AMERICAN JOURNAL OF EPIDEMIOLOGY
Vol. 102, No. 6

Printed in U.S.A.

EPIDEMIOLOGIC STUDIES OF CORONARY HEART DISEASE AND STROKE IN JAPANESE MEN LIVING IN JAPAN, HAWAII AND CALIFORNIA: PREVALENCE OF CORONARY AND HYPERTENSIVE HEART DISEASE AND ASSOCIATED RISK FACTORS[1]

M. G. MARMOT,[2] S. L. SYME,[2] A. KAGAN,[3] H. KATO,[4] J. B. COHEN,[2] AND J. BELSKY[5]

Marmot, M. G. (School of Public Health, U. of California, Berkeley, CA 94720), S. L. Syme, A. Kagan, H. Kato, J. B. Cohen and J. Belsky. Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: Prevalence of coronary and hypertensive heart disease and associated risk factors. *Am J Epidemiol* 102:514–525, 1975.

A study of coronary heart disease (CHD) among Japanese migrants compared with Japanese living in Japan provided the opportunity to study factors possibly responsible for the high rates of CHD in America as compared with Japan. Comparable methods were employed in examining 11,900 men of Japanese ancestry aged 45—69 living in Japan, Hawaii and California. The age-adjusted prevalence rates for definite CHD as determined by ECG were: Japan 5.3, Hawaii 5.2 and California 10.8/1000. For definite plus possible CHD the rates were 25.4, 34.7 and 44.6. The prevalence of angina pectoris and pain of possible myocardial infarction, determined by questionnaire, showed a similar gradient. Elevated serum cholesterol showed a Japan-Hawaii-California gradient, but the prevalence of hypertension in Japan was intermediate between the prevalence in Hawaii and the higher prevalence in California. The three geographic locations were compared as to prevalence of CHD at comparable levels of blood pressure and cholesterol. At each blood pressure level and at each cholesterol level, the greater prevalence of CHD in California persisted. These facts, plus the near universality of smoking in Japan, suggest that conventional risk factors only partly explain the observed gradient in CHD.

Received for publication September 9, 1974, and in final form June 12, 1975.

Abbreviation: CHD, coronary heart disease.

[1] From the Epidemiology Program, School of Public Health, University of California at Berkeley; Honolulu Heart Study, Honolulu, Hawaii; and the Atomic Bomb Casualty Commission, Hiroshima and Nagasaki, Japan.

Supported by: Grant No. 5 PO1 NB06818 from the National Institute of Neurological Diseases and Stroke, Grant No. HL14783 from the National Heart and Lung Institute, the National Heart and Lung Institute Intramural Program, and by funds of the National Heart and Lung Institute made available to the Atomic Bomb Casualty Commission through the Atomic Energy Commission.

Computing assistance was obtained from the Health Sciences Computing Facility, University of California at Los Angeles, sponsored by National Institutes of Health Special Research Resources Grant RR-3.

[2] Program in Epidemiology, School of Public Health, University of California at Berkeley.

[3] Honolulu Heart Study, Honolulu, Hawaii.

[4] Department of Epidemiology and Statistics, Atomic Bomb Casualty Commission, Hiroshima, and Hiroshima Branch, Japanese National Institute of Health, Hiroshima, Japan.

[5] Formerly Department of Medicine, Atomic Bomb Casualty Commission.

The combined articles in this issue on "Epidemiologic Studies of Coronary Heart Disease and Stroke in Japanese Men Living in Japan, Hawaii and California," are available on request from: Epidemiology Research Unit, Dept. of Biomedical and Environmental Health Sciences, School of Public Health, University of California, Berkeley, CA 94720.

blood pressure; coronary heart disease; epidemiology; glucose; lipids; migrants; mortality

Introduction

Worth et al. (1) confirmed Gordon's finding of a gradient in coronary heart disease mortality among men of Japanese ancestry, increasing from Japan to Hawaii to California (2, 3). The three cohorts of Japanese men in Japan, Honolulu and the San Francisco Bay Area were examined to see if disease prevalence followed the same gradient.

The present paper reports the prevalence of coronary and hypertensive heart disease as well as the prevalence of high blood pressure and elevated serum cholesterol, triglyceride and glucose found on examination of the three study groups. Other papers from this study report details of the research plan (4), methodology for comparison of diet (5), the relationship between diet and biochemical measurements (6), summary statistics of the characteristics of the three populations (7) and, in this series, detailed analyses of blood pressure (8) and biochemical measurements (9).

Methods

Subjects studied. The data in this report are for men of Japanese ancestry aged 45–69 at time of examination: 2141 men were studied by the Atomic Bomb Casualty Commission in Hiroshima and Nagasaki, Japan; 8006 men were studied in Honolulu, Hawaii; 1844 men were studied in the San Francisco Bay Area, California.

Additional details regarding the development of the study samples, age distributions, and response rates are reported in the Introduction to this series (10).

