

THE ODYSSEY - SUMMER 1963

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Itsumi - This is the original report my
father prepared for NIH after
he went to Hawaii + Japan.
I thought you could practice
your English + learn some
history about the project at
the same time.

Lorann

Dr. William Zukel and I travelled from San Francisco to Honolulu on June 12. Dr. Abraham Kagan had preceded us by a week or so. We spent a couple of days discussing matters with Joe Stokes and the crew at Queen's Hospital and with Dick Lee and Bob Worth at the University. Then Bill and Abe returned to the mainland, while I remained collecting information relevant to the plans for a study of cardiovascular disease of Japanese (see Appendix for a report of this activity). During this time I met Dr. Richard Park, who was scheduled to enter our school in September, and spent a pleasant time with Dr. Carl Peterson. Carl is still P.M.O. for the Navy and most recently had been doing a very nice investigation of an outbreak of polio on Kwajalein.

Hawaii is still much as advertised. Some of the entrepreneurs regret the loss of the carriage trade as the islands become more accessible to less favored segments of our population. I did not get to the outer islands this trip and spent the whole time in a hotel on the strip. Waikiki has been defined as "Miami Beach with greasy music." And it does have the air of a sunburned honky-tonk.

I arrived in Tokyo the evening of Thursday, June 27, and was met at Haneda Airport by Dr. Kenzaburo Tsuchiya, Associate Professor of Preventive Medicine at Keio University. The next day Dr. Tsuchiya took me to Keio University and that afternoon I presented a lecture on cardiovascular disease epidemiology. This was attended by Dr. Harashima, Professor of Preventive Medicine; Dr. Toyama, Professor of Preventive Medicine; Dr. Tsuchiya; Dr. Sakurai, Dozent in Preventive Medicine; and other members of that department; Dr. Matsuda of the Japanese R.I.H.; Dr. Sasaki of ^HKirosaki University; and representatives of the Department of Internal Medicine of Keio University. The University is located near

the Meiji Shrine, in the area of the 1964 Olympic Games where the construction activity is frenzied. The Medical School was almost totally destroyed by the fire raids of World War II but has been rebuilt completely so the laboratories look as though they were only a few hundred years old.

Trains in Japan are crowded in summer and I was unable to get a reservation for Hiroshima until Monday, July 1. While in Tokyo, I stayed at the Imperial Hotel. The old building is now a somewhat venerable relic of Frank Lloyd Wright's youth and is a very interesting and unusual structure. Organic it may be, but it is certainly ornate. Prices are moderate by U. S. standards, although the dining rooms' rates are a bit excessive. Most of the dining rooms serve western-style foods, but somehow never quite like mother used to make, unless perhaps mother came from Honshu. There is a sukiyaki-tempura palace there, but I was advised that Japanese sneer at their best efforts. (Incidentally, the finest meal I had in Japan was a superb tempura lunch—unfortunately the location of the restaurant is a complete mystery to me.) The hotel is very conveniently located in the Maranouchi District, two long blocks and a thousand temptations away from the Ginza.

The trip to Hiroshima was a delight. It took almost 12 hours, passed through the major cities of Japan, and covered a vast variety of landscape. The train was Tsubame #1, a limited express and luxurious. I think anyone visiting Japan should plan a train excursion somewhere. And I advise him to be an ugly American and take the parlor car. This adds three or four dollars to a very modest fare and where else can you feel like a millionaire for half a day for four dollars?

I arrived in Hiroshima on the evening of July 1 and spent the morning of July 2 with Dr. George Darling. The discussion related to Dr. Darling's judgment of the stability of the ABCC for future operations and something of the policy under which the research program is presently conducted.

Last year the future of ABCC was jeopardized for a time by a strike of the technical and service workers. To a considerable degree, the strike was used for political purposes to discredit the motives of the United States' interests in Japan. Dr. Darling's position was that unless the Japanese people locally and the Japanese government were enthusiastically in favor of continuing the ABCC's work, the effectiveness of the program was so seriously compromised that there would be little use in continuing. Ultimately the situation was resolved acceptably and amicable relations reestablished. Although difficulties could recur, the maintenance of ABCC seems assured for some years to come. Initiating a study designed to continue for five years or so does not seem too great a gamble.

Research activities at ABCC are now subject to review not only by the American representatives and agencies concerned but also by representatives of the Japanese N.I.H. Although this complicates the administrative aspects of clearing a new project, there is no reason to believe that a well-conceived research activity should be hampered by this requirement.

Control of research conducted within the ABCC must reside with personnel of the ABCC. This is entirely reasonable, with one exception. The change over of American professional personnel is quite rapid and it is manifestly impossible to assure that a person as yet unknown who may

enter the unit at some time in the future will have an especial interest or competence in a project started long before his arrival. Although the ABCC administration may be committed to a particular protocol, the quality of work on a project outside the main stream of ABCC's mission can only be assured by the assignment of additional personnel with primary responsibility for that project.

At the present, ABCC policy permits conduct of a study in collaboration with activities elsewhere by mutual agreement to adhere to a common protocol. In effect, this is a Federal union of two autonomous states with surrender of autonomy only within the limits of the agreement. Presumably, this pattern entails the participation only of ABCC personnel and the agreement may be abrogated by unilateral action. The assignment of personnel from another agency to conduct the study is considered acceptable. The acceptability of this may be related to the extent to which those personnel are identified as ABCC staff, rather than staff of the other agency. Obviously the success of this would be importantly affected by the personalities of the persons concerned.

I believe that the establishment of a separate unit located at ABCC would not be acceptable, nor, if acceptable, feasible.

Since the primary mission of ABCC is to study radiation effects, a study of cardiovascular disease with quite a different orientation would, I believe, require financing to cover those added expenses such a study would entail. Salaries of professional personnel might be covered directly by the N.R.I., but all other expenses probably would have to be handled by contract between ABCC and N.H.I.

Presently, one person, a Japanese physician Dr. Ishizumi, is considered to be a full-fledged epidemiologist, although the special

interests of Dr. L. Friedman, Dr. Phair, and Dr. Morrow are epidemiologically oriented. Dr. Yano, on his return, will undoubtedly bring strong epidemiologic interests. Generally, however, Japanese physicians have little interest in or appreciation for epidemiology. My friends at Keio University told me that there is really no place in Japan where a person may secure adequate training in epidemiology. Thus, I believe an essential part of any project of the kind proposed must be the assignment of a thoroughly competent American epidemiologist to ABCC.

The afternoon of July 2 was spent in discussion with Dr. Lawrence Friedman, the Chief of Medicine. Dr. Friedman is a young, capable internist from Yale who is thoroughly enjoying his time at ABCC and is extending himself to make this a profitable time professionally. He is impressed by the great value of this population for the study of a variety of diseases. In all ways I found him cooperative, enthusiastically so, and a pleasure to work with.

Wednesday, July 3, Dr. Friedman was off to Kyoto and I spent the day with Drs. Phair and Morrow. These men are both from medical residencies at Yale and are assigned here via the Division of Radiological Health, BSS, USPHS. They are engaged in the regular work of the examination clinic and the medical ward, and, in addition, have initiated special projects using the data accumulated here.

Conversations have been in progress for several months between Dr. Friedman and Dr. ~~Robert~~ Kimura of Kurume University about the development of an epidemiologic study of cardiovascular disease in the ABCC population. Dr. Kimura has a long standing interest in these problems and has been associated with some of the operations of Dr. Ancel Keys, as well as pursuing independent studies. An assistant of Dr. Kimura's prepared a

massive protocol for such a study and this was submitted to Dr. Freedman for review. This constitutes an omnibus proposal to:

- (1) estimate the prevalence and incidence of CHD, CVA, HHD, and RHD in the ABCC population;
- (2) determine the effect of radiation exposure on the frequency of these diseases;
- (3) study a variety of associated factors relevant to the principal etiologic hypotheses for these diseases;
- (4) establish careful evaluation of the degree of arterial disease in persons coming to autopsy; and
- (5) correlate autopsy findings with clinical and epidemiologic data.

