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THE EPIDEMIOLOGY OF DIABETES MELLITUS IN HIROSHIMA AND NAGASAKI

INTRODUCTION

The populations of the Atomic Bomb Casualty Commission (ABCC) have provided a unique opportunity to investigate the epidemiology of a number of diseases in Hiroshima and Nagasaki, Japan.[1] An earlier detailed study of diabetes mellitus by Rudnick and Anderson of about one third of the Hiroshima sample demonstrated that the prevalence of diabetes was comparable to that of Oxford, Massachusetts, and commented on the reversal of sex ratio in Japanese diabetes.[2] Many features of diabetes mellitus are remarkably different in Japan and Western countries. Atherosclerosis, ketoacidosis, and juvenile diabetes are rare in the Japanese. On the other hand, retinopathy, proteinuria, and ketone response to noreprinephrine are comparable to Western experience. These data have recently been reviewed elsewhere.[3]

Reported here are the data on diabetes mellitus collected from the entire ABCC study population at the 1st and 2nd examinations (1958-60, 1960-62) and a comparison of the epidemiology of this disease in Hiroshima and Nagasaki. The differences in the two communities provide some

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measure of the variation possible within national boundaries and between males and females.

Nature of the population

A sample of about 20,000 persons from Hiroshima and Nagasaki was selected from information derived from the 1950 Japanese National Census. Persons were selected according to their location in the cities at the time of the atomic bombings. The purpose of the ABCC study is to determine the long term health status of persons exposed to varying amounts of

TABLE 1. CONTACTING RESULTS BY EXAMINATION CYCLE AND CONTACTING CATEGORY

1960-62 cycle	*1958-60 cycle—Contacting categories*							
	Total	*1*	*2*	*3*	*4*	*5*	*6*	*7*
Total	19,877	14,923	1,710	1,586	196	96	22	1,344
Contacting categories								
1 Examined	14,451	13,348	784	231	38	47	3	0
2 Refused	1,384	556	765	24	15	16	8	0
3 Moved—address known	1,790	419	42	1,243	81	4	1	0
4 Moved—address unknown	182	58	21	46	53	1	3	0
5 Too ill to come	40	23	8	0	0	9	0	0
6 No contact	275	237	26	3	2	0	7	0
7 Deceased	1,702	261	45	31	3	18	0	1,344
8 Contact incomplete	53	21	19	8	4	1	0	0

ionizing radiation. The details of the selection procedure and an analysis of sociologic features of the population have been given elsewhere.[1,4]

The study was begun in 1958, and the entire sample scheduled for examination at two-year intervals. Most patients were seen in the morning about 1 to 3 hours after breakfast. A medical history was taken and a physical examination performed after a urine specimen and blood had been taken. Chest X-ray, ECG, and various other laboratory tests were performed. Between 1958 and 1962 about 90 per cent of sample members still living in the two cities were examined (Table 1).[5,6]

MATERIALS AND METHODS

The blood pressure readings were taken by a Japanese nurse. The cuff was applied to the left arm in the sitting position. Diastolic values were recorded as the point of cessation of sounds. The first reading obtained was used for analysis. Height was

measured without shoes. Weight was measured with the patient wearing only a dressing gown, the weight of which was subtracted from the observed value. After data for height and weight had been obtained on the entire population in 1958-60, the relation between these two measurements was established by Seigel,[7] who fitted least square curves to express the relation of logarithm of weight on height, by age and sex. In the present analysis, the expected weight according to height (as calculated from Seigel's formula) divided by the observed weight provided the basis for dividing the population into three groups. Light-weight persons were those 6 per cent or more below expected weight, normal-weight persons were those from 5 per cent below to 11 per cent above expected weight, and heavy persons were those 12 per cent or more above expected weight.

Information about family history of diabetes was taken from the replies given during the first cycle of examinations in 1958-60. Serum cholesterol was determined by the method of Abell, *et al.*[8] During the 1958-60 cycle, casual urine specimens were collected. Starting October 1960 in Nagasaki and November 1961 in Hiroshima, clean voided urine specimens were routinely analyzed. Glycosuria was determined with Benedict's reagent until June 1960. After July 1960 the urine was first tested with Combistix and positive results confirmed with Benedict's reagent. This procedure was adopted because some of the slow-appearing faint trace results with Combistix were negative when tested with Benedict's reagent.

