to the 2- to 3-month-old group. The data from the Handbook were accepted without modification; therefore, the method and accuracy of those measurements could not be ascertained.

Although this method seemed to be an effective way to collect large amounts of growth data on twins after birth, it did not produce perfect longitudinal data, and there were certain differences in the number of subjects in each age group.

Zygosity classification

The zygosity of the twins was determined primarily by a questionnaire¹⁶ that was used widely in Japan and that, in the present study, was completed by the mothers in both groups. The zygosity types were monozygotic, unclassified, and dizygotic, according to the similarity score, which was calculated by using five questions regarding the physical similarity and confusion of identity between the twins. The accuracy in classifying their twins was nearly 98%, although about 10% of pairs were unclassified.¹⁶ The

accuracy was a trade-off according to the percentage of unclassified pairs.

For the school applicants group, zygosity was diagnosed also by the use of many genetic markers for those twin pairs who were actually admitted to the school.³ The twins in the present study were classified as 1159 monozygotic, consisting of 557 male-male and 602 female-female pairs; 675 dizygotic, consisting of 170 male-male, 174 female-female, 163 male-female, and 168 female-male pairs; and 195 unclassified, consisting of 106 male-male and 89 female-female pairs. As zygosity testing is very rare in Japan, this is the largest sample to date for a study on growth data of twins in Japan that includes both correct age and specified zygosity.

Preliminary analyses and data combination

Before the data of the two groups were combined, weight and height in both groups were examined in detail. The results are described elsewhere (Ooki et al. *Twin Research*, mentioned above). Birth complications of mothers or twins, such as placenta previa, placental abruption, coiling of the umbilical cord, neonatal asphyxia, growth-discordant twins, and twin-to-twin transfusion syndrome, were observed to varying degrees. None of these were grounds for exclusion from the study. In general, it was very difficult to set clear and consistent inclusion/exclusion criteria, as more than 10% of the present subjects had at least one of the

complications mentioned above. Moreover, no subjects showed apparent retardation of physical growth at the time of data collection. The preliminary analyses are summarized as follows. (1) The twins in the maternal associations group had one-week shorter gestations than the twins in the school applicants group. (2) Body size parameters at birth, namely weight, length, chest circumference, and head circumference were slightly smaller in the maternal associations group. Nevertheless, both birth weight itself according to gestational weeks and the percentage difference in relative birth weight within pairs were nearly the same compared to the birth weight norms of the general twin population in Japan.¹⁷ (3) The two groups were very similar to each other in body weight and height from birth through 6 years of age, as shown in Figure 1. For example, the range of body weight difference between the groups (the school applicants group minus the maternal associations group) at the 50th percentile of the raw data was from -1.30 kg to 1.30 kg for males and -0.37 kg to 1.50 kg for females. These findings suggested that the groups were not very different, at least in their physical development. Moreover, in both groups the data seemed to reflect normal physical development after birth. All data samples were used, irrespective of the data source, in order to maintain the sample size, stabilize the monthly measurement values, and not overestimate monthly measurement values from birth to one year of age.

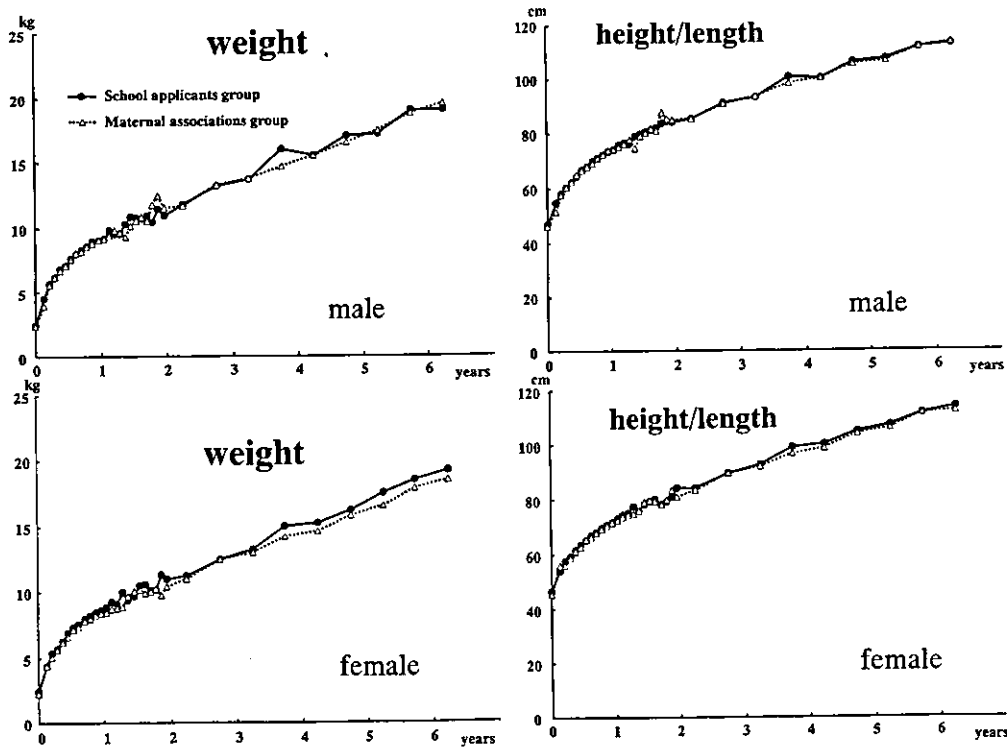


Figure 1. The 50th percentiles of body weight and height/length from birth to six years of age (raw data).

Statistical analysis

Birth complications were not grounds for exclusion from the following analysis. Usually, the growth standards of singletons *in utero*, determined by body size at birth according to the gestational weeks, are presented according to sex and/or parity (primiparity or multiparity), whereas after birth the standards are presented according to sex alone. In the case of twins, at least two additional factors that are not relevant to singletons might also be considered: the birth order of the twins and their zygosity (monozygotic or dizygotic).

First, the factors that affected the body weight and height/length of twins at selected ages were confirmed by stepwise regression analysis, with a threshold significance level of 0.05. The variables considered were sex, birth order of the twins, gestational weeks, maternal and paternal age upon the birth of the twins, parity, zygosity, presentation, the birth year of the twins, and the group to which the subjects belonged. For qualitative variables, the following codes were used: sex, female 0, male 1; birth order, first-born 1, second-born 0; zygosity, monozygotic 0, dizygotic 1; presentation, non-vertex 0, vertex 1; group, maternal

associations group 1, school applicants group 0. The numbers of subjects on whom data were missing as to parity, presentation, zygosity, gestational age, maternal age, and paternal age were 4, 446, 390, 52, 36, and 8, respectively. There were no missing data for sex, birth order, or birth year of the twins.

Growth charts were developed from the results of the regression analysis. The selected percentiles (3rd, 10th, 25th, 50th, 75th, 90th, and 97th) of body weight (kg), height/length (cm), and body mass index (kg/m^2) at each age were calculated, and growth curves were drawn by means of a spline function. Body mass index (BMI) is mathematically equal to the Kaup index, which has been widely used in Japan as an index for the physique or obesity of a child younger than 6 years. Though several problems were pointed out regarding BMI as an indicator of child obesity, this index has become a world standard.¹⁸ Table 1 shows the number of subjects using data analysis according to age and group.