The hypotheses on which the studies are to be based have not been presented specifically, but the nature of the study design indicates quite clearly that the following are to be tested:

1. CHD results from a diet high in total calories and high in fat, probably in association with little physical activity.
2. HHD is importantly related to salt ingestion.
3. The association of CVD in Japanese with hypertension and with atherosclerosis is uncertain and is to be quantitated.
4. The causal factors in RHD are obscure and are to be explored broadly.

Much of the orientation of the study proposal can be deduced from the items on the tentative questionnaire. These include lifetime residence, lifetime occupation, sports, diet, smoking, alcohol consumption, and cardiac pain. Presumably this represents information to supplement a variety of data already being collected.

I do not know how to evaluate the protocol. The references are largely to Keys, certain Japanese workers, and the WHO recommendations for methods of measurement and diagnostic criteria. As presently constituted, the plan does not fit too well the idea of a comparative study between Japan and the United States. However, with relatively minor modifications, coordination could be achieved.

Much depends on the attitude Dr. Kimura may display toward a close collaborative effort, and especially whether he would react positively to the presence here of an American epidemiologist who would carry a major part of the responsibility (and authority) in the conduct of the study.

In the 1958-60 cycle of examinations, the sample size of persons eligible for examination was 13,026 (4,938 males and 8,088 females) of all ages. Of these, 9,814 were examined (88 per cent of these still reside in Hiroshima), divided into 3,554 males and 6,260 females.

Age group	All categories		Not exposed	
	Male	Female	Male	Female
20-29	527	848	111	193
30-	726	1,745	190	447
40-	619	1,202	154	280
50-	813	1,414	193	348
60-	649	758	170	188
70+	220	293	77	74
Totals	3,554	6,260	895	1,530

Data from the cardiovascular examinations done during this time have been studied by Dr. Shoichi and Dr. Katsuhiko Yano. The prevalence of a variety of cardiovascular diseases was determined, compared with Framingham data, and related to exposure to ionizing radiation and other variables. The findings have been presented in a series of reports and a summary paper has been submitted for publication.

The prevalence of hypertension and hypertensive heart disease increased with age and showed no especial differences between the sexes. The prevalence rates (age adjusted to the Hiroshima city population) were for males, 29 per cent hypertension and 5 per cent hypertensive heart disease, and for females, 25 per cent hypertension and 4 per cent hypertensive heart disease (including both definite and possible diagnostic categories).

ASHD prevalence per 1,000 was:

Age	Hiroshima		Framingham	
	Male	Female	Male	Female
30-	1	0	6	2
40-	3	2	9	10
50-	14	8	59	23
Total age adj.	6	3	22	11

Thus, although the rates were almost 4 x higher for Framingham, the age and sex differentials were very similar.

Mean systolic BP was 132 for males and 130 for females; diastolic was 83 for males and 82 for females; serum cholesterol was 155 for males and 163 for females. There was a definite increase with age for BP and

cholesterol, between ages 30 and 70. For serum cholesterol, the percentages of persons with extreme values were:

	≤ 180	≥ 200	≥ 220
Male	21	10	5
Female	29	14	6

Correlation coefficients

	Sys BP	Diast BP	Weight	Heart Size
Serum cholesterol				
Male	0.04	0.04	0.20	0.12
Female	0.09	0.10	0.18	0.08

Certainly, these are not impressive, although the higher correlations with weight may be important.

An estimate of relative risk of ASHD prevalence (Obs./Exp.) was completed for several characteristics. Generally, the risk increased with increase in systolic BP, diastolic BP, serum cholesterol (males only), weight, and heart size. For males, the relative risk for nondiabetics was 0.9 and for diabetics, 2.1. These ratios for serum cholesterol are especially interesting.

Cholesterol

	<160	160-199	200+
Male	0.7	1.2	1.9
Female	1.1	1.0	0.9

The differences are not significant for either sex.

No occupational differences of note were found, although there was a tendency for higher social levels of occupations to have higher serum cholesterol.

An additional relevant study currently in progress is an analysis of cerebral vascular disease as a cause of death. This work is being done by Dr. John Phair. The idea is to accumulate the death certificate data over a 12 year period from the population identified at the 1950 census. The death certificate diagnoses will be related to autopsy findings where possible, and for those persons included in the adult health study, further information is available and will be included in the study. Even preliminary results of this inquiry are not yet available, but Dr. Phair has gathered some interesting impressions.

1. Many of the deaths recorded as due to CVA are probably in error; the subject may have suffered a CVA some time in the past but that event would not be considered a proximal cause of death.

2. At autopsy, an appreciable proportion of the persons assigned to CVA show evidence of recent occlusive coronary artery disease.

3. A preponderance of the persons with CVA are found at autopsy to have thrombotic rather than hemorrhagic disease of the cerebral vessels.

These impressions are of very great significance in evaluating the differential patterns of cardiovascular disease between Japan and the United States.

Schroeder, H. A. Degenerative cardiovascular disease in the Orient. I. Atherosclerosis. J. Chr. Dis. 8:287-311 (Sept.) 1958.

Schroeder, H. A. Degenerative cardiovascular disease in the Orient. II. Hypertension. J. Chr. Dis. 8:312-333 (Sept.) 1958.

J. Chr. Dis. Oct., 1958. Neurologic Diseases. "Stroke Review"

From Hiroshima to Osaka, I was introduced to domestic Japanese air travel. The plane was a Fokker Friendship F27, which sounds like something with open cockpit and hostesses wearing goggles but is a high wing monoplane with turbojet engines. This was All Nippon Airlines--very Japanese--I never found a schedule in English. But with the careful guidance of innumerable clerks and other airlines' people, I was always placed aboard the proper plane at the proper time. Both ANA and Japan Airlines are proud of their F27's, Viscounts, and assorted pure jets; but there are many routes served by aging DC6's and aged DC3's.

Osaka is a bustling city of some 3,000,000 people, which is reputed to be virtually devoid of culture, devoted to the quest for money. This may be so, but Kyoto, about half an hour away, has enough culture for ten cities.

Kyoto is most interesting. It was the capital of Japan for about 1,000 years until the Tokugawa Shoguns moved the seat of power to Tokyo, and remained the Imperial residence for 200 years more until Meiji restored the Imperial line to power and set up shop in Tokyo. Thus shrines, temples, and royal villas have spawned and despite the inevitable toll of fire and other disaster, enough remain to satisfy the most ardent sightseer. Kyoto was spared by the U. S. Air Force during World War II because of the many national treasures (and small strategic importance).

Shopping, too, is especially delightful in Kyoto. There are many superb specialty shops for jewelry, brocade, Kyoto dolls, and paintings and wood-block prints, as well as the usual wares. All the same things can be purchased in Tokyo or Osaka but not in such picturesque surroundings.

Incidentally, the rain in Kyoto was torrential, so my plans were sharply curtailed. Rain is to be expected almost anywhere in Japan in

summer. Generally, it is wetter than the rain in Honolulu but not so wet as San Francisco's rain.

The Osaka visit was for the M.I.H. and Kyoto was for fun. In Osaka, I met Drs. Reader, Hollingshead, and Roberts and we made a project site visit for a proposed study of diabetes in Japanese. We were treated with much formality but with great hospitality. The hospitality becomes a little embarrassing because it is obviously expensive and we are supposed to be rendering impartial judgments. I think the only way to handle the situation is to submit graciously to the inevitable and assume that one's rectitude is so shining that it is unthinkable that it could be suborned by such actions. Anyway, that is what we did, somewhat to the discomfiture of our borrowed study section secretary.

Back to Hiroshima and back to work on July 12. More discussions with ABCC staff and then on July 16, a trip to Hakata (Fukuoka). (The difference between Hakata and Fukuoka is not clear to me but seems to be something like Manhattan and New York City.) There we met Dr. ~~Nabor~~ Kinura of Kurume University. Kurume University is one of the few private universities in Japan. It was established by a local tycoon, the head of the Bridgestone Tire Company. Apparently some years ago, this industrialist decided to memorialize himself in this way, pirated a faculty from other universities, and set up the shop.