The urine was tested for protein with sulfosalicylic acid and positive reactions confirmed by the nitric acid ring test. For the 1958-60 cycle the result of the nitric acid ring test was recorded in Hiroshima and the sulfosalicylic acid test was recorded in Nagasaki. In July 1960, Combistix were used to test for protein in both cities. Positive reactions continued to be confirmed with nitric acid. The nitric acid test result continued to be used in Hiroshima but the Combistix test was recorded in Nagasaki. Blood sugar was determined in both cities by a modification of the method of Folin and Malmros.[9] Protein precipitation was accomplished with sulfate-tungstate, and ferricyanide was used for the final color reaction; however, the techniques were slightly different in the two cities (Hiroshima,[10, 11] Nagasaki[12]). The normal range was determined to be 80 to 110 mg/100 ml. in Hiroshima and 80-120 mg/100 ml. in Nagasaki. Nevertheless, the same diagnostic criteria were applied for the diagnosis of diabetes mellitus. Exchange of protein-free filtrates and testing of unknown samples from Yamaguchi Medical College (Dr. Shibata) and the 406th Medical General Laboratory at Camp Zama, Japan, have shown differences between Hiroshima and Nagasaki to be approximtely five per cent.

Criteria for the diagnosis of diabetes

Patients found to have glycosuria during their regular clinic visit were advised to have an oral glucose tolerance test. After an overnight fast 1.75 g. of glucose per kg. of body weight was given and diabetes mellitus diagnosed if the two-hour blood sample contained 140 mg/100 ml. or more glucose. If an oral glucose tolerance test could not be obtained, a postprandial blood sugar determination was requested. For this test the subject was advised to have 2 to 3 bowls of rice. A blood sample was taken two hours later. The same two-hour level of blood sugar as for the glucose tolerance test was required for a positive diagnosis. If neither test could be done, a fasting blood sugar of 125 mg/100 cc. was accepted. If even this blood test was not obtained, 3+ to 4+ sugar in the urine was considered as diabetes mellitus.

TABLE 2. PERCENTAGE OF PERSONS WITH DIABETES AND NONDIABETIC GLYCOSURIA

Sex	Age	1958-60 Number	1958-60 Diabetes	1958-60 Nondiabetic glycosuria	1960-62 Number	1960-62 Diabetes (A)	1960-62 Nondiabetic glycosuria (B)	Ratio A/A+B
				Hiroshima				
Male	<20	248	. .	3.2	123	0.8	2.4	18.8
	20–29	527	0.8	4.9	333	0.6	3.0	
	30-39	729	1.2	6.3	711	3.0	6.1	32.8
	40–49	619	4.5	8.7	509	5.3	9.6	35.5
	50–59	815	8.7	10.9	684	9.4	11.8	44.1
	60–69	650	8.5	13.1	624	12.3	14.3	46.4
	70+	221	9.5	13.6	223	11.2	13.0	46.3
	Total	3,809	. .	. .	3,207	. .	. .	41.7
Female	<20	307	0.3	3.3	168	. .	. .	. .
	20–29	849	0.9	4.5	540	0.2	1.3	12.5
	30–39	1,729	0.9	3.7	1,597	0.8	1.7	32.5
	40-49	1,202	1.5	3.4	1,096	0.8	1.6	33.3
	50–59	1,417	3.2	4.5	1,254	2.6	2.7	49.3
	60–69	759	2.6	5.1	853	2.9	3.5	45.5
	70+	294	3.1	4.4	286	4.6	6.6	40.6
	Total	6,577	. .	. .	5,794	. .	. .	41.0
				Nagasaki				
Male	<20	155	. .	. .	61	. .	. .	
	20–29	400	. .	2.0	190	. .	0.5	
	30–39	412	. .	2.4	323	1.9	4.0	
	40–49	349	1.4	6.0	212	2.4	3.3	
	50–59	368	1.1	5.4	235	2.1	5.5	
	60–69	206	3.9	7.8	175	3.4	4.6	
	70+	28	3.6	10.7	34	2.9	2.9	
	Total	1,918	. .	. .	1,230	. .	. .	39.7
Female	<20	155	0.7	3.9	62	. .	3.2	
	20–29	536	. .	1.9	274	. .	0.7	
	30–39	1,025	0.3	1.2	777	0.3	. .	
	40–49	388	0.8	1.3	295	1.7	1.4	
	50–59	325	1.9	1.9	234	0.4	1.3	
	60–69	153	1.3	2.0	135	2.2	2.2	
	70+	50	. .	4.0	48	. .	4.2	
	Total	2,632	. .	. .	1,825	. .	. .	38.8