The size deficit in twins was calculated as the percentage difference between the value of the general population and that of the twins divided by the value of the general population. Size

Table 1. Number of subjects according to sex, age, and group.

		weight				height/length			
		male		female		male		female	
		M group	S group	M group	S group	M group	S group	M group	S group
	at birth	966	1022	899	1154	944	957	868	1092
0 year	2-3 months	95	152	68	149	91	138	62	136
	3-4	481	514	469	554	456	490	448	534
	4-5	357	199	315	275	351	193	312	270
	5-6	171	202	157	201	164	191	152	193
	6-7	420	374	405	425	410	367	389	419
	7-8	209	98	216	103	201	97	211	98
	8-9	159	95	141	108	157	94	138	98
	9-10	337	263	320	304	327	259	312	302
	10-11	242	132	263	137	238	129	262	132
	11-12	178	100	145	88	174	98	142	88
1 year	0-1	318	288	358	358	314	285	348	352
	1-2	94	78	93	58	90	76	91	58
	6-7	178	97	135	117	178	95	134	116
	7-8	94	61	75	79	95	61	75	78
2 years	0-6	335	236	344	265	328	234	333	259
	6-12	91	69	67	56	85	67	68	56
3 years	0-6	545	647	528	719	540	648	527	715
	6-12	155	65	147	65	153	65	147	68
4 years	0-6	201	239	203	257	198	239	206	259
	6-12	90	120	89	113	88	120	91	115
5 years	0-6	192	244	190	245	192	244	190	247
	6-12	72	103	54	110	70	103	54	110
6 years	0-6	171	323	184	364	171	324	181	371

M group: Maternal associations group.

S group: School applicants group

deficits were calculated using the 50th percentile values of the growth standards presented by the Ministry of Health and Welfare (now reorganized as the Ministry of Health, Labor and Welfare) in 1990.¹⁵ All data were analyzed using SAS® for Windows.¹⁶ The growth curves were smoothed by the PROC TRANSREG procedure, with the 'pspline' model specified.

Ethical issues

The mothers in the maternal associations group all cooperated voluntarily in this research, mainly through their associations. Informed consent concerning the statistical analysis of the data in the school applicants group was obtained from each twin and his or her parents in writing as part of the application process.

RESULTS

The results of the stepwise regression analysis are shown in Table 2. Gestational weeks, sex, parity, zygosity, and birth order significantly affected both birth weight and birth length. None of the other variables — that is, the maternal and paternal age upon the birth of the twins, presentation, the birth year of the twins, or the group — met the 0.05 significance level for entry into the model. Lasting effects of gestational weeks and sex were found with statistical significance up to at least 3 years of age. The contributions of other factors were negligible and mostly disappeared by 6 to 12 months of age.

The coefficient of determination (R^2) of gestational weeks rapidly decreased with age, while the effect of sex did not. Physical growth from birth to 3 years of age was calculated according to sex and gestational weeks. The results are shown in Tables 3 and 4. The gestational weeks were divided into two groups: 25-36 weeks (preterm delivery) and 37-41 weeks (term delivery). The difference in weight or height/length between the preterm and term groups was calculated as the percentage difference between the value of the term group and that of the preterm group divided by the value of the term group. Between the term and preterm groups, the difference in weight was nearly 20% at birth, rapidly decreased until 3 months, and was within 5% after 6 months. As to height/length, the difference was nearly 6% at birth and gradually decreased after birth. Since there were many detailed standards for birth weight and length in twins according to gestational weeks³, growth charts after birth were calculated separately for males and females without taking gestational periods into consideration, following the system used to calculate standards for singletons.²⁰

The 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentile curves of weight and height/length from birth to 1 year of age are presented in Figure 2, and those from 1 to 6 years of age are presented in Figure 3. The 3rd, 10th, 25th, 50th, 75th, 90th, and 97th percentile curves of BMI from birth to 6 years of age are presented in Figure 4.

The size deficits of twins in weight and height/length from birth to 6 years of age are presented in Figure 5. The weight deficit of

Table 2. The results of stepwise regression analysis for weight and height/length.

	weight						height/length													
	gestational age		parity		sex		birth order		zygosity		gestational age		parity		sex		birth order		zygosity	
	R ² (%)	p	R ² (%)	p	R ² (%)	p	R ² (%)	p	R ² (%)	p	R ² (%)	p	R ² (%)	p	R ² (%)	p	R ² (%)	p	R ² (%)	p
birth	39.78	**	1.91	**	0.88	**	0.76	**	0.08	*	36.56	**	1.09	**	1.33	**	0.25	**	0.11	*
3 months	12.28	**	-	n.s.	7.34	**	0.47	**	-	n.s.	18.03	**	0.18	*	6.91	**	0.16	*	-	n.s.
6 months	3.44	**	0.63	**	8.21	**	0.53	**	-	n.s.	6.24	**	0.44	*	10.46	**	-	n.s.	-	n.s.
9 months	4.36	**	0.32	*	8.18	**	0.43	*	-	n.s.	6.30	**	-	n.s.	8.03	**	-	n.s.	-	n.s.
1 year	3.98	**	-	n.s.	8.66	**	-	n.s.	-	n.s.	6.22	**	-	n.s.	6.07	**	-	n.s.	-	n.s.
2 years	1.17	**	-	n.s.	8.32	**	-	n.s.	-	n.s.	1.61	**	-	n.s.	5.99	**	-	n.s.	-	n.s.
3 years	0.69	**	-	n.s.	4.16	**	-	n.s.	-	n.s.	0.84	**	-	n.s.	2.49	**	-	n.s.	-	n.s.

*: p<0.05, **: p<0.01.

None of the other variables (maternal and paternal age upon the birth of the twins, presentation, the birth year of the twins, or subject group) met the 0.05 significance level for entry into the model.

R²: coefficient of determination

Table 3. The 50th percentiles of weight from birth to 3 years of age according to gestational weeks (preterm vs term delivery).

	weight									
	male					female				
	25-36 weeks (preterm)		37-41 weeks (term)		difference	25-36 weeks (preterm)		37-41 weeks (term)		difference
	n	kg	n	kg	%	n	kg	n	kg	%
birth	677	2.13	1276	2.61	18.4	656	2.04	1348	2.54	19.7
3 months	344	5.82	636	6.26	7.0	332	5.31	662	5.84	9.1
6 months	245	7.52	540	7.79	3.5	262	7.00	558	7.37	5.0
9 months	199	8.42	397	8.74	3.7	205	7.96	405	8.17	2.6
1 year	208	9.09	386	9.33	2.6	229	8.48	473	8.80	3.6
2 years	209	11.80	355	11.86	0.5	206	10.93	394	11.26	2.9
3 years	400	13.70	771	13.83	0.9	383	13.05	836	13.33	2.1

Difference=(T-P)/T x 100. P: weight of preterm delivery, T: weight of term delivery.