Japanese universities are of three major kinds: (1) National, (2) Prefectural and City, and (3) Private. Among the medical schools there are about half a dozen that are considered to be the very best, all of them in National Universities (Tokyo, Nagoya, Osaka, Kyoto, and some other-- often Tokyo University is considered to be in a class by itself). In the second rank are some of the Prefectural, City, and private universities.

Everyone acknowledges, however, that very fine scholars may be found in any of the schools.

Dr. Kimura has been engaged in population studies of CHD for some years, including some cooperative study with Dr. Ancel Keys some time ago. Currently he is maintaining surveillance over three villages on Kyushu, one a fishing village, and the other two rice growing. He had previously indicated his interest in studies in ABCC and had proceeded to develop fairly well detailed plans toward this end. Negotiations have lagged in recent months; however; and it appeared that Dr. Kimura did not have the resources to proceed at this time. Because involvement of Japanese scientists is important to the future ABCC operations and because Dr. Kimura clearly had a prior claim established, we discussed the matter with him very frankly and presented three alternatives for him to choose:

- (1) Dr. Kimura to proceed with ABCC personnel to conduct a study.
- (2) Dr. Kimura to withdraw from future plans in ABCC.
- (3) Dr. Kimura to become a cooperating member of the tripartite study group (ABCC-NHI-Kimura) to proceed with plans for the study.

After some discussion, Dr. Kimura elected the third alternative, and the last impediment to the plans for Hiroshima was cleared away. *Daijoubu!*

I spent the night in Hakata and the next morning boarded another of those fine Japanese trains for Nagasaki.

Nagasaki harbor is a deep slash into the hills from the sea. The topography is such that when the A-bomb was dropped on the torpedo works at the head of the harbor, the main part of the city was protected by a hill mass and spared the general destruction that Hiroshima suffered. Perhaps for this reason and perhaps because Nagasaki was second choice,

the place is not such a focus for emotional protest as Hiroshima. During the Shogunate, a few Dutch traders were permitted to maintain a station on an island in the harbor, Japan's only contact with the outside world.

The ABC operation in Nagasaki is on a reduced scale, but is carried on in the same pattern as at Hiroshima. Dr. and Mrs. Leonard Sagan, from Mill Valley, were my host and hostess in Nagasaki. Along with the usual bonds of interest between Gaijin nesting in Japan, we shared reminiscences about the Bay Area. They live in a beautiful old house on the bluff overlooking the harbor, built by an Englishman very soon after Japan was opened to the Western world, at the beginning of the Meiji era about 100 years ago. The house is western style, but with the inevitable Japanese nuances that make a charming combination. The harbor below is extremely busy with coastal shipping and the Mitsubishi shipbuilding ways where the large oil tankers are made for shipping lines all over the world.

Nagasaki to Hakata by train, then the next morning (July 19) a plane to Tokyo and then to Sendai on Northern Honshu. Sendai was headquarters for the 11th Airborne Division during the occupation and I had heard many stories of it from my friends in the days in Korea, many of whom were stationed there. Sendai seemed very much a country village after the cities of the South. It seems less westernized and less preoccupied with industrial advancement. Also, it is the home of Tohoku University and on the 20th of July, Dr. Freedman and I met with Dr. Takahashi, the Professor of Preventive Medicine, and several members of his staff. Dr. Takahashi has been studying the geographic distribution of hypertension and cerebral vascular disease and has many interesting ideas concerning the association of these conditions with each other and with other variables.

We visited Matsushima. There are three especially famous shrines in sites of great natural beauty, Miyajima (near Hiroshima), Matsushima, and Amanohakodate (which I could not visit). At Matsushima there is a large bay, liberally sprinkled with beautiful islands. The shrine is Buddhist, and consists of niches carved into a rock cliff.

In the evening of 20 July, I returned to Tokyo and on Sunday Dr. and Mrs. Tsuchiya took me to Nikko. Nikko is in the mountains about two hours from Tokyo and is the center of a lake resort area and the site of perhaps the most fabulous shrine in Japan. Half the young people in Japan seem to have put on walking boots, shouldered knapsacks, and set off into the mountains. Every department store in Tokyo has a large, busy department selling all manner of hiking, camping, and mountain climbing gear.

The shrine, Toshogu, was established by Iyeyasu Tokugawa, the founder of the Tokugawa Shogunate, to insure himself a comfortable eternity. After that time, buildings were added until the present complex is huge and unbelievably gaudy. It's as though William Randolph Hearst had had several generations of heirs, each determined to outdo his forbears in erecting and collecting on the San Simeon site. I am not sure if it is beautiful; parts of it are and certainly the setting is. The hillside is covered with huge, ancient cedars which also line a road, the Nikko-kaido, which was the route of the shoguns travelling from Tokyo.

There are several beautiful waterfalls in the Nikko National Park, but the day we went to view the most famous, Kegon Falls, it was very Japanese. That is, it was invisible behind a blanket of fog.

Back to Tokyo and the Imperial Hotel, which had begun to seem like home. A word about hotels. In Kyoto, I stayed in a Japanese Inn (Ryukan). This was very exotic and charming and uncomfortable. After a couple of hours of sitting on the floor, my bones demanded a return to upholstered

chairs. Japanese dinner is edible, especially if one is hungry--sometimes, of course, it can be delicious, but this is not typical Japanese food. Breakfast was, for me, out of the question. I was presented with a bowl of miso-soup (soya bean stock, extremely salty), pickles (vegetables pickled in brine), rice, and an assortment of unidentifiable delicacies, none of which resembled bacon and eggs. I took refuge in being a rich, ugly American and went to the Miyako Hotel for orange juice, hot cakes, and coffee.

Half the hotels in Japan are called New or Grand. (In Osaka, the Grand Hotel is much newer than the New Osaka). And they have a distinctly British flavor, especially as regards food service. The dinner menu at the Sendai Grand Hotel read so:

A. Potage, fish meuniere, meat, dessert, beverage	<u>¥</u> 600
B. Potage, fish meuniere, meat, dessert, beverage	<u>¥</u> 900
C. Hors d'oeuvre, potage, fish meuniere, meat, dessert, beverage	<u>¥</u> 1,200
D. Hors d'oeuvre, potage, fish meuniere, meat, dessert, beverage	<u>¥</u> 1,500

Since I was only there one evening, the difference between these, other than price and appetizers, remains a mystery.

Single rooms, the only kind I became familiar with (that's for my wife's attention), are somewhat more compact than is usual in the States, but they are very efficiently arranged and quite comfortable.

Generally there are two pillows on the bed.

"Try the top one," he said softly.

"Now you must try the bottom one," he insisted adamantly.

Where only one is provided, it is invariably the bottom one.

For people who do not wish to go to Japan but must, the Tokyo Hilton

is like all the other Hiltons. The Okura in Tokyo is also quite plush. I enjoyed the Imperial.

Japanese are almost unfailingly courteous when you meet them socially or in some kind of business dealing. But on the streets, trains, buses, elevators, only the fittest survive. Taxi drivers were recruited from the unused *hauckaze* and are still at war. With everybody. Occasionally the streets are marked with traffic lanes, but the lanes are wide enough for trucks or Detroit iron so three Japanese cars fit two lanes and that's the way they play it.

Baseball is widely popular, both amateur and professional. Certain common expressions are not translated so the radio announcer informs the audience that there are two out by, "Two down, *desu*."

The sumo tournament in Nagoya generated great excitement and bouts were televised almost every evening for about three weeks. Taisho, grand champion for an unprecedented 6 or 7 years, was defeated roundly by a couple of lesser lights and they had to meet in a special play-off match to settle the matter. Confirmed sumo addicts take note: I think the winner was Kitabayama.

