THE 2000 SIEVERT LECTURE—LESSONS FROM ATOMIC BOMB SURVIVORS IN HIROSHIMA AND NAGASAKI

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SHORT HISTORY OF STUDIES ON ATOMIC BOMB SURVIVORS

People in Hiroshima and Nagasaki, without distinction of age or sex, experienced for the first time in human history exposure to massive doses of instantaneous ionizing radiation that was produced by the detonation of atomic bombs in August 1945. Such tragedies should never be repeated, but it is true that these unfortunate experiences have greatly enhanced our knowledge of the health effects due to exposure to ionizing radiation. Immediately after the atomic bombings, Japanese researchers initiated studies on the casualties caused by the bombings. Soon thereafter, Japan was occupied by the Allied Forces and initiative for the conduct of these studies was placed in the hands of the United States military mission, and the Japanese researchers were requested to join this mission for cooperation.

Based on the findings of this mission, the United States government established the Atomic Bomb Casualty Commission (ABCC) in Hiroshima and Nagasaki in 1947 and 1948, respectively, under the auspices of the National Academy of Sciences (NAS). The purpose was to study late health effects in the people exposed to the atomic bomb radiation. To attain this purpose smoothly, branch laboratories of the Japanese National Institute of Health (NIH) were attached to ABCC in 1948.

ABCC conducted studies on the atomic bomb survivors for 28 years thereafter, and during this time the United States provided most of the necessary funds and guidance for the operation of ABCC while the Japanese NIH undertook recruitment of Japanese investigators, advised on scientific matters, and also made efforts to secure the cooperation of the Japanese government, local organizations, and atomic bomb survivors. During the period when Japan was occupied by the Allied Forces, there were many restrictions for Japanese researchers in conducting studies on atomic bomb survivors, but after the Peace Treaty became effective in 1952, these restrictions were removed and active programs began in various institutions including local universities in Hiroshima and Nagasaki. The results of these studies have been summarized annually since 1959 at the meetings of the Research Council on Late Health Effects of Atomic Bomb Radiation.

From the need to further continue the research studies for an extended period, ABCC was reorganized in April 1975 into the Radiation Effects Research Foundation (RERF) based on Japanese law, with its finance, operation, and scientific responsibilities shared equally by the governments of Japan and the United States through the Japanese Ministry of Health and Welfare and the United States NAS under contract with the U.S. Department of Energy. The objective of RERF is clearly given in its Act of Endowment, which prescribes that it will contribute to the maintenance of the health and welfare of atomic bomb survivors and to the enhancement of the health of all mankind. RERF succeeded the research program of ABCC, adding to the latter's existing program new study projects beneficial to atomic bomb survivors.

ABCC-RERF studies are necessarily limited to the effects of acute, single-dose, whole-body, mixed gamma-neutron radiation, but their comprehensiveness and long prospective duration make them the most definitive descriptions of the late effects of radiation in humans. For this reason, the entire world relies heavily on ABCC-RERF data to set radiation standards, as demonstrated in the reports of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), the International Commission on Radiological Protection (ICRP), the International Atomic Energy Agency (IAEA), and the Committees on Biological Effects of Ionizing Radiation (BEIR Committees). It is almost certain that ABCC-RERF data will remain as a major source for the quantitative risk estimates.

The intent of this lecture is not to review the results of ABCC-RERF studies, but to draw certain lessons from these studies. Topics to be discussed here are exposed population (population at risk), exposure dose, relative risk and attributable risk versus absolute risk, and long-term follow-up health data.

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EXPOSED POPULATION (POPULATION AT RISK)

Epidemiological methods for assessing the health risks of radiation involve identifying the numerator of those with health abnormalities among the denominator population defined by exposure dose or the exposed population (population at risk). Long-term follow-up observations are usually required of an exposed population as a fixed cohort.

The current research program of ABCC-RERF began as a series of platform protocols based on a fixed cohort of about 120,000 survivors who were listed in the Japanese National Census of October 1950. Since the ABCC-RERF cohort consists of persons who survived the acute effects of the bombings and were still alive in late 1950, it has been pointed out that the results may reflect a resistant subpopulation of survivors who are not representative of overall human risk.

In this connection, some scientists contended that mortality in the ABCC-RERF cohort is biased because survivors might be healthier than those who did not survive, and thus the radiation effects observed in survivors might be underestimated (Stewart 1973; Kneal and Stewart 1978; Rotblat 1977). The ABCC-RERF cohort is, of course, a selected one, but it is important to show the magnitude of the effects of such selection on the induction of cancer by atomic bomb radiation.

In this regard, epidemiological, clinical, and radiobiological studies have been extensively carried out by ABCC-RERF researchers to clarify such bias. However, all the results obtained have failed to show any difference in the radiation sensitivity of the survivors as a function of their radiation dose. Examples of these data are shown in Figs. 1 and 2 (Tachikawa and Kato 1969; Nakamura et al. 1993). It was thus concluded that the effects of selection through the exclusion of deaths prior to 1950, if any, appear to be very small.

