

The Health of Atomic Bomb Survivors: A Decade of Examinations in a Fixed Population¹

JOSEPH L. BELSKY,² KIYOSHI TACHIKAWA,
AND SEYMOUR JABLON³

*Departments of Medicine and Statistics, Atomic Bomb Casualty Commission
Hiroshima and Nagasaki, Japan,
U.S.A. National Academy of Science-National Research Council, and
Japanese National Institute of Health of the Ministry of Health and Welfare*

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More than 25 years after the atomic bombings of the Japanese cities of Hiroshima and Nagasaki, the late effects of radiation on the health of the survivors are still incompletely known. However, the Atomic Bomb Casualty Commission (ABCC) continues to monitor morbidity and mortality of A-bomb survivors.

The ABCC is a binational endeavor; the parent organizations are the U.S. National Academy of Sciences-National Research Council (NAS-NRC) and the Japanese National Institute of Health (JNIH) of the Ministry of Health and Welfare (1). The late R. Keith Cannan, who, for many years, as Chairman of the Division of Medical Sciences of the NAS-NRC, had general responsibility for ABCC on the U.S. side, has reviewed the history of the Commission (2). Miller (3) has summarized the major findings as to delayed radiation effects. Dr. James Hollingsworth (1) reviewed the major findings from 1948-1959. The present report concerns the following decade (1958-1968) during which a new study plan was put into effect. In the late 1950's, ABCC completed the organization of a program based on a revised study cohort designed to permit large-scale epidemiologic studies on the effects of sublethal whole-body radiation. The cohort selection was based on a Special Survey of A-bomb Survivors made in 1950. In brief, nonirradiated, distally located survivors as well as subjects not present in the cities at the time of the bomb were matched by age and sex with survivors who sustained variable amounts of radiation. Selection and characterization are described in detail elsewhere (4-6).

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² Present address: Division of Medicine, Danbury Hospital, Danbury, CT 06810.

³ Present address: Follow-Up Agency, National Academy of Sciences-National Research Council, Washington, DC 20006.

THE POPULATION

All persons, in both cities, verified to have been within 2000 m of the bursts, were chosen for study. To these were matched, by age and sex, a group whose members were in the environs but at distances where there was little or no radiation (3000–3499 m in Hiroshima and 3000–3999 m in Nagasaki) and a nonirradiated control group which was not present within the cities at the time of the bombing (ATB). The final study population of 109,000 persons, including survivors and control subjects (Life Span Study population) is followed for mortality at the level of the death certificate. A subsample (originally numbering about 20,000 in 1950), has undergone biennial physical examinations since 1958 (the Adult Health Study–AHS). The programs of study of these populations have been formally approved by the governments of Japan and the United States.

Within the framework of the Adult Health Study program, which is the basis for the present report, the numbers of subjects (minus those deceased or who moved out of the cities) of the first and fifth 2-year examination intervals, or cycles, are shown in Table 1 by estimated A-bomb radiation dose (see below), sex, and city. The fraction of each original subgroup who continued to return for clinical examinations is shown for Cycle 1 (1958–1960) and Cycle 5 (1966–1968) in Table 2. Figures for the intervening periods are intermediate between those shown. It can be seen in the tables that a great majority of subjects living in the city returned for examinations over the decade from 1958–1968. Those more heavily irradiated participated slightly more, but the difference between this group and the nonexposed was very small.

TABLE 1
ADULT HEALTH STUDY, NUMBER OF SUBJECTS (MID-CYCLE)

Cycle	Hiroshima					Nagasaki					
	Total	NIC ^a	Estimated radiation Dose, Rad ^b			Total	NIC ^a	Estimated radiation Dose, Rad ^b			
			0-9	10-99	100+			0-9	10-99	100+	
Male											
1958-1960	4712	1206	1535	1043	730	2527	636	657	311	628	
1966-1968	4149	1065	1366	897	637	2314	582	609	280	567	
Female											
1958-1960	7991	2039	2558	2112	981	3369	851	916	421	815	
1966-1968	7437	1910	2402	1932	902	3230	806	882	397	781	

^a Not in the city at time of bombing.

^b Total estimated radiation dose in rad (10).