Japanese written language was created purposefully by assigning Chinese Kanji to the sounds of their spoken language. This forced marriage is not a happy one. There is continual language reform and simplification and many well-educated people cannot read some things written not so long ago. (We have difficulty with early English, admittedly, but I think their problem is more severe.) A Japanese typewriter I saw in operation in Hiroshima had 4,900 characters. The secretary did not take dictation on it. The newspapers use some 1,800 characters. Besides the Kanji, there are two forms of simplified characters, Hiragana and Katakana. One of

them (I've forgotten which) is used only for direct syllabic transliteration of foreign words and phrases. Because of the variety of meanings associated with each character, the language is better suited to conveying emotional content than to unambiguous scientific communication. Ken Tsuchiya made a very significant comment to me in discussing a paper written by a colleague, "I know what he feels but I am not sure what he thinks."

The cheery comments of the stewards and stewardesses on the BQ&C flight to Hong Kong were not much more easily understandable than Japanese, but somehow sounded more familiar. Fortunately, "Scotch and water" is widely understood.

Off the starboard side, Hong Kong appeared as a green agrarian place with a long jet size runway jutting into the bay. However, the flight pattern took the plane around and in from the south, and then the crowded city came into view.

The Peninsula Hotel is a mid-Victorian establishment hard by the bay on Kowloon side. My clothes closet was nearly as large as a Japanese hotel room. The ceilings are high and there is a fan dead-center, which has been rendered obsolete by air-conditioning that keeps the room at a temperature suitable for a person reared in a drafty manorial hall in England. The mechanism can be turned up but not off.

Hong Kong is enduring the most severe drought of its history. Bath between 6:30 and 7:30 P.M. or not at all. The dirty bath water is left in the tub for scrubbing and flushing. There is a carafe of ice water for drinking and one quart bottle for brushing teeth and incidental washing up. Water is really too precious for internal use but there are many substitutes.

The city is one gigantic bazaar. All the artifacts of man, precious or shoddy, clever or foolish, licit or illicit, are here in one huge counter display to be pawed over, drooled over, mullied over. Dollars, pounds, pesos, or triple distilled tears of Tasmanian virgins--any currency will buy. And like any street peddler's display, the whole affair has an air of impermanence. The customers, the management, and the staff, all are transient, even those who are born, spend their lives, and die here.

This is surely one of the places entitled to be called a crossroads of the world. The U.S.S. Kearcarge was in port and the drunken swabbies were cracking heads and making friends for the United States. I have met the Lord Mayor of Sidney and two of his most irreverent constituents, and a Swiss-Californian who is here to sell Brazilian land to Chinese refugees.

The harbor swarms almost as busily as the city. Naval vessels, freighters, tankers, and passenger liners, junks, tugs, sampans, and motor cruisers bob up and down and course back and forth, and the whole scene is stitched together by the Star Ferries wearing a path between Kowloon and Hong Kong. The ferry trip is the greatest duty-free bargain of all--HK\$0.20 for first class and HK\$0.10 for second class (HK\$1.00 = US\$0.19). For 3 cents one may spend 10 minutes as a Malayan pirate, an intrepid explorer carving a small piece of empire for the Queen, or a Tiger Balm tycoon en route to the bank.

Thai International #703 to Bangkok on Saturday, 27 July, departing at 15:00 hours.

And so we bid a fond farewell to Hong Kong, Jewel of the Orient, to add another gem to the string. Like MacArthur, we promise to return,

after enough paydays have passed to restore us to relative financial health. This is a Convair 990, started by TAI and SAS and the flight is superb. We duck around towering cumulus that rise several thousand feet above our cruising altitude.

Bangkok overnight. This was badly planned. I arrived late in the afternoon and left early the next morning. This effectively kills sight-seeing. And there is much to see in Bangkok.

The city looks something like Fresno, California, except there are not as many tall buildings in Bangkok. It is very large, low, and colorful. The new government buildings are likely to be bright and the temples are riotous. The pagodas are stupa type, quite different from Japan, and the walls are bright mosaics. The tile roofs also are brightly colored and this, too, is a marked contrast with the Japanese temples. The emerald Buddha is lovely.

After the British influence in Japan and Hong Kong hotels, in Bangkok there is a modest French air. I had a bidet in the bathroom. Hotel food is very inexpensive, drinks moderate, and room rate rather high. But the room would sleep a platoon of infantry--perhaps it has.

My schedule was fouled up because the flight from Hong Kong was cancelled and I had to take an earlier one. I tried to reach Dr. Dilok Yenbutra by phone as soon as I arrived but he had just left his office and had no home phone. He waited faithfully at the airport and the next morning came to the hotel just in time to drive me to the airport and say goodbye.

Lunch on board a Comet is a study in applied relativity--my spoon moves back and forth, the plane moves in one direction at over 500 mph, the earth is going in another at some 1,000 mph, and the whole bloody system

is hurtling through space with still more movements within movements. To compute the motion of that maraschino cherry on the spoon from some outside reference point poses quite a difficult problem. The Comet IV is pure jet, a little smaller than the 707, DC8, or 990. Certainly the wings are much shorter and the plane is not quite so stable a platform as the ones we are used to. But who can ride a Comet without feeling a little like James Bond, gazing moodily out the perspex window from high above the North Atlantic. Actually, this perspex window was high above Malaya. The time change from Bangkok to Kuala Lumpur is, strangely, half an hour.

In Hong Kong, the sports pages were filled with the International Cricket Match and there was play by play broadcast of the action on radio. The last I heard, the West Indians had two batsmen who scored over 150 runs in their innings and apparently were going to slaughter their worthy opponents as soon as play recommenced after tea.

I arrived in Kuala Lumpur via Malayan Airways Comet IV from Bangkok on Sunday, July 28. Riding a jet into the K.L. Airport is an exciting experience. As the plane descends, it slides along a hillmass, then swoops into a sharp left bank as another hill looms dead ahead. From there on the approach is straight into the runway and the pilot flies lower and lower and lower over a very heavily settled area, and drops onto the runway at the first possible moment. As soon as all three wheels are down, the jets are reversed and the wheel brakes are applied sharply. With all these procedures working well, the plane stops just as the runway ends. A new airfield, presumably one with a little more margin for error, is under construction.

Dr. Ma Kian Joe delivered me to the Hotel Merlin, a very pleasant and comfortable menage, generally maintained at about the temperature of the

penguin quarters at the San Diego Zoo. The lobby, floors, and dining room swarm with attendants--mostly quite young, mostly male. For example, the elevators are modern automatic devices but each carries a full-time pilot to spare the guest the indignity of pushing his own buttons. Right now there are six attendants standing around the main entry chatting desultorily about whatever occupies them--perhaps plotting a revolution. At peak demand, perhaps two of them would be wildly busy.

KI has been in the grip of a drought, severe enough to call for some minor rationing, although nothing like the Hong Kong stringencies. However, I brought thunder, lightning, and tropical showers with me, and there has been rain for some part of every day. When the clouds open, they open wide, and the effect is roughly like standing under a full flowing water tap. One can readily understand the evolutionary pressure that selected our forebears with nostrils pointing downward.

Monday, Dr. Ide and Dr. James Chin took me in tow to introduce me around and I had a most pleasant chat with Dr. Duguid, IMR Director. His many years of interest in coronary artery disease provided a support from which to hang the conversation. He thoroughly mistrusts any and all conclusions about disease that derive from "statistical" studies, so we argued pleasantly.

The schedule at IMR calls for work to begin about 8:30 and end at 4:30, with lunch from 1:00 to 2:00. Many people dine so late the hour is ridiculously fashionable, maybe 10 or 11 o'clock. The long famine between lunch and dinner is bridged by tea and whatever caloric value can be extracted from gin and tonic.

Monday afternoon, Jim Chin gave me a first installment of his adventures among the blood groups, I heard from Paul Rasch about his schistosomes, and Fred Dunn and I had dinner together.