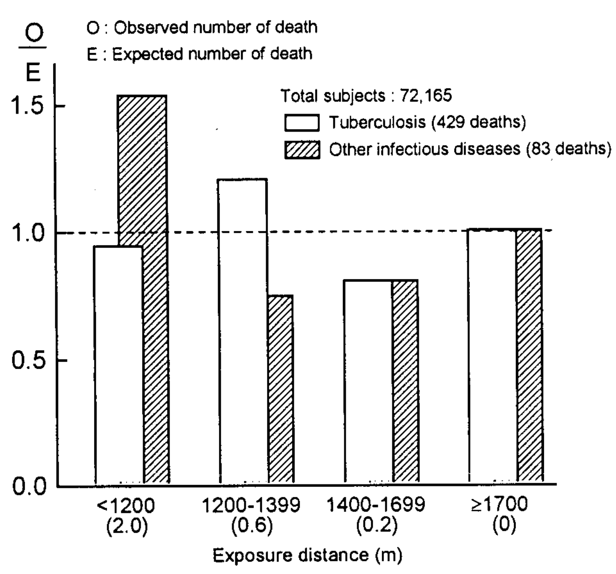

Fig. 1. Mortality from tuberculosis and other infectious diseases by exposure distance, October 1946–September 1950, Hiroshima (from Tachikawa and Kato 1969).

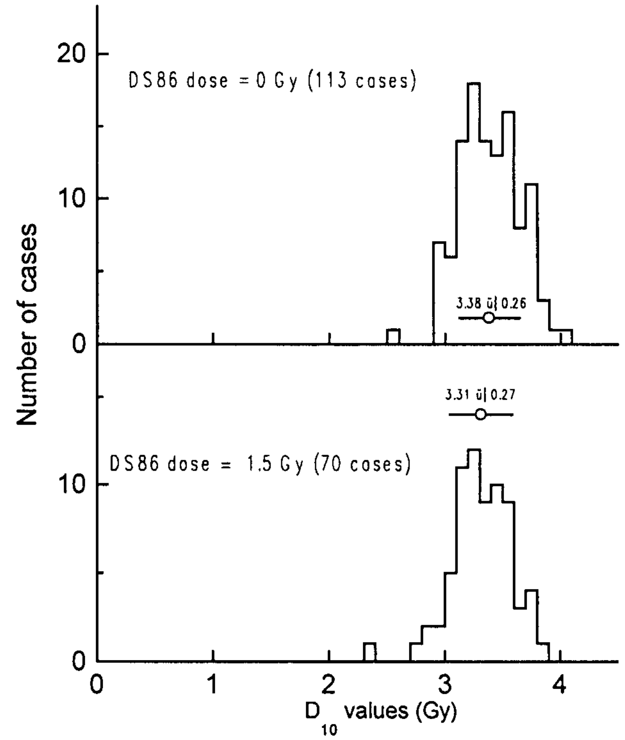

Fig. 2. Distribution of lymphocyte radiosensitivity (D_{10} values) between the distally and proximally exposed (from Nakamura et al. 1993). D_{10}: x-ray dose required to produce the death of 90% of lymphocytes.

In Hiroshima and Nagasaki, the identification of the exposed population as denominator was inevitably delayed because of the confusion after the war. In the case of the Chernobyl accident, however, a greater delay has occurred and so far only the numerator has been emphasized. This is regrettable, and every effort should be made to provide an appropriate denominator as soon as possible to pursue long-term follow-up studies of persons after radiation exposure.

EXPOSURE DOSE

Radiation dosimetry is essential for identifying the exposed population so that the dose-response relationships can define the health risks of radiation. All ABCC-RERF studies have been dependent on radiation dosimetry. Currently, Dosimetry System 1986 (DS86) created and monitored by a U.S.-Japan joint group of experts is used. Although DS86 is considered to be the best scientific dosimetry system at this stage, it has been indicated that DS86 has problems such as discrepancies between calculated and measured gamma and neutron doses at long distances.

It was thus decided in 1989 to establish the U.S. and Japanese Committees to continue to review these issues

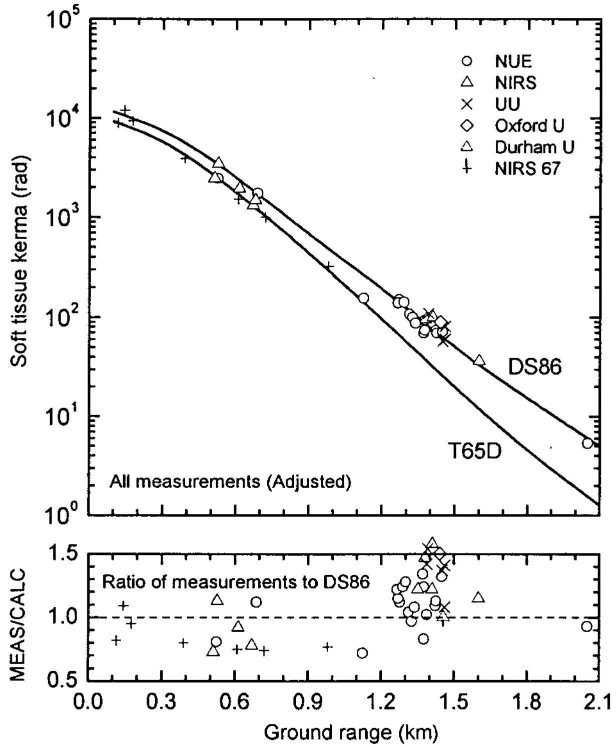

Fig. 3. Thermoluminescence measurements of gamma rays: Comparison of theoretical calculations with measurements (free-field kerma in soft tissue vs. distance from hypocenter at Hiroshima; from Maruyama et al. 1987).