TABLE 2
PERCENTAGE OF PARTICIPATION IN EXAMINATIONS

Class	Cycle	Total	Male	Female	Hiroshima	Nagasaki	NIC ^a	0-9 Rad	10+ Rad
Total sample	1958-60	74.8	71.9	76.7	75.8	72.6	72.3	74.6	76.3
	1966-68	63.4	58.2	66.9	64.5	61.1	60.6	64.5	64.2
Total sample	1958-60	80.4	79.3	81.1	81.9	77.2	76.6	80.4	82.6
Minus deceased	1966-68	74.3	72.0	75.6	76.6	69.3	69.9	75.3	76.1
Total sample	1958-60	89.9	89.2	88.9	88.5	90.1	87.3	87.9	90.6
Living in city	1966-68	85.3	84.7	85.7	85.0	86.3	83.9	85.6	86.0

^a Not in the city at the time of bombing.

CLINIC PROCEDURES AND THE CULTURAL MILIEU

The clinical examination reflects traditional patterns of recorded histories and physical findings on standard forms. Laboratory tests on blood, urine, and stool, as well as chest films, are also obtained at each biennial visit. Any necessary further tests and observations are performed on follow-up clinic visits.

It is important to emphasize that all clinic subjects are examined without overt knowledge of their radiation status. However, it would be naive to suggest there is no observational bias. For various reasons, an individual survivor could readily inform the ABCC clinic physician, a Japanese doctor, that, for instance, his "back discomfort" was present since the bombing. In addition, as recorded material accumulated, chart review could suggest evidence that the subject might be a survivor of the atomic bombing.

The population is fixed, and accountability for every member is important. For those too ill to attend the clinics, there is a home visit program. Periodic checks on the subject's *koseki* (a local vital statistics register unique to Japan), and notification of death in each instance serve additionally to ensure data on each participant.

The examinations must be viewed within the indigenous cultural milieu that ABCC has worked since 1947. Since these examinations are voluntary, what influences over 85% of those eligible to continue to return every other year for their "check up" is not completely known. Certainly, the nonexposed control subjects must know that their "A-bomb disease" potential is nil.

Many feel that the "American" examination is more beneficial, even though virtually all clinical procedures are carried out by Japanese physicians. A hopefully normal report, traditional participation in group activities, willingness to contribute to the research endeavor, satisfaction with the clinic routine, acceptance of ABCC as an integral part of the community, and probably other factors, also apply.

DOSE ESTIMATION FOR A-BOMB SURVIVORS

In analyses before 1966, intensity of sublethal atomic bomb radiation received by survivors was measured only by distance from the detonation area. Studies (7, 8) since that time have resulted in individual total dose assignments (9) to virtually the entire cohort.

Thus, atomic bomb doses in rad (the simple sum of gamma plus first collision neutrons) can be used to map a continuous dose effect, judge thresholds for special observations, and yield data in forms relevant to current discussion. Nevertheless, these figures are recognized to be estimated values. The degree of inexactness is not known, but may be as high as 30% (10). Table 3 lists mean gamma and

TABLE 3
ESTIMATED MEAN AIR DOSE (RAD) FOR SELECTED DISTANCES FROM THE HYPOCENTER^a

Distance (meters)	Hiroshima			Nagasaki		
	Gamma	Neutron	Total	Gamma	Neutron	Total
600-649	1443	1465	2908	4415	370	4785
1000-1049	219	160	379	784	30	814
1500-1549	19	8	27	102	1	103
2000-2049	1.9	0	1.9	<20	0	<20

^a Adapted from Milton and Shohoji (10).

neutron doses for selected distances from the hypocenter, a landmark directly beneath the point of explosion. The table emphasizes two important considerations: in Hiroshima the neutron component was greater, while at similar distances from the hypocenter the intensity of total radiation (gamma plus neutron) was greater in Nagasaki.

The major effort of the biennial examinations of the Adult Health Study is to judge, via periodic clinical appraisal of large numbers, the general health of the population. It is important to note that this serves especially to identify trends that can be pursued in greater detail.

In combination, detailed studies and regular examinations provide insights not only into some effects associated with A-bomb radiation, but also health (disease) trends over time, and permit age, sex, and intercity comparisons. The following sections attempt to review only some of these aspects. Age is given as that at the time of the bomb in recognition of possible different biologic responses to radiation at different periods of growth and development.

LATE RADIATION EFFECTS

Analysis of the results of the regular biennial examinations over Cycles 1–5 (1958–68) (11) revealed that, at this level, there were no significant uniform differences between heavily irradiated, lightly irradiated, and control subjects except for diseases of the thyroid gland and of the eye.

