STUDY OF TWINS WITH HYPERTENSION

By Goro Mimura

Until the present, essential hypertension has been presumed as a hereditary disease from the results of the study of families and twins. (Weitz, 1923; Allan, 1933; Ayman, 1934; Hines, 1937; Platt, 1947, 1961; Miyao, Mimura, Terai, 1968). The comparison between monozygotic and dizygotic twins offers a convenient means for studying some problem of human heredity. Monozygotic twins arising from the division of a single fertilized zygote have the same genetic endowment. Dizygotic twins, on the other hand, arising from the fertilization of two ova by two spermatozoa are related in the same way that brothers and sisters are. The study of twins with essential hypertension is necessary to solve the mutual relation between heredity and environment which influences the development of essential hypertension. As a result of previous genetic study of essential hypertension, it can be presumed that hypertension is transmitted by a Mendelian dominant one-gene, (Weitz, 1923; Ayman, 1934; Miyao, 1953) therefore this disease can be regarded as a clinical entity of qualitative character. But according to our recent genetic study and other investigators' results, (Oshiro, 1964; Miyao, Mimura, Terai, 1968; Hamilton, Pickering, Roberts, Sowrg, 1954); it is quite clear that blood pressure is a continuous character. If blood pressure genetically is of quantitative character, to classify blood pressure into hypertension normotension and hypotension respectively at a certain level as different qualitative character is questionable. From the above mentioned opinion, firstly I should like to point out the difference of resemblance of blood pressure between monozygotic twins. From the clinical points of view, hypertension will be diagnosed in the case of excessive blood pressure at a certain level, nevertheless blood pressure is continuous character. Therefore secondly I should like to state the difference of concordance ratio of hypertension between monozygotic and dizygotic twins.

MATERIALS AND METHODS

The data for twins used in this paper is a summary of the data which was already published in Japan (Miura, 1941; Oka, 1952; Matsuoka, 1957; Kuboi, 1962) as well as my recent data. 208 pairs of monozygotic twins and 145 pairs of dizygotic twins were divided into five age groups as follows: (a) under 10, (b) 11-19 (c) 20-39 (d) 40-59 (e) over 60.

The correlation coefficiency and the average difference of basal blood pressure of each pair in these group were calculated. Next in the case of under 6 mm.Hg. of the difference of basal blood pressure in each pair, we considered that there can be a resemblance of basal blood pressure, hence we calculated the concordance ratio of this resemblance in both twins. Furthermore, the reaction of blood pressure of twins which were induced by many different stimuli were examined.

Finally, the concordance ratio of hypertension in both twins were calculated.

RESULTS AND DISCUSSION

1. Correlation coefficient of basal blood pressure in various age groups of twins.

The correlation coefficient of basal blood pressure in monozygotic and dizygotic twins which were divided into five groups is shown in Table 1. The correlation coefficient of basal blood pressure in the monozygotic twins were observed according to age, with the exception of the 40-59 age group. On the contrary, in the dizygotic twins such a definite tendency according to age was not obtained. A significant difference between monozygotic and dizygotic twins was observed only in the under 10 age group, contrary to expectation.

Department of Geriatrics, Institute of Constitutional Medicine, Kumamoto University, Kumamoto, Japan.

This cause may be due to unequal numbers of the cases examined in each age group. Be that as it may, there can be no doubt that environmental factors can influence the regulation mechanism of blood pressure. Oka (1952) also observed a significant difference of basal blood pressure between young monozygotic and dizygotic twins. But in contrast with our results, Awano and Takahashi (1966) did not recognize a significant difference both in twins of the younger and older age groups.

2. Resemblance of basal blood pressure in twins.

The average difference of basal systolic blood pressure in the various age groups of twins is shown in Table II. The average difference of basal blood pressure in monozygotic twins in the under 10 year-old group is 2·64 mm.Hg., in the 10 - 19 age group=3·29 mm.Hg. 20-40 age group= 4·95 mm.Hg., 40-60 age group=7·91 mm.Hg. over 60 age group=11·2 mm.Hg. respectively. In the dizygotic twins, the average difference of basal systolic pressure was found to be greater than that of monozygotic twins. Similar results were reported by Verschuer and Zipperlen (1922) viz. that the average difference in systolic pressure in 112 monozygotic twins was 5·1 mm.Hg. and in 82 dizygotic twins 8·4 mm.Hg.. Weize (1923) reported that the average difference of systolic blood pressure in 145 pairs of monozygotic twins was 5·04 mm.Hg., on the other hand, in 109 pairs of dizygotic twins the average difference of systolic blood pressure was observed to be 9·36 mm.Hg.. Oka (1952) reported also similar results, namely the average difference of systolic blood pressure in 30 pairs of monozygotic twins was 3·73 mm.Hg. and in 17 pairs of dizygotic twins 9·12 mm.Hg.. Next, in those cases showing under 6 mm.Hg. difference of basal systolic pressure in each pair of twins, the resemblance of basal blood pressure was regarded as positive in this study.