in each country. Both committees have been cooperatively promoting their activities up to the present. Final conclusions are not yet obtained, but the followings are commonly recognized by both committees:

1. Measured gamma doses are 10–15% higher than DS86 doses at the distance of 1 km or greater as shown in Fig. 3 (Maruyama et al. 1987);
2. Measured-to-calculated thermal-neutron activation ratios show an increasing trend with an increasing distance as shown in Fig. 4 (Straume et al. 1992); and

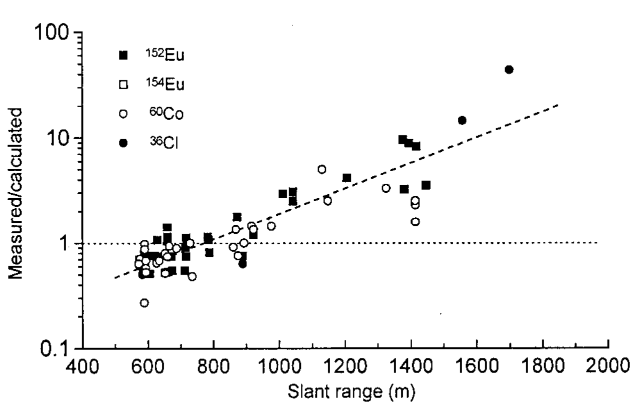

Fig. 4. Measured-to-calculated thermal neutron-activation ratios in Hiroshima at various distances from the epicenter (Straume et al. 1992).

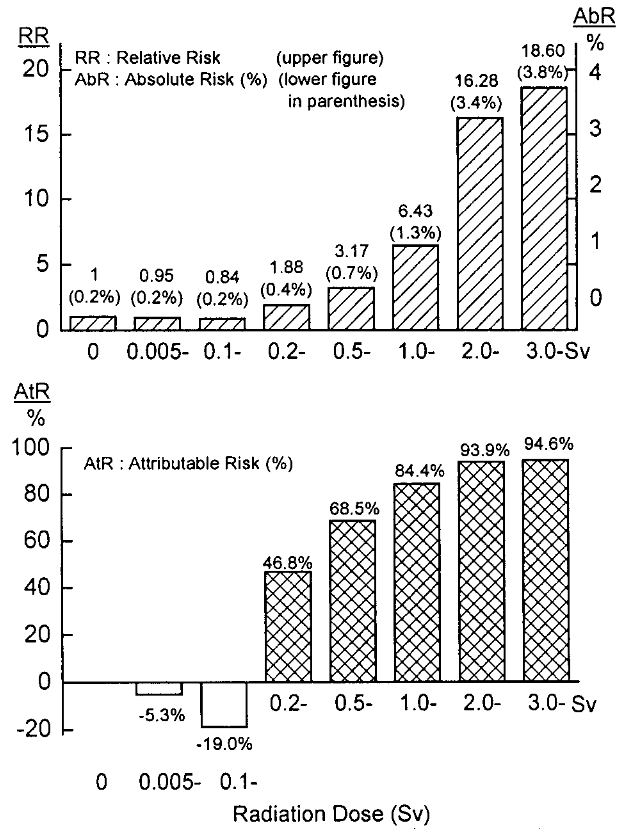

Fig. 5. RR, AbR (upper) and AtR (lower) of leukemia mortality by radiation dose, 1950–1990 (both sexes and all ages).

3. Copper samples are now being analyzed to measure fast-neutron activation.

Although these issues will be discussed at the joint conference of the U.S. and Japanese dosimetry committees, it is expected that the discrepancy in gamma dose at distances may lead to a slight increase in calculated doses at around 2 km and radiation risk assessment will not be greatly affected. It is also considered that the discrepancy in neutron doses may not greatly affect the total dose equivalent because gamma rays contribute much more to the total atomic bomb radiation dose equivalent than neutrons.

Dosimetry-related efforts at RERF involve the use of biological end points and the newly evolving and promising method of electron spin resonance of tooth enamel. The biodosimetry is of two types: (1) chromosomal aberrations with detection enhanced by fluorescence *in situ* hybridization, and (2) flow cytometric methods to detect somatic mutation in red blood cells and lymphocytes. These results contribute substantially to the development of methods and validation of biological dosimeters, as well as provide insights into mechanisms of radiation effects. To our disappointment, the methods have not clarified the issue of biological variability because without an independent physical dosimeter we are fundamentally unable to distinguish between biological variability and DS86 error. We hope that this

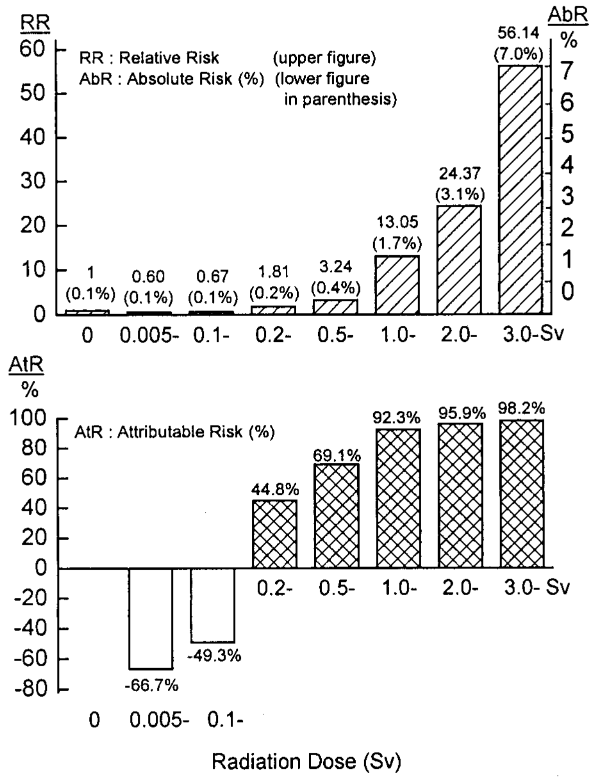

Fig. 6. RR, AbR (upper) and AtR (lower) of leukemia mortality by radiation dose, 1950–1990 (both sexes and under 10 y).