This is not unexpected in the clinic population of about 16,000 followed for 10 years and in which only one-half were exposed to variable doses of total body radiation. The numbers of survivors and controls are too small to generate sufficient numbers of specific conditions or diseases for analysis. The clinical examinations were carried out by a large number of different physicians over the decade under consideration. When this group was studied by death certificates from 1950 (the date of establishment of the cohort) or by a researcher trained in a special aspect, radiation-related effects were noted.

Cancer in general (12), and leukemia (13) and thyroid cancer (14, 15) in particular, have been shown in other studies to be more prevalent among heavily irradiated A-bomb survivors. In addition, persons heavily exposed appear to be at greater risk of cancer of the breast (16), lung (17), and salivary glands (18). Increased cancer risk has been most recently evident in those exposed when they were less than 10 years old (19).

DISEASES OF THE THYROID

This category includes all thyroid diseases except cancer. In females of all ages at the time of the bomb in Hiroshima, and in those less than 20 years of age ATB in Nagasaki, the prevalence of thyroid diseases rises with dose. Figure 1 shows this for females in the fifth cycle (1966–1968). The number for males is too small to yield meaningful rates, but the data (not given here) from the 2-year examinations (11) suggest a possible radiation relationship also.

Simple and nontoxic nodular goiters constitute approximately 75% of the diagnoses. The remainder include thyroiditis and disorders of thyroid function in about equal proportions.

During observations over 16 months in 1958–1959, Hollingsworth *et al.* (20) examined more than 5000 subjects of the AHS in Hiroshima. They found that simple nontoxic goiters were predominant among thyroid disorders. Nodules and

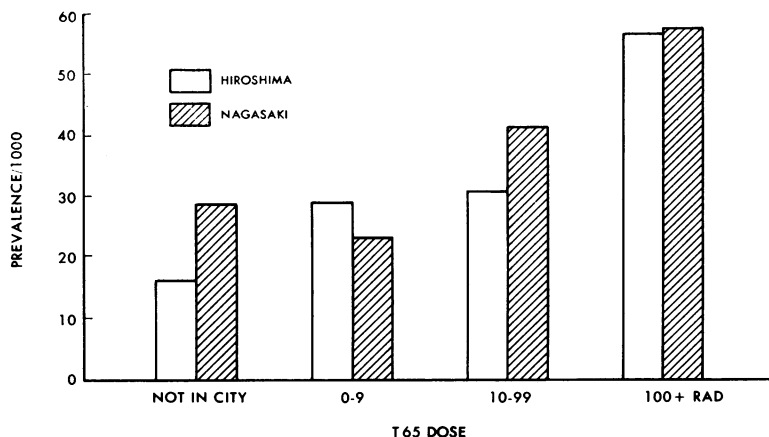


FIG. 1. Prevalence of diseases of the thyroid, fifth examination cycle, by radiation dose and city for females age 0-19 ATB.

hyperthyroidism were more frequent in the group proximal to the hypocenter. Although these investigators were cautious in ascribing these findings to radiation from the atomic bombs, the persistence of these trends in Hiroshima females throughout the five cycles makes these observations even more convincing. Moreover, in Nagasaki, where a special study was not undertaken, radiation-related thyroid disease is also seen, especially for females who were young when irradiated.

Radiation effects may be more readily noted in subjects with dietary (goitrogen) or genetic disposition to hyperplasia of the thyroid gland, but data on these points are not available. Radioactive fallout, specifically iodide nuclides, is not considered to be a factor, city wide (21), but the possibility of radiation-induced or augmented hypothyroidism cannot be ruled out in view of studies of Marshall Islanders (22). Studies in process will measure serum thyroid-stimulating hormone levels in a further effort to assess thyroid function in A-bomb survivors. During 1962-1963, tests (unpublished) of thyroid function and antibodies in more than 1000 subjects did not show significant differences between exposed and nonexposed groups.

DISEASES OF THE EYE

This is a heterogeneous group of diagnoses made during the screening examinations and influenced by many short-term intensive investigations. For the entire group examined, average prevalence rates increased generally with A-bomb radiation dose.

