RERF update RERF

*News & Views from the US–Japan Radiation Effects Research Foundation*

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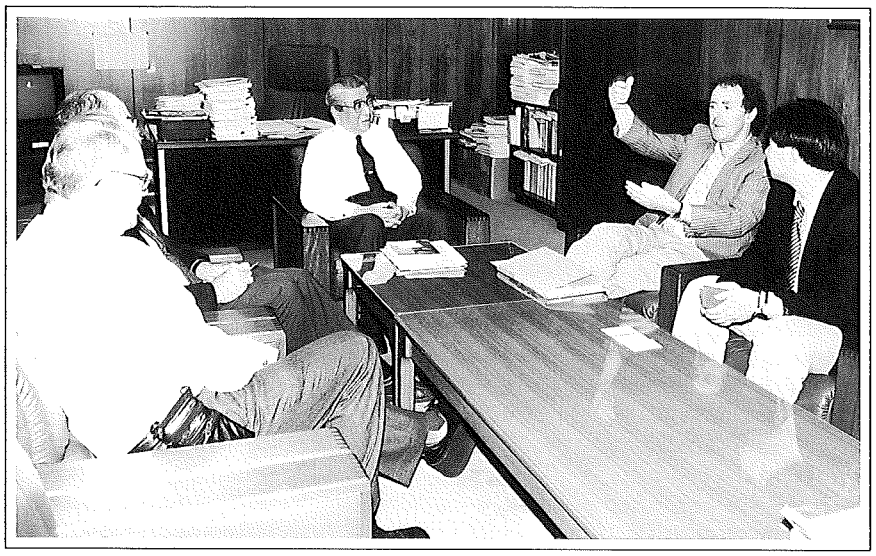
# *International Television Coverage Will Incorporate RERF Research Findings*

Worldwide interest in the effects of radiation exposure has not waned with the relaxing of Cold-War tensions. Making frequent headlines are instances of environmental contamination related to weapons' manufacturing, nuclear-power-plant mishaps, and the disposal of radioactive substances. Realizing that radiation research is indeed a "hot" topic, correspondents from three countries recently visited the RERF Hiroshima Laboratory.



Y OGASAWARA

***In early December, John Slater of the British Broadcasting Corporation, second from right, meets with RERF Chairman Itsuzo Shigematsu, center, RERF Chief of Research Seymour Abrahamson, left, and RERF Vice Chairman Mortimer Mendelsohn, seated to the left of Abrahamson.***

## *United Kingdom*

On 2 December, **John Slater** of the British Broadcasting Corporation (BBC) consulted with RERF directors about the BBC's plans to produce a two-hour documentary on the international politics and the environmental and health consequences of radiation. Scheduled for 1995, the show will mark the 100th anniversary of Wilhelm Rœntgen's discovery of X rays and the 50th anniversary of the atomic bombings.

"Mr Slater sought a historical perspective on RERF's research program—what studies were undertaken during the early years and how they have evolved into the present long-range study," explained RERF Chief of Research **Seymour Abrahamson**.

## *Australia*

In mid-November, **Raymond Quint** of Film Australia interviewed Abrahamson, Epidemiology Department Chief **Kiyohiko Mabuchi**, and Statistics Department Research Scientist **Shoichiro Fujita** to get information for a documentary to be titled "The Forgotten Force."

"At the end of World War II, this region of Japan—the Hiroshima and Kure area—had been under the administration of the Australian Occupation Forces," explained Abrahamson. "Mr Quint was particularly interested in learning if any diseases now occurring among surviving members of the Australian military forces, especially cancers, could be associated with radiation exposure accumulated during the time they had been stationed in the Hiroshima area [1945–1946].

"Dr Fujita was asked to calculate possible doses received using certain recalled locations, as well as to calculate the worst-case situation—time spent at hypocenter," Abrahamson continued. "For the former group, the dose estimate was 0.1 mGy. For the latter group, the maximum possible dose was estimated at 1.4 mGy. These doses are in the range received from simple diagnostic medical exposures or from one year of natural background radiation." According to Abrahamson, the reporters were told that the risk of cancer from such exposures would be extremely low.

## *South Africa*

On 25 October, producer **Jan Horn** and a South African Broadcasting Corporation television crew stopped off at the Hiroshima Laboratory to interview Abrahamson. Seeking perspective on the aftereffects of the Chernobyl reactor accident, the crew learned about RERF research and later recorded video footage of the thriving city of Hiroshima to contrast with the environs of the Chernobyl nuclear power plant. ❑

## In This Issue

## Perspectives: *Invited Guest Editorial*

# Understanding Risk Estimates

***by Dale Preston, Department of Statistics, RERF***

Cancer-risk estimates derived from the ABCC–RERF Life Span Study (LSS), as presented in LSS mortality and incidence reports, play a central role in assessing radiation risks. In particular, LSS reports are one of the main sources for the widely used risk estimates and radiation-protection standards developed by groups such as the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), the International Commission on Radiological Protection (ICRP), the US National Academy of Sciences' Advisory Committee on the Biological Effects of Ionizing Radiation (BEIR), and the National Radiological Protection Board in the United Kingdom. Several scientists from RERF have been directly involved in preparing a number of these reports. From my experience with some of these efforts, I have learned much about how people use and interpret RERF risk estimates and those from other studies, and I have considered what we can do to improve the presentation and understanding of information on radiation risk. My concerns include the following: underemphasis of the reasons for the noncomparability of risk estimates from various studies; overemphasis of statistical significance in comparing results from various studies; and overinterpretation of the variability in site-specific risk estimates, both within and between studies. Each of these issues could be considered in more detail, but in this guest editorial I can only address a more basic misunderstanding of what many people view to be the RERF risk estimates.

Although the LSS reports present much data and many risk estimates, these reports tend to emphasize, and readers focus on, single-number site-specific summary measures of radiation relative risk. Such summaries are often cited as *the* risk of radiation in the LSS cohort (or even more broadly) and are often compared with similar summary measures for other populations. A serious problem with such simple summary measures is that they ignore important variability in the relative risk. For example, the summary estimate of the excess relative risk (ERR) at 1 Sv (RBE 10 weighted colon dose) in the LSS between 1950 and 1990, computed using standard methods in recent LSS mortality reports, is 0.43 with 95% confidence bounds of 0.33, 0.54. However, sex-specific estimates of the ERR are 0.26 and 0.64 for males and females, respectively. Neither of these estimates is contained in the confidence interval for the simple summary ERR, and indeed the 95% confidence intervals for the sex-specific estimates do not include the standard estimate of 0.43. However, the sex difference in the relative risk is often acknowledged in statements to the effect that women appear to be more sensitive to the effects of radiation than men, but insufficient attention is paid to the finding that estimates of excess absolute rates or projected lifetime risks are essentially the same for men and women.

Another often misunderstood aspect of the typical RERF summary risk estimates involves the effect of age at exposure. Although ERRs following radiation exposure are generally accepted to be increasing with decreasing age at exposure, this effect is not explicitly included in the computation of the typical risk estimates. Many people believe that the usual LSS risk estimates represent risks for a person of about the average age at exposure in the cohort, that is, a person about 28 years old at exposure. However, relative-risk estimates that ignore age effects are lower than estimates that explicitly allow for effects of age at exposure on risk. In contrast to the "average" sex-specific values given above, ERR estimates for 28-year-old male and female survivors are 0.36 and 0.75, respectively. This discrepancy arises because the usual summary estimator implicitly gives the most weight to groups with the largest number of deaths, that is, to those exposed at later ages.

The above comments are primarily concerned with ERR estimates. LSS reports also include simple average esti-

*continued on page 4*

## News Briefs

### ✓ RERF Chairman Honored by Epidemiologists' Group

RERF Chairman **Itsuzo Shigematsu** has been elected an honorary member of the International Epidemiological Association (IEA) in recognition of his contributions to the IEA and to the field of epidemiology in Japan and throughout the world.