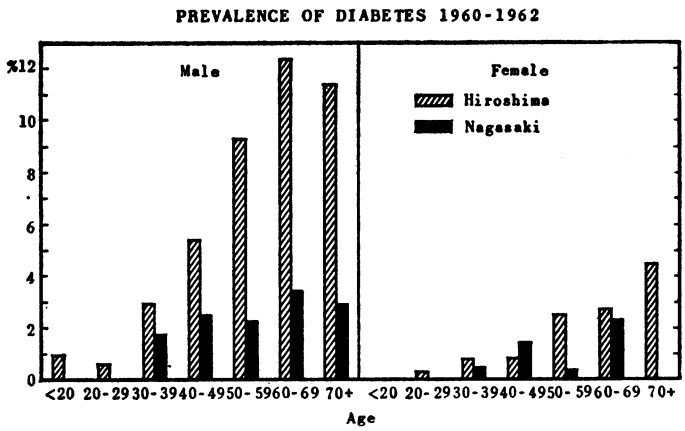

FIG. 1

RESULTS

Prevalence. The prevalence of diabetes and glycosuria (including trace tests) are shown according to age, sex, and city in Table 2 and Figure 1. A number of features of the data are of interest.

1. The well known increase in diabetes and glycosuria with age was clearly demonstrated in Hiroshima males and was probably present in Hiroshima females. In Nagasaki, however, neither sex showed a clear pattern.

2. In Hiroshima, more males than females had diabetes and glycosuria. A similar difference was seen in Nagasaki but it was not statistically significant.

3. Diabetes and glycosuria were considerably more common for both sexes in Hiroshima than in Nagasaki.

4. The rates for diabetes and glycosuria have increased in almost all age groups between the two examinations for Hiroshima males. In other groups the rates for diabetes did not increase and the prevalence of glycosuria decreased, as would be expected on the basis of the change in method for testing urine sugar. (Benedict's reagent as a screening test is less specific for glucose than Combistix.)

The differences between the cities and between males and females are remarkable. Careful inquiry into the methods used in both cities proved them to be comparable. Support for the comparability of data from the two cities is derived from the ratio of diagnoses of diabetes to persons with glycosuria (Table 2). In males and females of Hiroshima, diabetes

was diagnosed more commonly in older persons with glycosuria. In Nagasaki there were not sufficient cases to analyze the data by age, but the over-all ratio was similar in males and females and both ratios were similar to those of Hiroshima.

Tabulation of the diagnostic procedures applied to those persons with glycosuria with and without a diagnosis of diabetes is shown in Table 3. Differences were evident between cities but not to any great extent between sexes within cities. In Nagasaki, glucose tolerance tests were performed

TABLE 3. FREQUENCY OF DIAGNOSTIC PROCEDURES, 1960-62

Category	*Hiroshima*				*Nagasaki*			
	Male	*%*	*Female*	*%*	*Male*	*%*	*Female*	*%*
				Diabetes				
Glucose tolerance test	107	49.4	38	34.5	20	87.0	9	75.0
Postprandial	22	10.2	16	14.6	1	4.4	1	8.3
Fasting blood sugar	48	22.1	34	30.9	..	. .	2	16.5
Urine only (3-4+)	40	18.4	22	20.0	2	8.7	..	. .
Total	217	100.1	110	100.0	23	100.1	12	99.8
				Nondiabetic glycosuria				
Glucose tolerance test	154	50.6	48	35.5	29	65.9	9	56.3
Postprandial	26	8.5	14	10.3	2	4.6	1	6.3
Fasting blood sugar	61	20.0	37	27.4	7	15.9	2	12.5
Urine only (trace, 1-2+)	63	20.7	36	26.7	6	13.6	4	25.0
Total	304	99.8	135	99.9	44	100.0	16	100.1

more often than in Hiroshima. Therefore, if anything, it might be anticipated that rates in Nagasaki would be overestimated as compared with Hiroshima.