Examination methods. Standardized interviews were used in the three centers. All subjects completed a self-administered questionnaire detailing various demographic and socioeconomic characteristics. Following this, a medical history questionnaire was completed giving full details of past and present health. The medical history questionnaire was administered by a nurse-interviewer in Japan and Hawaii and was self-administered in California. In Hawaii and California, blood pressure with the subject seated was taken by a nurse; in Japan it was taken by a physician. Duplicate measurements were taken; systolic and phase V diastolic blood pressures were recorded, and the first measurement used. Details of examination methods are reported elsewhere (4).

A 50 gm glucose load was given early in the clinic procedure and blood drawn one hour later. Subjects were non-fasting. California subjects who reported a history of diabetes were not given a glucose load. Serum cholesterol, uric acid and glucose values were determined in San Francisco for the California and Hawaii cohorts and in Hiroshima for the Japanese cohort. Serum triglycerides for all three cohorts were determined in San Francisco. Procedures were devised to control variation within and between laboratories, and analysis indicated that the methods used yielded comparable data from the two laboratories (9).

Conventional 12 lead electrocardiograms were performed using a Sanborn electrocardiograph at 25 mm per second. Copies of all ECG tracings were sent to the Laboratory of Physiological Hygiene in Minnesota for objective ratings according to the revised Minnesota code (11). Tracings sent to Minnesota were not identifiable by area by those reading the ECG's.

Diagnostic criteria. To avoid the possible non-comparability of clinical judgments among the three study areas, only standardized procedures were used to assess prevalence.

Angina pectoris and pain of possible myocardial infarction were determined by

means of the London School of Hygiene-Cardiovascular Questionnaire (11). A diagnosis of angina pectoris was made if the subject reported pain in the chest in the appropriate location while walking uphill or hurrying and if the pain went away in 10 minutes or less when the subject stopped or slowed down. Possible history of myocardial infarction was said to exist if the subject had experienced a severe pain across the front of the chest which lasted for half an hour or more.

Prevalence of CHD was restricted to the finding of abnormal Q and QS patterns on ECG. Minnesota codes 1-1-1 through 1-1-7 constituted definite CHD and 1-2-1 through 1-3-6 constituted possible CHD.

World Health Organization criteria were used to classify hypertension: i.e., hypertension represents a systolic blood pressure $\geq$ 160 mm Hg and/or a diastolic blood pressure $\geq$ 95 mm Hg; normotension implies both systolic blood pressure $\leq$ 140 mm Hg and the diastolic pressure $\leq$ 90 mm Hg; borderline hypertension represents the residual category, i.e., the systolic blood pressure $\leq$ 160 mm Hg and the diastolic blood pressure $\leq$ 95 mm Hg, but pressures are not simultaneously below both 140 mm Hg systolic and 90 mm Hg diastolic.

Left ventricular hypertrophy was defined solely on the basis of the ECG, and was diagnosed in the presence of a high voltage ORS complex and ST-T wave abnormalities (Minnesota codes 3-1 plus 4-1, 4-2 or 4-3 plus 5-1, 5-2 or 5-3). Hypertensive heart disease was considered to be present if the subject had hypertension as defined above plus ECG evidence of left ventricular hypertrophy.

The decision as to the levels at which a biochemical or physiological variable should be considered a "risk" factor in a given population is an arbitrary one and should ultimately be determined on the basis of long-term outcome. Available data suggest that for cholesterol and blood pressure, and perhaps for the other risk factors as well, the risk of subsequent development of CHD increases at each increasing level of the parameter (12). For ease of presentation, however, we have chosen commonly used arbitrary cutpoints.

Results

Prevalence of coronary heart disease. The prevalence of coronary heart disease, as defined by ECG, and the prevalence of two classes of chest pain, as determined by standard questionnaire, are presented in table 1. With the low prevalence rates observed, especially in Japan, the confidence intervals around the age-specific rates are wide relative to the magnitude of the rate. We have therefore summarized these as age-adjusted prevalence rates. Age-adjustments were performed by the indirect method using the three populations pooled as the standard from which the standard age-specific rates were derived. There is no difference in prevalence

Table 1

Prevalence of coronary heart disease as determined by ECG and standard questionnaire for Japanese males by geographic location

Observational base and diagnosis	Age-adjusted prevalence/1000		
	Japan	Hawaii	California
ECG			
Definite CHD*	5.3	5.2	10.8
Definite and possible CHD†	25.4	34.7	44.6
Questionnaire			
Angina pectoris‡	11.2	14.3	25.3
Possible infarction‡	7.3	13.2	31.4
(No. of men)§	(2141)	(8003)	(1834)

* Major Q/QS abnormalities: Minnesota Codes 1-1-1 through 1-1-7.

† Definite and possible CHD = major and minor Q/QS abnormalities: Minnesota Codes 1-1-1 through 1-3-6.

‡ Cardiovascular questionnaire (Rose and Blackburn, 1968).

§ The numbers of men in each of the tables vary due to differences in the numbers of missing values.

of definite CHD between Japan and Hawaii, but the California Japanese have more than twice the rate of the other two cohorts. When the criteria for CHD are broadened to include lesser Q/QS abnormalities, i.e., definite and possible CHD, a Japan-Hawaii-California gradient of increasing prevalence is seen.