Tuesday morning, Paul came by the hotel with an assistant and a driver and we took a tour through Malaya's countryside to Kuala Pilar for a session of snail collecting. The paddies were sparsely populated and the best collecting turned out to be in the effluent from a privy. But who wants to live forever? There is a fair variety of snails available for the taking, none of them highly prized as foodstuff. Paul's schistosome is apparently a bird parasite and is of cosmic rather than immediate concern. Several of the crew recently spent two weeks with a malaria survey unit on an island off the east coast of Malaya and among the souvenirs of the trip, Paul returned with a very black beard and a falciparum positive blood smear. He kept the beard but knocked the falciparum with chloroquin.

Wednesday, Jim continued the review of his studies. He is collecting materials for study of defined genetic characters from patients in a leprosy hospital near Kuala Lumpur, from Malay aborigines, and certain other groups as the opportunity presents. The genetic markers are ABO and MN blood group systems (and some work with Diego), secretor factor, glucose-6-phosphate dehydrogenase deficiency, and, for some samples, abnormal hemoglobins and haptoglobins. Aside from the aborigines, the aim is to study the use of these genetic markers as predictors of variations in risk of disease. At the leprovarium, Jim expects to collect materials from 1,000 Chinese males, and relate the findings to the language group to which they belong and to the type of leprosy. Leprosy there is graded on a 5 point scale from pure tuberculosis, through three intermediate classes to pure lepromatosis.

Jim has also collected data from tuberculin testing of large samples of school children, using PPD-S, PPD-B, PPD-E, and PPD-Y. The results are very difficult to analyze, but there appears to be a large proportion of

indeterminate reactions (the antinode of the distribution is about 9 mm) which are closely related to Baitoy bacillus.

Wednesday afternoon was spent with Nyven Marchette and Al Rudnick. Nyven is working on the isolation of atypical mycobacteria, with somewhat disappointing results so far; on an agent related to spotted fever; and on Q fever. Antibodies to Coxiella burnetii are widely distributed among rodents in Malaya.

Al is continuing and extending his studies of hemorrhagic dengue. Human cases are still occurring in Singapore where Dr. Lim Kok An is studying the problem, and last year cases began to occur in Penang. All of the cases reported are children and they show very marked HI and neutralizing antibody response to dengue. Two viruses have been isolated from sera of patients. The disease appears to be similar to that encountered in Bangkok in 1958 and subsequently, and conceivably represents a southward extension of the agent. Al is concentrating his vector studies on Aedes aegypti and Aedes albopictus and is surveying monkeys as possible reservoir hosts of a sylvatic cycle.

Thursday, Jim and I visited the Aborigine Hospital and the Leprosarium. The Aborigine Hospital is the center of a network of some 40 medical aid stations distributed over the country. Dr. Malcolm Bolton, the Medical Director, visits the stations about once a month by helicopter. Between visits, contact is maintained by shortwave radio, and acutely ill persons may be brought to the hospital by helicopter whenever necessary. Tuberculosis, malaria, and trauma are the most common identifiable conditions requiring medical care, but there is no information available on cause of death for a high proportion of the total mortality, for the

cases never come to medical attention. There are about 45,000 aborigines, comprising a number of language groups, largely living a very primitive, semi-nomadic life in the jungle. Presently, Dr. Bolton is contending with a hospital epidemic of measles. As with other primitive peoples, measles in this group is an exceedingly grave disease.

At the Leprosarium, Dr. John Pettit, in charge of research, demonstrated a number of patients illustrating various phases of the disease, and took us on a tour of the wards and the settlement. There are some 2,600 people in the hospital and living in the community. The establishment is a very pleasant place and exudes an air of concern for the welfare of the inhabitants. Very impressive. The case load is divided between old disease with serious permanent disability and relatively recent cases under intensive therapy. The deficit of persons between these extremes is testimony to the use of chemotherapeutic agents and foretells a sharp decline in the community as the old cases die and are not replaced.

Friday, 2 August, was Mohammed's birthday. Several thousand Muslims paraded through downtown K.L. and only the infidels kept their shops open. In the afternoon, Fred Dunn told me the story of his studies of aborigines and brought me up-to-date on monkey malaria. He is doing intensive surveys of the prevalence of intestinal parasites among different aborigine groups, divided by place of residence, by means of livelihood, and by language group. As I mentioned earlier, there are about 45,000 aborigines in Malaya, with about 5,000 Negritos, 30,000 Senoi, and 10,000 Proto-Malay. The Negritos are very primitive, nomadic hunters who roam the jungles of Northern Malaya; they are very like the Negritos of the Philippines. The Senoi may be divided into two major language subgroups,

the Temia and Semai, and show varying degrees of acculturation. The Proto-Malay are similar to the Malay by physical characteristics.

Late in the afternoon, the entire ICWRT contingent converged on the airport to greet Dr. and Mrs. Hubert Loncin. This pleasant custom is an established tradition for new arrivals. The Loncins were deposited in a government chalet immediately and thus were spared the problem of settling in a hotel, then finding temporary quarters as a base for house hunting.

The British Colonial Service and many industrial firms routinely provided quarters for their employees serving in Malaya and the Malayan government adopted the practice after independence. In addition to permanent housing, the government has established temporary facilities in some of the cities, the chalets. In the compound are a number of apartments, and a central mess. Amahs and baby-sitters are available and tea is served to the apartments in the morning and afternoon.

We are accustomed to outdoor living in California, but in Malaya the houses and apartments are customarily wide open, with no screens. Mosquito coils are burned to repel these invaders and the hardier arthropods are kept in check by a plentiful supply of gekkos, which cruise the walls and ceiling snapping up the unwary bugs and periodically sounding off in amazingly loud and resonant tones.

Saturday, I went with Al and his crew on a mosquito collecting tour. We visited a Malay Kampong, a Chinese squatters community, and an Indian settlement--all pretty much at the bottom of the economic heap. House collecting in K.L. is much like that around Buttonwillow, except that the houses here are on higher stilts and the mosquitoes are more

restless. We also spent a short time doing a biting collection of Aedes albopictus. Although this is a time honored method, I had never seen it in operation before.

On Saturday evening, Paul Basch was host at a cocktail party to celebrate the Lencins' arrival. My enthusiasm for local color was at a low ebb that night and Sunday as I had my turn with the traveler's curse. Enteroviform is the paracea recommended here as enthusiastically as in Mexico and one should try to include some within the weight allowance.

This is not, I trust, related to the preceding, but a word on Malayan fruit is in order. The hotels insist on serving canned grapefruit juice for breakfast, but there are excellent local pineapple, bananas, and papaya. Rambutan are red, prickly fruit about the size of a golf ball. When the husk is removed, the fruit looks and tastes like a grape with a large central seed. Mangostine have a very thick husk with a white fruit divided into sections; the fruit is sweet and a little tart. A former queen of England is said to have offered to trade a kingdom for mangostine. But above all, the durian demands attention. When ripe, the durian falls to the ground and since it is hard, larger than a papaya, heavy, covered with spines, and the durian tree is very tall, its arrival is impressive. The fruit is cream colored and soft and is indescribably foul. If one could concoct a mixture of onion, garlic, very ripe cheese, and sugar, this might approach the taste and odor of a durian. I am told that a taste for durian can be acquired by trying it three times, but after my first attempt, I am unable to place any value on this acquired taste. However, the people who like them have almost an obsession for them.

Monday, August 5, and my time of exile is drawing to a close. The morning was spent with Hubert and the afternoon with Fred. Tuesday, more

of the same, plus a session with Don Eyles and McWilson Warren on monkey malaria. Wednesday, Fred, Hubert, Bob Wolfe, and I visited an aborigine village. At noon, Hubert, Jim Chin, and I met with Dr. Manohoran, District Medical Officer in Selangor State, for discussion of industrial medical care in Malaya. The afternoon was spent tidying up loose ends.

Wednesday night, Jim, Fred, Al, and Paul accompanied me to dinner at Le Coq d'Or for our tearful farewell.