### ✓ RERF Chairman Journeys to Ukraine and China

At the second Chernobyl–Sasakawa Medical Symposium, held in Korosten, Ukraine, on 13 October, RERF Chairman **Itsuzo Shigematsu** delivered a lecture titled, "Lessons from the Hiroshima and Nagasaki atomic-bomb survivors."

Also representing RERF at this meeting were **Shizuyo Kusumi**, Department of Clinical Studies, and **Yoshisada Shibata**, chief of the Nagasaki Laboratory's Department of Epidemiology and Biometrics.

A few days later in Kiev, Shigematsu met with the director of the Ukranian Scientific Center of Radiological Medicine, **Anatoly E Romanenko**, and staff members at their new clinic facilities.

In Beijing, on 19 October, Shigematsu reviewed the 40-year-long atomic-bomb-survivor research program of ABCC–RERF in a lecture at the Asia Congress on Radiation Protection. While in China, Shigematsu also met with the director of the Laboratory of Industrial Hygiene, **Wei Kedao**, and eight members of his staff who had studied at RERF.

### ✓ Vice Chairman Moderates International Biomarkers Meeting in US

RERF Vice Chairman **Mortimer Mendelsohn** moderated a day-long international workshop on the use of biomarkers for worker-health monitoring, held in Washington, DC, on 24 September. The workshop was sponsored jointly by the Office of Environment, Safety and Health; the Office of Environmental Restoration and Waste Management; and the Office of Energy Research, US Department of Energy (DOE).

*continued on page 10*

# Cardiovascular Disease in Atomic-bomb Survivors

*A reanalysis of data collected over 32 years suggests an increase in the incidence of myocardial infarction among Adult Health Study participants exposed to radiation when under 20 years old.*

***by Kazunori Kodama, Department of Clinical Studies, RERF***

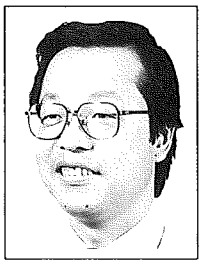
Investigating the relationship between atomic-bomb (A-bomb) radiation and cardiovascular disease (CVD) has been of great interest at the Atomic Bomb Casualty Commission–Radiation Effects Research Foundation (ABCC–RERF) since the early 1960s; CVD is important because of its high mortality and morbidity rates in Japan. However, relatively little research has been conducted on the late effects of A-bomb radiation on CVD, mainly because of the difficulty in obtaining accurate information and because of CVD's long latent period.

In 1992, **Y Shimizu et al** reported noncancer mortality, 1950–1985, in the Life Span Study (LSS) population (*Radiat Res* 130:249–66, 1992). This report described a definite increase in the mortality of CVD in the high-dose group (≥2 Gy) of A-bomb survivors. However, determining whether this increase in mortality was a direct effect of A-bomb radiation or an indirect effect—such as through known risk factors of CVD, or a combination of both was difficult.

A CVD study of RERF's Adult Health Study (AHS)* population was initiated in 1965 as part of the Ni-Hon-San Study, a collaboration between RERF and the Honolulu Heart Program to analyze the incidence of, and risk factors associated with, stroke and coronary heart disease in Japan, Honolulu, and San Francisco.

In 1979, the incidence of AHS coronary heart disease (CHD) between 1958 and 1974 was summarized by **TL Robertson et al** as part of an investigation of possible late effects of exposure to ionizing radiation (RERF Technical Report 12-79). During these 16 years of follow-up, 218 CHD cases were observed. Among the heavily exposed women from Hiroshima CHD incidence was significantly higher, but not among women from Nagasaki nor among men from either city.

**K Kodama et al** described continued high incidence for both stroke and CHD in heavily exposed Hiroshima females for the period 1955–1978, excluding autopsy diagnoses (RERF Technical Report 22-84). The relative risk (RR) for the 1-Gy group (tentative 1965 dosimetry system) compared with the 0- to 0.09-Gy group was 1.5 for stroke and 2.3 for CHD among Hiroshima females.



*Kodama*

In 1988, when the CHD observation period was extended to 1984 (for a total of 26 years) and an analysis was performed using Dosimetry System 1986 (DS86) doses, a continued and more significant increase in the incidence of myocardial infarction (MI) in heavily exposed females, mainly in Hiroshima, was seen. The RR of the 2-Gy group compared with the 0-Gy group was 2.7 for MI among females, with a RR of MI particularly high among those exposed when less than 20 years old. In March 1988, the RERF Scientific Council recommended continuation of the study, with careful analysis to exclude confounding factors.

In this article, the results of a reanalysis of MI incidence will be summarized. The observation period was extended to 1990 (32 years) in Hiroshima.

## *Materials and methods*

The AHS sample comprised 19,961 subjects in 1950 when established; 16,921 subjects were examined at least once during the period of this study; and 10,824 subjects with DS86 doses were available for MI incidence determinations.

When clinical-diagnosis reports, electrocardiograms, death certificates, or autopsy reports suggested MI, the medical charts of the AHS participants were reviewed using methods consistent with previous studies. The diagnostic criteria for MI, described in past RERF reports, were applied without change. The accuracy of diagnosis was classified into four grades as done previously, but only two grades, "definite" and "probable," were employed in this analysis.

For all subjects, the incidence rate for MI was obtained by calculating person-years from the first examination to the onset of disease, to death, or to the last examination date. The city-, sex-, and age-adjusted incidence rates of the various dose groups were compared and tested.

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***Table. Cox regression analysis of the incidence of myocardial infarction***

| Variable | Relative risk |
|---|---|
| Radiation dose: 1 Gy vs 0 Gy | 1.10 |
| Age: 10 years' difference | 2.03[a] |
| Sex: male vs female | 2.10[a] |
| SBP: difference of 10 mm Hg | 1.18[a] |
| Cholesterol: difference of 10 mg/dL | 1.04[b] |
| Smoking: 10 cigarettes per day | 1.29[a] |

Note: SBP = systolic blood pressure.

[a] $p < .001$

[b] $p < .05$

** The AHS population originally consisted of 20,000 atomic-bomb survivors and controls from Hiroshima and Nagasaki matched by age and sex. Since 1958, these participants have voluntarily returned to the RERF clinics for biennial medical examinations.*

## Cardiovascular Disease

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### *Results*

In 1991, the observation period for CHD in Hiroshima was extended to 1990, and the data were analyzed for radiation effects, with consideration of possible confounding by known CHD risk factors, such as age, sex, hypertension, serum cholesterol, and smoking. A significant increase was observed in the incidence of MI in heavily exposed survivors. It was, however, difficult to determine from this analysis whether the dose response conformed to the linear, quadratic, or threshold model, even though there appeared to be an increase in the incidence only among those who received doses higher than 2 Gy (see the Figure). The RR at 1 Gy was 1.14, which was far smaller than the RR for cancers. The number of excess cases per $10^4$ person-gray-years was 1.94, with the excess most significant among those less than 20 years old when exposed. No difference was seen in the radiation effect by sex, time since exposure, or city. When a Cox regression analysis including known CHD risk factors was done, the direct effect of radiation almost disappeared, indicating a strong possibility that the increased incidence of MI in the heavily exposed survivors resulted from known CHD risk factors (see the table on page 3). In March 1992, RERF's Scientific Council recommended further careful investigation to confirm whether radiation-related atherogenesis was observed. The known risk factors for CVD, including socioeconomic factors, may be playing a role and thus deserve study.