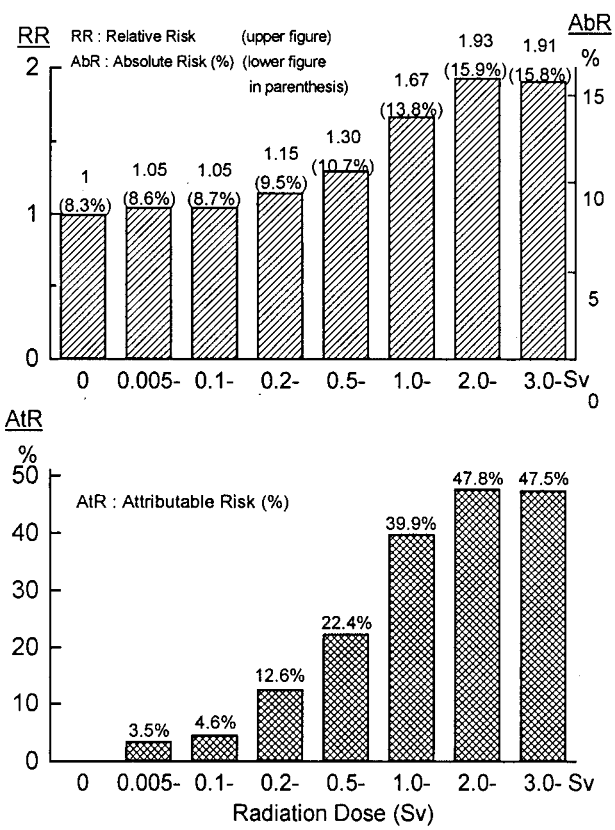

Fig. 7. RR, AbR (upper) and AtR (lower) of solid cancer mortality by radiation dose, 1950–1990 (both sexes and all ages).

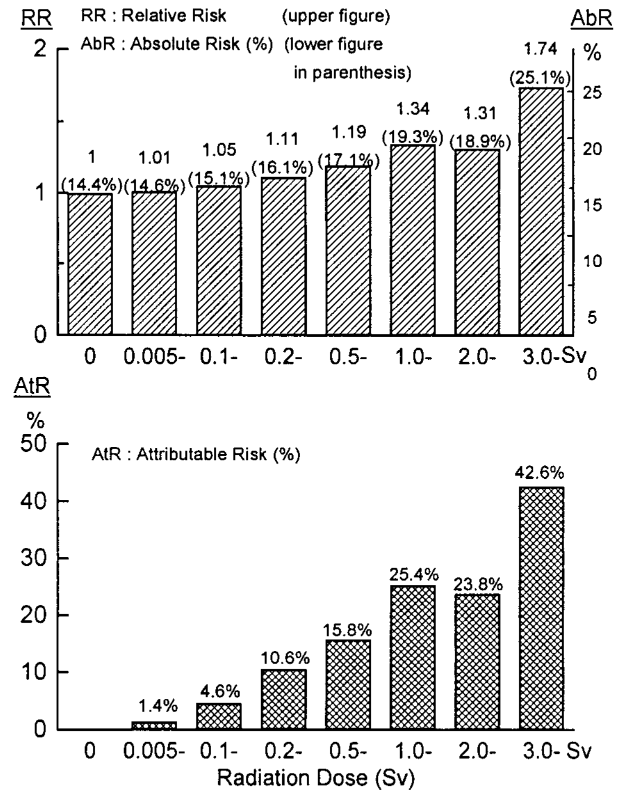

Fig. 8. RR, AbR (upper) and AtR (lower) of solid cancer mortality by radiation dose, 1950–1990 (both sexes and over 40 y).

impasse can be broken by physical dosimetry based on tooth enamel.

RELATIVE RISK (RR) AND ATTRIBUTABLE RISK (AtR) VERSUS ABSOLUTE RISK (AbR)

According to the definition in *A Dictionary of Epidemiology* (Last 1995), RR is the ratio of the risk of disease or death among the exposed to the risk among the unexposed, and AtR is the rate of a disease or other outcome in exposed individuals that can be attributed to the exposure, while AbR is the observed or calculated probability of an event in a population under study, as contrasted with the RR.

RR and AtR are often used to express the degree of association between disease or death and exposure, but AbR is the fundamental index for assessing the frequency with which a radiation-induced disease or death occurs. For example, RR and AtR calculated from leukemia mortality during 1950–1990 among atomic bomb survivors (both sexes and all ages) exposed to 3 Sv or more were 18.6 and 95%, respectively, as shown in Fig. 5, indicating a strong association between radiation and leukemia. However, AbR shown in the same figure was 3.8%, suggesting that nonetheless most of the survivors are not so vulnerable to leukemia.