In Hiroshima the radiation relationship was statistically stronger than in Nagasaki. Among Hiroshima females, prevalence increased significantly with dose for those aged 0-19 ATB in each cycle except the third; for those aged 20-29 ATB in the second, third, and fifth cycles; and for those aged 40-49 ATB in the second and fourth cycles. For males aged 0-19 ATB, a significantly increased prevalence of disease was notable in the first and second cycles.

Younger persons ATB may have been the most sensitive to radiation-associated eye conditions (Fig. 2). Also, Miller (23) has reported more refractive errors among proximally exposed children compared with those more distant from the detonation. However, the conclusions based on the cycle examination data cannot necessarily be taken to apply to every particular eye condition in this group. The irregularities in the association of disease with radiation among age, city, or sex

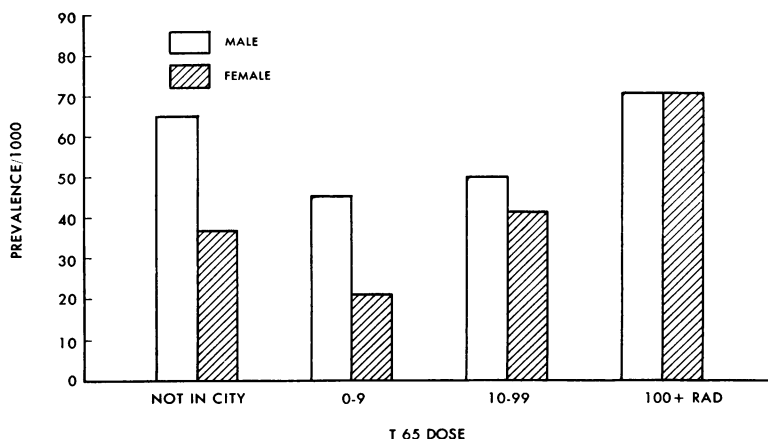


FIG. 2. Prevalence of diseases of eye, fifth examination cycle, by radiation dose and sex for Hiroshima, age 0-19 ATB.

groups may be attributable, in part, to the many different observers associated with prior cataract substudies (24-31).

Of the group of eye conditions discussed in this section, the diagnosis of cataracts is the major condition in Hiroshima (43.6% of the total) and the second most prominent in Nagasaki (21.1%). Since the prevalence ratios of cataracts to refractive abnormalities are markedly different in the two cities, it may be that a large observational bias is, in fact, present.

Alternatively, it may be that neutrons, which contributed significantly to total radiation exposure only in Hiroshima (9), are much more effective than gamma radiation for the induction of cataract. A dose-dependent effectiveness for neutron induction of lenticular abnormalities has been shown in experimental animals (32).

Studies now in progress concerning aging and visual acuity and accommodation may yield further insight into eye conditions.

OTHER CONDITIONS

The survey of a decade of clinic examinations has uncovered a variety of other radiation-related trends; some are statistically significant for a portion of the period under discussion, others are suggestive. For instance, the prevalence of tuberculosis was increased in males exposed to 100+ rad at age 20-29. This was not uniform and occurred only during the second, third, and fifth cycles. Since healthy, military-age males were notably absent from the civilian population (and accordingly also from the ABCC clinical cohort), a bias in favor of less robust young persons who were exposed to the A-bombs is probable.

For all other infective, parasitic, and degenerative diseases, there was no relationship with A-bomb radiation during 1958-1968.

Another aspect, which was reexamined with the new dosimetry, concerns growth among persons exposed to high doses of A-bomb radiation. In general, these persons seem shorter and lighter in weight at the completion of their growth period.

GROWTH AND DEVELOPMENT IN EXPOSED CHILDREN

For both cities and for both sexes, Fig. 3 shows shorter adult stature for the subjects aged 0-19 who received 100+ rad ATB. The measurements used in the

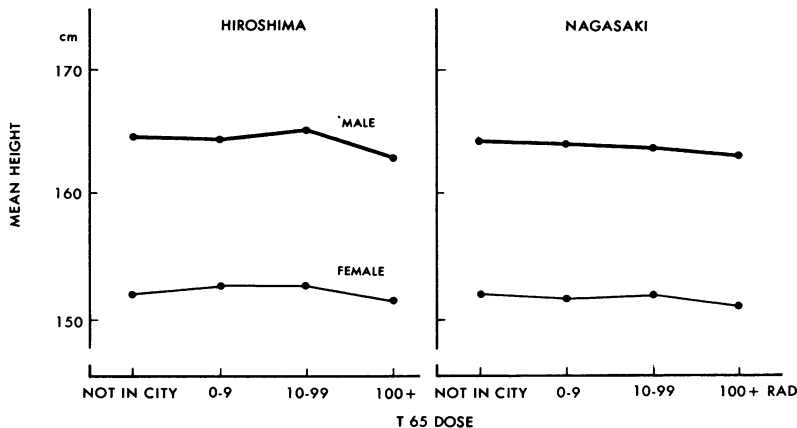


FIG. 3. Mean standing height, fifth examination cycle, by radiation dose, sex, and city, age 0-19 ATB.