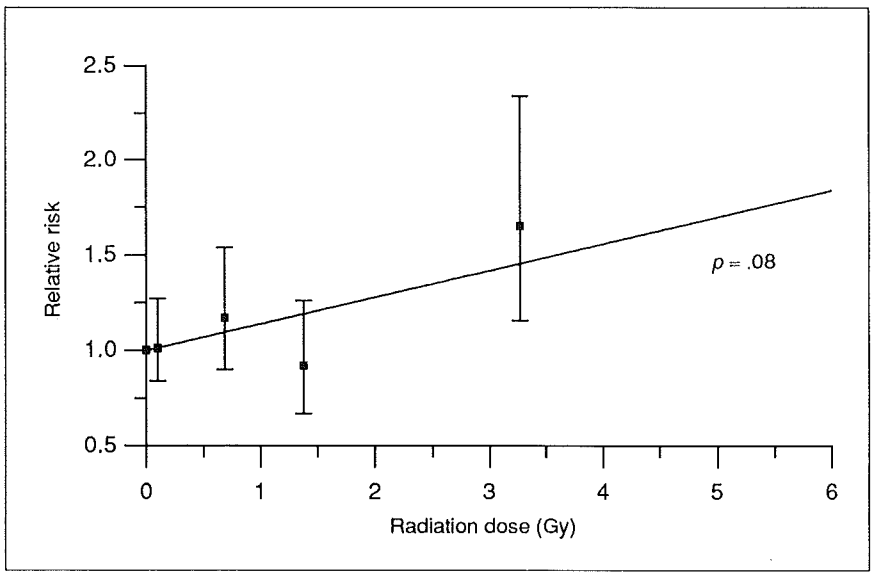


FIGURE REVISED BY Y KATAYAMA

***Figure. Dose response for incidence of myocardial infarction for men and women, 1958–1990, Hiroshima and Nagasaki. Bars indicate 90% confidence intervals of relative risk.***

In addition to MI incidence, the various endpoints of atherosclerosis, such as the prevalence of aortic-arch calcification, changes in blood coagulability, and the prevalence of isolated systolic hypertension, were also analyzed for radiation effects, and all endpoints showed radiation effects, which supports the possibility of a real relationship between radiation and atherosclerosis.

### *Conclusion*

The incidence study of MI in the AHS population for 1958–1990 suggested that a radiation-related increase in the incidence of MI occurred mainly in subjects exposed at ages less than 20 years and that the increase began in the last few years of the study period. Before final conclusions are drawn, however, further detailed analysis with consideration of other confounding factors is necessary. In addition, continuing accumulation of new cases is vitally important to increase the power of the analysis. ❑

## Perspectives

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mates of the excess absolute rate (EAR). Although some measure of the number of excess cases is important, the EAR estimates in most LSS reports are of limited use as a summary measure of risk because these estimates do not allow for changes in the excess rate with time and, thus, are highly dependent on the length of follow-up. The changes in the EAR with time are among the most striking features of the LSS excess risks. A summary measure ignoring this provides little useful information. Comparison of LSS EAR estimates and simple absolute risks from other studies without carefully considering temporal variation and other factors affecting these EAR estimates can be quite misleading.

Inadequacies of the standard risk estimates such as those described above are well known to many involved in preparing the ICRP, BEIR, UNSCEAR, and similar reports. Indeed, in recent years members of these groups have made concerted efforts to deal with the problems noted above. However, these groups have neither the time nor the resources to develop better methods for presenting and summarizing radiation-risk estimates. I believe that RERF researchers and others involved in the analysis of data on radiation and cancer can do more to explain the limitations of the current risk estimates and to develop new methods that provide clearer, more-comprehensive summaries of radiation risks.

Much of our work on the next LSS mortality report is focused on developing simple but meaningful risk summaries that explain important aspects of the variability in the excess cancer risk seen in the LSS. Among other things, the new report will de-emphasize misleading summary measures and make greater use of simple graphs and tables to illustrate variation in the absolute number of excess cases, in the excess relative and absolute rates, and in projected lifetime risks for the LSS cohort. In addition to this work on the LSS mortality report, joint analyses are being carried out to help clarify the nature of intersite variability in the LSS cancer-incidence data.

This year we hope to produce a number of reports and *Update* articles describing some of our ideas and results. We welcome suggestions from *Update* readers on how we can improve the presentation of our findings. ❑

# Cholesterol Levels in the Adult Health Study, 1958–1986

*Similar age cohorts studied across several generations appear to exhibit worsening trends in total-serum-cholesterol levels, a possible factor in the apparent increased mortality from coronary heart disease among female atomic-bomb survivors.*

***by Michiko Yamada, Department of Clinical Studies, RERF***

The long-term follow-up of the Adult Health Study* (AHS) cohort of atomic-bomb survivors offers a vast amount of information for epidemiologic research, including biennial measurements of total serum cholesterol (TC) collected since 1958 for about 10,000 persons, ranging from adolescents to the elderly. These data provide an invaluable opportunity to elucidate not only the longitudinal changes in TC levels in a Japanese cohort over 30 years but also the relationship between exposure to ionizing radiation and TC.

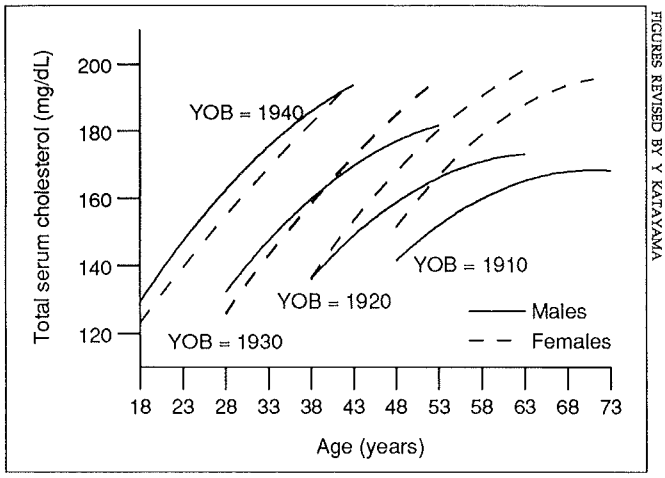
## *Subjects and methods*

The study sample comprised 9633 subjects, including 3437 males (Hiroshima: 2416; Nagasaki: 1021) and 6196 females (Hiroshima: 4602; Nagasaki: 1594) who had participated in at least one clinical examination between 1958 and 1986. The radiation-exposed group included 5514 persons for whom radiation dose estimates were greater than zero, and the unexposed group included 4119 persons with dose estimates of zero. Subjects diagnosed with medical conditions that might affect TC levels were not included.

Modeling and parameter estimating were carried out using the mixed-effects model of Laird and Ware (*Biometrics* 38:963–74, 1982), which includes the growth curves as a special case. The objectives of the growth-curve method are to characterize the temporal pattern of change in the serial measurements obtained longitudinally and to examine factors that may cause changes in this pattern. This method is identical to the usual regression technique except that for a specific individual, rather than across several individuals, the serial observations are assumed to be normally distributed with a mean and variance and somehow related to certain independent (growth-related) variables such as age, height, and weight. The nonindependence of the serial measurements for an individual is also considered. For the $i$th individual, denote the dependent variable as

$$y_i = y_{i1}, y_{i2}, \ldots, y_{ij}$$

to represent the measurements obtained from the $j_i$ AHS examinations participated in by person $i$, where $y_i$ is the set of values of (natural log of) TC. We assume that the growth model of $y_{ij}$ in person $i$ is related to his/her age and body mass index (BMI), where BMI = (weight ÷ height$^2$) × 100. That is,




FIGURES REVISED BY Y. KATAYAMA

***Figure 1. Cholesterol growth curves in Hiroshima males and females. Predicted curves for persons with Dosimetry System 1986 estimates of zero. Predicted body-mass-index growth curve was used. YOB = year of birth.***

$$y_{ij} = \beta_{0i} + \beta_{1i}(\text{age}_{ij}) + \beta_{2i}(\text{age}^2_{ij}) + \beta_{3i}(\text{BMI}_{ij}) + \beta_{4i}(\text{BMI}_{ij} \times \text{age}_{ij}) + \beta_{5i}(\text{BMI}_{ij} \times \text{age}_{ij2}) + e_{ij} \quad . \qquad (1)$$

Each individual is associated with his/her own growth model, equation (1), and his/her own set of growth parameters, $\beta = (\beta_{0i}, \ldots, \beta_{5i})$. However, he/she may also be considered a random observation from a population consisting of similar individuals and possessing its own growth curve and parameters, $\beta = (\beta_0, \ldots, \beta_5)$. This is called the random-effects model for the analysis of longitudinal data under the growth-curve setting. One of the goals of growth-curve analysis is to identify factors that distinguish the subpopulation, that is, factors that alter the growth parameters and thus the overall shape of the growth curve. This analysis examines the following factors—city, sex, year of birth minus 1945 (year of birth [YOB*]), and Dosimetry System 1986 (DS86) radiation dose—and their interactions, which may affect the population growth curve by modifying the values of $\beta$.