In the monozygotic twin groups under 10 years, the concordance ratio of the resemblance of basal systolic pressure was observed to be 93·2% as shown in Table III. On the other hand, in the same group of dizygotic twins the concordance ratio of the resemblance of basal systolic pressure was lower than that of monozygotic twins. This tendency was also observed in other older twin groups and the concordance ratio of the resemblance of basal systolic blood pressure gradually decreased according to the increase of age, not only in dizygotic twins but also in monozygotic twins. This interesting phenomenon can suggest that various environmental factors which had been active for a long time after separation of twins could influence the genetic mechanism which controls blood pressure. But from the result of the significant difference of the resemblance of basal systolic blood pressure between monozygotic and dizygotic twins, it can be concluded that the hereditary factor in the control mechanism of blood pressure is much greater than the environmental factors. Oka (1952) also reported similar results in young twins, namely the concordance ration of resemblance of basal systolic blood pressure in 30 pairs of monozygotic and in 17 pairs of dizygotic twins were observed to be 73·33% and 47·06%, respectively. Verschuer and Zipperlen (1929), Curtins and Korkhaus (1931) already reported similar results.

3. Reaction mechanism of blood pressure induced by stimuli.

Having determined the basal blood pressure, 17 pairs of monozygotic twins and 10 pairs of dizygotic twins in the over 30 year group were administered various stimuli, e.g. breath-holding test, cold pressure test and exercise test, which raises blood pressure: deep breathing test standing test which decrease blood pressure were performed.

After a breath holding test of twenty seconds, blood pressure was determined. Table IV. shows the percentage distribution of the difference in blood pressure in 16 pairs of twins. A difference of the reaction of blood pressure induced by breath holding test between monozygotic and dizygotic twins was not observed, contrary to expectation.

TABLE I

CORRELATION COEFFICIENT OF BASAL SYSTOLIC BLOOD PRESSURE OF VARIOUS AGE GROUPS IN TWINS

Age group (years)	Monozygotic Twin		Dizygotic twin	
	No. of cases	C.C.	No. of cases	C.C.
under 10	44	0·94	21	0·60
10 - 19	110	0·91	90	0·78
20 - 39	21	0·90	17	0·89
40 - 59	23	0·94	10	0·88
over 60	10	0·73	7	0·67

TABLE II

AVERAGE DIFFERENCE IN BASAL SYSTOLIC BLOOD PRESSURE IN TWINS

Age group (years)	Monozygotic Twin		Dizygotic Twin	
	No. of cases	Difference in blood pressure mm. Hg.	No. of cases	Difference in blood pressure mm. Hg.
under 10	44	2·64	21	6·48
10 - 19	110	3·29	90	6·84
20 - 39	21	4·95	17	7·06
40 - 59	23	7·91	10	20·80
over 60	10	11·20	7	28·00

TABLE III

CONCORDANCE RATIO OF RESEMBLANCE OF BASAL SYSTOLIC BLOOD PRESSURE OF VARIOUS AGE GROUPS IN TWINS

Age group (years)	Monozygotic Twin		Dizygotic Twin	
	No. of cases	C.R. (%)	No. of cases	C.R. (%)
under 10	44	93·2	21	66·7
10 - 19	110	85·5	90	58·9
20 - 39	21	81·0	17	58·8
40 - 59	23	65·2	10	20·0
over 60	10	50·0	7	0·0

In the cold pressure test, which was conducted by soaking the left palm in 4°C ice water for one minute, blood pressure was determined. The percentage distribution of the differences in the blood pressure induced by cold stimuli in twins is shown in Table IV. From this result, it can be presumed that the reaction of blood pressure to the cold pressure test is more identical in the monozygotic twins than in the dizygotic twins.

A bending and stretching of the knees twenty times was also conducted as a test. The blood pressure was determined one minute after the exercise. Table IV shows the percentage distribution of the differences in blood pressure in twins. This data shows almost similar results as the other.

Next the deep breathing test was performed. The blood pressure was determined after deep breathing for one minute. The percentage distribution of the differences in blood pressure in twins is shown in Table IV.

Finally, in the one minute standing test blood pressure was determined. The results are shown in Table IV. The latter two tests indicate that the differences in the blood pressure in the monozygotic twins is less than that of dizygotic twins.

In all five tests, the significant difference between monozygotic and dizygotic twins was observed only in the cold test. Oka (1952) reported that in five similar tests the significant difference of systolic blood pressure was observed only in the cold pressure test. Hines *et al* (1957) also obtained a significant difference between monozygotic and dizygotic twins in the cold pressure test. In my experiments, the significant differences between monozygotic and dizygotic twins were observed in the cold pressure test. From the above mentioned five tests, it is my opinion that a genetic factor is involved in the control mechanism of blood pressure.

Concordance ratio of hypertension in twins

The difference in the concordance ratio of hypertension between monozygotic and dizygotic twins suggests the importance of heredity as an aetiological factor of hypertension. Essential hypertension has been clinically diagnosed, in the case of excessive blood pressure at a certain level. Therefore in the case of subjects over 40 year-old diagnosed as essential hypertension, if systolic blood pressure is over 150 mm.Hg. and diastolic pressure is over 90 mm.Hg., then in the case of subjects under 40 year-old, diagnosis criterion of systolic blood pressure must be over 140 mm.Hg.