To summarize, diabetes and glycosuria were more common in Hiroshima than in Nagasaki and in both cities males were more often affected than females. These differences appear to be real and not attributable to methodology. Also, the age specific rates for glycosuria and diabetes have risen in Hiroshima males between the first and second cycle examinations.

Incidence. New cases of glycosuria and diabetes detected in the second examination provided data for the calculation of two-year incidences (Table 4). In Hiroshima males the age specific rates increased between examinations and the high incidence figures reflect this. The incidences in other groups were derived from persons with constant rates for diabetes.

Radiation exposure. The prevalence and incidence of diabetes and glycosuria were examined from the standpoint of radiation exposure according to conventional comparison groupings and with particular emphasis on persons located within 1,400 meters of the hypocenter. No effect of previous exposure to ionizing radiation could be detected. All other analyses were therefore conducted without regard to prior exposure to radiation.

Family history. A family history of diabetes was obtained from about 5 per cent of persons in Hiroshima and from 2.5 to 2.0 per cent of persons

TABLE 4. TWO-YEAR INCIDENCE OF NONDIABETIC GLYCOSURIA AND DIABETES IN PERSONS SEEN FOR BOTH EXAMINATIONS

Sex	*Age*	*Number*	*Glycosuria*	*Per cent*	*Diabetes*	*Per cent*
		Hiroshima				
Male	<19	123	3	2.4	1	.8
	20–29	331	8	2.4	2	.6
	30–39	702	36	5.1	18	2.5
	40–49	489	29	5.9	18	3.7
	50–59	653	50	7.7	28	4.3
	60–69	591	56	9.5	36	6.1
	70+	210	16	7.6	9	4.3
Female	<19	168	..	..	..	..
	20–29	539	6	1.1	..	..
	30–39	1,589	19	1.2	7	.4
	40–49	1,091	13	1.2	5	.5
	50–59	1,238	18	1.5	10	.8
	60–69	840	17	2.0	12	1.4
	70+	279	12	4.3	8	2.9
		Nagasaki				
Male	<19	61	..	..	..	..
	20–29	190	1	.5	..	..
	30–39	322	12	3.7	6	1.9
	40–49	210	5	2.4	4	1.9
	50–59	233	11	4.7	4	1.7
	60–69	172	5	2.9	4	2.3
	70+	34	1	2.9	..	..
Female	<19	61	1	1.6	..	..
	20–29	273	1	.4	..	..
	30–39	777	..	..	1	.1
	40–49	293	2	.7	3	1.0
	50–59	233	2	.9	1	.4
	60–69	134	2	1.5	2	1.5
	70+	47	1	2.1	..	..

in Nagasaki, thus reflecting the different rates of disease in the two communities (Table 5). The percentage of positive family histories from males and females did not differ.

In Hiroshima, diabetes occurred more often in persons with a positive family history. In males a positive family history was associated with a twofold increase in diabetes rates, whereas in females the increase was fourfold. These differences between sexes are statistically significant.

TABLE 5. FAMILY HISTORY OF DIABETES

		History positive			*History negative*		
Sex	*Age*	*Number*	*Diabetes*	*Per cent*	*Number*	*Diabetes*	*Per cent*
			Hiroshima				
Male	Total	145	20	13.8	3,032	196	6.5
	<40	46	3	6.5	1,119	21	1.9
	40+	99	17	17.2	1,933	175	9.1
Female	Total	279	20	7.2	5,587	90	1.6
	<40	100	6	6.0	2,289	12	0.5
	40+	179	14	7.8	3,298	78	2.4
			Nagasaki				
Male	Total	35	1	2.9	1,190	22	1.9
Female	Total	72	..	..	1,742	12	0.7

In Nagasaki, on the other hand, the rates for diabetes in persons with a positive family history were not significantly different from those with negative histories. The number of cases was small, however, so that the lack of effect of a family history in Nagasaki cannot be established in this size sample.

