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Twin Database of the Secondary School Attached to the Faculty of Education of the University of Tokyo: Lifecourse Database of Twins

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This article profiles the historical twin databases of the secondary education school attached to the Faculty of Education at the University of Tokyo. The school was established in 1948. Every year, about 50 pairs of twins of all sex and zygosity combinations and aged 11–12 years take an examination, and about 10–20 pairs are admitted based on the results. Three data sets exist: one for applicants (11–12 years), one for junior and senior high school students (12–18 years), and one for graduates (18–79 years). Record linkage of these three databases should facilitate several important research projects; for example, the lifecourse genetic epidemiologic studies and verification of so-called developmental origin of health and disease hypothesis.

■ **Keywords:** longitudinal twin data, life course epidemiology

The secondary education school of the University of Tokyo is known in Japan because many twins study at the school. The school was established in 1948. When the school was established, twin studies were burgeoning in Japan. Since its establishment, the school has adopted a unique entrance system. The school gathers applications from twins in addition to applications from the general student population. About 50 pairs of twins aged 11–12 years, of all sex and zygosity combinations, and living in the Tokyo metropolitan area, take an entrance examination. From the results, about 10–20 twin pairs are admitted each year (Ooki & Asaka, 2006; Ooki et al., 2004). The school provides ongoing education for the 6 years of junior and senior high school. Of the 120 students in each grade, there are about 20–40 twins (10–20 pairs). During their 6 years of enrolment, the twins participate in observational studies for educational and related projects.

As shown in Figure 1, three data sets exist: one for school applicants (age 11–12 years), one for enrolled students (12–18 years), and one for graduates (18–79 years). Theoretically, all applicants include students, and students include graduates. Although an extraordinarily large amount of data on twin pairs exists in these databases, the same items were not necessarily gathered or obtained. Not all of the data have been exhaustively and effectively combined as yet; however, part of this database has been analyzed. All data from the retrospective perinatal and neonatal periods through childhood, school age, and adulthood are theoretically linkable using individual specific identification numbers, though in practice the linkage has only been partially completed thus far.

Database of the Junior High School Applicants (1948–2012)

Applicants and their parents are the subjects of this database. Mothers of all of the twin applicants complete and return a Twins Protocol Questionnaire, the format of which has remained fairly constant especially since 1981. The questionnaire gathers information on family structure, obstetrical findings, the twins' physical growth, zygosity and placentation, and motor and mental development from birth through 11–12 years of age. Information on socioeconomic status has recently been excluded because of privacy concerns. One parent of each applicant, usually the mother, or both parents, participates in a medical interview conducted by two or three interviewers, in which responses to the

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TABLE 1

Basic Characteristics of the Applicants Database

N		1,205 pairs
Method of data collection		Handed questionnaire and interview
Year of data collection		1981–2011
District		Tokyo metropolitan area
Birth year of twin pairs	Mean ± *SD* (range)	1980 ± 8 (1968–1999)
Sex of twin individuals	M/F	1,119/1,291
Zygosity		
Monozygotic	MM/FF	348/435
Dizygotic	MM/FF/MF/FM	97/89/73/60
Suspended	MM/FF	29/39
Insufficient information	MM/FF	19/16
Age of twin pairs at data collection (years)	Mean ± *SD* (range)	11.9 ± 0.4 (11–12)
Maternal age at twins birth (year)[a]	Mean ± *SD* (range)	29.2 ± 3.9 (19–43)
Paternal age at twins birth (year)[b]	Mean ± *SD* (range)	32.0 ± 4.6 (19–53)
Gestational age (weeks)[c]	Mean ± *SD*	37.5 ± 2.2
Parity	1	641 (53.2%)
	2	446 (37.0%)
	3–5	117 (9.7%)
	Unknown	1 (0.1%)
Neonatal condition (twin individuals)	Healthy	1,898 (78.8%)
	Hyposthenia (not so healthy)	325 (13.5%)
	Neonatal asphyxia	130 (5.4%)
	Unknown	57 (2.4%)

Note: [a]Four missing values,[b]14 missing values,[c]15 missing values. *SD* = standard deviation; M = male; F = female.