My impressions of the visit to K.L. are necessarily tentative and based on imperfect knowledge, but I will present them nevertheless. The ICMCF group are busy, productive, and happy. They have many complaints and are not reluctant to voice them, but the complaints are almost universally directed toward relatively minor administrative affairs and not professional matters. I do not believe these "minor administrative affairs" should be considered unimportant, however. K.L. is a long way off, and despite good will at both ends, when difficulties arise, they often are difficult to resolve. In the exchange of correspondence, misinterpretations occur and misunderstandings arise. Since these aspects comprise a major part of the continuing link with home on the part of the expatriates, I strongly suspect that they are of greater concern in K.L. than in S.F. To a considerable extent, the problems will be minimized if communication is free and frequent and if the people there are assured and reassured that someone on this side is on their side and earnestly fighting their battles for them.

Occasionally, problems of supply affect the progress of the work but not, I think, often or seriously. The intellectual and professional quality of the ICMCF people is of the highest order and their personal

relations are marked by a healthy respect for each other. There was surprisingly little friction apparent to my observation for people who have been placed in such close and continued association.

Conditions of work - space, help, equipment - are excellent and opportunities for research abound in Malaya. In many important areas, the surface has barely been scratched.

The problem of getting Hubert off to a rousing start was not handled. Unfortunately, the difficulty was greater than I had anticipated and I was there too early for Hubert to be well settled. Insofar as I could determine, the technical difficulties of conducting a worthwhile survey of cardiovascular disease in Malayan populations are not especially formidable. I believe that Hubert will be able to adapt his plans sufficiently to accomplish this. Dr. Danaraj presented a more serious difficulty. He expressed this to Dr. Din and Dr. Duguid:

1. The project proposed by Dr. Loncin could not be done.
2. If it should be done, local people should do it.

The inconsistency of these two comments apparently did not trouble him and his attitude was hostile and petulant. Since the disposition of the IMR relative to the medical school still had not been resolved and since the ICMRT's place in all this was equally uncertain, the best posture of ICMRT staff (and visiting firemen) re Loncin vs. Danaraj seemed to be one of studied unconcern. When I left, Hubert planned to meet Danaraj but not to incite or confront. Perhaps the pressing problems confronting Dr. Danaraj will occupy his attention to the exclusion of such minor matters as this. Dr. Din was occupied with problems of state, recruiting physicians in the Philippines, so I was unable to see him. In any case, Dr. Danaraj had already indicated that he looked on attempts to

work through Mr. Din as a threat to his own virility and thus it appeared that further moves in this direction at that time would not be desirable.

Without meeting Danaraj, the various references to his activities left me with a strong distaste for him. He seemed inordinately touchy and stiff-backed, petty, unreliable, and self-serving. Fred assured me that these impressions were not wholly accurate and that the man has many excellent qualities. Perhaps so, but I would not want my future to depend on his good offices unless I was damned sure that his own aspirations were linked with my success. And then I would be wary.

One last point about the KL ICMRT staff. Several members expressed to me their concern about future employment. The "fellows" face difficulties in promoting their own causes from such a distance. If anything can be done in San Francisco to inform them of opportunities for employment, this would be a worthwhile service. If they are to be offered posts within ICMRT on a continuing basis, an early offer and frequent communication of the state of negotiations would help to allay their concern.

The ICMRT "staff" presents a somewhat more complex problem. For reasons which are a little difficult for me to understand, the administrative change in designation of the "fellows" made them acutely aware of the lack of stability of their own positions. Thus, although their situation has not changed, they "feel less stable." I believe that if there are plans for transferring some of the staff to tenure positions, that early communication of these plans would be of great benefit. In any case, there is a need for free discussion of the probable future outlook for these people with respect to regular academic positions.

Thursday morning, August the 8th, I had a quick and easy flight from Kuala Lumpur into Singapore and was registered into a huge room at the

Raffles Hotel, courtesy of Malayan Airlines. Without any prompting on my part, the airline concluded that this was properly an overnight stay required by the nature of the airline's schedule, so they picked up the tab. So my long cherished dream of sipping a ginlet, sprawled in a comfortable chair, in the fabled Raffles Hotel was realized.

I called Bill Brown after lunch, went to the University to meet him. We spent the afternoon discussing his situation. He had been there only a few days and thus had not had an opportunity to begin work or even to unpack all of his gear, but he believes that his situation there was going to be very suitable for productive work. He was very happy with the reception he had received by the University of Singapore's staff and by their attitude toward his presence. The space set aside for his laboratory was entirely adequate, although in order to keep his equipment and himself working efficiently, he will surely need a room air conditioner.

A quiet night in the luxury of the Raffles Hotel, then off to the airport on Friday morning and then aboard a Pan Am flight, headed home.

The Pan Am plane settled into Saigon with a solemn warning from the plane steward that no photographs could be taken on the way in, on the ground, or on the way up, since this was a military zone. The airfield looked military, all right, very much like an airforce base somewhere in Texas, except greener, with American Air Force planes scattered all over the landscape. The stay was brief and no one set fire to himself while I was there. Then on to Manila. The Manila Airport was equally unexciting. Hopping about from one country to another in this way is about as illuminating as viewing the cities of the United States during 20 minute stopovers in the railroad depots.

The next stop was Guam. The flight in was marked by a particularly lovely sunset and we arrived at the island about 11 P.M., Guam time. So,

here I was, practically back in the United States and having my first brush with United States' customs officials. This one, however, was relatively painless since these guys didn't want any money; all they wanted was that I should tell them what I had. Dwayne Reed was on hand to meet me and we conversed through the slats of the enclosure that keeps the pure from the impure, while the customs officials look through the gear. Then he took me to his home and we were up late speaking of things epidemiologic and Guamanian. The next day, we went to the Guam Memorial Hospital, where I met the other members of the NINDS Field Station staff and was given a thorough introduction to their study. That evening, we went to the Naval Hospital and observed a very amateur performance of "You Can't Take It With You." The next day, more discussion of the project; then late in the evening, back to the airport to continue home in the tender care of Pan American.

Dwayne is scheduled to spend a year on Guam to work on the closing phases of a five-year study of amyotrophic lateral sclerosis. Unaccountably so far, the incidence of this disease among the Chamorro is fantastically high. Dr. Furland of the NINDS has been engaged in studies of this disease since sometime in the early 1950's. Along about 1958, a long-term study was initiated, presumably to investigate genetic mechanisms in the etiology of ALS. A registry of newly discovered ALS cases was established, and as each case was admitted to the registry, a comparison subject was selected. The idea, then, is to determine the frequency of occurrence of cases among first degree relatives of the cases admitted to the registry and among the comparison subjects. The notion was that if the disease is genetically determined, then there would be an aggregation in the families of the cases. This undoubtedly correct but a shared environmental toxic agent or an

infectious process would, of course, also show familial aggregation. Therefore, unless the data collected fits neatly into a specific genetic hypothesis, the results of this study may very well leave the issue in doubt. Dwayne is interested in looking at some of the other notions that have been suggested as possibly playing a part in the causation of ALS, such as nutritional toxic substances. The crew are also discussing the desirability and procedures for conducting physical examinations of the families of the study subjects. It seems probable that some such examination will be done.

Most of the discussion that Dwayne and I had dealt with considering the alternative methods of study. I think a thorough analysis of death certificate data of the last few years would add appreciably to the value of the study and that a well-planned survey examination of a defined population segment should be a part of the study whether or not all family members of the index cases are examined. Some family studies are under way and I think these should be intensified to provide more information against which to test genetic hypotheses.

Dwayne and I discussed at length the possibility that he may return to Berkeley for further study of epidemiology when his tour in Guam is completed. He would be a welcome addition to our post-MPH group, since about that time Dick Emmons will be finishing his work and when he leaves we won't have a folk singer in the lot.