Angina pectoris and possible myocardial infarction are diagnosed by questionnaire. Both of these show the same Japan-Hawaii-California gradient in prevalence and, as with CHD by electrocardiogram, the differences between California and Hawaii are greater than the Japan-Hawaii differences.

Doubt may be raised about the use, in linguistically different populations, of a questionnaire which was developed in English and only subsequently translated into Japanese. It has been shown that the cultural background of the respondents and the mode of administration of the questionnaire can affect prevalence estimates (3). However, the fact that the prevalence estimates, based on questionnaire responses, of angina and, to a lesser extent, of possible myocardial infarction are parallel to prevalence numbers of CHD determined by electrocardiogram, suggests that the differences in prevalence are real and not simply a function of differential response to the questionnaire.

Prevalence of hypertension and hypertensive heart disease. Given the previously reported inverse relationship between stroke and cardiovascular disease mortality among the three Japanese populations, the prevalence of hypertension in the three groups is of considerable interest (table 2). California Japanese have a higher prevalence of definite hypertension and higher mean blood pressures than the other cohorts and, with the exception of the oldest and the youngest age groups, the Japan cohort has a higher prevalence of hypertension than is seen in Hawaii. The detailed blood pressure distributions are reported separately by Winkelstein et al. (8).

The prevalence of hypertensive heart disease and of left ventricular hypertrophy (LVH) is presented in table 3. Hypertensive heart disease is defined as a combination of hypertension and left ventricular hypertrophy on ECG. Despite the lower prevalence of hypertension in Japan, a higher prevalence of hypertensive heart disease is observed in Japan than in California. This suggests that the occurrence of LVH as defined by ECG occurs more frequently in Japan than in the other two cohorts, regardless of blood pressure level. This is confirmed in table 3.

Prevalence of biochemical abnormalities. The distributions of the biochemical variables in the three populations by age are presented in a companion paper (9). Here attention is confined to the means and the proportions of individuals whose values for these variables lie above arbitrarily defined cutpoints.

The prevalence of hypercholesterolemia (serum cholesterol $\geq$ 260 mg/100 ml) and mean serum cholesterols are shown in table 4. There is a Japan-Hawaii-California gradient of increasing prevalence of elevated serum cholesterol and of increasing mean serum cholesterols. The lower cholesterol levels in the oldest group might in part be the result of the type of sample usually represented in a cross-sectional examination; the oldest, sickest group being underrepresented.

The comparison of serum triglyceride levels is complicated by the fact that the subjects in the study were non-fasting. Results must therefore be interpreted with caution and the use of conventional cutpoints becomes questionable. For this reason, the 80th percentile for the pooled data from all three sites was selected as the criterion of elevation, and the proportion of individuals in each age-area group falling above that arbitrary cutpoint (280 mg/100 ml) is compared (table 5). There is no clear difference between Hawaii and California, but both the American cohorts show a very much higher prevalence of elevated serum

TABLE 2

Prevalence of hypertension and mean blood pressure for Japanese males by age and geographic location*

Age	Mean blood pressure and prevalence of hypertension (per 1000)	Japan	Hawaii	California
45–49	Hypertensives/1000	139.5	142.5	234.8
	Mean systolic (mm Hg)	125.7	128.3	132.5
	Mean diastolic	80.6	81.8	87.5
	(No. of men)	(294)	(1832)	(707)
50–54	Hypertensives/1000	194.6	183.3	286.8
	Mean systolic	130.4	131.8	136.3
	Mean diastolic	82.4	82.2	88.6
	(No. of men)	(442)	(2788)	(509)
55–59	Hypertensives/1000	255.0	199.1	263.6
	Mean systolic	136.0	134.2	141.7
	Mean diastolic	84.8	82.6	89.4
	(No. of men)	(451)	(1592)	(264)
60–64	Hypertensives/1000	280.6	247.9	384.2
	Mean systolic	140.0	138.4	143.4
	Mean diastolic	83.1	82.0	89.0
	(No. of men)	(506)	(1335)	(164)
65–69	Hypertensives/1000	318.0	352.8	423.8
	Mean systolic	143.4	141.2	147.3
	Mean diastolic	83.0	81.1	89.3
	(No. of men)	(434)	(451)	(151)
Age-adjusted rate of hypertensives/1000		223.7	194.4	315.8
(No. of men)		(2127)	(7998)	(1795)

* Hypertension = systolic blood pressure ≥160 mm Hg and/or diastolic blood pressure ≥95 mm Hg.

TABLE 3

Prevalence of hypertensive heart disease and left ventricular hypertrophy for Japanese males by geographic location

Diagnosis	Age-adjusted prevalence/1000		
	Japan	Hawaii	California
Hypertensive heart disease*	9.3	1.4	4.6
Left ventricular hypertrophy†	16.4	5.7	6.1
(No. of men)	(2127)	(7998)	(1795)

* Definite hypertension (systolic ≥160 mm Hg or diastolic ≥95 mm Hg) plus left ventricular hypertrophy on ECG.