Table 4. The 50th percentiles of height/length from birth to 3 years of age according to gestational weeks (preterm vs term delivery).

	height/length									
	male					female				
	25-36 weeks (preterm)		37-41 weeks (term)		difference	25-36 weeks (preterm)		37-41 weeks (term)		difference
	n	cm	n	cm	%	n	cm	n	cm	%
birth	619	44.6	1247	47.4	5.9	606	44.0	1313	46.8	6.0
3 months	314	58.7	618	60.6	3.1	318	56.9	637	59.2	3.9
6 months	235	65.9	533	67.0	1.6	249	64.1	549	65.5	2.1
9 months	193	70.0	389	71.1	1.5	201	68.5	399	69.5	1.4
1 year	204	73.4	383	74.3	1.2	225	71.9	461	73.1	1.6
2 years	206	84.9	349	85.5	0.7	200	83.2	383	84.0	1.0
3 years	400	93.2	767	93.6	0.4	383	92.0	831	92.6	0.6

Difference=(T-P)/T x 100. P: height/length of preterm delivery, T: height/length of term delivery.

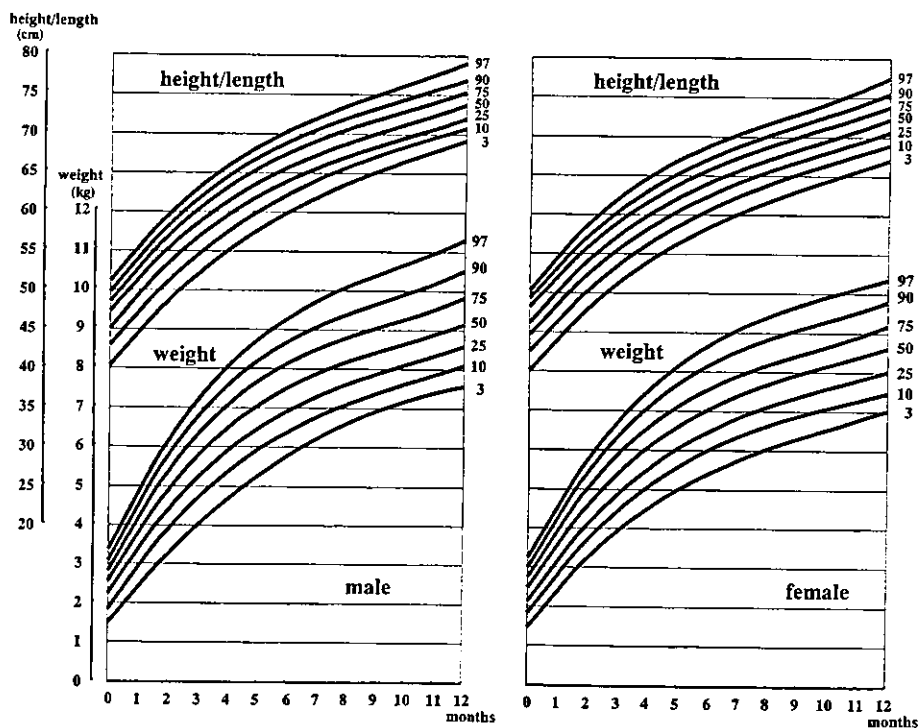


Figure 2. Body weight and height/length of twins by age percentiles from birth to 1 year of age.

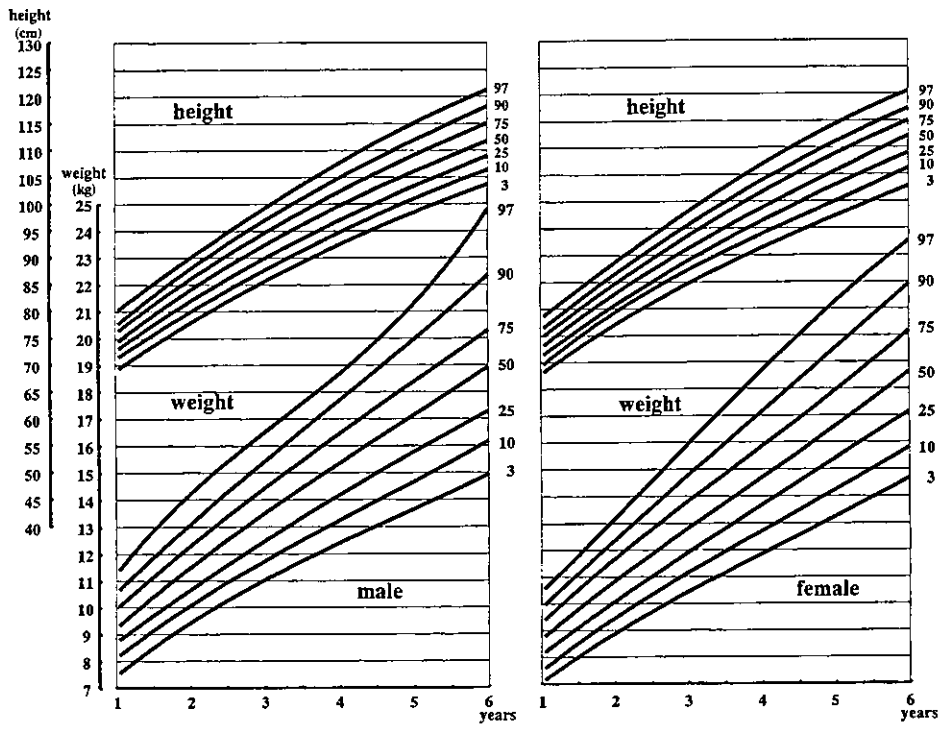


Figure 3. Body weight and height of twins by age percentiles from 1 to 6 years of age.

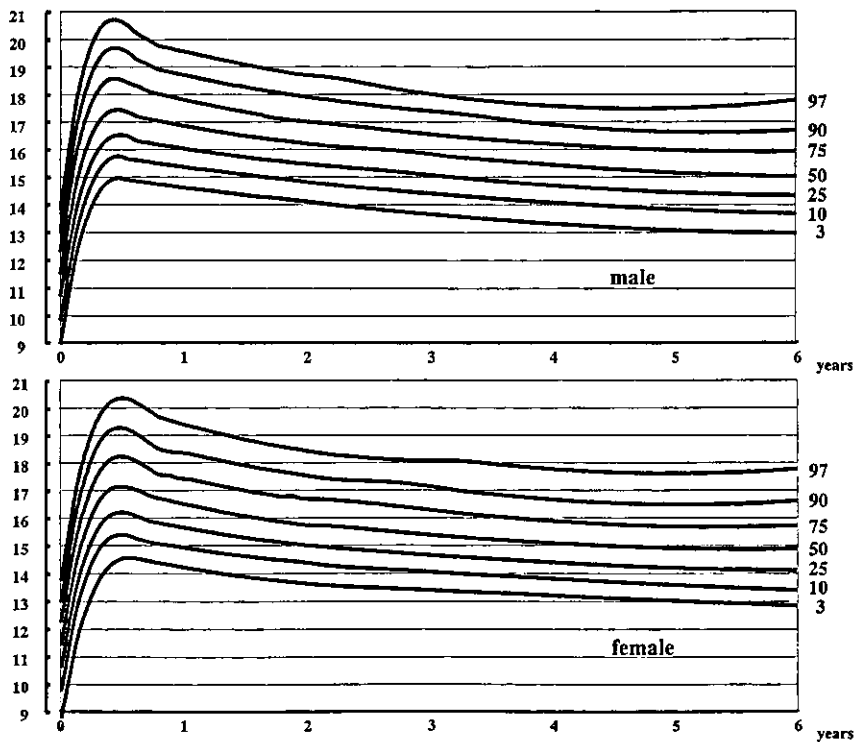


Figure 4. Body mass index of twins by age percentiles from birth to 6 years of age.