Height-weight-ratio. Table 6 shows the prevalence of diabetes by height-weight ratio. The increased rates for diabetes in persons above normal weight for their height was evident in both cities and sexes. Since only a small change in weight with age occurs among Japanese adults, the total values can be compared without age adjustment. Such a comparison showed the greatest effect of weight was in the heavy categories with only a slight advantage in the light groups. It is noteworthy that in both cities heavy persons constituted a higher percentage of female than male diabetics. Reference to the nondiabetic populations, however, revealed the same relative excess of heavy females. For both sexes, heavy persons constitute

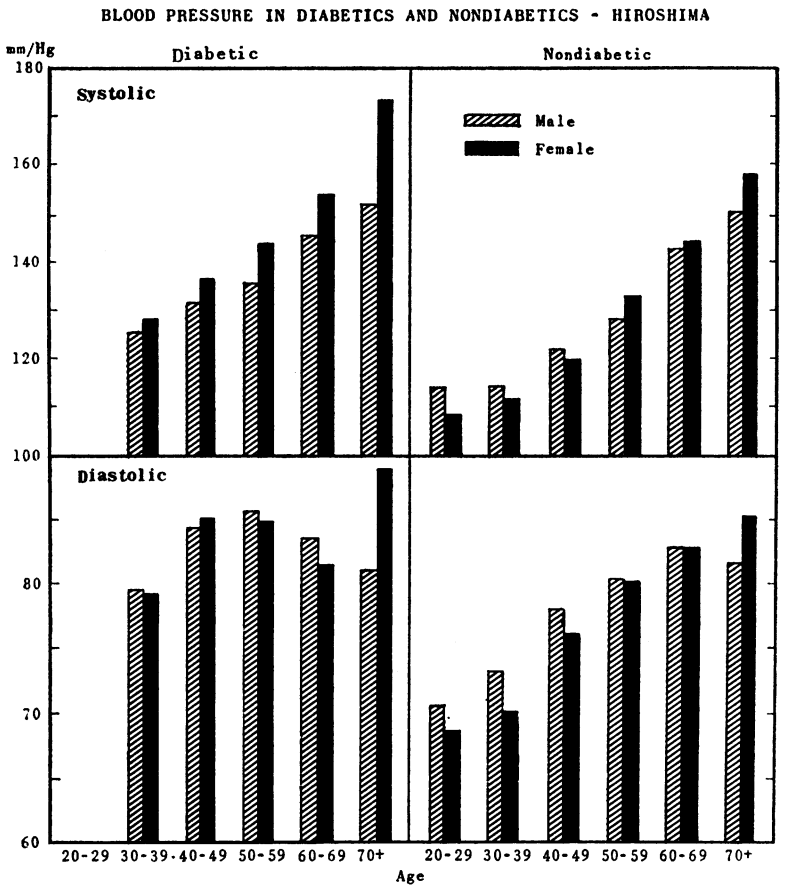

FIG. 2

about twice the percentage of the diabetic as compared to the nondiabetic populations.

In summary, diabetes is more frequent in heavy persons and the increased rates associated with increased weight are similar for both sexes. Neither the increasing prevalence of diabetes with age nor the preponderance of diabetes in males appears attributable to the relation between height-weight ratio and diabetes since weight does not change appreciably with age and more females are heavy as compared with males.