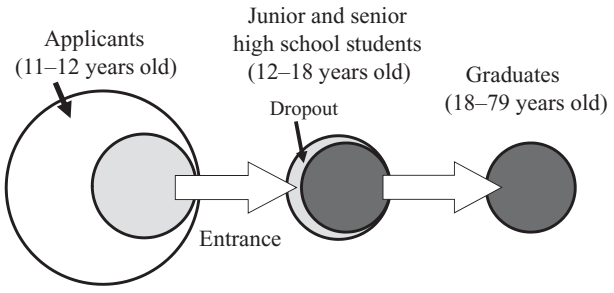

FIGURE 1

The relationship of the three databases.

questionnaire are checked carefully. A total of 1,205 parents of applicants have returned questionnaires to date. Moreover, data from the *Maternal and Child Health Handbook* have been obtained since 1992. This handbook is presented by the Ministry of Health and Welfare to all pregnant women, and includes detailed obstetric records written by obstetricians and a detailed record of the child's general growth until 6 years, written by the parents at home or by medical staff at regular mass health examinations. We can use this data as a standard for questions regarding the growth and development of Japanese children. Zygosity has been determined by means of questionnaire (Ooki & Asaka, 2004). All same-sexed twins and their mothers completed the zygosity questionnaire, on the basis of which twins' zygosity was determined with greater than 95% accuracy. No subjects showed apparent growth retardation at 11–12 years of age. This data set undoubtedly represents one of the largest and most thorough sets of accurate growth data on twins in Japan (Ooki & Asaka, 2005), especially since zygosity testing is very rare in Japan. The basic characteristics of the database are presented in Table 1. Growth and development features of twins in childhood were extensively analyzed for maternal and child health (Ooki, 2005a, 2006; Ooki & Yokoyama, 2003, 2004) and were found to not be markedly different from that of the general Japanese twin population (Kato, 2004), at least regarding physical growth within the normal range. Several genetic studies have also been performed (Ooki, 2005b, 2005c, 2005d, 2008). The data on 1948–1980 applicants have not yet been analyzed.

Database of the Junior and Senior High School Students (All Students After 1975)

Once twin applicants are admitted to the school, twins and their parents take a medical examination, which gathers detailed anthropometric and physical measurements. The blood pressure of twins and their parents is also measured. Blood specimens are taken, but these are permitted to be used only for the purposes of zygosity diagnosis and medical checks at present. These examinations, including zygosity diagnosis based on DNA/genetic markers, are performed by the twins' medical examination committee (Ooki & Asaka, 2004).

We gather predominantly longitudinal data on physical growth and development and medical conditions — for example, eyesight and allergic disease — through the results of the health examination performed each year at the Japanese School of Health Law. These results as a whole are presented as school health statistics by the Ministry of Education, Culture, Sports, Science and Technology. Information on singleton students is gathered as control

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TABLE 2

Numbers of Subjects According to Sex Combination and School Grade of Students

		Twin pairs						Singletons		
Grade	Age	MZM	MZF	DZM	DZF	DZOS	Total	Males	Females	Total
First	12–13	119	140	18	24	28	329	1,132	1,079	2,211
Second	13–14	116	136	20	21	27	320	1,069	1,023	2,092
Third	14–15	114	128	17	19	25	303	953	907	1,860
Fourth	15–16	112	128	17	21	26	304	919	880	1,799
Fifth	16–17	106	122	13	18	25	284	857	817	1,674
Sixth	17–18	100	121	15	18	25	279	813	754	1,567

Note: Birth year of twin pairs ranges from 1962 to 1987. First grade students are followed longitudinally. The data on 2000–2012 enrollees have not yet entered. MZM = monozygotic males; MZF = monozygotic females; DZM = dizygotic males; DZF = dizygotic females; DZOS = dizygotic opposite sex.

TABLE 3

Numbers of Subjects in the Graduates Database According to Birth Year and Sex-Zygosity Combination

Birth year of twins	Age	MZM	MZF	DZM	DZF	DZOS	Total
1993–1983	18–29	23	40	6	11	7	87
1982–1973	30–39	37	53	7	9	11	117
1972–1963	40–49	68	70	9	9	12	168
1962–1953	50–59	73	77	14	6	13	183
1952–1943	60–69	80	85	10	10	11	196
1942–1933	70–79	38	29	7	9	7	90
Total		319	354	53	54	61	841 (Pairs)

Note: MZM = monozygotic males; MZF = monozygotic females; DZM = dizygotic males; DZF = dizygotic females; DZOS = dizygotic opposite sex.

data. The number of subjects is shown in Table 2. This is basically longitudinal data; students of the first grade are followed for 6 years.