It is very difficult to find hypertensive twins. In this study I examined 32 pairs of twins over 30 years of age. In these twins, I found 5 pairs of monozygotic twins and 3 pairs of dizygotic twins with hypertension. Out of 5 pairs of monozygotic twins, concordance was found in 4 pairs (75%), while out of 2 pairs of same-sexed dizygotic twins, concordance was found in 1 pair (50%) and 1 pair of opposite-sexed dizygotic twins was discordant. Because my data alone is not sufficient, I gathered other reports of hypertensive twins in Japan as shown in Table V. Out of 39 pairs of monozygotic twins, concordance of hypertension was found in 27 pairs (69·2%), while out of 12 pairs of same-sexed dizygotic twins, concordance was found in only 4 pairs (33·3%).

The difference between monozygotic and dizygotic twins is highly significant. These studies of twins suggest that the appearance or non-appearance of hypertension can be due mainly to genes of blood pressure, but there is no doubt that environmental factors will also affect its development. To solve the participation of environmental factors in the development of hypertension, it is necessary to compare the concordance ratio of hypertension in the same and in different environments. Table VI shows the environmental condition in development of hypertension. Out of 23 pairs of monozygotic twins in the same environment concordance of hypertension was found in 15 pairs (65·2%), while out of 16 pairs of monozygotic twins in different environments, concordance of hypertension was found in 12 pairs (75%). Out of 9 pairs of dizygotic twins in the same environment, concordance of hypertension was found in 3 pairs (33·3%), and out of 7 pairs of dizygotic twins in different environments, concordance of hypertension was found in 1 pair (14·3%). These results indicate that there is no significant difference of concordance in the monozygotic twins as regard environment. In the dizygotic twins, in the same environment the concordance of hypertension was considerably large compared with that of the dizygotic twins in different environments. These results suggest that there is a complicated relation between heredity and environment in the development of essential hypertension. In the future, a follow up study of twins in the hypertension and normotension groups will be necessary to appreciate the relationship between hereditary factors and environmental factors.

SUMMARY

The study of twins is a very important means to solve the hereditary mechanism of essential hypertension. The resemblance of the difference in blood pressure of the monozygotic twins were stronger than that of the dizygotic twins and the reaction of the blood pressure to various stimuli was more identical in the monozygotic twins than in the dizygotic twins.

The concordance ratio of hypertension in the monozygotic twins was significantly higher than that of the dizygotic twins.

TABLE IV

PERCENTAGE DISTRIBUTION OF DIFFERENCES IN BLOOD PRESSURE INDUCED BY VARIOUS STIMULI IN TWINS

Difference in blood pressure mm. Hg.	Breath holding test Systolic pressure		Cold pressure test		Exercise test		Deep breathing test		Standing test	
	MZ (%)	DZ (%)	MZ (%)	DZ (%)	MZ (%)	DZ (%)	MZ (%)	DZ (%)	MZ %	DZ (%)
0		11·11	7·14				17·65	20·0	12·50	20·0
2 - 4	23·53	44·44	21·43	20·0	21·43	10·0	41·18	20·0	18·75	10·0
6 - 8	17·65		35·71	10·0	14·29	10·0	5·88	20·0	25·00	20·0
10 - 12	29·41		21·43	10·0	28·57	20·0	23·53		18·75	10·0
14 - 16	5·88	22·22	7·14	10·0	7·14	10·0	11·76	40·0	12·50	20·0
18 - 20	5·88	11·11	7·14	10·0	21·43					10·0
over 20	17·65			40·0	7·14	50·0			12·50	10·0

Reading to 2mm accuracy

TABLE V

CONCORDANCE AND DISCORDANCE OF HYPERTENSION IN TWINS

Reporter	MZ			Same-sexed DZ			Opposite-sexed DZ		
	No. of pairs	Concordant	Discordant	No. of pairs	C.	D.	No. of pairs	C.	D.
Watanabe (1942)	1	1	0						
Oka (1952)	1	1	0				1	0	1
Misao & Yanase (1955)	1	1	0	1	0	1			
Awano & Takahashi (1966)	31	20	11	9	3	6	2	0	2
Mimura (1972)	5	4	1	2	1	1	1	0	1
	39	27	12	12	4	8	4	0	4

TABLE VI

ENVIRONMENTAL CONDITION IN DEVELOPMENT HYPERTENSION IN TWINS

	MZ	DZ	
		Same-sexed	Opposite-sexed
Same environment	15/23 (65·2 %)	3/7 (42·9 %)	0/2 (0 %)
Different environment	12/16 (75·0 %)	1/5 (20·0 %)	3/9 (33·3 %) 0/2 (0 %)
			1/7 (14·3 %)
TOTAL	27/39 (69·1 %)	4/16 (25·0 %)	

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