## *Results*

The parameters in the estimated growth curve of ln(TC) include city, sex, YOB*, city × sex, city × YOB*, sex × YOB*, city × sex × YOB*, and dose × sex as fixed effects. That is, all coefficients of dose not including sex are zero, indicating that radiation effects are apparent only in females. In the first step, to present the temporal trends of TC apart from radiation effects, we adjust for dose by substituting zero for dose in the growth curve of TC. To calculate the expected values of ln(TC), the predicted values of BMI from the BMI growth function were used.

The model is difficult to interpret because of its many

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** The AHS population originally consisted of 20,000 atomic-bomb survivors and controls from Hiroshima and Nagasaki matched by age and sex. Since 1958, these participants have voluntarily returned to the RERF clinics for biennial medical examinations.*

## Cholesterol Levels

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interaction terms, so it is not shown in detail here. It can be said, at least, that variations in the TC levels with age are modified by gender, place of residence, and year of birth. More-detailed descriptions of the differences require graphical presentation.

### *Effects of sex and birth year on the TC growth curves*

Figure 1 shows the predicted TC levels for Hiroshima men and women born in 1910, 1920, 1930, and 1940. TC levels increased with age. The greatest change occurred in younger female subjects, for whom the average increase over the 28 years was about 70 mg/dL, whereas the smallest change occurred in older males, for whom the average increase during the same period was slightly more than 20 mg/dL. The changes experienced by the Nagasaki subjects were somewhat smaller. For both cities, the rate of increase in TC levels declined gradually in males with age, whereas the rate remained virtually constant in females until age 60 years. Differences in the TC levels based on sex were small under age 40 years but increased with aging.

TC levels at a given age were higher for those born later. The cohort effect, represented by 10-year intervals, was greater for those born later (for example, in 1930 and 1940), with an average difference of more than 20 mg/dL. However, the average difference for those born earlier (for example, in 1910 and 1920) was about 10 mg/dL. The effects of these 10-year intervals in birth cohort on the TC levels appeared to be similar in men and women.

### *Effects of place of residence on the TC growth curves*

TC levels were consistently higher for residents of Hiroshima than for residents of Nagasaki (both men and women). Effects of birth cohort and sex on the TC growth curves were similar in the two cities.

### *Effects of varying BMI on the TC growth curves*

BMI had a general tendency to increase with age in both men and women, up to about age 60 years in men and up to the mid-60s in women, followed by a decrease with further aging.

The general effect of the BMI is to elevate TC levels, but only a small part of the changes in TC could be explained by changes in the BMI during the study period.

### *Effects of radiation*

As mentioned earlier, radiation effects are apparent only in females. To examine this radiation effect, we estimated a parsimonious model of the TC growth curve by using only the data on women ($n = 6198$). In this parsimonious model, radiation effects were highly significant ($\chi^2_4 = 42.80$, $p < .00001$). Next, we examined whether radiation effects varied for women of different ages by including the interaction of dose with YOB*. The test of zero simultaneous effect was nonsignificant ($\chi^2_6 = 4.07$, $p = .67$), indicating that age at exposure does not alter the radiation effect.

Figure 2 shows the predicted TC growth curves for women born in Hiroshima during 1910, 1920, 1930, and 1940 for whom DS86 dose estimates were 0 Gy or 2 Gy. TC levels in the exposed women were higher than in the non-exposed, with the difference increasing slightly with age but attenuating past the age of 65. The maximum difference at 1 Gy, occurring at around age 48 years, is only about 2 mg/dL. The 95% confidence bounds for the TC level at age 48 with a BMI of 0.203 for the non-exposed Hiroshima women born in 1930 are 184 mg/dL and 187 mg/dL, with a point estimate of 185 mg/dL. The corresponding values for women exposed to 1 Gy are 186 mg/dL and 189 mg/dL, with a point estimate of 187 mg/dL. Although the shapes of the growth curves for 0-Gy and 2-Gy exposures appear to differ by year of birth, this is due to variation in ages at which TC levels were measured for the various birth cohorts and not due to differences in radiation effects.

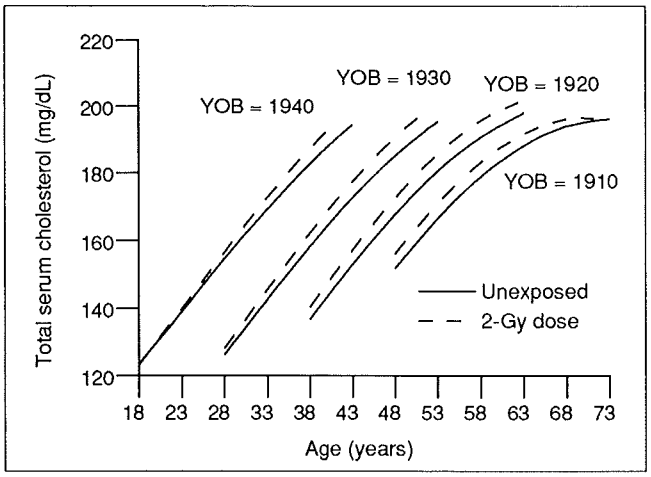



***Figure 2. Total-serum-cholesterol growth curves in Hiroshima females, by radiation exposure. YOB = year of birth. Body mass index predicted for the appropriate radiation level was used.***

### *Discussion*

This study is one of the few long-term investigations of such a large Asian population. The observed increase in TC experienced by AHS cohort members of comparable ages across generations was more dramatic than in most longitudinal studies conducted on non-Asian, for example, North American, populations. The rapid increase of, and strong cohort effect on, TC suggest that the effects of factors related to behavior, life style, and environment that vary across generations and that are responsible for worsening of the TC profile have grown stronger with time.

Although detailed information on nutrition was not available for our study, clearly Japanese dietary habits are undergoing rapid "westernization," especially in urban areas. (Results of an AHS mail survey conducted from 1983–85 indicate that fat intake is greater in Hiroshima than in Nagasaki, which might explain the intercity variation in TC.)

A plausible explanation for the difference in radiation effects among the women in this study is that menopause occurs earlier in women exposed to radiation, which in turn accelerates the elevation of TC levels. (For a report on the early onset of menopause among Nagasaki women, see M Soda and J Cologne, *RERF Update* 5[2]:3, 1993.)