figure were made during the fifth cycle (1966-1968), at a time when the youngest subjects were 21 years old. Significant differences ($P \leq 0.01$) are found only for Hiroshima males; but an overall relation of diminished growth to A-bomb seems clear. Additional analyses have shown that both male and female children who were heavily irradiated in Hiroshima are, on the average, shorter adults (33). The mean difference between those exposed at ages under 5 years to 100+ rad compared with nonexposed children was about 4 cm ($P \leq 0.001$).

Observations regarding weight are similar. Especially in Hiroshima, males and females show significantly ($P \leq 0.001$) lower body weight among those exposed to 100+ rad when less than 20 years old.

Any explanation of growth differences must take into account possible growth arresting factors, such as malnutrition, and the ages at which diets were nutritionally deficient. In addition, physical and psychological stresses were certainly prevalent in wartime.

Deficient linear growth is reported for Marshall Island boys who were exposed when they were less than 5 years old to radioactive fallout resulting from bomb testing in 1954 (34). In these cases, hypothyroidism was presumably primarily responsible. An association between thyroid dysfunction and exposure to the A-bomb is under study at ABCC. However, it may be impossible to prove that a total-body radiation effect on growth was mediated by thyroid disease.

A syndrome consisting of small stature, microcephaly, and mental retardation has been reported among children who were exposed to A-bomb radiation while in utero (23, 35, 36). Some growth retardation was also found among heavily exposed children (37, 38), but the dose effect was estimated by distance. More recent publications (39, 40) have strengthened these conclusions using dose estimations to the mother. Our observation in conjunction with these other studies seem to support the conclusion that the sensitivity of the child to radiation effects on the growth process did not necessarily end at the moment of birth.

These conclusions on growth and development of heavily irradiated children are strengthened when the evidence of suggestively smaller heart and thoracic diameters among those aged 0-19 ATB who received high doses of radiation is revealed in clinical screening (11). These measurements were made on standard X-rays

TABLE 4
TRENDS AMONG A-BOMB SURVIVORS; 1958-68

Class	ICD classification ^a	Male/female	Intercity ^b	Changes ^c with age	Time
Tuberculosis	001-019	M > F	H < N	—	Dec
Syphilis	020-029	H: M > F	H < N	Inc	Dec
Parasitic diseases	120-138	N: M < F	H < N	—	Dec
Diabetes	260	M > F	M: H > N	Inc	Inc
Arteriosclerotic heart disease	420-422	M > F	—	Inc	Inc
Hypertensive heart disease	440-443	—	H < N	Inc	Inc
Diseases of blood	290-299	M < F	—	—	Dec
Cholesterol		M < F	—	—	Inc
Glycosuria		M > F	H > N	Inc	Inc
Total WBC		M > F	—	—	Dec

^a International Classification of Disease, 7th Revision.

^b H = Hiroshima; N = Nagasaki.

^c Incidence: Inc = Increased; Dec = Decreased.

of the chest routinely obtained every biennium. In addition, somewhat lower blood pressures have been recorded among heavily irradiated subjects.

CHANGES OVER TIME AND OTHER TRENDS

As a longitudinal population study, the current examination program has persisted for 15 years at this writing.

It was not expected that for most observations during these years there would be any very large trend in health status. Some of the changes which were noted may be real, others may reflect trends in local medical practice or emphasis by physicians with particular interests. Several observations show marked differences between the cities of Hiroshima and Nagasaki. Some of these are listed in Table 4. In none of these items were irradiated persons at apparently greater risk.

DIABETES MELLITUS

The prevalence of diabetes mellitus increased sharply from Cycle 1 to Cycle 5 (Fig. 4), doubling in older people and increasing by an even larger factor in those less than 40 years of age ATB. It is likely that there was more intensive screening for diabetes after the early interest in the epidemiology and characteristics of this disease in Japan (41-43).