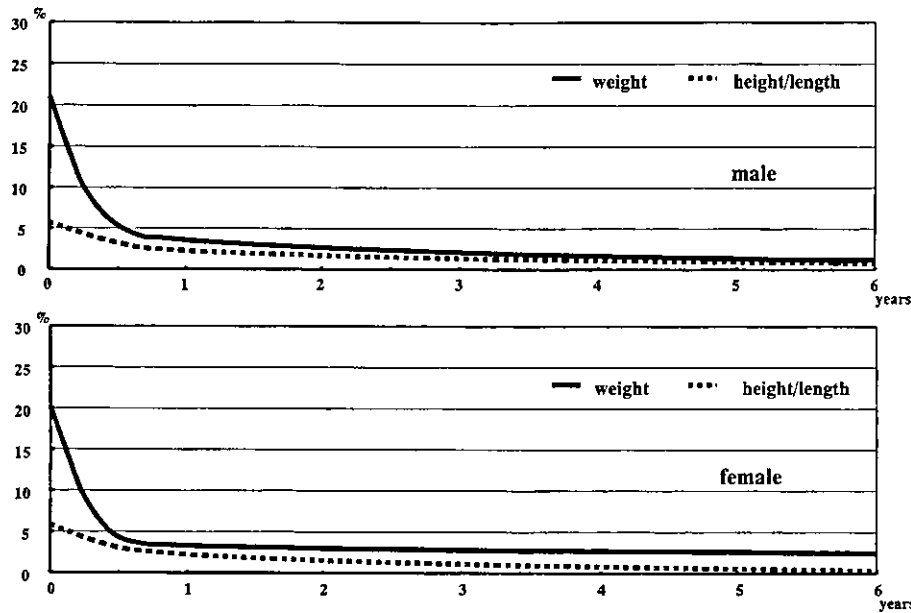


Figure 5. Size deficit of twins as to the 50th percentiles compared with general population from birth to 6 years of age.

twins in the 50th percentile was more than 20% at birth relative to the growth standards of the general population. However, the deficit decreased rapidly, to approximately 5% within the first 6 months, and diminished thereafter. The length deficit of the twins at the 50th percentile was approximately 6% at birth and gradually decreased, reaching about 3% by 7 to 8 months of age. It then decreased slightly thereafter.

DISCUSSION

There are no growth charts for twin children in Japan despite the rapid increase in multiple births and the increasing need to provide appropriate information to parents and nursing staff. Most studies reported so far regarding the physical growth of twins after birth in Japan had very small samples and therefore only roughly classified age after birth. The present data are the largest twin sample in Japan to provide accurate age after birth and information on zygosity.

The effects of parity, birth order, and zygosity in twins on their birth weight and length, irrespective of gestational age, have been extensively reported.²¹⁻²³ Nevertheless, in the present study those effects were small and mostly disappeared at an early age, as shown in Table 2. Although lasting effects of gestational periods were observed statistically, we found, as can be seen in Tables 3 and 4, that these effects decreased constantly after birth and the impacts themselves were not necessarily large except at birth. The effects of gestational age on birth weight or length have been analyzed many times in greater detail.³ Moreover, the growth standards of the general population do not correct the effects of gestational periods to reflect the actual conditions of physical growth.²⁰

To estimate the difference between the general population and twins, the present data should be treated in the same way. Therefore, in this study the growth charts for the twins were differentiated only by sex.

Compared with the general population, the twins' size deficit was greatest at birth but decreased dramatically in the first 6 to 12 months, reaching as little as approximately 2%, around 1 kg for weight and 1 cm for height, by 6 years of age. This finding was consistent with the data reported by Wilson.¹¹ It was very difficult to determine when or whether twins fully catch up to singletons, as the present study did not use a complete birth cohort containing singletons. Since it is found here that most of the size deficit of twins compared to the general population is gone by 6 years of age, there is no practical necessity for specific growth charts for twins after that age.

The limitations of the present study were as follows. First, the data were obtained from retrospective records, and the methods of measurement were not necessarily consistent. Nevertheless, the data on physical growth did not reveal a large difference between the maternal associations group and the school applicants group, as shown in Figure 1. This suggested the absence of any fatal methodological problems in data collection.

The second limitation was that these data were semi-longitudinal rather than cross-sectional. Specifically, data on the same individual were used according to the recorded times. For example, some twins provided almost longitudinal data. On the other hand, others provided only birth weight. Additionally, the number of subjects in each age group varied considerably, as shown in Table 1. Consequently, the range of measurements in each age group becomes smaller than it would be in complete cross-sec-

tional data, such as the standards for the general population.¹⁵ The clinical use of 3rd percentiles and 97th percentiles of this growth charts as indicators of growth retardation is not necessarily appropriate.

Third, as all data were derived from normally developed twins, the norm for the early days after birth may have been overestimated. It is difficult to specify the direct effects of these selection biases. However, compared with the hospital data, which usually include many high-risk subjects, the present data seem to reflect more closely the physical growth features of the general twin population.³

Fourth, as the birth years of the present subjects ranged from 1968 to 2002, a period of 35 years, yearly trends in physical growth may also be considered. Fortunately, no birth-year effects were observed in the present study, as mentioned in the results of the stepwise regression analysis. According to the physical growth standards of the general population, birth weight in Japan began to decline after 1975, with the result that body size is smaller until several years after birth. The reduction in infant body size has been attributed to other factors, too, such as lifestyle changes. Although the growth standards presented by the Ministry of Health and Welfare in 1990¹⁴ were used in the present study, the difference between twins and singletons was smaller according to the growth standards presented in 2000. Given this trend, it is difficult to achieve a meaningful comparison of twin growth and singleton growth. Body weight and height after school entrance in both groups of subjects were not analyzed, because the present data did not accommodate the much larger secular trends at this life stage.

Fifth, physiological body weight loss after birth was not assessed because of a lack of appropriate data. Such weight loss was presented as to the growth standards in the general population.¹⁵

Finally, the merits and demerits of combining the data of the two subject groups should be discussed. One reason why we combined the data was that the groups were of similar size. Preliminary analysis showed that the body size parameters of the twins at birth were slightly lower in the maternal associations group, whereas physical growth after birth was nearly identical between the groups. Moreover, it is not always the case that growth charts are developed based on only one group of subjects. Usually, complicated methods of weighting measurements and modifying those measurements according to the number of subjects and so on are part of the development of growth charts; see, for example, "2000 CDC Growth Charts: United States".²⁴ For the present data, no special corrections were performed. Some unexpected selection biases or confounding may have occurred. These effects would be estimated by comparing the data to less biased, more representative, and nationwide data on twins.