Late last fall, Guam was hit by a bad hurricane. The eye passed over the island and winds of some 150 knots were recorded. A very considerable portion of Agaña was hid waste. Guam Memorial Hospital is a handsome building of concrete and glass, sitting up on a promontory, and was exposed to the full blast. The wind went through the large glass windows on one side and swept out through the large glass windows on the other side,

leaving piles of twisted, water-soaked debris. The patients had been evacuated to the Naval Hospital, but large quantities of supplies and many records were lost. The main portion of the hospital has been put back in working order but one wing is still exposed to the elements. The NINDB suffered some losses in the storm and, of course, some of the NINDB staff lost valuable personal possessions.

The Pan American Airways around the world trip flight headed east, stopped in Wake, and then in Honolulu. This time, the customs officers were all too willing to accept money.

I spent a couple of hours with Bob Worth at the airport while waiting for a flight on to San Francisco and reviewed with him the prospects for conducting the cardiovascular disease studies in Hiroshima. This is the first time that Honolulu has seemed to me to be almost home.

A short trip in and back to hearth and home on the evening of August 13, older, tired, poorer, and if not wiser, at least a little better informed.

THE END

APPENDIX

CARDIOVASCULAR DISEASE AND JAPANESE MIGRATION

I. Introduction

The movement of significant numbers of Japanese from their homeland to Hawaii and California, and their establishment and progressive acculturation provides an unusual opportunity for the investigation of the influence of environmental factors on patterns of morbidity and mortality. A gradient of increasing risk of death from coronary heart disease (CHD) and of decreasing risk of death from cerebral vascular disease (CVA) appears to have been established and is probably related to variations in diet (see section on prior work done on this subject). No data are available to permit evaluation of morbidity, or to relate these to place of birth, length of residence, occupation, physical activity, smoking, blood pressure, or other relevant variables. The diet and serum lipid data are based on very small samples and present cholesterol determinations only. An intensive study of characteristics already shown to be associated with variation in the risk of cardiovascular disease is of exceptional interest in these populations because the range of variation for many of them is much greater than can be found in populations within the United States.

II. Objectives

1. To describe the variations in mortality and morbidity from coronary heart disease, hypertensive disease, and cerebral vascular disease between population samples or persons of Japanese descent in Hiroshima, Hawaii, and California.
2. To study the relation of various environmental factors and individual characteristics to these variations in disease.

III. The Study Population

There are about 150,000 persons of Japanese ancestry on the Island of Oahu and, of these, approximately 15,000 (45-64) are middle-aged males. This, then, constitutes our study universe. The only way of identifying these people by name and address would appear to be through the Bureau of the Census enumeration listings from the 1960 census. Some loss of the more mobile portions of this population is inevitable.

Mailed questionnaires are to be sent to each Japanese male aged 35 to 64 at the time of the 1960 census. The questionnaires will be fairly brief, calling for identifying information, birthplace and birthdate, immigration, occupation, smoking, diet, and medical history. These data, together with detailed tabulations of the characteristics of Japanese adult males from the 1960 census, will serve to identify and describe a population for the study of cardiovascular disease mortality. Mortality data will be collected by searching the death certificate files of the Hawaii State Health Department for CV deaths in this age, sex, and ethnic group. The completeness of the census data will permit an evaluation of the distortion produced by those failing to respond to the questionnaire and this mortality study will serve to validate the findings in the more intensive study of morbidity in a small population sample.

For the intensive morbidity study, there are several means of identifying specific population groups which could conceivably be of use in studying cardiovascular disease among persons of Japanese descent resident in Hawaii.

1. Registration of persons of Japanese ancestry was required early in World War II. Depending on the extent of information collected at that time, this group might be useful as a cohort whose mortality experience

could be investigated over some 20 years. Other than this, no reasonable means of using this population is apparent.

2. A probability sample of some 2,000 households has been drawn by the Bureau of the Census for the study of stomach and lung cancer. Some modification of the current study design would be necessary if this group were to be used, for some additional information would be needed by interview and a screening examination of the adult males is required. Grafting our operation onto this study would be relatively inexpensive and not too difficult administratively. However, the response rate from the sample queried by the Bureau of the Census was about 40 per cent and this introduces an intolerable bias. The study directed by Dr. Haenzel of cancer of stomach and lung is very similar in over-all design to that which we propose for cardiovascular disease. In Japan, a sample survey of 1,190 households has been conducted in Miyagi Prefecture and cases are collected from the hospitals. In Hawaii, a probability sample of about 2,000 households has been drawn by the Bureau of the Census, requests for participation in the study have been mailed, and some interviews have been completed. The cases are to be collected from the hospitals of Oahu. The status of the study in the Los Angeles area is not known to me.

The interview schedules for the population surveys include data on sex, residence, date and place of birth, birthplace of parents, education, migration, religion, marital status, and race and birthplace of spouse. There are a dietary history with emphasis on rice in the diet, smoking history, occupation, something on habits and customs of living, and very casual inquiry as to health status. Similar questionnaires are to be completed for the cases, with some additional medical history and data on family composition.

Very minimal modifications should serve to make these forms suitable for a CV study. The medical history is not adequate and additional data on physical activity, father's occupation, and such are needed.

3. In 1958-59, the National Health Survey conducted a special study of Oahu on a sample of some 3,200 households. No examinations were done. This sample is presumed to be a representative sample of the island's population, and may be representative of the Japanese segment. If Japanese are represented in the sample proportionately, there should be about 1,000 households in this group. The information already available for this sample would be very valuable, but the problems involved in finding persons at addresses now 4-5 years old may be formidable.

4. About 1,800 middle-aged adult male Japanese are enrolled in the Kaiser Health Plan. Comprehensive medical care is available to the subscribers and they are encouraged to take advantage of the opportunity to have periodic physical examinations. With modest modification, this examination, together with a detailed interview, could serve the purposes of this study. In addition to examinations repeated at intervals, the medical records of the Kaiser Health Plan would provide valuable data on the occurrence of new disease in the study group.

5. Conceivably, another sample could be drawn by the Bureau of the Census, independent of the cancer study sample. However, this would leave unsolved the problem of the inadequate response rate.

Considering all of these factors, the most suitable study group is the Kaiser Health Plan subscribers. This poses the fewest problems in follow-up, should yield a good response rate, and when evaluated in light of the mortality study, the biases in this population should be within tolerable limits. The probability sample presents serious difficulties

in following morbidity and if the response rate is so low, any advantage it has in representativeness is lost.

IV. Previous Studies on this Subject

Information already available on the risk of coronary heart disease in Japanese in Hawaii is contained in the following list. Where indicated, there is also some statement of the variation in risk between Hawaii and Japan or the mainland United States. Insofar as I can determine, this list is exhaustive.

1. Gordon, T. Mortality experience among the Japanese in the United States, Hawaii, and Japan. Pub. Hlth. Rep. 72:513-553 (June) 1957. This is a presentation of mortality data for the period 1949-52. The death rate, all causes, for Japanese in the United States is lower than that for Caucasians. However, the over-all death rate for Japanese males in Japan is higher than that for Japanese males in the United States. For deaths attributed to diseases of the heart, there is a clear gradient for males up to the age of 65 years, with low rates in Japan, intermediate rates in Hawaiian Japanese, and higher rates in U.S. Japanese (the latter approximately double the rates for Japanese in Japan). An inverse gradient is observed for deaths due to vascular lesions of the central nervous system and here the rates for Japanese in Japan are approximately twice as high as the rate for Japanese in the United States. Gordon's look at the percentage of Japanese in Hawaii and mainland U.S. indicates that the age group 45-54 should consist of predominantly native-born persons by 1960. Thus he predicts, on the assumption that the differential rates are the result of cultural-environmental determinants, that there should be a marked increase in heart disease mortality for Japanese men in this age group. Data should now be available from the Hawaii State Department of Health to test this prediction.