Blood pressure. Figure 2 shows the blood pressures of diabetics and nondiabetics in Hiroshima. Diabetics had higher blood pressures and the

TABLE 6. PREVALENCE OF DIABETES BY HEIGHT-WEIGHT RATIO

Sex	Sategory	Diabetes	No Diabetes	Total	Diabetes Per cent
		Hiroshima			
Male	Light	47	866	913	5.2
	Normal	81	1,415	1,496	5.4
	Heavy	77	495	572	13.5
	Unknown	11	210	221	5.0
Female	Light	20	1,579	1,599	1.3
	Normal	37	2,341	2,378	1.6
	Heavy	47	1,180	1,227	3.8
	Unknown	6	578	584	1.0
		Nagasaki			
Male	Light	2	288	290	0.7
	Normal	16	659	675	2.4
	Heavy	5	193	198	2.5
	Unknown	..	61	61	..
Female	Light	2	479	481	0.4
	Normal	4	875	879	0.5
	Heavy	5	335	340	1.5
	Unknown	1	117	118	.9

TABLE 7. BLOOD PRESSURE BY HEIGHT-WEIGHT RATIO, HIROSHIMA

		Light		*Normal*		*Heavy*	
Sex	Age	Diabetes	No diabetes	Diabetes	No diabetes	Diabetes	No diabetes
		Systolic					
Male	<40	140.0	109.8	115.6	114.2	124.0	118.6
	40-59	133.8	121.2	135.2	126.4	133.7	132.5
	60+	145.7	137.5	142.0	144.0	155.1	151.6
Female	<40	..	107.3	126.8	109.1	127.2	114.9
	40-59	108.3	121.6	137.1	123.9	153.8	133.8
	60+	146.6	137.2	163.2	143.6	159.7	154.2
		Diastolic					
Male	<40	81.7	68.5	72.4	71.6	81.8	76.7
	40-49	82.6	76.9	87.0	79.9	86.6	86.4
	60+	81.4	79.4	81.7	83.2	85.7	88.3
Female	<40	..	67.3	77.8	68.8	79.8	73.6
	40-59	69.3	75.1	82.9	77.5	89.6	83.2
	60+	79.1	79.4	83.6	82.2	86.0	87.2

differences seemed greater in females. However, since diabetics are heavier for fixed height than nondiabetics and since a relation between weight and blood pressure has been demonstrated by others, the data were recalculated according to height-weight classification. The results are shown in Table 7. When height-weight ratio was taken into consideration, the blood pressures of diabetics remained higher than the remaining nondiabetic population. This was most marked in systolic but variable in diastolic values. Most of the variability in diastolic pressures was due to lower values in persons

TABLE 8. CHOLESTEROL

Sex	*Age*	*Diabetes*		*No diabetes*		*Statistical test*
		Number	*Mean*	*Number*	*Mean*	
			Hiroshima			
Male	<40	12	171.4	456	152.0	..
	40+	69	169.4	533	162.2	..
Female	<40	7	245.6	765	153.0	P = <0.5
	40+	32	206.8	867	178.9	P = <.001
			Nagasaki			
Male	<40	5	150.6	235	145.5	..
	40+	13	175.1	389	155.4	..
Female	<40	1	192.0	542	149.3	P = <.001
	40+	7	173.0	404	166.2	..

age 60 or over. This might be due to high mortality rates in diabetic persons with high diastolic pressure readings.

Cholesterol. Serum cholesterol determinations were made on a portion of the diabetic and nondiabetic population during 1960-62. The results are shown in Table 8. The values for diabetics are higher than for nondiabetics, but the differences are statistically significant only for females.

Proteinuria. Table 9 shows the outcome of urine protein tests. Trace tests were not included. The data have several interesting features. Proteinuria was much more common in Hiroshima in both sexes. Examination of the methods used in the two cities revealed that the technique in Nagasaki was probably more sensitive than that used in Hiroshima, thus tending to obscure the extent of the difference between the cities. This discrepancy in the rates for proteinuria in the two cities is the subject of a separate study.[18] Proteinuria was considerably more frequent in diabetics and the

data suggest that diabetic females have higher rates for proteinuria than diabetic males. In nondiabetics, proteinuria was more common in males than in females in both cities.

ABO blood groups. An analysis of the distribution of ABO blood groups in the two cities revealed no significant differences between them and no difference in the prevalence of diabetes between sexes withn cities.