Although selection bias should be quite low in a population-based study, it is almost impossible to conduct this type of twin study in Japan at the present time. Nevertheless, it is extremely important to present objective growth charts for infant twins using

the best available methods. Moreover, there exists much less information on the physical growth of higher-order multiples such as triplets. The growth charts developed in the present study will be more useful than those of the general population to estimate the growth of higher-order multiples.

In conclusion, the present study reveals the physical growth characteristics of twins in Japan and shows the need for early-childhood growth charts for twins, though the present data also suggest that such charts are not necessary for twins after 6 years of age. The present charts are the first objective ones for twins in Japan, and will be especially useful for child and maternal health.

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Language development of Japanese twins in childhood based on maternal reports

Syuichi OOKI

Twins tend to lag behind singletons in their language development, though the causes of this are as yet unknown. Language development of twins is typically evaluated using the standards for the singletons in Japan, and the results often suggest that twins suffer from poor development. The present study was performed to resolve this situation. The subjects were 937 (maternal associations group) and 1092 (school applicants group) twin mothers and their twin children of known zygosity. Relative to general population norms, twins in the maternal associations group were about one to two months delayed in terms of age at first spoken word. Nevertheless, about 95% of twins have started speaking at least one word at 18 to 19 months, as singletons do. According to maternal reports from the school applicants group, monozygotic males, compared with singletons, showed the largest delay throughout childhood; this delay was partly attributed to the effect of 'twin language'. Language development was more similar to that of monozygotic pairs than that of dizygotic pairs. In conclusion, the results of present study suggested that language development of twins partly differ from that of singletons and that estimation of language development specifically for twins are needed.

Key words : twins, language development, database, zygosity, twin language

I Introduction

In Japan, as in other developed countries, multiple birth rates have been increasing. Higher rates of twin births since 1987 have been attributed to both the higher proportion of mothers treated with ovulation-inducing hormones and to the increasing use of in-vitro fertilization (Imaizumi and Nonaka, 1997). Under such circumstances, there is an increasing need to provide appropriate information to parents and nursing staff on the biological characteristics of twins, such as their intrauterine growth, physical growth after birth, and motor and language de-

velopment.

Since the classical study performed by Day (1932), it has become a well known fact that twins tend to lag behind singletons in terms of language development (Tomasello et al., 1986; Hay et al., 1987; Akerman, 1987; Akerman and Thomassen, 1991, 1992; Thorpe et al., 2003; Rutter et al., 2003), although the causes of this delay are unknown and appear to be complex. Because there are no large scale data to show this tendency directly in Japan, language development of twins must be evaluated using the standards for the general population, that is, essentially the standards for singletons. As a result, many twins

may be regarded as showing poor development, causing their parents much anxiety and concern. In general, the professional advisors for the growth and development of children, such as pediatricians and public health nurses, do not have adequate information to answer the questions concerning these children's language development that are asked by the parents. To resolve this situation, it is essential to obtain objective data on language development based on a large sample of Japanese twins.

In Japan, the developmental norm for the 'age at first spoken word' was presented together with other milestones regarding motor development in childhood by the Ministry of Health, Labor and Welfare. The purpose of the present study was to compare language development of twins with that of the general population. Moreover, some features of language development reported by mothers, which were unique to twins, were also analyzed for practical use in maternal and child health care for multiples.

II Methods

1. Subjects and Outline of Data Collection

Many countries, including some in Asia, have constructed or have been constructing large population-based twin registries, whereas no systematic twin registry exists in Japan (Ooki et al., 2003). There are mainly three types of data sources regarding multiples in Japan: vital statistics, data from large hospitals, and a volunteer-based database. The volunteer-based database covers the gap between vital statistics and hospital data, and is larger than and more unbiased than hospital data and contains more detailed information than do vital statistics. In addition, data regarding the condition of the twins after birth can be collected in the volunteer database: this is data that both vital statistics and hospital

data seldom contain. This background information represents continuous data on twins in childhood and on their families that the author has been gathering for the purpose of contributing to twins' health care and to the genetic epidemiologic study of twins and their families (Ooki and Yokoyama, 2003, 2004; Ooki et al., 2004). The data used in this study were a portion of this body of data.

The present sample consisted of two independent groups of subjects. A detailed description of both groups is given in Table 1. The first group of subjects consisted of 937 mothers from the several associations for the parents of multiples throughout Japan (maternal associations group). Birth years ranged from 1986 to 2002. The data from this group was gathered in 2002 and 2003 intensively. The age of twins at data collection was from 0 to 15 years. The second group of subjects consisted of 1092 mothers and their twin children living in the Tokyo metropolitan area, with all of the twins attending secondary school attached to the faculty of education of the University of Tokyo from 1981 to 2003 (school applicants group). Birth years ranged from 1968 to 1991. The present style of systematic data collection has been performed since 1981. Twins were all 11 or 12 years of age at data collection. No subjects in both groups were severely retarded from the medical point of view with regard to physical growth and motor and language development at data collection.

Information regarding family structure, obstetrical findings on the mothers, the physical growth of twins, zygosity, and motor, language, and mental development of twins, the medical history of twins and parents, behavioral problems of twins, and others were gathered as core items from both groups by means of mailed or personally distributed questionnaires. Since

Table 1 Basic Characteristics of Present Data

	Maternal associations group	School applicants group
n	937 pairs	1092 pairs
method of data collection	mailed questionnaire	handed questionnaire and interview
year of data collection	2002-2003	1981-2003
district	all around Japan	Tokyo metropolitan area
birth year of twins	1986-2002 (mean 1995, SD 3.8)	1968-1991 (mean 1978, SD 6.4)
age of twins at data collection	0-15 years (mean 6.0, SD 3.8, median 5)	164 pairs at 11 years and 928 pairs at 12 years
sex of twins		
male individuals	971	1026
female individuals	903	1158
zygosity	zygosity questionnaire	zygosity questionnaire and/or DNA/genetic markers
monozygotic (male-male)	230	327
monozygotic (female-female)	203	399
dizygotic (male-male)	95	75
dizygotic (female-female)	108	66
dizygotic (male-female)	95	68
dizygotic (female-male)	112	56
suspended (male-male)	46	30
suspended (female-female)	31	36
insufficient information (male-male)	11	19
insufficient information (female-female)	6	16
questions as to language development	age at first spoken word (by month)	maternal subjective estimation of their twins' language development throughout childhood

SD: Standard Deviation

these data were gathered not in the same periods, each item of the questions was not necessarily in the same format. For the school applicants group, one of the parents of each applicant, usually the mother, participated in a medical interview by two or three interviewers (the author being an interviewer from 1987 on) in which their responses to the questionnaire were checked carefully.