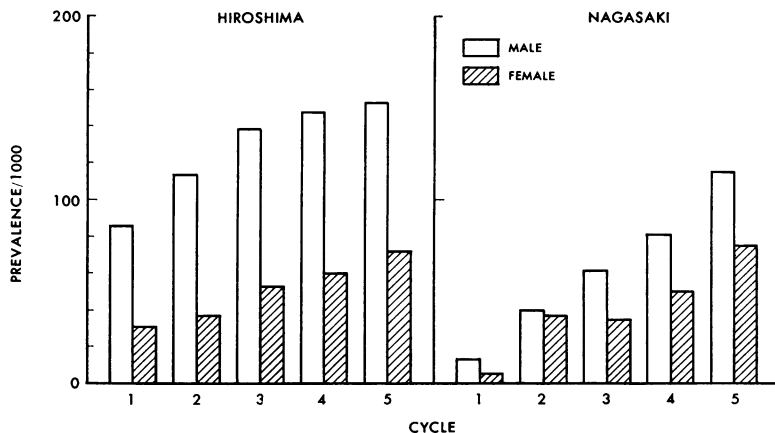


FIG. 4. Prevalence of diabetes mellitus by cycle, sex, and city, age 40-49.

The prevalence of this disease rose with age in both cities except in ages 50+ ATB.

Age-related diminishing glucose tolerance is well known, but this seems unable to account for the steep increase with time noted here. Other factors that may be important are changing diagnostic criteria, more intensive testing, and a gradual dietary change to include Western foods.

Males, in both cities, showed higher rates than females throughout the five cycles (Fig. 4). This difference would not be expected to be affected by changing diagnostic effort or change in technique for glucose determination. Complications of diabetes were not studied, but very few insulin-dependent cases were seen.

DISEASES OF BLOOD AND BLOOD-FORMING ORGANS

The major component of this group of conditions is Fe-deficient anemia. In Hiroshima, changes in prevalence were not striking; however, in Nagasaki, especially among females, prevalence dropped very sharply from extraordinarily high levels to a level comparable with Hiroshima. This may reflect the special interest of investigators concerned with refractory and iron-deficiency anemia in Nagasaki over the period 1959–1962, a decrease in intestinal infestation (shown by a parallel decrease in ova and parasites in stool), and general improvement in diagnosis and treatment in both communities.

SERUM CHOLESTEROL

The serum cholesterol values showed large increases from the first to the fifth cycles—from mean levels of the order of 150–160 mg/100 ml to 170–190 mg/100 ml. This may reflect increased westernization of the diet.

In summary, A-bomb survivors health over the second decade after the bombs seems to reflect expected findings in a country which had rapidly applied the benefits of modern technology. Degenerative diseases, and particularly ischemic heart disease, have increased; diabetes and cholesterol levels have increased. Chronic infectious and parasitic illnesses have decreased. Little clinically diagnosable impact of A-bomb radiation is seen in specific entities except thyroid hyperplasia (simple goiter). However, a somatic effect of radiation is noted in the shortened adult stature of those heavily irradiated in childhood. Neither heretofore unknown diseases nor unusual manifestations of well-known conditions have been found.

MORTALITY AND CANCER

Since the ABCC study cohort is fixed, it can only age relentlessly; there is no input of young persons. Deaths, especially in the older groups, continuously subtracted subjects. However, the annual mortality rates in the examined group showed no significant relationship to A-bomb radiation, nor was there a consistent difference between Hiroshima and Nagasaki. Thus, we must look to studies other than the routine clinic examinations for more details. The 5-fold larger population sample (Life Span Study) of which the clinically examined group is a part does reveal continuing increased mortality among heavily exposed persons (12). This seems to be associated with deaths due to cancer, other than leukemia, and in recent years is seen predominantly among those exposed at ages less than 10 years. Since this finding is based on death certificates, confirmation must await correlation between clinical observations and analysis of findings at autopsy.

It is of interest that cancer of the stomach, for which Japan ranks highest among

developed countries (44), has not been found consistently increased among heavily exposed survivors. One reason may be the high rate in controls which obscures possible small differences due to radiation. More intensive case-finding studies are now under way, based on epidemiologic evidence of higher risk in those with abnormalities in gastric acid and blood pepsinogen levels (45).