Diagnoses

The diagnoses for thyroid diseases (ICS 250-254), tuberculosis (ICS 001-019), and heart and cerebrovascular disease (ICS 410-434, 330-334, 352) were tabulated for diabetics and nondiabetics in Hiroshima. There were too few diabetics in Nagasaki to make comparisons. The only statistically significant difference was in the frequency of diagnosis of heart and cerebrovascular disease. These diagnoses were more common in diabetic females of all ages. Although the individual comparisons for the two age groupings below and above age 50 were not statistically significant, the test for all females was significant (p.-.02-.01).

TABLE 9. PROTEINURIA

	Diabetes			*No diabetes*			
Sex	*Number*	*Positive*	*Rate*	*Number*	*Positive*	*Rate*	*Test*
				Hiroshima			
Male	215	33	15.3	2952	181	6.1	P = .01
Female	110	26	23.6	5595	310	5.5	P = .01
				Nagasaki			
Male	23	1	..	1197	34	2.8	..
Female	11	1	..	1802	41	2.3	..

DISCUSSION

The data in the present report were derived from a broad health survey of similarly systematically selected population samples in Hiroshima and Nagasaki. Tests for urine sugar were conducted in the same way in the two cities and criteria for the diagnosis of diabetes were uniform. Data were available from two consecutive examinations of the sample populations. Diabetes and glycosuria were more common in Hiroshima than in Nagasaki in both sexes. The differences were sizeable and not explicable by methodology. Explanations for these differences have been considered in

detail elsewhere.[8] Possible environmental and socioeconomic differences between the populations in the two cities were not considered sufficient explanations. It is believed that genetic strongholds fostered by geographic stability of the populations are more likely to account for the different rates between the two cities.

The present study was designed to tabulate certain features of diabetes mellitus and to make comparisons between cities. The city comparisons were hampered by the paucity of diabetes in Nagasaki. Two features, however, warrant further investigation. There may not be a greater risk of diabetes in persons with a positive family history for diabetes in Nagasaki. This is in contrast to the Hiroshima data and data from Western studies. The number of subjects was too small, however, to establish this fact. Confirmation would require studies of a larger population.

Another remarkable difference between the cities is in the prevalence of proteinuria. It had been noted previously that proteinuria was more frequent in Hiroshima than in Nagasaki. This subject will be considered in detail in a subsequent analysis.[13] Diabetes was also more common in Hiroshima, and the present analysis demonstrated a higher rate of proteinuria in diabetic subjects. This increased rate in diabetics was not sufficient, however, to explain the difference between cities; in nondiabetics the discrepancy persisted.

In Hiroshima and Nagasaki, diabetes and glycosuria were more common in males than in females. The differences were great in Hiroshima and slight in Nagasaki. The possible explanations for the difference between the sexes and comparisons with other studies have been considered in detail elsewhere.[8] The reason suggested was that males have a greater predisposition to diabetes which was obscured in countries where females gained a great deal of weight during adult years. This thesis is further supported by the recent observation that 70 per cent of diabetics in India are male, whereas in Natal 64 per cent of Indian diabetics are female. Campbell belives "this may be a measure of the emancipation experienced by women in Natal." He comments also that obesity is common in Natalian Indian women.[14]

The present anlysis detected a number of circumstances in which females differ from their nondiabetic counterparts to a greater extent than males. The increased prevalence of diabetes in the presence of a positive family history was greater in females than in males. The difference in serum cholesterol values when compared to nondiabetics was greater in females than males. Proteinuria also showed a greater increase in diabetic females than in diabetic males. Blackard, *et al.*[5, 15] and Rudnick and Anderson[3] have

noted higher rates of retinopathy in diabetic females, and the latter authors also mentioned higher rates of symptoms, neuropathy, and cataracts in diabetic females. In addition, diagnoses of heart diseases and cerebrovascular diseases were more common in diabetic females but not in diabetic males.

Thus, there is evidence that diabetic Japanese females are subject to higher rates of the disorders associated with diabetes. This is of particular interest in view of the greater frequency of diabetes in Japanese males. No features detected in the present study were more common in male diabetics. Yano and Ueda described an increased rate for coronary heart disease in diabetic males but not in females in this same study population.[16] This does not, however, constitute evidence for an effect in males greater than in females since the number of cases in females was too small for analysis.