2. Zygosity classification

The zygosity of twins was determined mainly by means of a zygosity questionnaire (Ooki and Asaka, 2004), which is used widely in Japan. Mothers of both groups answered this zygosity

questionnaire. Zygosity diagnoses using many DNA/genetic markers were performed in addition to the zygosity questionnaire for those twin pairs of the school applicants group who were admitted to the school (Ooki and Yokoyama, 2003). Zygosity determined by many DNA/genetic markers occurred prior to that determined by questionnaire. When zygosity determination by DNA/genetic markers was regarded as the gold standard, the accuracy of the zygosity questionnaire was 97.5% (199/204), though 8.9% (20/224) of pairs were not classified by questionnaire (Ooki and Asaka, 2004).

In total, 726 monozygotic (MZ) and 265 dizygotic (DZ) with 101 unclassified zygosity were

determined for the school applicants group, and 433 MZ and 410 DZ with 94 unclassified zygosity were determined for the maternal associations group. This is one of the advantageous features of present data, as zygosity diagnosis of the same-sex twins is seldom performed in Japan.

3. Questions as to language development and statistical analyses for the maternal associations group

With regard to language development, the age at first spoken word was asked about by month. The present data was based on maternal retrospective reports according to the age of the twins at data collection. The data were mainly based on their memory or records in the "Maternal and Child Health Handbook". The growth data of children based on mass examinations in Japan are usually recorded in this Handbook, and the author advised the mothers to refer to these records when completing the questionnaire. If mothers could not remember events in their children's language development, the author recommended in the questionnaire that they should not necessarily complete questionnaire using incorrect answers.

In analysis, only those twins whose first spoken word occurred between 6 to 25 months were used in consideration with the growth standards presented by the Ministry of Health, Labor and Welfare (Takaishi et al., 1992; Kato et al., 2002). Data were missing for 636 twins of varying ages out of 1874 (937 pairs). Of 1238 answers, 31 were excluded because these data did not meet the above mentioned inclusion criteria. Therefore, 1207 answers, representing 614 males and 593 females, were used in analysis.

In the statistical calculation, the following adjustment was performed. Because the data answered by mothers was by month and contained

about 30 days interval, 0.5 months was added assuming that the age at first spoken word in each month was normally distributed.

First, factors that affect the age at first spoken word of twins were confirmed by stepwise regression analysis, with a threshold significance level of 0.15. The variables considered were sex, birth order of twins (first-born or second-born), birth complications of mothers or twins, gestational age (weeks), maternal and paternal age at twin birth, parity, zygosity (MZ or DZ), birth weight (g), motor development (age at sitting with head steady), and age of twins at data collection. Birth complications of mothers or twins included, for example, placenta previa, placental abruption, coiling of the umbilical cord, neonatal asphyxia, twin-to-twin transfusion syndrome, and so on. Age at sitting with head steady was limited between one and nine months with reference to the norms presented by the Ministry of Health, Labor and Welfare (Takaishi et al., 1992; Kato et al., 2002). Age of twins at data collection has an inverse relationship with the birth year of twins.

For qualitative variables, the following codes were used: sex, female: 0, male: 1; birth order, first-born: 1, second-born: 0; birth complications, yes: 1, no: 0, zygosity, MZ: 0, DZ: 1; parity, primiparity: 0, multiparity: 1.

Next, cumulative frequency distribution regarding the age at first spoken word was calculated, and compared with those presented by the Ministry of Health, Labor and Welfare (Takaishi et al., 1992; Kato et al., 2002), wherein the values of cumulative relative frequency for selected months after birth were presented. Standards of the general population in 1990 and 2000 were used considering twins' birth year.

Cumulative frequency distribution regarding the age at first spoken word according to sex

was also calculated. The means, standard deviations, and median of the age at first spoken word were calculated according to sex and zygosity.

4. Questions as to language development and statistical analyses for the school applicants group

For the school applicants group, the following two questions regarding maternal subjective estimation of their twins' language development were asked. The first question was, 'In childhood, was your twin children's language development delayed compared with that of contemporary singletons?' The mothers selected one answer from following three items. 1, not delayed; 2, slightly delayed; 3, considerably delayed. The second question was, 'To what degree was the language development of your twin children alike during childhood?'. The mothers selected one answer from following three items. 1, no difference (very similar); 2, slight difference; 3, clear difference. Maternal subjective estimation of their twins' language development was analyzed according to sex and zygosity.

All statistical analyses were performed using SAS® for Windows (1997). Smoothing of the cu-

mulative frequency distribution was performed using the PROC TRANSREG program, specifying the "pspline" model.

5. Ethical issues

The mothers in the maternal associations group cooperated voluntarily in this research, mainly through the president of their associations. It was clearly mentioned in the questionnaire that only statistical analysis was performed on the data obtained.

Informed consent concerning statistical analysis of the data in the school applicants group was obtained in writing from each twin and their parents as part of the application process.

III Results

1. Maternal associations group (age at first spoken word)

The results of the stepwise regression analysis were shown in Table 2. Factors affecting the age at first spoken word were sex ($p < 0.0001$) and motor development ($p = 0.0003$) at 0.01 significance level. In these cases, females and earliness of sitting with head steady showed a tendency toward earliness for the age at first spoken

Table 2 The results of the stepwise regression analysis for the age at first spoken word

	p	coefficient of determination (R^2)
sex	< 0.0001	0.0205
motor development (sitting with head steady)	0.0003	0.0121
birth complications of mothers or twins	0.0382	0.0039
parity	0.0535	0.0034
age of twins at data collection	0.0764	0.0029
zygosity	0.0928	0.0026
birth order of twins	n.s.	
maternal age at twin birth	n.s.	
paternal age at twin birth	n.s.	
gestational weeks	n.s.	
birthweight (g)	n.s.	

Subjects were maternal associations group ($n = 1057$).