Adult Twin Database of High School Graduates

The information on all graduates of the school has been updated regularly. The distribution of birth year and sex-zygosity combinations of this cohort is shown in Table 3. A total of 841 pairs of twins, consisting of 673 monozygotic (MZ; 319 male–male and 354 female–female) and 168 dizygotic (DZ; 53 male–male, 54 female–female, and 61 opposite-sex), have graduated from this school through March 2012. Cumulative frequencies according to the combination of sex and zygosity are increasing almost proportionally year by year. Zygosity is diagnosed strictly by the best method available, given the year of entrance. For example, many anthropometric characteristics and blood groups were used in the early years. More recently, genetic markers and DNA polymorphisms are used (Ooki et al., 2004).

Twins are followed longitudinally (Ooki et al., 2004), and three follow-up studies have been performed (Ooki & Asaka, 2006). All three surveys included questions about occupation, marital status, number of children, body weight and height, drinking habits, smoking habits, food preferences, medical history, especially for lifestyle-related diseases, and so forth. The database was reconstructed for future studies. Family data have also been collected. The fourth follow-up survey is planned any time soon.

Ethical Issues

The statistical analysis of the data was clearly written in the application document, and the detailed explanations concerning data collection by questionnaire and interview, and blood sampling for zygosity examination and health checks were added as another paper from 1999. Moreover, informed consent was obtained from each twin and his or her parents in writing from 2001 on. The data analysis was also permitted by the ethical committee of this school. Zygosity diagnosis using DNA sample was permitted through the ethical committee of the Graduate School of Medicine, University of Tokyo.

Limitations

The greatest limitation of this cohort is its selection bias based on the sampling process itself. The subjects lived in the Tokyo metropolitan area when they were enrolled at the school, and all took the entrance examination. Thus, they are not representative of Japanese children in general with regards to socioeconomic status and abilities. This selection bias would be deleterious to some study designs. Moreover, the zygosity imbalance in favor of MZ twins, in contrast to the small sample size of DZ pairs, especially in the students and graduates group, clearly differs from the MZ/DZ ratio of the twin population in Japan (Imaizumi & Nonaka, 1997). This difference may be as a result of the entrance process. It is, however, difficult to estimate the long-term effects of this selection bias.

Perspective

The main focus of each database is shown in Table 4. This school is no doubt one of the most important sources in the

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history of Japanese twins. Numerous data is in existence as a result of over 60-year-old history of the school, not all of which are organized or established as databases as yet for systematic analysis from the same platform, unfortunately. Record linkage of the present three databases would make several important research projects possible; for example, the lifecourse genetic epidemiologic study and verification of so-called fetal origin of adult disease hypothesis (Barker, 1998), or developmental origin of health and disease hypothesis (Gluckman & Hanson, 2006). It is very difficult to perform lifetime follow-up studies, especially for twins; the existing datasets exceptionally permit this type of pioneering twin research in Japan, although the sample size and data quality are insufficient for many studies. Considering these characteristics and limitations, we need to maintain and make the most use of this historically important cohort in Japan.

TABLE 4
Summary of the Database

N (pairs)	Applicants 1,205	Students 454	Graduates 841
Age (years)	11–12 (data was obtained from pregnancy)	12–18	18–79
Participants	Twins and their parents	Twins and singletons control	Twins and their family members
Zygosity assessment	Questionnaire	DNA/genetic markers	The best possible method (mainly DNA/genetic markers)
Method of data collection	Handed questionnaire and interview	Medical examinations	Mailed questionnaires and medical examinations
Data of blood specimen	No	Twins and their parents (only for zygosity determination and medical check)	Participants of medical examination of first and second follow-up survey
Follow-up	Impossible	Possible	Possible
Main focus	Effects of intrauterine/obstetrical conditions and family environment on later development, physical growth and motor and language development of early twin children, diseases often occurring in the early children, problem behavior	Physical growth and development, diseases often occurring in the school children, allergic disease, myopia and related diseases	Genetic study of lifestyle (eating, smoking, drinking, and sleep habits, stress reaction, physical exercise, and so on) and lifestyle-related disease, metabolic syndrome, cognitive ability, and longevity, psychology as to twinship, verification of FOAD (fetal origin of adult diseases) hypothesis or DOHaD (developmental origin of health and disease) hypothesis

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