† Left ventricular hypertrophy = Minnesota codes 3-1 plus 4-1, 4-2 or 4-3 plus 5-1, 5-2 or 5-3.

triglyceride than the Japanese cohort. The mean serum triglycerides, in general, show a Japan-Hawaii-California gradient.

One hour post-load serum glucose, rather than blood glucose, was used to assess the prevalence of hyperglycemia. The glucose levels, shown in table 6, are therefore 30–35 mg/100 ml higher than the corresponding blood glucose figures would have been (14). Various biochemical criteria have been used in other studies to assess diabetes and these vary greatly. Whichever criteria are used, comparatively high cutoff points will result in few false positives and many false negatives, while the reverse will be true if the cutoff points are comparatively low. Here, a cutoff point of 200 mg/100 ml was used and the resulting prevalence figures are referred to as hyperglycemia rather than diabetes. It may be seen that the frequency of hyperglycemia is approximately equal in Hawaii and California, but both the American

TABLE 4

Prevalence of hypercholesterolemia and mean serum cholesterol for Japanese males by age and geographic location*

Age	Serum cholesterol	Japan	Hawaii	California
45–49	≥260 mg/100 ml (rate/1000)	27.9	131.4	138.9
	Mean serum cholesterol (mg/100 ml)	179.8	219.4	223.4
	(No. of men)	(287)	(1819)	(720)
50–54	≥260 mg/100 ml (rate/1000)	33.9	135.8	198.4
	Mean serum cholesterol (mg/100 ml)	182.5	219.4	228.2
	(No. of men)	(442)	(2783)	(514)
55–59	≥260 mg/100 ml (rate/1000)	30.6	132.7	161.0
	Mean serum cholesterol (mg/100 ml)	181.5	218.7	226.8
	(No. of men)	(457)	(1582)	(267)
60–64	≥260 mg/100 ml (rate/1000)	27.1	127.1	160.5
	Mean serum cholesterol (mg/100 ml)	182.2	216.7	223.6
	(No. of men)	(517)	(1330)	(162)
65–69	≥260 mg/100 ml (rate/1000)	27.6	73.8	189.5
	Mean serum cholesterol (mg/100 ml)	180.9	211.1	224.0
	(No. of men)	(435)	(447)	(153)
Age-adjusted prevalence/1000, serum cholesterol ≥260 mg/100 ml		31.6	124.0	162.5
(No. of men)		(2138)	(7961)	(1816)

* Serum cholesterol ≥260 mg/100 ml.

cohorts show a greater frequency than Japan.

The California figures probably represent an underestimate of the true prevalence of hyperglycemia, as subjects who reported that they had ever been told by a doctor that they had diabetes were not given an oral glucose load. Hence, a comparison of data based on the presence of either an elevated serum glucose and/or a positive history of diabetes is presented in table 6. This raises the prevalence estimates in all three geographic locations, but produces little change in the differences between them.

The relationship of blood pressure and serum cholesterol to CHD. A higher prevalence of electrocardiographic and symptomatic evidence of CHD has been observed in California. In general, there is a Japan < Hawaii < California gradient, with relatively smaller differences between Japan and Hawaii than between Hawaii and California. It is of interest to note that the frequency of elevated cholesterol levels in the three areas does not precisely parallel the CHD prevalence. For cholesterol elevation there are substantial differences between Japan and the two American cohorts, and smaller differences between Hawaii and California.

It is also surprising that the distribution of hypertension did not parallel the CHD distribution. For hypertension, Japan has prevalence levels intermediate between the lower levels in Hawaii and the higher levels in California.

A closer study of these relationships is presented in figures 1 and 2. For any given level of blood pressure (figure 1), the Japan-Hawaii-California gradient in CHD prevalence persists. Given the differences in blood pressure distributions between the cohorts, it is possible that these broad blood pressure groupings do not satisfactorily "control" for differences in blood pres-

TABLE 5

Prevalence of hypertriglyceridemia and mean serum triglyceride for Japanese males by age and geographic location*

Age	Serum triglyceride	Japan	Hawaii	California
45-49	≥280 mg/100 ml (rate/1000)	79.5	272.1	278.4
	Mean serum triglyceride (mg/100 ml)	149.1	235.8	241.7
	(No. of men)	(264)	(1742)	(722)
50-54	≥280 mg/100 ml (rate/1000)	64.5	278.8	269.4
	Mean serum triglyceride (mg/100 ml)	142.7	247.7	250.2
	(No. of men)	(372)	(2679)	(516)
55-59	≥280 mg/100 ml (rate/1000)	62.0	242.9	251.9
	Mean serum triglyceride (mg/100 ml)	140.7	225.6	237.3
	(No. of men)	(371)	(1523)	(270)
60-64	≥280 mg/100 ml (rate/1000)	38.4	180.5	262.2
	Mean serum triglyceride (mg/100 ml)	125.8	200.3	231.3
	(No. of men)	(443)	(1280)	(164)
65-69	≥280 mg/100 ml (rate/1000)	41.1	193.5	187.5
	Mean serum triglyceride (mg/100 ml)	123.6	198.6	220.7
	(No. of men)	(365)	(434)	(153)
Age-adjusted prevalence/1000, serum triglyceride ≥280 mg/100 ml		61.4	245.5	251.9
(No. of men)		(1815)	(7658)	(1825)

* Serum triglyceride ≥280 mg/100 ml.