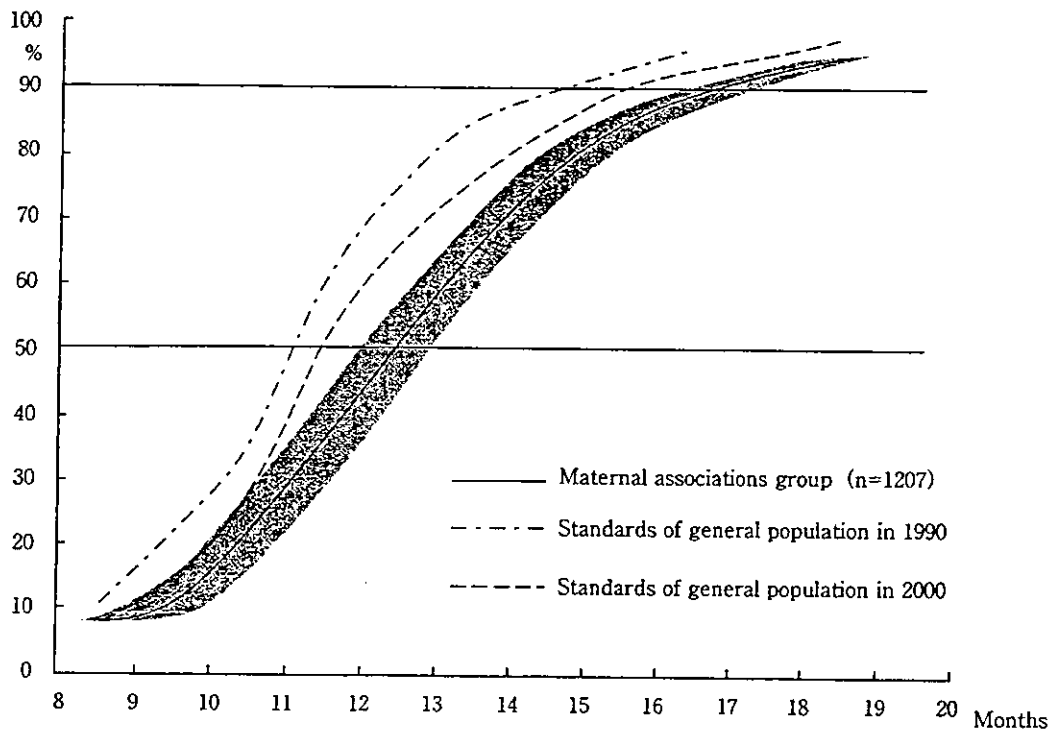


Fig. 1 Cumulative frequency distribution of twins for the age at first spoken word compared with standards obtained from the Japanese general population

word, though the contributions of these factors themselves were not so large. Not significant at 0.01 significance level birth complications ($p=0.0382$), parity ($p=0.0535$), age of twins at data collection ($p=0.0764$), and zygosity ($p=0.0928$) were also selected. In these cases, no birth complications, multiparity, younger age of twins (recent birth year), and DZ twins showed a tendency toward earliness for the age at first spoken word.

Cumulative frequency distribution compared with general population norms are shown in Figure 1. Only the range between 8.5 and 18.5 months is presented, which is how general population norms are presented. As mentioned earlier in the methods section, the present data was obtained by month. For example, if mothers answered that the age at first spoken word was 8 months, the data contained information from just

8 months and 0 days to 8 months and 30 days (nearly 9 months). In general, an interval of about one month was considered. Therefore, both the earliest and the latest patterns were presented; thus, the results were shown as area. Compared with general population norms, that in the maternal associations group was about one to two months delayed. Nevertheless, about 95% of twins had begun speaking one word at 18 to 19 months.

Cumulative frequency distributions according to sex are shown in Figure 2. Males were slightly delayed compared with females.

Mean and median months of the age at first spoken word according to sex and zygosity combination are shown in Table 3. Mean months of age at first spoken word was significantly earlier in females than in males ($p<0.0001$). This tendency was observed irrespective of zygosity, except

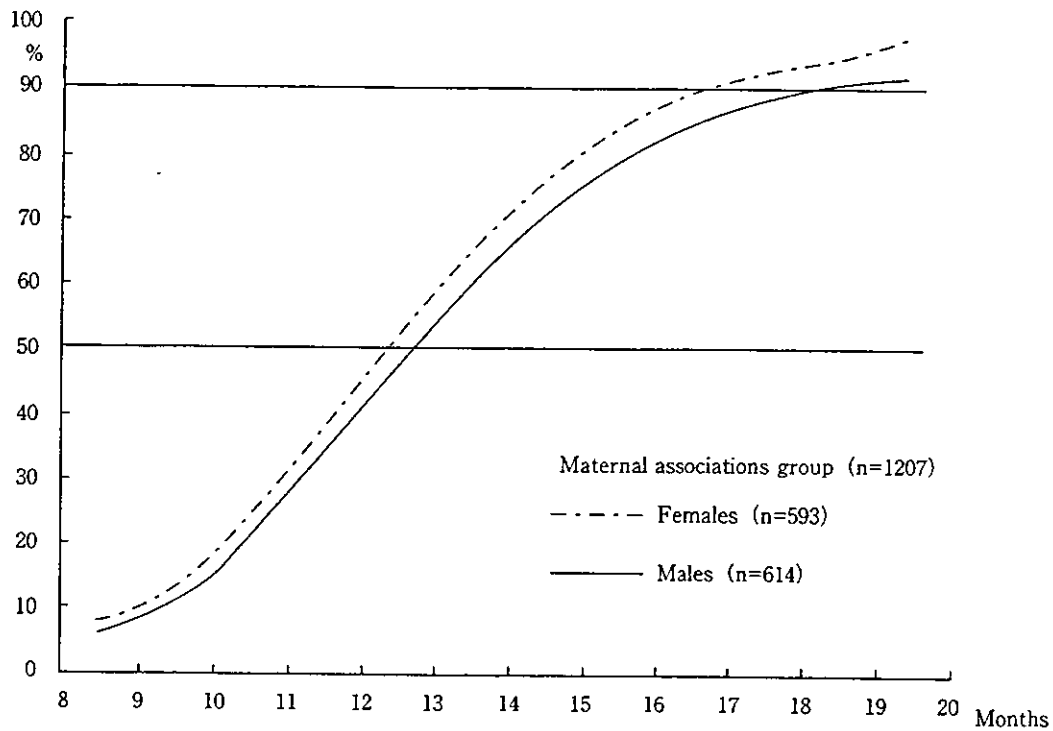


Fig. 2 Cumulative frequency distribution of twins for the age at first spoken word according to sex

Table 3 Mean and median months for the 'age at first spoken word' for the maternal associations group

	n (twin individuals)	median	mean	SD	sex difference	
					Variance	p
MZ males	319	13.5	14.7	3.8		
MZ females	285	12.5	13.9	3.5	equal	0.0082
same-sex DZ males	112	14.0	14.8	4.0		
same-sex DZ females	138	12.5	13.2	3.7	equal	0.0009
opposite-sex DZ males	132	13.0	14.3	4.0		
opposite-sex DZ females	140	12.5	13.7	3.7	equal	0.1894
all males	616	13.5	14.6	3.9		
all females	593	12.5	13.7	3.5	equal	< 0.0001

MZ: Monozygotic, DZ: Dizygotic, SD: Standard Deviation

Subjects were maternal associations group.

All males and all females contain twin individuals of unclassified zygosity.

T-test was performed as to sex difference of means.

for opposite-sex DZ. There was no tendency for the language development of males of opposite-sex DZ to be more rapid than that of males of same-sex DZ.

2. School applicants group (maternal subjective estimation of their twins' language development)

Maternal estimation of their children's development of language relative to that of contempo-

Table 4 Answers to the question 'In infancy, was your twin children's language development delayed compared with that of contemporary singletons?'

	n (twin individuals)	not delayed %	slightly delayed %	considerably delayed %	sex difference	
					χ^2	p
MZ males	627	58.5	28.6	12.9	47.3	< 0.0001
MZ females	774	75.5	18.4	6.2		
same-sex DZ males	134	73.1	18.7	8.2	1.2	0.5571
same-sex DZ females	122	74.6	20.5	4.9		
opposite-sex DZ males	112	60.7	26.8	12.5	4.2	0.1222
opposite-sex DZ females	110	73.6	18.2	8.2		
all males	966	60.9	27.2	11.9	52.5	< 0.0001
all females	1101	75.4	18.4	6.2		

MZ: Monozygotic, DZ: Dizygotic

Subjects were school applicants group.