If we observe people in a more vulnerable age group such as under 10 y old, RR and AtR from leukemia

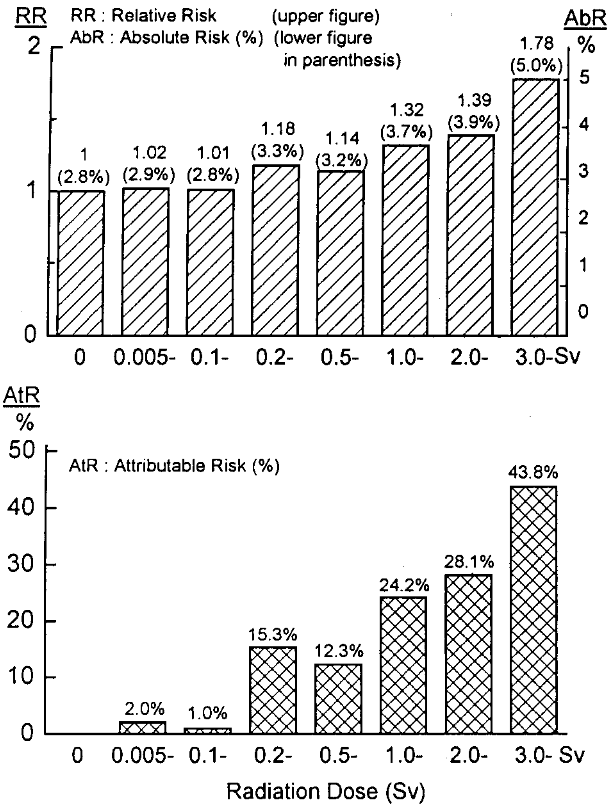

Fig. 9. RR, AbR (upper) and AtR (lower) of stomach cancer mortality by radiation dose, 1950–1990 (both sexes and ages).

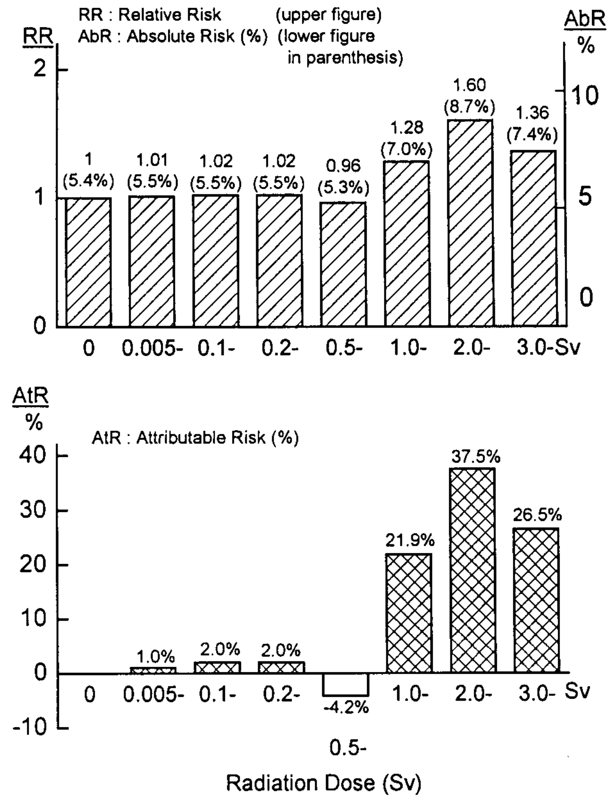

Fig. 10. RR, AbR (upper) and AtR (lower) of stomach cancer mortality by radiation dose, 1950–1990 (both sexes and over 40 y).

mortality for both sexes is 56.1 and 98%, respectively, and AbR is 7.0% as shown in Fig. 6. This means that, although the association between radiation and leukemia is much stronger than that for all ages, 93% of survivors under 10 y old are still resistant to leukemia even for exposure of 3 Sv or more. Clues to the pathogenesis of leukemia may be obtained from the epidemiological and molecular-biological analyses by applying the case-control study method to those who contracted leukemia as cases and those who did not as controls.

Similar observations were also made on solid cancer, stomach cancer, and lung cancer. In the case of solid cancer mortality during 1950–1990 for both sexes and all ages, RR and AtR for 3 Sv or more were 1.9 and 48%, respectively, while AbR was 15.8%, indicating that about 84% of those heavily exposed to radiation are not susceptible to solid cancer as shown in Fig. 7. Fig. 8 shows RR, AtR, and AbR in solid cancer mortality for those over 40-y of both sexes. These figures for 3 Sv or more are 1.7, 43%, and 25.1%, respectively.

Similarly, RR and AtR for 3 Sv or more were 1.8 and 44%, respectively, for stomach cancer mortality (1950–1990, both sexes and all ages) and 2.2 and 53%, respectively, for lung cancer mortality (1950–1990, both sexes and all ages), while AbR was 5.0% for the former and 2.1% for the latter as shown in Figs. 9 and 11. If observations are made for those over 40 y old, these figures are 1.4, 27% and 7.4%, respectively, for RR, AtR, and AbR of stomach cancer mortality, and 2.1%, 52%, and 3.3%, respectively, for those of lung cancer mortality as shown in Fig. 10 and Fig. 12. Case-control study methods should also be attempted to compare those who contracted these cancers with those who did not.