Our current finding suggests that the elevated TC level associated with radiation exposure contributes to increased mortality from coronary heart disease among radiation-exposed women (see K Kodama, p 5, this issue; Y Shimizu et al, RERF Technical Report 2-91 and *Radiat Res* 130:249–66, 1992). ❑

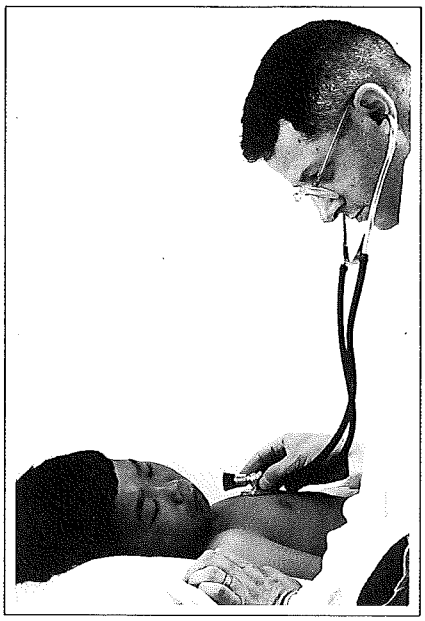
# Miller's Memories of ABCC–RERF, 1953–1990: Part 1

*Long involved in the activities of the Radiation Effects Research Foundation and its predecessor, the Atomic Bomb Casualty Commission, the author relates an informal mixture of scientific and personal anecdotes spanning more than three decades.*

***by Robert W Miller, Clinical Epidemiology Branch, National Cancer Institute, Bethesda, Maryland***

## *Why and how*

On 20 November 1953, I arrived in Hiroshima via pediatrics, radiation biology, and troop train. Three years earlier, upon completing my training in pediatrics, I did not feel finished. Specialty training seemed too narrowing, so I obtained a little-sought-after fellowship in radiation biology sponsored by the US Atomic Energy Commission (AEC) to train a few physicians in this new broad-spectrum field. After five months each at Duke University for classroom work and Western Reserve University for laboratory studies, the Korean War started. I was called to military service and because of the fellowship was assigned to the Atomic Energy Project at the University of Rochester for two years. After bleeding 96 dogs each day in studies of X-ray lethality, I brightened my outlook by making rounds of the pediatrics ward. There I learned that when X-ray films were ordered for small children they were routinely subjected to fluoroscopy (high doses), as required by the Radiology Department. An unfriendly meeting with its chairman and his staff led to a change in policy, to my review of the literature on potential hazards of medical radiation to children, and to the now-famous studies by **Louis Hempelmann** of infants who had received radiotherapy for thymic enlargement.



PHOTOS COURTESY OF ROBERT W MILLER

***The author, in 1954, examining a participant in the ABCC pediatrics study.***

When I heard that **John Morton,** professor of surgery at the University of Rochester, was to spend six months as interim director of the Atomic Bomb Casualty Commission (ABCC), it seemed that my own short assignment there would add clinical experience to what I had already learned. I was interviewed by **Grant Taylor,** the departing director of ABCC, and agreed to a one-year term. Soon after, I was in Honolulu for an overnight stay in a $4-a-night hut in a jungle (now the International Market) across the street from its parent, the Moana Hotel, then to Wake Island and Tokyo by Pan American sleeper DC-6—the berth was in what is now known as the overhead luggage rack. Next, a night at the marvelous Imperial Hotel [designed by Frank Lloyd Wright and razed many years ago] in Tokyo, and from there to Hiroshima by US troop train.

## *Early pediatrics studies*

Being in Japan at that time was like being seven years old again and seeing many things for the first time. It was enchanting, and the work was fascinating. We examined about 20 children a day in the clinic, as Japanese children's songs played on a tape recorder in the waiting room. The patients were 9–19 years old. There was much to learn, much to teach, and fun all the time.

That clinic, which was alive with people and the charm of the children, is now occupied by RERF's Research Information Center. Our half-dozen young nurses were supervised by **Yaeko Hirayama**, a former midwife, who had the personality of a lovable top sergeant. ABCC's chief nurse was **Wakayo Ueda**, who worked with two American nurses from Duke University. The world may never have seen better nursing service in a clinic.

**Wataru W Sutow**, whom I was to replace as chief of pediatrics, was finishing his analysis of child development after in-utero exposure. **Margaret (Pat) Sullivan** from Duke was the other US pediatrician in the department. Pat was a superb clinician, with a special capacity for endearing herself to the children and their mothers. She and Wat went on to become pioneers in pediatric cancer chemotherapy at the MD Anderson cancer hospital in Houston. Also on the staff was **Earl Reynolds**, an anthropologist, who was finishing his collection of data. Among the clinic personnel were eight Japanese pediatricians and psychometric testers. The youthful staff gave ABCC a campus-like atmosphere.

At that time clinical research at ABCC, as elsewhere, was based on instinct rather than on strict scientific design. Chronic-disease epidemiology had not yet emerged from its famous forebear, infectious-disease epidemiology. The ABCC genetics program was an exception because of its mathematical basis. As a substitute for radiation dose, we used distance from the hypocenter. These figures were kept in the Biostatistics Department to avoid observer bias that may well have occurred had the distances been recorded on the clinic charts. My plan was to summarize the findings for a publication at the end of my tenure.

The most noteworthy observation, already known from studies by **Murphy** and **Goldstein** in Philadelphia, was small head size and severe mental retardation among children born of mothers who had received radio-

*continued on next page*

# Miller's Memories, Part 1

*continued from page 7*

therapy early in pregnancy. Murphy had been a professor at my medical school, where he loved to tell of these findings. It is remarkable that I witnessed the evolution of this story over the next 47 years.

**George Plummer** was the first to publish on this condition among Hiroshima survivors—seven children with severe mental retardation after in-utero radiation exposure (ABCC Technical Report 29-C-59). There seemed to be nothing more to do until a US television crew came for a story. Their questions led me to realize that we had no denominator for the seven cases. Review of the data raised the number of cases to 15, and another 18 were found with small head size but without mental retardation. Later this lesser effect was found to be six times more common than severe mental retardation.

Other findings of interest were the occurrence of leukemia before 1955 in 18 persons under 19 years old who had been within 1530 m of the hypocenter, visual impairment (due to myopia?) in 20% of the children who were exposed when 6–9 years old and within 1800 m of the hypocenter, compared with 9% among those children of the same ages who had been further away. No such difference was found among the group under age 6, and we wondered if it would occur when they reached the same age as the older cohort. Twenty-six children had persistent effects from the blast or burns. The most common late effect, we sensed, was fear of late effects—at times disabling.

In writing up the results, access to the distance from hypocenter for each child was denied by Biostatistics on the grounds that the data belonged to it alone. This obstacle was overcome by nocturnal visits to the Biostatistics files.

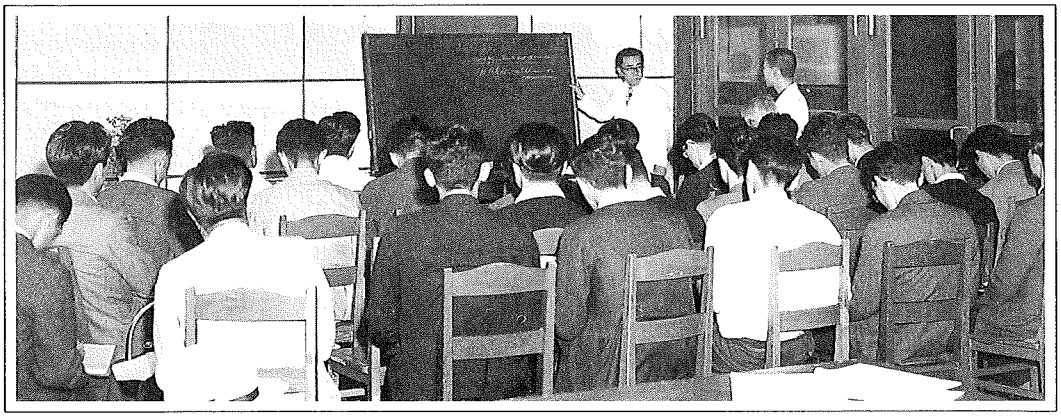
## *American superstars visit ABCC, staff member takes to the sea*

Several extracurricular events were worthy of note.

On 12 February 1954, Dr Morton and I were walking through the reception area of ABCC when **Joe DiMaggio** and **Marilyn Monroe** came through the front door. They were on their honeymoon, accompanied by **Bobby Brown**, who had played baseball for the NY Yankees while a Stanford University medical student. They had come to see Brown's classmate, **Jack Lewis,** an internist at ABCC. Within milliseconds everyone at ABCC poured into the area, and we were no longer alone with the superstars. Brown eventually became the president of the American League.