TABLE 6

Prevalence of hyperglycemia and history of diabetes for Japanese males by age and geographic location*

Age	Prevalence of hyperglycemia/1000			Hyperglycemia and/or history of diabetes (prevalence/1000)		
	Japan†	Hawaii	California	Japan	Hawaii‡	California
45-49	72.6	141.4	164.8	153.2	172.1	206.7
50-54	133.0	179.8	160.8	183.5	220.7	225.5
55-59	91.7	220.7	217.2	154.2	270.5	280.9
60-64	153.3	259.8	186.3	230.0	316.8	285.7
65-69	146.7	319.2	264.9	223.3	361.6	351.0
Age-adjusted rate	113.1	201.6	192.2	175.0	244.7	256.5
(No. of men)	(1195)	(7977)	(1805)	(1195)	(7911)	(1805)

* Serum glucose ≥200 mg/100 ml one hour after 50 gm glucose load. No glucose load was given to diabetics in California, but they had a serum glucose measured and included in the tabulations.

† In Japan, subjects who were examined in the evening did not have a post-load glucose determination.

‡ For 66 subjects in Hawaii, the history of diabetes was unknown.

sure. To assess this possibility the mean blood pressures within each hypertension category were compared between cohorts. The differences in means were small for both systolic and diastolic blood pressures, suggesting that differences in blood pressure alone do not account for the differences in CHD.

Figure 2 shows that the Japan-Hawaii-California CHD gradient persists at each level of serum cholesterol. There are too few subjects in Japan with elevated serum

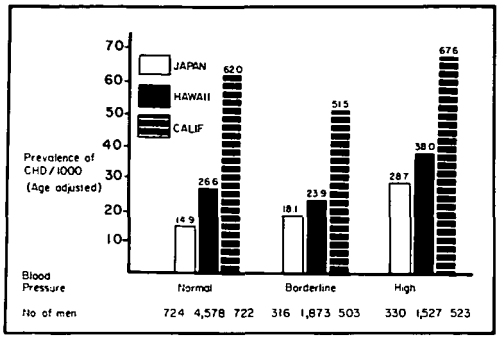

FIGURE 1: Prevalence of "all CHD" (age-adjusted rate/1000) at categorical levels of blood pressure for Japanese males by geographic location. CHD = Minnesota code 1:1 on ECG or angina or myocardial infarction determined by questionnaire. Normal, borderline, high—WHO criteria.

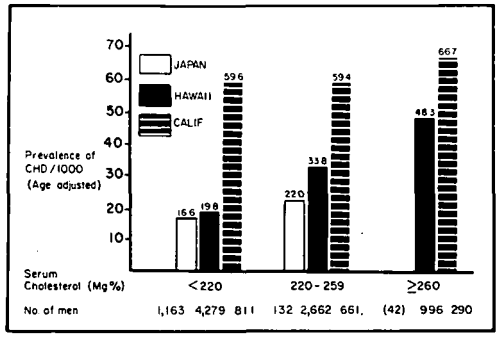

FIGURE 2: Prevalence of "all CHD" (age-adjusted rate/1000) at categorical levels of serum cholesterol for Japanese males by geographic location. CHD = Minnesota code 1:1 on ECG or angina or myocardial infarction determined by questionnaire.

cholesterol to compute CHD prevalence numbers. Once again the possibility was assessed that differences between the cohorts in the underlying distributions of serum cholesterol are inadequately taken care of by using these broad serum cholesterol groupings. There was a 20 mg/100 ml difference in mean serum cholesterol between Japan and the other two cohorts in the $\leq$ 220 mg/100 ml category. This is consistent with the possibility that the lower CHD prevalence in Japan in this low cholesterol category is a result of lower serum cholesterol levels in Japan. However, the mean serum cholesterols by location, within each of the two higher cholesterol groupings were very close. This suggests that the cholesterol groupings "220–259" and "$\geq$260 mg/100 ml" do control for serum cholesterol differences. The fact that within these categories the Californian Japanese have a higher CHD prevalence indicates that differences in serum cholesterol do not completely account for the Japan-Hawaii-California differences in CHD prevalence.

The Mantel-Haenszel procedure (36) was used to examine these CHD prevalence data, controlling simultaneously for age, blood pressure and serum cholesterol. Controlling for these three variables, and taking the Japan CHD rate as 1, the relative risk (strictly, relative prevalence) in Hawaii is 1.6 and in California is 2.1.

Smoking and CHD. Figure 3 presents the prevalence of CHD, controlling for current smoking pattern. Within each smoking category, the Japan-Hawaii-California CHD gradient persists. For Japan and Hawaii, the high prevalence in the ex-smoker category is likely the result of individuals changing their smoking habits consequent upon developing the disease. It should be pointed out that although smoking is very common in Japan, fewer smokers in Japan are "heavy" smokers as compared with Hawaii and California (7). Hence the apparent difference in CHD prevalence between California and Japan among smokers may be overstated.