All males and all females contain twin individuals of unclassified zygosity.

Table 5 Answers to the question 'To what degree was the language development of your twin children alike during infancy?'

	n (twin pairs)	no difference %	slight difference %		clear difference %	
			males were delayed	females were delayed	males were delayed	females were delayed
MZ pairs ¹⁾	670	85.5	6.1		8.4	
male pairs ²⁾	299	84.3	7.4		8.4	
female pairs ³⁾	371	86.5	5.1		8.4	
same-sex DZ pairs ¹⁾	133	62.4	8.3		29.3	
male pairs ²⁾	70	54.3	12.9		32.9	
female pairs ³⁾	63	71.4	3.2		25.4	
opposite-sex DZ pairs	108	55.6	8.3		36.1	
			5.6	2.8	26.9	9.3

MZ: Monozygotic, DZ: Dizygotic

Subjects were school applicants group.

1) Zygosity difference was significant by χ^2 test ($\chi^2 = 49.3, p < 0.0001$)

2) Zygosity difference was significant by χ^2 test ($\chi^2 = 34.7, p < 0.0001$)

3) Zygosity difference was significant by χ^2 test ($\chi^2 = 16.3, p = 0.0003$)

rare singletons in childhood is shown in Table 4. Significant ($p < 0.0001$) sex difference was observed by χ^2 test (males vs. females; $\chi^2 = 52.5, p < 0.0001$). About 40% of mothers of males and 25% of mothers of females answered that there were varying degrees of delay in language development relative to that in singletons. Considering zygosity, this tendency was obvious with

regard to MZ twins.

Maternal estimation of the similarity of language development within twin pairs is shown in Table 5. A significant influence of zygosity on similarity was observed by χ^2 test (MZ vs. same-sex DZ; $\chi^2 = 49.3, p < 0.0001$). It can be seen that about 85% of MZ pairs were regarded to show 'no difference' from their co-twins in terms

of language development in childhood, whereas 54.3% of DZ males, 71.4% of DZ females, and 55.6% of opposite-sex DZ were regarded to show 'no difference'. More than 25% of mothers of DZ twins reported 'clear difference' in development between children. The delay in males was marked in opposite-sex DZ pairs.

IV Discussion

1. Maternal associations group (age at first spoken word)

Though the present data was limited to only maternal reports for the age at first spoken word, considerably significant effects of sex and motor development were observed. On the other hand, no effects of birthweight and gestational age were observed. These factors appeared not so influential regarding the age at first spoken word. Recently, using systematic collection of detailed twin data from the Avon Longitudinal Study of Parents and Children, Rutter et al. (2003) concluded that obstetric/perinatal features do not account for the slower language development in twins relative to that of singletons.

As shown in Figure 1, compared with norms of the general population, maternal association groups showed a delay of about one to two months for age at first spoken word. The first possible explanation for this was essential delay of development in twins compared with that in singletons, though the reasons for this delay were unclear. Another possible explanation derives from the difference in the data collection method between the general population and the present subjects. The present data was based on maternal retrospective reports, mainly by means of a mother's memory or records in the "Maternal and Child Health Handbook". It is possible that the higher the age of the twins at data collection became, the more unreliable was the

memory of the mother, particularly if she depended only on memory. But regression analysis showed no strong effect of age at data collection on the age at first spoken word, as shown in Table 2. Moreover, no direct correlation was found between age at first spoken word and age of twins at data collection ($n=1207$, $r=-0.072$, n.s.). On the other hand, developmental norms presented by the Ministry of Health, Labour and Welfare were determined based on observation during health examinations, performed around the same time throughout Japan, on more than ten thousand subjects. The results were recorded in the questionnaire as binary data of 'possible' or 'impossible', and values were added up according to the real age after birth (Takaishi et al., 1992; Kato et al., 2002). This difference in data collection method can not be adjusted for, and represents a limitation of the present questionnaire survey.

2. School applicants group (maternal subjective estimation of their twins' language development)

An effect of sex difference on language development throughout childhood was clearly observed. This tendency was widely recognized in twins as well as in singletons. Males were delayed compared with females. The causes were more complicated in twins in consideration of the effect of their co-twin. According to Garitte et al. (2002), apropos of language development, it is more advantageous for a male twin to have female co-twin than a male co-twin. An effect of the sex difference of the co-twin was not clearly observed in this study, partly because of limited questions.

As shown in Table 4 and Table 5, both members of MZ male pairs may be delayed to nearly the same degree, with the result that twin pairs

became relatively similar, whereas DZ male pairs of twins may be delayed to varying degrees, with the result that twin pairs became dissimilar.

It has been reported that patterns of parent-child interaction and communication have environmentally mediated effects on language and account for twin-singleton differences in language development (Rutter et al., 2003). The present study gathered no data on mother-to-twin interaction in terms of language development.

Language development of twins is very complicated, and is influenced by sex and zygosity in their various combinations. Moreover, the influence of so-called 'twin language' has often been reported (Hay et al., 1987; Bakker, 1987; Dodd and McEvoy, 1994; Bishop and Bishop, 1998; Thorpe et al., 2001). In general twin language is often observed to be used only within certain twin pairs, and it cannot be understood by others. As yet, there is no established definition of twin language. About 40% of twin pairs show twin language, typically occurring in the second year of life and decreasing considerably over the next 16 months (Thorpe et al., 2001). Twin language has more often been observed in males and MZ pairs, causing delay of language development. According to the results of maternal reports shown in Table 4, MZ males showed the largest delay relative to development in singletons, which finding partly supports the above findings regarding twin language.

Maternal subjective reports may be very informative concerning total language development throughout childhood, as mothers are typically able to observe their twin children more frequently and attentively than anyone else can. As shown in Table 5, language development in childhood was obviously similar between MZ pairs compared with that between DZ pairs, ir-

respective of sex combination. Zygosity classification of same-sex twins in childhood was very rare in Japan. Moreover, zygosity misclassification at birth by means of easy placental findings occurred in about 25-30% of MZ twin pairs (Ooki et al., 2004). Therefore, mothers of same-sex twins often did not know the correct zygosity of their children. Taking these circumstances into consideration, the similarity between MZ twins, who have identical genetic composition, compared with that between DZ twins, whose genetic similarity is only 50%, slightly suggested a role of genetic background in language development. Dale et al. (1998) reported considerable genetic contribution to language development by performing the detailed genetic epidemiologic twin study of the largest sample based on more than 3000 pairs of twins.

3. Over the course of this study

Contrary to the rapid increase of multiple birth rates in Japan, little attention has yet been paid and limited information obtained concerning physical growth, motor and language development of multiples in childhood, and many problems related to the nurturing and rearing of multiples.

The lag in language development of twins behind singletons has been reported many times in western countries (Tomasello et al., 1986; Hay et al., 1987; Akerman, 1987; Akerman and Thomassen, 1991, 1992; Thorpe et al., 2003; Rutter et al., 2003). Though this tendency has been experientially recognized, there existed no objective data on a large subject sample in Japan to demonstrate this phenomenon. In general, three main reasons for delayed development have been suggested: obstetric complications, twin-specific features, and postnatal differences in family interaction.