The anthropologist member of the pediatrics staff, Earl Reynolds, decided on an unusual way to return home with his wife and two teenaged children. He had a small boat built and, after some practice outings, was

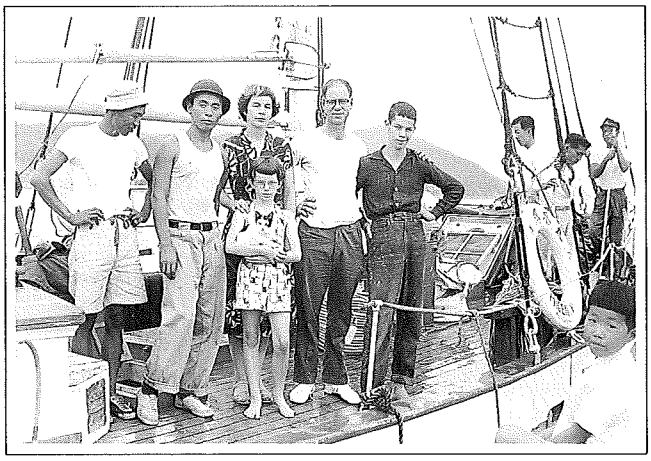
***Right, in August 1949, Wataru Sutow (Department of Pediatrics, 1948–1953) lectures to members of his department. Below right, Yaeko Hirayama, a former midwife whose supervision of the nursing staff was invaluable amidst the bustle of the early pediatrics activities at ABCC.***



RERF ARCHIVES

***Above, in 1954, ABCC statistician Marvin Kastenbaum poses with members of the nursing staff.***

ready to leave for Hawaii with several Japanese crewmen who did not speak English. Naval officers from US ships visiting the area looked at the boat and crew and said they would be lost at sea. Forty-seven days after their departure from Japan, they arrived in Hawaii. Earl published an account of the voyage in *The Saturday Evening Post* and promptly set sail again. Eventually, he defied a ban on ships in waters near a nuclear-test site in the South Pacific and was arrested. His wife, Barbara, a writer of children's books, often returned to Hiroshima, where she was held in high esteem as a pacifist.



***Above, Michihiko Hachiya, author of the book* Hiroshima Diary, *and his wife, Yaeko, in September 1959. Below, in September 1954, Earl Reynolds of the ABCC pediatrics staff and his wife Barbara with their childen a few minutes before their departure from Hiroshima by sailboat. At left are two members of their non-English-speaking crew.***

## *ABCC and the* Lucky Dragon

On 1 March 1954, a US nuclear weapons test at Bikini resulted in fallout on the Marshall Islands and its vicinity. About two weeks later, a Japanese fishing boat, the *Lucky Dragon*, arrived in Tokyo with its 23 fisherman, who had been living amidst heavy fallout dust. They had been fishing for tuna in the fallout area. Dr Morton led an ABCC group to Tokyo, where they were permitted to examine the men. Newspapers were full of stories concerning the men and the contaminated fish, considered a threat to all Japan. (See *RERF Update* 5[1]:10–13, 1993; 5[2]:8–10, 1993; 5[3]:7–9, 1993.) In June, ABCC was visited by an American reporter who was well regarded by the US Embassy, or so we were told by **Frank (Tax) Connell,** the acting director of ABCC, just before he left for Tokyo to welcome the new director, **Robert H Holmes.** For an hour I told the reporter what we were doing in pediatrics, and as he rose to leave, he asked in an informal tone if he and his family should worry when Japanese newspapers reported that yesterday's rainwater contained 20,000 radiation counts. I said that one has to compare the 20,000 with the number of counts in rainwater known to be uncontaminated. One should be aware, I added, that in the US the unit of measure was the milliliter, so we would say 20 counts per millimeter per minute. In Japan the unit of measure was the liter, so the 20,000 represented counts per liter per minute. The next day there were Japanese reporters all over the place to interview **Lowell Woodbury,** the chief of Biostatistics, and me because of our insults to Japanese scientists. Lowell had been quoted by the American reporter as saying that the Japanese did not take into account natural radioactivity in fruits and vegetables, and I had been quoted as saying that they exaggerated radiation exposures by 1000 times. That was my introduction to the new director, who started his term handling that "hot potato."

## Hiroshima Diary *by Michihiko Hachiya*

Several cultural events highlighted my time in Japan. Soon after my arrival someone gave me a rough draft translation of **Michihiko Hachiya**'s *Hiroshima Diary*. The power of the account was heightened by some residual Japanese-English in the writing. **Warner Wells,** a surgeon from the University of North Carolina on the staff of ABCC, had learned of the work, which had appeared in an obscure medical journal of the Communications Ministry. Hachiya was the director of the Communications Hospital (*Teishin Byoin*) in Hiroshima. Wells arranged for the work's translation at ABCC with the help of **Neal Tsukifuji.** The book lost some of its Japanese "feel" but gained a fine literary polish with further editing in North Carolina. When it was published in the US, in 1955, it received critical acclaim on the front pages of major book-review supplements, such as that of *The New York Times*. The book was translated into more than a dozen languages, became an international best seller, and is still in print. Hachiya accepted only a small sum for his work which he put into an educational fund for atomic-bomb orphans. It was said, perhaps in jest, that publishers in Tokyo, unaware of the book's origin, asked to have it translated into Japanese. After I read the draft, I came to know Hachiya well enough to appreciate his fine mind and literary ability. I rejoiced in the success of his book as it became known throughout the world. ❑

*Editor's note: Robert W Miller's recollections will be continued in an upcoming issue of* RERF Update.

# Facts & Figures

## *Coefficient of Variation in Radiation-induced Micronuclei*

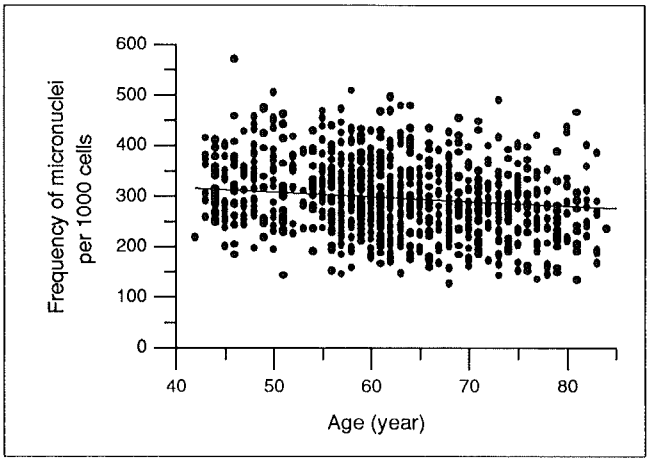
***by John B Cologne, Department of Statistics, RERF***

Many researchers use the coefficient of variation (CV)* to summarize dispersion in a measure of radiation sensitivity. The CV is defined for observations having a common statistical distribution, which implies a common mean and variance. Confusion regarding use of the CV may therefore arise when regression methods are used, because the mean of the observations (and possibly the variance also) depends on values of the regression covariate and therefore is not identical for all observations.

For example, **S Ban et al** (*Radiat Res* 134:170–8, 1993) reported that in-vitro radiation sensitivity of peripheral-blood lymphocytes—as measured by the frequency of micronuclei induced by 2 Gy of X rays—decreases with the subject's age (Figure 1). Although the residual standard deviation after adjustment for age appears to be constant (70.4 micronuclei per 1000 cells), the CV changes with subject age because the mean induced frequency depends on age. The CV for these data increases nonlinearly (in the mean) from 22.4% at age 42 years to 25.4% at age 80, as shown in Figure 2.