LONG-TERM FOLLOW-UP HEALTH DATA

One of the core research programs at ABCC-RERF is the Adult Health Study (AHS), which has been following a subsample of 20,000 survivors since 1958 using biennial health examinations. The AHS physical and laboratory examinations provide valuable insight into emerging and nonfatal effects of radiation as well as serving as a source of important biological samples for biodosimetry and related activities.

The clinical studies often confirm and even presage the mortality-based studies. Recent examples of clinical findings include the evidence for thyroid, parathyroid, and menstrual malfunction and the subtle and still unexplained changes that occur in calcium metabolism as a function of radiation dose.

Besides these, long-term follow-up health data obtained from AHS are useful for evaluating the prospective outcomes of health conditions observed at the beginning of study. Two examples of such study will be

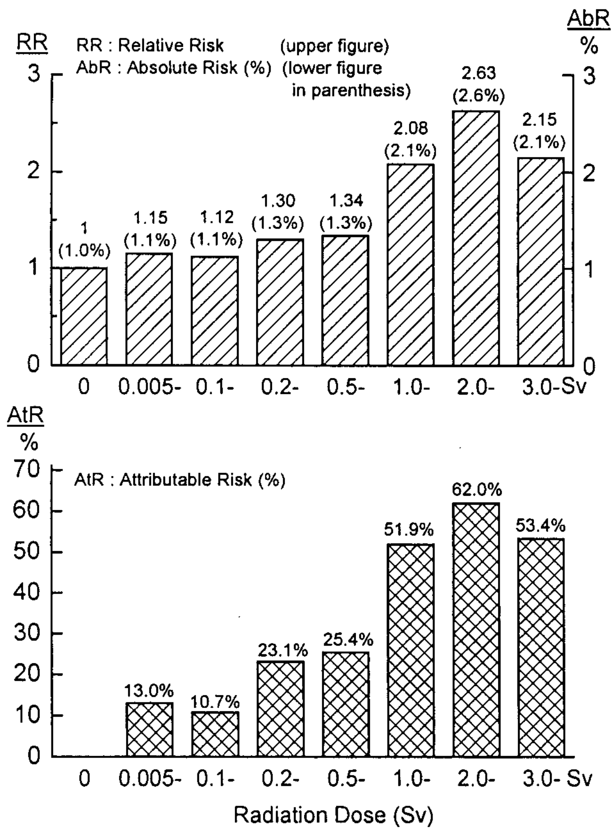

Fig. 11. RR, AbR (upper) and AtR (lower) of lung cancer mortality by radiation dose, 1950–1990 (both sexes and all ages).

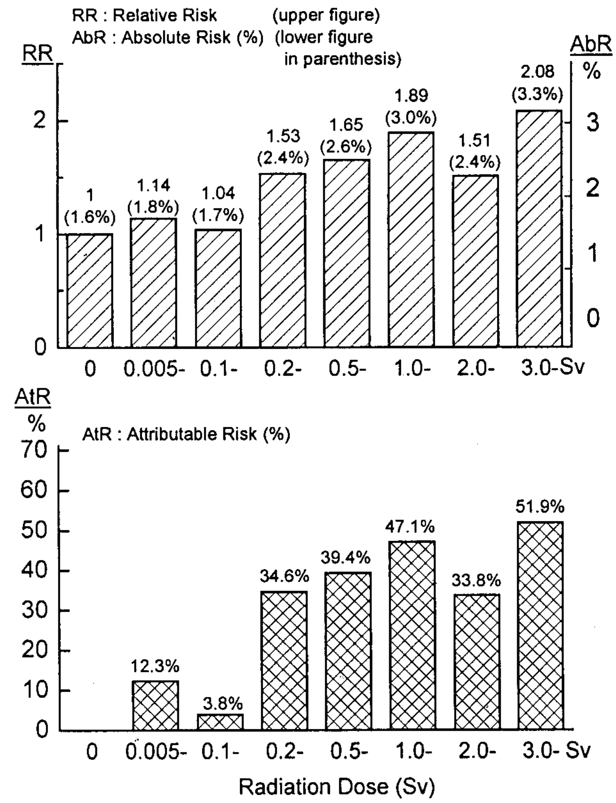

Fig. 12. RR, AbR (upper) and AtR (lower) of lung cancer mortality by radiation dose, 1950–1990 (both sexes and over 40 y).

introduced here. One is a case-control study of short and long lives which were intended to identify the factors that promote longevity or contribute to short lives and to utilize its information for prevention of diseases and health promotion.[†]

AHS participants aged 56.1±3.5 who underwent the periodical health examination during 1968–1970 (the sixth cycle of biennial examinations) were the subjects of the study. Those who died before 65 years of age were regarded as cases and those who lived more than 80 years of age as controls as shown in Fig. 13. 178 cases and 356 controls were randomly selected from both groups by matching on residence (Hiroshima or Nagasaki), sex, and year of birth as shown in Table 1, and each item of physical and laboratory examinations indicated in Table 2 at the beginning of observation were compared between the two groups.

Statistically significant differences between the two groups were observed in some areas such as high blood pressure, low total cholesterol levels, smoking, high and low body mass index (BMI), high and low physical activity, proteinuria, inappropriate dietary habits and radiation, suggesting that these might be predicting factors of short lives as shown in Table 3.