The absence of more definite findings may lie in the inability to diagnose all conditions in the living subject, the large variability in accuracy of clinical examinations which involved many physicians, and the long latent period for cancer.

ACCELERATION OF AGING

It has been difficult to come to grips with this provocative subject. Despite a large body of experimental work which suggests that morbidity from nonspecific causes is increased in irradiated animals, the design of an epidemiologic study among humans is difficult. Hollingsworth *et al.* (46) studied age-related tests in a small portion of the clinic group, and found no difference in responses of A-bomb survivors compared to nonirradiated controls. These observations are currently being extended to the entire clinic sample of about 16,000 subjects.

Changes in physiologic function which differentiate normal persons from irradiated survivors are sought. But whether the result can be properly called "premature aging" is debatable, and no clear hypotheses are agreed upon (47).

PSYCHOLOGIC AND SOCIAL SEQUELAE

These areas are the most elusive, and no definitive studies have been undertaken. Of all the possible gauges of delayed effects of the atomic bomb, accurate measurements regarding survivors' attitudes, habits, and fears are the most difficult to obtain. Certainly, Americans cannot use their cultural preconceptions, or even language, in a proper scientific enquiry among Japanese.

Regarding A-bomb survivors, Lifton (48) has written concerning a unique and overwhelming encounter with death, and the aftermath of fear of late effects even into future generations. His extensive insights are based on interviews with 75 persons, of whom only 33 were selected from a list of 90,000 survivors. It is not clear whether his conclusions apply to a larger portion of the population, and attitudes measurable in large-scale surveys are needed.

On the other hand, there is evidence, by means of a self-administered questionnaire completed by about 12,000 members of the Adult Health Study group, that exposed persons, even 20 years after the bombs, experienced more nonspecific symptoms than nonexposed persons. The effect of this on their life patterns is not known. As Lifton pointed out, the survivors have been made aware of radiation effects by the news media and a variety of benevolent and political organizations.

Matsumoto (49) has gathered data that reflect patterns among the study population which do not support some conceptions regarding suicide and marriage trends among the survivors. Figures for 1950–1965 showed no higher rates for suicide among heavily exposed compared with Japanese national vital statistics. The percentage of those who were not married 14 years after the bomb was no greater among heavily exposed groups compared with lightly and nonexposed subjects.

This does not mean that there was no fear of marriage or genetic consequences, or that survivors were able readily to find employment. Such surveys that have been accomplished suggest only that there is no clear evidence of a significantly affected life pattern.

CYTOGENETIC STUDIES

Chromosome alterations consisting of dicentrics, ring forms, and breaks are increased in heavily exposed survivors (50). Although these alterations seem to reflect a specific radiation effect (51), to date, no disease or functional abnormality has been associated with these cytogenetic findings. Continued study, including cloning of abnormal cells found in irradiated survivors, is part of the ongoing program.

RELEVANCE TO THE PRESENT AND FUTURE

Controversy over the uses of technologic advances finds a major outlet in potential hazards of radiation. Japan, possibly at a greater rate than the United States and other industrial nations, is building nuclear sources for power. To those concerned with setting standards for radiation protection, the long-term consequences of the atomic bombs are important and useful (52).

Examination and follow-up of Japanese who are still alive after experiencing variable doses of A-bomb radiation provide a unique opportunity for the science of health protection. Observations on cancer, accelerated aging, cytogenetic changes, mutations in offspring, etc., must continue, at least for the lifetime of the survivors.

Studies to date have shown that those irradiated during the period of rapid growth and development—from conception to adolescence—appear to be most susceptible to abnormalities. This knowledge is applicable to future health policies among nations where radiation hazards will be an increasing by-product of progress.

SUMMARY

Since 1958 a population of about 16,000 exposed and sex- and age-matched nonexposed persons have been examined biennially at the Atomic Bomb Casualty Commission in Hiroshima and Nagasaki, Japan, to judge late effects of A-bomb radiation. The biennial checkups, in contrast to more probing studies with which they are compared, have shown few radiation-related effects.

Screening examinations have revealed changes over time (1958–1968) in disease patterns and certain intercity aspects. In this survey, those who experienced the A-bomb disaster and survived seem generally to be as healthy as nonirradiated persons, though risks for specific late effects cannot be dismissed, particularly among those who were children at that time.

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