Use of the CV is further complicated when the variance is a function of the mean, such as with logistic regression or Poisson regression. One common statistical distribution, the log-normal distribution, has a constant CV. The Poisson distribution, however, has a CV equal to the inverse of the square root of the mean. Many data also display overdispersion; that is, the variance is greater than expected. With such data, common statistical practice is to report the estimated variance function (the relationship between the variance and the mean) rather than the CV. ❑

$$*\mathrm{CV} = \frac{100 \times (\text{standard deviation})}{\text{mean}}$$




FIGURES REVISED BY K KANEOKA

***Figure 1. Frequency of micronuclei induced by 2-Gy in-vitro X-ray exposure in 1000 peripheral-blood lymphocytes as a function of a subject's age. The solid line is the least-squares linear regression of induced frequency on age.***

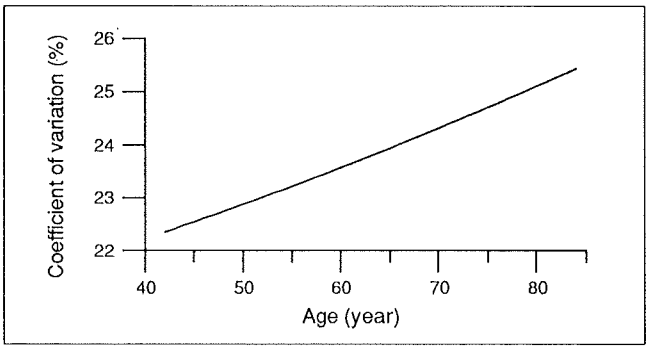



***Figure 2. Coefficient of variation (CV) in 2-Gy-induced micronucleus frequency as a function of a subject's age. The CV is the ratio of the residual standard deviation (70.4) to the mean (shown as the solid line in Figure 1) expressed as a percent.***

## News Briefs

*continued from page 2*

New legislation requires the DOE to use biomarkers for estimating the occupational exposure of all its workers. The meeting examined the scientific, legal, and practical issues involved in carrying out this mandate. DOE plans to publish the proceedings of this meeting.

### ✓ RERF Epidemiologist Attends Meeting about Chernobyl Effects

**Yoshisada Shibata**, chief of the Nagasaki Laboratory's Department of Epidemiology and Biometrics, joined European scientists at a meeting, 19–20 October, in Kiev at the Ukrainian Research Center for Radiation Medicine, where epidemiological studies on Chernobyl-accident-related medical effects and the establishment of an national registry of affected persons were discussed. In Minsk, Belorussia, Shibata met with **Alexey Ye Okeanov**, director of the Belorussian Research Center for Medical Technologies. Shibata obtained cancer-incidence data—in particular, data on thyroid cancer in Belorussia.

### ✓ Participation in Regional and International Meetings

Five members of the RERF Department of Statistics (**D Preston, D Pierce, D Pawel, R DeLongchamp**, and **JB Cologne**) were invited to attend a one-day workshop at the Japanese Institute of Statistical Mathematics, Tokyo, on the theory and application of discrete multivariate methods in the health sciences. Participants hope to promote applied statistics research in Japan and to encourage Japanese statisticians from other institutions to conduct research on applied statistics problems associated with the analysis of RERF data.

In mid-October, Department of Genetics Chief **Akio A Awa** attended a meeting on establishing cytogenetic nomenclature for chromosome aberrations detected by whole-chromosome painting. At the two-day meeting, nine cytogenetics experts from five nations actually observed under the microscope all detectable forms of chromosome aberrations using either bicolor or multicolor painting methods.

Department of Radiobiology Chief **Mitoshi Akiyama** was one of 30 participants at a National Research Council–National Academy of Sciences-sponsored workshop on dose reconstruction for epidemiological uses, held 25–27 October, in Washington, DC. He helped draft a summary document on biomarkers and biologic dosimetry. ❑

# Recent Scientific Publications

*Editor's note: As announced in the summer 1993 issue of* RERF Update, *the RERF Technical Report Series, begun in 1959, will be terminated after processing of 1992 manuscripts is completed. Henceforth, summaries of journal articles based on approved RERF manuscripts will accompany the complete journal citation. Other selected summaries of interest also will be published occasionally. Reprints, when available, can be obtained from the RERF Publication and Documentation Center, 5-2 Hijiyama Park, Minami-ku, Hiroshima, 732 Japan.*

## Publications in the Open Literature

**Noncancer disease incidence in the atomic bomb survivors: 1958–1986.** FL Wong, M Yamada, H Sasaki, K Kodama, S Akiba, K Shimaoka, Y Hosoda. *Radiat Res* 135:418–30, 1993 (based on RERF Technical Report 1-92).

**Proliferative and nonproliferative breast disease in atomic bomb survivors. Results of a histopathologic review of autopsy breast tissue.** M Tokunaga, CE Land, Y Aoki, T Yamamoto, M Asano, E Sato, S Tokuoka, G Sakamoto, DL Page. *Cancer* 72:1657–66, 1993 (based on RERF Technical Report 9-92).

**Radiation-associated lung cancer: a comparison of the histology of lung cancers in uranium miners and survivors of the atomic bombings of Hiroshima and Nagasaki.** CE Land, Y Shimosato, G Saccomanno, S Tokuoka, O Auerbach, R Tateishi, SD Greenberg, S Nambu, D Carter, S Akiba, RJ Keehn, P Madigan, TJ Mason, M Tokunaga. *Radiat Res* 134:234–43, 1993 (based on RERF Technical Report 20-92).

**Stable chromosome aberrations among A-bomb survivors: an update.** DO Stram, R Sposto, DL Preston, S Abrahamson, T Honda, AA Awa. *Radiat Res* 136:29–36, 1993 (based on RERF Technical Report 13-92).

**Application of generalized estimating equations to a study of in vitro radiation sensitivity.** JB Cologne, RL Carter, S Fujita, S Ban. *Biometrics* 49:927–34, 1993 (based on RERF Commentary and Review 2-92).

**Influence of death certificate errors on cancer mortality trends.** DG Hoel, E Ron, RL Carter, K Mabuchi. *J Natl Cancer Inst* 85:1063–8, 1993 (based on RERF Commentary and Review 2-91).

## Publication of Interest Using RERF Data

**A comparison of the risks of leukaemia in the offspring of the Japanese bomb survivors and those of the Sellafield workforce with those in the offspring of the Ontario and Scottish workforces.** MP Little. *J Radiat Prot* 13(3):161–75, 1993.

## Approved Research Protocols

**Molecular analysis of skin cancers in atomic-bomb survivors.** T Mizuno, T Seyama, T Ito, KS Iwamoto, N Nakamura, M Akiyama, Y Shimizu, M Tokunaga, M Kishikawa, S Tokuoka, K Mabuchi, JE Trosko. **RERF RP 3-93.**

On the basis of the assumption that specific physical and chemical carcinogens, by activating oncogenes or inactivating tumor suppressor genes, leave unique "molecular fingerprints" in the DNA sequences of the altered tumor genes, this project has been designed to characterize these changes in the ras oncogenes and the p53 tumor-suppressor gene of skin cancers in atomic-bomb (A-bomb) survivors, who have a high excess risk of developing these types of tumors. Also, because a close relationship exists between exposure to ultraviolet (UV) light and skin carcinogenesis, both UV and ionizing radiation may influence neoplastic transformation in A-bomb survivors. We will investigate the roles of these specific radiations in tumorigenesis.

From a set of about 23 skin-cancer tissue specimens of highly exposed A-bomb survivors and about twice that number of controls who are matched by age, sex, histologic types, and location relative to the A-bombings and to any shielding, DNA will be extracted and analyzed using polymerase chain reaction-single strand conformation polymorphism, polymerase chain reaction-restriction length polymorphism, and direct sequencing.