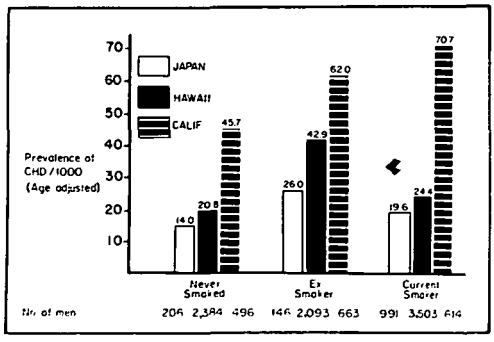

FIGURE 3: Prevalence of CHD in Japan, Hawaii, and California controlling for smoking. CHD = Minnesota code 1:1 on ECG or angina or myocardial infarction determined by questionnaire.

It will be noted that for these last analyses a combined category of "all CHD" was used to increase the number of cases. There are many suggestions that angina pectoris and other manifestations of coronary heart disease may be epidemiologically distinct. However, since the patterns of variation in angina and in prevalence of CHD (defined by ECG) between geographic sites are quite similar in the present study, it seems reasonable to combine them. In California, where the prevalence of CHD was highest, analyses were done separately on the symptom categories and ECG categories. These separate categories showed essentially the same relationships to serum cholesterol, blood pressure and smoking as did the combined category of "all CHD".

Discussion

The findings indicate that Japanese living in California have a higher prevalence of all manifestations of CHD than do Japanese living in Hawaii or Japan and that Japanese in Hawaii, for three of the four measures used, have higher rates than Japanese in Japan. Before these findings can be accepted, the possibility that they may be due to biases inherent in cross-sectional examination or to artifacts of diagnostic methods should be examined.

Clearly, if a disorder has equal incidence in two populations, the prevalence rates should be proportional to the survival rates, other things being equal. It is unlikely that lower survival rates are responsible for the lower prevalence rates in Japan and Hawaii since case-fatality rates for Japanese under study in Hiroshima and Nagasaki are reported to be quite low (15), and since this proposed high case-fatality rate is not consistent with the gradient in CHD mortality reported by Gordon (2, 3) and largely confirmed by our own mortality surveillance (1). It is possible that non-response due to factors other than death may have biased the prevalence estimates. For this factor to have produced the gradient of prevalence rates observed, non-respondents in California would have to have been at much lower risk of CHD than non-respondents in Hawaii and Japan. Based on our mortality surveillance studies, there is no evidence that this is the case. In addition it may be argued that the lower response rates to examination in Hawaii and California as compared with Japan may have biased the prevalence estimates; but as non-respondents may in general have poorer health than respondents (37), the bias would be in the direction of lowering the rates in Hawaii and California and could not account for the observed prevalence differences.

The possibility remains that these differences in prevalence represent variation in diagnostic methods. This is especially likely with a questionnaire used for international comparisons, with the difficulties encountered in translation and different modes of administration (13). However, all ECG's were centrally coded in a uniform fashion. The fact that the prevalence estimates from the questionnaire generally show geographic variations similar to the trends in prevalence determined by ECG, and that both these prevalence estimates show a gradient similar to that predicted by Gordon's mortality report, is support for the validity of the observed gradient in CHD.

It should be further borne in mind that when ECG items are compared this is not the same as comparing the degree of atheroma in the coronary arteries and it is possible that the relationship between various ECG items and "true" coronary heart disease may differ slightly in these Japanese populations from the relationship that is assumed to exist in Caucasian populations. This is currently under investigation in the present study.

Hypertensive heart disease is far more common in Japan than in the American cohorts, a finding which would not have been predicted from the blood pressure distributions. This high prevalence of left ventricular hypertrophy, which is more a

function of high voltage of the QRS complex than of ST-T wave changes, has been found in other studies in Japan where the possibility was raised that the high voltage seen on ECG was a function of thin chest wall in the Japanese rather than of increased myocardial bulk (16, 17). However, high voltage cannot be considered to be totally physiological as Japanese men and women who display this finding have a substantially increased risk of subsequent CHD mortality (15). This increased risk of CHD mortality among subjects with left ventricular hypertrophy is in accordance with findings from white men and women in Framingham (18). The apparent discordance between prevalence of hypertensive heart disease and prevalence of hypertension between Japan and California may also be partly a function of the circumstances surrounding the measurement of blood pressure. The study sample from Japan has been under observation through three cycles of examinations whereas the data from the Hawaii and California samples are from a first cycle of clinical examinations. The experience in Hiroshima and Nagasaki, as well as in Framingham (19), has been that blood pressure recordings were higher in the first cycle than in subsequent cycles and it is possible therefore that the blood pressures of the American cohorts are spuriously high relative to those in Japan. This possibility could explain only part of the differences in blood pressure distributions observed and certainly does not account for the Hawaii-California differences.