The epidemiological study being conducted in Tecumseh, Michigan, is the best source of comparative information from the West.[17] In Tecumseh, diabetes is more common in females than in males, so these data would help to establish whether the findings associated with diabetes in Japanese females were dependent on sex or on prevalence of diabetes. In Tecumseh, coronary heart disease was more prevalent in diabetics of either sex, as compared with the total population in corresponding age and sex groups. Also, diabetes was correlated with systolic and diastolic blood pressure and relative weight only in females. Thus, it would appear that the higher rates of abnormalities associated with diabetes in Japanese females indicate a phenomenon which may apply to all females rather than being limited to females in Japan.

A summary of the relation of sex hormones to diabetes in animals has been presented by Houssay.[18] In general, the evidence shows a greater predisposition to diabetes in males and alleviation of diabetes by the administration of female sex hormones. If it is correct that predisposition to the easily detectable abnormality of carbohydrate metabolism in diabetes is greater in males, the finding of higher rates of abnormalities associated with diabetes in females is remarkable and would constitute additional evidence for the independence of carbohydrate abnormality and associated pathological lesons in diabetes.[19] It has recently been suggested that carbohydrate tolerance is different in males and females and that excretion of sugar in the urine at a given blood sugar level is also different in the two sexes. According to data from the U. S. National Health Survey, at any blood sugar level, glycosuria is more common in males than in females.[20] Conversely, in persons with glycosuria, if the same criteria for diabetes were used in both sexes, a diagnosis of diabetes would be made more often in females than in males.

In the present study the diagnosis of diabetes in persons with glycosuria was made with equal frequency in the sexes suggesting that the situation in Japan may differ from that in the United States. In addition, the urine samples in the U. S. Health Survey were obtained about one and one half hours after the glucose drink, and the urine results correlated with the one-hour blood sugar. The results of these particular circumstances of testing may not be applicable to the circumstances of testing in the present study and may also differ because of variations in diet, patterns of obesity, and perhaps racial characteristics. Further study of this important subject is in progress using methods that would permit direct comparison of data with those obtained in the United States. The prevalence of glycosuria and diabetes in Hiroshima males increased at the second examination. It is possible that interest in the disease was stimulated in Hiroshima by the studies of Rudnick and Anderson,[8] thus resulting in an increasing awareness of the disease. This suggestion can probably be discarded since a similar change was not seen in Hiroshima females.

Another explanation is that the males now reaching the age of increasing rates of diabetes were for some health reason not in the army during World War II and one expression of this is a higher prevalence of adult-onset of diabetes. Although this factor has been considered in ABCC studies in the past, there is no evidence on the subject. In addition, if this were so, the same phenomenon should be detected in Nagasaki males, but it is not. Also, the increased rates in all age groups makes this an unlikely explanation.

A final possibility is that the prevalence of diabetes is increasing among Hiroshima males. Japan has been undergoing far-reaching socioeconomic changes since the war and factors such as westernization of foods might have an impact on Hiroshima before Nagasaki and on males before females. There are no other data bearing on this problem at the present time, but this represents an important area of future investigation.

SUMMARY

Data have been presented on the finding of glycosuria and the diagnosis of diabetes mellitus during four years of a long term study of the health of population samples of Hiroshima and Nagasaki. Diabetes and glycosuria are much more common in Hiroshima than in Nagasaki and in both cities these findings are more frequent in males than in females. The prevalence of diabetes appears to be increasing in Hiroshima males. Findings in diabetics were compared with nondiabetics. In general, Japanese diabetics

are similar to diabetics in other countries concerning their increased risk of obesity, hypertension, proteinuria, hypercholesterolemia, and cardiovascular and cerebrovascular diagnoses. This is of particular interest in the light of evidence that ketosis and severe abnormalities of carbohyrate metabolism are rare in Japan as compared to Western countries.

Despite a lower prevalence of diabetes in Japanese females than in males, the abnormalities associated with diabetes appear to occur more commonly in female diabetics than in male diabetics.

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