**Epidemiologic study of antiadult T-cell leukemia-associated antigen antibodies in the Adult Health Study sample, Nagasaki.** K Oishi, Y Shibata, M Akahoshi, T Nakamura, S Nagataki, M Tsujihata,T Matsuo, M Tomonaga, K Shimaoka. **RERF RP 4-93.**

The C-type retrovirus is recognized to be of great importance as a tumor marker in adult T-cell leukemia (ATL). The proposed study has the following two major objectives: 1) to examine the relationship between the positive rate of antiadult T-cell leukemia-associated antigen (anti-ATLA) antibodies and radiation dose in the Adult Health Study subjects, Hiroshima and Nagasaki, and 2) to examine how the antibody titers, the presence of ATLA, the ratio of T-cell subsets, and the presence of abnormal lymphocytes in the peripheral blood are related to radiation dose in antibody-positive cases.

Recently, various immunological abnormalities and disorders such as ATL and HTLV-I associated myelopathy (HAM) have been reported. We propose, therefore, to conduct a preliminary study on anti-HTLV-I antibody positive atomic-bomb survivors in Nagasaki, an HTLV-I endemic area, to elucidate whether immunological abnormalities are present in the survivors in terms of the frequency of autoantibodies and the quantity of immunoglobulins. If abnormalities are found in the HTLV-I–infected subjects, they will become an important factor in the comparative analysis of immunology data from Nagasaki and Hiroshima.

**Longitudinal study of hormone indicators of menopause in perimenopausal female atomic-bomb survivors.** TP Rose, M Soda, M Yamada, H Sasaki, M Akahoshi, JB Cologne, K Kodama. **RERF RP 5-93.**

Recent research findings at the Radiation Effects Research Foundation on menopause among female atomic-bomb (A-bomb) survivors in Nagasaki showed an increased incidence in the early onset of menopause for women with greater exposure to atomic-bomb radiation. The sources of information on menopause were medical records and self-reports. This proposed study will measure the levels of two important perimenopausal hormones, follicular-stimulating hormone (FSH) and estradiol ($E_2$), over the next four years in the 1940–45 female birth cohort of A-bomb survivors. A quality-control study will be conducted to evaluate the sources of variability in these hormone assays. Results will be used as hormone indicators of menopause to estimate the rate ratio of the incidence of early onset of menopause among women exposed to radiation compared with unexposed women. Also, information on symptomatology will be collected. This approach assumes that biochemical indicators provide empirical, more-valid measures of change and can be

*continued on next page*

# Recent Scientific Publications

*continued from page 11*

used to describe the temporal relationship between radiation exposure and early menopausal hormone changes. In contrast to western lifestyles, confounding life-style factors such as alcohol consumption, smoking, and exogenous hormone use are likely to be minimal in this sample.

**Breast-cancer incidence among atomic-bomb survivors, 1950–1990.** M Tokunaga, CE Land, S Tokuoka, T Ikeda, M Soda, K Mabuchi. **RERF RP 6-93**

We propose to extend through 1990 the study of breast-cancer incidence among members of the Radiation Effects Research Foundation (RERF) Life Span Study (LSS) sample. This will be the fifth in a series of similar surveys, which previously covered the periods 1950–69, 1950–74, 1950–80, and 1950–85. As in previous studies, the proposed investigation will be aimed at complete ascertainment of cases from locally available sources, including local hospitals and clinics, tumor and tissue registries, and death certificates, through the RERF tumor registry. Attempts will also be made, on a pilot basis, to ascertain cases from nonlocal sources such as tumor registries in cities other than Hiroshima and Nagasaki, and the feasibility of including the resulting data in the overall analysis will be evaluated. Final selection of cases will be made by the investigators after reviewing all collected diagnostic materials. Whenever possible, histological subtyping will be done after tissue samples are reviewed.

The purpose of the proposed study, like that of its predecessors, is to characterize the LSS sample in terms of female-breast-cancer risk in relation to radiation dose, age at the time of the bombings, attained age, and calendar year of onset. If sufficient numbers of male-breast-cancer cases are found, similar analyses will be performed for male-breast-cancer risk, to the extent possible, and comparisons will be made by sex. If cases from nonlocal sources, such as distant tumor registries, are incorporated into the analysis, available information on the residence histories of LSS sample members will be used to adjust observed rates for differences in case-ascertainment efficiency related to migration from Hiroshima and Nagasaki.

**Molecular analysis of thyroid cancers among atomic-bomb survivors.** T Ito, T Seyama, T Mizuno, KS Iwamoto, N Nakamura, M Akiyama, Y Shimizu, Y Hayashi, N Tsuda, S Tokuoka, K Mabuchi. **RERF RP 7-93.**

Elevated risk of thyroid cancers among the atomic-bomb (A-bomb) survivors, compared with the nonexposed population, suggests that some genetic events related to thyroid cancer must be caused by ionizing radiation. As a first step in an attempt to clarify these genetic events, the reverse transcription and polymerase chain reaction (RT-PCR) method will be used to amplify D10S170-RET fusion transcripts, that is, the activated oncogene, from paraffin-embedded blocks of thyroid-cancer tissue from A-bomb survivors. This assay exclusively amplifies the activated form of the RET oncogene and thus can clarify the involvement of this gene in thyroid-cancer development among A-bomb survivors.

**Cytogenetic study in the Adult Health Study population by fluorescence in-situ hybridization (FISH).** Y Kodama, M Nakano, K Ohtaki, AA Awa, M Kodaira, K Kodama, T Honda, DJ Pawel. **RERF RP 8-93.**

Using the fluorescence in-situ hybridization (FISH) technique with whole-chromosome DNA probes, the frequencies of translocations in peripheral lymphocytes of atomic-bomb survivors will be measured to seek relationships between aberration frequency and radiation dose and between aberration frequency and age at the time of exposure and to compare the dose-response curves of translocations in Hiroshima with those of Nagasaki.

## RERF Technical Reports Published in Japanese

*Editor's note: Since 1989, only selected Japanese-language technical reports have been published by RERF under separate cover. Following is a partial listing of these reports. As space permits, the remainder of the list will be included in future issues of* RERF Update.

**Allowing for random errors in radiation exposure estimates for the atomic bomb survivors data.** DA Pierce, DO Stram, M Vaeth. **RERF Technical Report 2-89.**

**Smoking and serum proteins in atomic bomb survivors in Hiroshima.** DO Stram, S Akiba, K Neriishi, RG Stevens, Y Hosoda. **RERF Technical Report 3-89.**

**Abdominal ultrasonographic screening of Adult Health Study participants.** WJ Russell, Y Higashi, T Fukuya, Y Hosoda, J Murakami, A Mizushima, A Kawashima, S Murayama, T Ohuchida, F Mihara, M Takagi, S Fujita. **RERF Technical Report 10-89.**

**Incidence of thoracic vertebral fractures among Adult Health Study participants, Hiroshima and Nagasaki, 1958–86.** S Fujiwara, S Mizuno, Y Ochi, H Sasaki, K Kodama, WJ Russell, Y Hosoda. **RERF Technical Report 12-89.**

**Congenital malformations, stillbirths, and early mortality among the children of atomic bomb survivors: A reanalysis.** M Otake, WJ Schull, JV Neel. **RERF Technical Report 13-89.**

**Serum ferritin and stomach cancer risk among A-bomb survivors.** S Akiba, K Neriishi, WJ Blot, M Kabuto, RG Stevens, H Kato, CE Land. **RERF Technical Report 14-89.** ❑


RERF **update** RERF

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RERF conducts research and studies—for peaceful purposes—on the medical effects of radiation on humans with a view toward contributing to the maintenance of the health and welfare of atomic-bomb survivors and to the enhancement of the health of all mankind.

*Editorial Policy*

Contributions to *Update* receive editorial review only and are not subjected to scientific peer review. Consequently, the opinions expressed herein are those of the authors only and do not necessarily reflect RERF policies or positions.

Units of radiation and radioactivity are given as found in the source material.

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