Diabetes is relatively common in Japan (20, 21). In the present study the prevalence of hyperglycemia is high, especially in Hawaii and California. Comparisons with other US populations are hindered by differences in methods used. However, when allowances are made for these differences and the problems inherent in comparisons of serum glucose with blood glucose, then it would appear that the prevalence of hyperglycemia in the (predominantly Caucasian) population sample studied in the US Health Examination Survey is intermediate between the prevalence in Japan and the prevalence in the two Japanese-American cohorts (22). Given this high prevalence of hyperglycemia, it will be of considerable interest to directly examine the relationship between diagnosed diabetes and CHD in Japanese-Americans, especially as it has been reported that CHD is a comparatively rare complication of diabetes in Japan (21).

The levels of serum cholesterol in Hawaii and California, although higher than in Japan, are lower than those reported in the US Health Examination Survey's population sample (23). The very low levels of serum cholesterol in Japan, where the prevalence of CHD is very low, are consistent with the established role of hypercholesterolemia as a risk factor. However, at equivalent levels of serum cholesterol, California Japanese still have higher CHD prevalence. Similarly, at equivalent levels of blood pressure, the high California prevalence persists. To make definite statements about relationship of risk factors to disease from prevalence figures would be inappropriate, but the cautious interpretation from these simple prevalence comparisons is that other factors interact with blood pressure and cholesterol in the etiology of CHD.

Certainly the role of blood pressure in the etiology of stroke and heart disease is far from simple. It is known in the United States that blacks have higher blood pressures than whites (24–26) but have lower prevalence and incidence of heart disease than do white Americans and higher prevalence and incidence of stroke (27, 28). In the present study, the Hawaii Japanese, whose reported rates of stroke mortality and CHD mortality are intermediate between Japan and California, have the lowest prevalence of hypertension. The prevalence of hypertension is high in both Japan and California, but is comparable to previ-

ous studies on Japanese men (17, 29, 30). The reason why high blood pressure should contribute to CHD in the California Japanese and to stroke in the Japanese in the home country is not clear. It may be, as has been suggested, that high blood pressure predisposes to CHD only in the presence of a particular set of factors, including elevated serum cholesterol, and that high blood pressure in the presence of other factors predisposes to stroke (31). The elucidation of these relationships must await the accumulation of precise incidence data.

As with any cross-sectional study, these prevalence data only relate current risk factor levels to existence of CHD. This may be a problem with smoking, for example, as current smoking habits do not reflect lifetime exposure. However, as the higher CHD prevalence in California was seen in each smoking category, it seems unlikely that these CHD differences are all due to differences in smoking.

If incidence data confirm that cholesterol, blood pressure and smoking differences do not completely explain these gradients in cardiovascular disease, then we must look elsewhere for explanations. These gradients may be a result of genetic factors, i.e., the migrant Japanese may be genetically different from those resident in Japan in ways that make them more susceptible to heart disease and less susceptible to stroke. This seems unlikely since such genetic differences would have to explain differences between Japanese in Hawaii and California as well as between migrants and home populations. It is more likely, then, that environmental factors play a role in these and other chronic diseases. Other migrant studies of CHD, chronic respiratory disease (32, 33) and many cancers (34, 35) have suggested that migrants commonly experience rates of disease intermediate between the levels in their home country and the levels in the adopted country, and the results of the present study are in accordance with that pattern.

The Japanese in America lead very different lives from the Japanese in the home country. Among other things, they eat different diets, they have different patterns of occupation and they live in a different social and cultural milieu. The relationship between the changes in these factors and CHD, both within and between study cohorts, will be the subject of later reports.

References

1. Worth RM, Rhoads G, Kagan A, et al: Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii, and California: Mortality. Am J Epidemiol 102:481–490, 1975
2. Gordon T: Mortality experience among the Japanese in the United States, Hawaii and Japan. Public Health Rep 72:543–553, 1957
3. Gordon T: Further mortality experience among Japanese Americans. Public Health Rep 82:973–984, 1967
4. Belsky JL, Kagan A, Syme SL: Epidemiologic Studies of Coronary Heart Disease and Stroke in Japanese Men Living in Japan, Hawaii and California. Research Plan. Atomic Bomb Casualty Commission Technical Report 12-71, 1971. Microfiched and stored at: Bay Microfilm, Inc, 737 Loma Verde Ave, Palo Alto, CA
5. Tillotson JL, Kato H, Nichaman MZ, et al: Epidemiology of coronary heart disease and stroke in Japanese men living in Japan, Hawaii, and California: Methodology for comparison of diet. Am J Clin Nutr 26:177–184, 1973
6. Kato H, Tillotson J, Nichaman M, et al: Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: Serum lipids and diet. Am J Epidemiol 97:372–385, 1973
7. Kagan A, Harris BR, Winkelstein W, et al: Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: Demographic, physical, dietary, and biochemical characteristics. J Chronic Dis 27:345–364, 1974
8. Winkelstein W, Kagan A, Kato H, et al: Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: Blood pressure distributions. Am J Epidemiol 102:502–513, 1975
9. Nichaman MZ, Hamilton HB, Kagan A, et al: Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: Distribution of biochemical risk factors. Am J Epidemiol 102:491–501, 1975