Another example is related to healthy worker effect (HWE), which refers to lower total mortality in workers

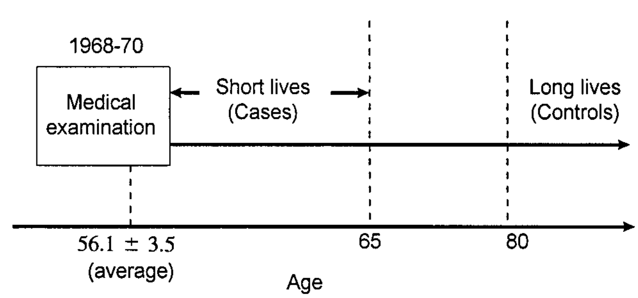

Fig. 13. Case-control study of short and long lives—study design.

Table 1. Number of cases and controls.[a]

	Men	Women	Total
Case	105	73	178
Control	210	146	356

[a] Case: Control = 1:2
Birth year: 1911 (average)
Age at examination: 56.1 ± 3.5.

[†] Kodama, K.; Kasagi, F.; Fujita, Y.; Yamada, M.; Fujiwara, S. Case-control study of short and long lives in the population of Atomic Bomb survivors. Proceedings of the 15th International Scientific Meeting of the International Epidimiological Association, Florence, Italy, 4 September; 1999 (oral presentation).

Table 2. Factors for analysis.

Variables:	-Diseases
	-Symptoms
	-Systolic blood pressure
	-Body mass index
	-Proteinuria
	-Hemoglobin
	-WBC count
	-Total serum cholesterol
	-ECG findings
	-Smoking
	-Dietary habit
	-Physical activity
	-Occupation
	-Radiation dose

Table 3. Factors to predict short lives.[a]

-High blood pressure
-Low total cholesterol
-Smoking
-High and low BMI
-High and low physical activity
-Proteinuria
-Inappropriate dietary habits
-Radiation

[a]Kodama, K.; Kasagi, F.; Fujita, Y.; Yamada, M.; Fujiwara, S. Case-control study of short and long lives in the population of Atomic Bomb survivors. Proceedings of the 15th International Scientific Meeting of the International Epidimiological Association, Florence, Italy, 4 September; 1999 (oral presentation).

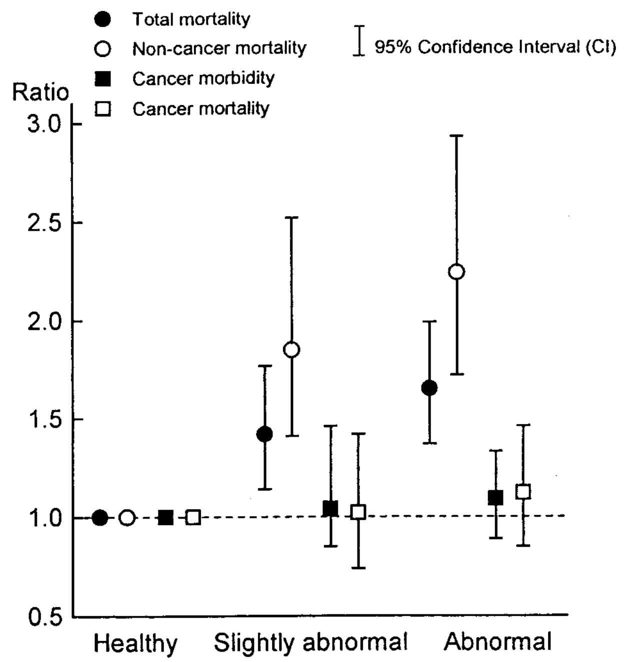

Fig. 14. Ratios of total mortality, non-cancer mortality, cancer morbidity and cancer mortality during 1970–1994 in 3 groups (healthy, slightly abnormal, and abnormal) screened by health examinations (Koyama 1999).

than in the general population. This phenomenon has been observed in many occupational studies, and one of the major sources of HWE is considered to be selection at employment or the so-called "healthy screenee effect." However, there has been much discussion as to whether the healthy screenee effect is observed not only for total mortality but also for cancers.

Although the AHS participants are not necessarily workers, AHS follow-up data were analyzed to obtain some suggestions on this problem (Koyama 1999). The study group consisting of 2,850 males aged 22–59 y sampled from a subcohort of 20,000 AHS participants was divided into 3 groups: healthy, slightly abnormal, and abnormal according to the combination of clinical and laboratory data (11 items such as hemoglobin, cholesterol, urinary protein, urinary sugar, blood pressure, obesity, audition, vision, electrocardiogram, chest x ray finding, past history) examined between 1 August 1967 and 31 July 1969.

The rates of total mortality, non-cancer mortality, cancer morbidity, and cancer mortality were then calculated based on the person-years of three groups during the observation period from 1 January 1970 to 31 December 1994. As shown in Fig. 14, the risks of cancer morbidity and mortality for "abnormal" were 1.09 (95% CI: 0.89–1.33) and 1.12 (0.85–1.46), respectively, compared with 1.65 (1.37–1.99) for total mortality and 2.24 (1.72–2.93) for non-cancer mortality. These risks for slightly abnormal were in the same tendency as those for abnormal, that is, 1.04 (0.85–1.46) and 1.02 (0.74–1.42) for cancer morbidity and mortality, respectively, and 1.42 (1.14–1.77) and 1.85 (1.36–2.52) for total mortality and non-cancer mortality, respectively.

These results indicate that the healthy screenee effect is seen for total mortality and non-cancer mortality, but not for cancer morbidity and mortality, suggesting that general health examinations are effective for prediction or prevention of total and non-cancer mortalities, but not of cancers. The problem is, however, that items of health examination for screening in this study are limited. More detailed health examinations should be attempted to confirm this conclusion.