2. Keys, A., Kimura, K., Kusukawa, A., Branta-Stewart, B., Larsen, N., and Keys, M. N. Lessons from serum cholesterol studies in Japan, Hawaii, and Los Angeles. *Ann. Int. Med.* 48:83-94 (Jan.) 1958. From the paper, the numbers and selection of study subjects cannot be sorted out exactly but apparently some 153 Japanese in Shima, 122 in Hawaii, and 45 in Los Angeles were studied. Probably in addition to these were 50 farmers from Koga and either 52 or 54 doctors from Fukuoka. For some of these groups (the men aged 40-49), special dietary studies were done. Mean cholesterol increased with age in the Shima and Hawaii groups; at age 50-59 the Shima mean was 170 mgm% and the Hawaii mean was 240 mgm%. Keys states the increase in B-lipoprotein cholesterol for males aged 40-49 was linearly related to the per cent of total calories in the diet derived from fat. The groups arrayed in the following order: Koga farmers < Shima miners < Shima clerks < Fukuoka doctors < Japanese in Hawaii < Nisei in Los Angeles.

3. Tarsen, N. P., and Bortz, W. Coronary atherosclerosis in ethnic groups. A series of 2,000 autopsies. *Hawaii Med. J.* 19:159-162 (Nov.-Dec.) 1959. The coronary arteries from 2,000 consecutive autopsies at Queen's Hospital were graded by degree of atherosclerosis. Almost half the subjects were Caucasian and about one-eighth were of Japanese ancestry. Caucasians had more severe atherosclerosis than did Japanese. Among Caucasians, severe disease was more frequent in males than in females, but among the Japanese there was no marked sex differential. In both groups the frequency of severe disease was 2 to 3 times greater in those over 50 years than among those less than 50 (the total age span was 20-70 years and there were 3-4 times as many subjects over 50 in each group except Japanese females, where the ratio was 1:1).

The findings in other ethnic groups are given and, according to the author, support the hypothesis that dietary differences is the most significant explanation for the observed variation.

4. Bennett, G. G., Tokuyama, G. H., and McBride, T. C. Cardiovascular-renal mortality in Hawaii. *Am. J. Public Health* 52:1418-1431 (Sept.) 1962.

Death rates for the major components of the cardiovascular-renal disease category for the years 1949-1956 were computed for several ethnic groups.

	AGE-ADJ. DR FOR MALES AGED 35-74 YEARS							
	Cont. U. S.	Total	Polynes.	Hawaii Chin.	Cauc.	Fil.	Japan.	Other
CVR	928	681	1,214	860	818	508	498	740
Coronary H.D. (420)	530	280	550	357	483	140	161	270
Hypertension								
♂ H.D. (440-3)	76	123	261	197	121	105	86	131
♀ H.D. (444-7)	11	9	13	7	11	4	8	14
CVA (330-334)	416	168	233	179	121	183	165	489

As expected, the Japanese had a low CHD death rate, but the Filipinos were still lower. Surprisingly, the Japanese did not have a very high CVA death rate, and were lower than all the groups except Caucasians.

5. _____, Mortality from cardiovascular-renal diseases in Hawaii, 1949-1956 (Ages 35-74). A joint project of Hawaii Heart Association and Hawaii State Department of Health, 1959.

This micrographed publication gives in more detail the data which served as the basis for the paper by Bennett et al. The proportionate mortality and the age specific death rates are given.

PER CENT OF TOTAL CV-M DEATHS

	Haw.	Cauc.	Chin.	Japan.	Fil.
CHD (420)	44.0	58.7	41.0	32.1	27.3
Hyp \bar{c} H.D.	20.9	13.9	23.0	17.3	19.8
Hyp \bar{s} H.D.	1.0	1.2	0.9	1.6	1.2
CVA	18.1	13.6	21.0	32.6	36.4

DEATH RATES 1949-1956

AGE	CHD		HYP \bar{c} HD		CVA	
	Cauc.	Japan.	Cauc.	Japan.	Cauc.	Japan.
35-44	67.4	34.1	12.6	13.4	8.4	23.8
45-	329.7	81.1	58.2	37.2	49.6	77.7
55-	788.5	252.7	160.3	135.9	163.5	282.6
65-74	2114.5	507.5	467.1	292.5	486.8	520.0

6. McBird, T. C. Ethnic heart survey in Hawaii: Project II.

A 10-year medical record of cardiovascular-renal disease in male plantation employees (1948-1958).

The medical records of 3,533 male plantation workers were reviewed for the period 1948-1958. Rates for new and previously existing disease were computed, but by ethnic group the only rates presented were some kind of period prevalence (this was not defined, but no other interpretation seems reasonable). The rates were not adjusted for age, nor for duration of observation.

	PREVALENCE/1,000	
	Cauc.	Japan.
CHD	139.3	46.3
Hyp. \bar{c} H.D.	69.7	75.0
Hyp. \bar{a} H.D.	282.8	211.8
OVA	16.1	30.9

I am told that the quality of medical data collected from this source is very low, probably the variations in quality related to ethnic background.

7. _____ Heart conditions and high blood pressure. Hawaii health survey report No. 4. Hawaii State Department of Health; June, 1962.

The Hawaii Health Survey, conducted from October 1958 to September 1959 was a special extension of the National Health Survey, with the cooperation of the Hawaii State Health Department and the Oahu Health Council. Approximately 3,300 household interviews were completed, representing about 12,500 persons.

PREVALENCE/1,000 OF HEART CONDITION AND HIGH BLOOD PRESSURE

		Cauc.	Japan.	Other
Heart Cond.	Total	16.5	10.1	10.5
	Male	19.7	13.3	13.3
	Female	11.3	7.2	7.3
High blood pressure	Total	22.7	21.2	27.5
	Male	16.8	17.3	21.5
	Female	28.7	24.9	30.7

PREVALENCE/1,000 OF HEART CONDITION AND HIGH BLOOD PRESSURE

AGE	Cauc.		Japan.		Other	
	Ht.	HBP	Ht.	HBP	Ht.	HBP
Under 25	3.9	3.4	6.0	-	2.6	3.0
25-44	18.9	18.9	8.6	18.1	8.9	25.4
45-64	55.8	87.2	13.3	66.9	34.6	100.5
65+	79.2	175.1	42.5	91.0	47.9	135.8

8. Bennett, C. G., Tokayama, G. M., and Bruyere, P. T. The health of Japanese Americans in Hawaii. Draft ms. to be published in Public Health Reports.

CIVILIAN POPULATION BY RACE, OAHU, HAWAII, 1960

Ethnic Group	Number	Per Cent
All	458,407	100.0
Japanese	149,166	32.5
Caucasian	139,814	30.5
Hawaiian	79,808	17.4
Filipino	44,105	9.6
Chinese	35,343	7.7
All others	10,131	2.2

Major in-migration of Japanese was from 1885 (especially after 1898) to 1921, when the Oriental Exclusion Act was passed.

DEATH RATES/1,000 BY AGE, 1959-61

Age	Can Japanese	Other Oahu	United States
All	4.4	5.5	9.5
Under 1	20.7	23.6	26.8
1-24	0.5	0.7	0.8
25-44	1.1	2.2	2.2
45-64	6.8	12.1	11.6
65+	39.9	69.2	60.5

This ms. is based on the Hawaii Health Survey. Additional information on the survey is contained in the U.S.P.H.S. publication, Health Statistics from the U. S. National Health Survey, Series C, No. 3; The Hawaii Health Survey, Description and Selected Results.

V. Space Requirements

The continuation of the study now underway under the direction of Dr. Joseph Stokes is desirable and it should remain centered in Queen's Hospital. No additional space is available there, however, so the study here proposed must be located elsewhere.

If the Kaiser Health Plan subscribers are to be studied, the examinations and interviews should be conducted in the Health Plan clinical facilities, notably the hospital and clinic near Waikiki. Additional space would be needed for the staff and this can probably be secured at the University of Hawaii. A new building is planned for the Pacific Biomedical Research Center for completion in 1964, and both Dr. Richard Lee and Dr. Robert Worth have indicated they would welcome the project there.

If some other population sample is to be established as the study group, then clinical and administrative space can be rented near Queen's

Hospital, or elsewhere, or secured in the Leahi Hospital, which was formerly a tuberculosis treatment facility and now has ample room available.