10. Syme SL, Marmot MG, Kagan A, et al: Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California: Introduction. Am J Epidemiol 102:477-480, 1975
11. Rose GA, Blackburn H: Cardiovascular Survey Methods. Monogr Ser No 56, Geneva, WHO, 1968
12. Report of Inter-Society Commission for Heart Disease Resources (J. Stamler, A. Lilienfeld, chairmen). Primary prevention of the atherosclerotic diseases. Circulation 42:A55-A95, 1970
13. Marmot MG, Syme SL, Kagan A, et al: The use of a standard questionnaire to diagnose angina pectoris in international studies. Presented at the sixth annual meeting of Society for Epidemiologic Research, Winnipeg, Canada, June 21-23, 1973
14. Committee on Statistics of the American Diabetes Association: Standardization of the oral glucose tolerance test. Diabetes 18:299-310, 1969
15. Johnson KG, Yano K, Kato H: Coronary heart disease in Hiroshima. Report of a six-year period of surveillance, 1958-1964. Am J Public Health 58:1355-67, 1968
16. Takahashi N, Kato K, Suzuki K, et al: Epidemiologic studies on hypertension and coronary heart disease in a Japanese rural population. III. Electrocardiographic findings in Chiyoda. Jap Heart J 5:37-48, 1964
17. Katsuki S, Hirota Y, Akazome T, et al: Epidemiological studies on cerebrovascular diseases in Hisayama, Kyushu Island, Japan. Part I. With particular reference to cardiovascular status. Jap Heart J 5:12-36, 1964
18. Kannel WB, Gordon T, Castelli WP, et al: Electrocardiographic left ventricular hypertrophy and risk of coronary heart disease. Ann Intern Med 72:813-822, 1970
19. Kagan A, Gordon T, Kannel WB, et al: Blood pressure and its relation to coronary heart disease in the Framingham study. Hypertension. Vol 7: Drug Action, Epidemiology and Hemodynamics. Proceedings of the Council for High Blood Pressure Research, American Heart Association. New York, American Heart Association, 53-81, 1959
20. Rudnick PA, Anderson PS: Diabetes mellitus in Hiroshima, Japan. Diabetes 11:533-545, 1962
21. Blackard WG, Omori Y, Freedman LR: The epidemiology of diabetes mellitus in Japan. J Chronic Dis 18:415-427, 1965
22. US Department of Health, Education, and Welfare, National Center for Health Statistics: Glucose Tolerance of Adults. United States 1960-1962. Vital and Health Statistics (PHS Publication 1000, Series 11, No 2), Washington DC, GPO, 1964
23. US Department of Health, Education, and Welfare, National Center for Health Statistics: Serum Cholesterol Levels of Adults. United States 1960-1962. Vital and Health Statistics (PHS Publication 1000, Series 11, No 22), Washington DC, GPO, 1967
24. McDonough JR, Garrison GE, Hames CG: Blood pressure and hypertensive disease among Negroes and whites: A study in Evans County, Georgia. Ann Intern Med 61:208-228, 1964
25. Borhani NO, Borkman TS: Alameda County Blood Pressure Study. State of California, Department of Public Health, June 1968
26. US Department of Health, Education, and Welfare, National Center for Health Statistics: Hypertension and Hypertensive Heart Disease in Adults. United States 1960-1962. Vital and Health Statistics (PHS Publication 1000, Series 11, No 13), Washington DC, GPO, 1966
27. Cassel JC, Heyden S, Bartel AG, et al: Incidence of coronary heart disease by ethnic group, social class, and sex. Arch Intern Med 128:901-906, 1971
28. Heyman A, Karp HR, Heyden S, et al: Cerebrovascular disease in the biracial population of Evans County, Georgia. Arch Intern Med 128:949-955, 1971
29. Suzuki K, Watanabe H, Takahashi N, et al: Epidemiologic studies on hypertension and coronary heart disease in a Japanese rural population. I. A study of blood pressure in Chiyoda. Jap Heart J 3:544-554, 1962
30. Imai K, Takikawa M, Maeda Y, et al: National survey of blood pressure and heart diseases in Japan. Public Health Rep 80:321-329, 1965
31. Switzer S: Hypertension and ischemic heart disease in Hiroshima, Japan. Circulation 28:368-380, 1963
32. Stamler J, Kjelsberg M, Hall Y, et al: Epidemiologic studies on cardiovascular-renal diseases: III. Analysis of mortality by age-sex-nationality. J Chronic Dis 12:464-475, 1960
33. Reid DD: Studies of disease among migrants and native populations in Great Britain, Norway, and the United States. I. Background and design. *In:* Epidemiological Study of Cancer and Other Chronic Diseases. Edited by W. Haenszel. Natl Cancer Inst Monogr 19:287-299, 1966
34. Haenszel W: Cancer mortality among the foreign-born in the United States. J Natl Cancer Inst 26:37-132, 1961
35. Haenszel W, Kurihara M: Studies of Japanese migrants. I. Mortality from cancer and other diseases among Japanese in the United States. J Natl Cancer Inst 40:43-68, 1968
36. Mantel, Haenszel W: Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst 22:719-748, 1959
37. Doll R, Hill AB: Lung cancer and other causes of death in relation to smoking. Br Med J 2:1070-1081, 1956