COMMENT

It is true that ABCC had been regarded with distrust and disfavor by atomic bomb survivors. The fact that the study results in the early days of ABCC were published only in the scientific journals in the western countries and little was known in Japan also gave rise to criticisms regarding the secrecy and the closed nature of ABCC. Furthermore, the atomic bomb survivors were much displeased with ABCC for only conducting studies and tests and providing no apparent treatment. Nevertheless, every research program of ABCC and RERF has the positive cooperation of atomic bomb survivors, as is evident by the fact that their participation rate in the AHS has been maintained at a high level of about 80% on an average for more than 40 y. This is attributable to the understanding and cooperation of atomic bomb survivors and countless others in the communities of Hiroshima and Nagasaki. It must also be borne in mind that it is, at the same time, because of the untiring efforts of the Japanese and American research scientists and all employees of ABCC-RERF.

Because of the advancing age of atomic bomb survivors, it is becoming more and more difficult to identify the effects of radiation from those of other factors, and health effects that are still unknown may appear with aging phenomena. On the other hand, those exposed at younger ages are just now reaching the cancer-prone ages. Furthermore, about 45% of the survivors are alive as of the present time. By age at the time of the bombings, about 80% of those less than 30 years of age and near 90% of those less than 10 years of age are still alive. Some evidence points to an even greater risk in the very young. We estimate that it will be another 20 years before the question of age sensitivity can be addressed properly, making this issue one of the primary reasons for continuation of the studies into the future.

Interests in radiation exposure issues have recently reached a world-wide scale, and ever since the Chernobyl accident rapidly increasing numbers of people want to learn from the Hiroshima and Nagasaki experiences. We believe that it is our duty to disseminate the lessons obtained from Hiroshima and Nagasaki as widely as possible.

Finally, I would like to add that the association of radiation exposure with leukemia and other cancers has been established during 5 decades of data collection among the atomic bomb survivors and control population, leading to understanding of the nature and magnitude of risk associated with radiation, but much more can be learned from further follow-up of the survivors and their children. Some of these lessons were introduced here.

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The detonation of atomic bombs over Hiroshima and Nagasaki in August 1945 resulted in horrific casualties. The long-term effects of radiation exposure also increased cancer rates in the survivors. But public perception of the rates of cancer and birth defects among survivors and their children is greatly exaggerated when compared to the reality revealed by comprehensive follow-up studies. Share: FULL STORY. The detonation of atomic bombs over the Japanese cities of Hiroshima and Nagasaki in August 1945 resulted in horrific casualties and devastation. The long-term effects of radiation exposure also increased cancer rates in the survivors. Following the atomic explosion over HiroshimaÂ In general, though, the healthfulness of the new generations in Hiroshima and Nagasaki provide confidence that, like the oleander flower, the cities will continue to rise from their past destruction. The pilot of the Enola Gay, Paul Tibbets, took this photo of the aftermath. Perhaps most reassuring of this is the view of the cityscapes themselves.Â This experience of can serve as lesson in the present when much of the public and even some governments have reacted radically to the accident in Fukushima--in the midst of tragedy, there remains hope for the future. Further Reading: The Radiation Effects Research Foundation site outlines the results of numerous studies regarding the survivors of Hiroshima and Nagasaki. After The Bomb. Survivors of the Atomic Blasts in Hiroshima and Nagasaki share their stories. Photographs by HARUKA SAKAGUCHI | Introduction By LILY ROTHMAN. When the nuclear age began, there was no mistaking it. The decision by the United States to drop the worldâ€™s first atomic weapons on two Japanese citiesâ€"Hiroshima first, on Aug. 6, 1945, and Nagasaki three days laterâ€"was that rare historical moment that requires little hindsight to gain its significance. World War II would end, and the Cold War soon begin. New frontiers of science were opening, along with new and frightening moral questions. As TIME noted in the week following the bombings, the men aboard the Enola Gay could only summon two words: â€œMy God!â€. Hiroshimaâ€™s devastation failed to elicit immediate Japanese surrender, however, and on August 9 Major Charles Sweeney flew another B-29 bomber, Bockscar, from Tinian. Thick clouds over the primary target, the city of Kokura, drove Sweeney to a secondary target, Nagasaki, where the plutonium bomb â€œFat Manâ€ was dropped at 11:02 that morning. More powerful than the one used at Hiroshima, the bomb weighed nearly 10,000 pounds and was built to produce a 22-kiloton blast.Â However, it's estimated roughly 70,000 to 135,000 people died in Hiroshima and 60,000 to 80,000 people died in Nagasaki, both from acute exposure to the blasts and from long-term side effects of radiation. READ MORE: Photos: Hiroshima and Nagasaki, Before and After the Bombs. Citation Information. Article Title. atomic-bomb survivors, called hibakusha in Japanese. The human consequences of the two atomic bombings are the history of the. struggle by the hibakusha to survive and regenerate their life and families as well as.Â This article considers. lessons for Homo sapiens from Hiroshima and Nagasaki for gaining the wisdom to. realize a nuclear-weapon-free world and end the nuclear weapon age. I. Human Decision to Use Two Bombs on Humanity.Â of approximately 140,000 in Hiroshima and 73,000 in Nagasaki died instantaneously or. within five months due to the combined effects of three components of physical energy. generated by nuclear fissions: blast wind (pressure), radiant heat, and ionizing radiation.