RERF update RERF

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

Volume 5, Issue 2 Hiroshima & Nagasaki Summer 1993

RERF and US DOE Scientists Exchange Ideas

On 14–16 April, RERF research scientists attended a workshop in Irvine, California, to promote collaboration with other researchers whose studies of radiation-exposed populations are sponsored by the US Department of Energy (DOE). Overlapping concerns, such as epidemiologic methodology, confirmation of results, and extrapolation from one exposed population to another, as well as data sharing, were discussed.

Apart from brief introductory remarks, the first day of the DOE-sponsored meeting was devoted to presentations by RERF scientists. The second day focused on presentations by DOE officials from organizations operating under the auspices of Deputy Assistant Secretary for Health **Harry Pettengill** and presentations by working scientists. During the final half-day session, three areas of potential collaboration were reviewed: 1) molecular epidemiology of exposed populations; 2) international research activities; and 3) data sharing and comprehensive epidemiologic data resources.

RERF Permanent Director **Mortimer L Mendelsohn** organized and introduced a discussion of molecular epidemiology. Clinical Studies Research Scientist **Saeko Fujiwara** discussed parathyroidism and calcium metabolism among atomic-bomb (A-bomb) survivors, and Department of Genetics Assistant Chief **Chiyoko Satoh** described the biochemical genetics program.

The following RERF department chiefs also presented overviews of their programs: **Mitoshi Akiyama**, Department of Radiobiology; **Kiyohiko Mabuchi**, Department of Epidemiology; **Dale Preston**, Department of Statistics; **Kazunori Kodama**, Department of Clinical Studies; **Akio Awa**, Department of Genetics; and **Jill Ohara**, Research Information Center.

RERF Permanent Director and Chief of Research **Seymour Abrahamson**, coordinator of the RERF presentations, moderated the first day's session.

The following scientists described their ongoing collaborative studies with RERF: **Elaine Ron**, National Cancer Institute (NCI)—site-specific cancer incidence and mortality among the A-bomb survivors; **Charles Land**, NCI—breast-cancer studies involving the A-bomb survivors; **William J Schull**—damage to the developing brain of the in-utero exposed; **James V Neel**—studies of the first-generation offspring of the A-bomb survivors.

Topics of DOE representatives were as follows: **Robert Goldsmith**—introduction and overview of the Office of Epidemiology and Health Surveillance and its future directions; **Terry Thomas**—community health surveillance and international activities; **Heather Stockwell**—worker health surveillance activities; and **Barbara Brooks**—environmental dose reconstruction activities.

Other scientific presenters, who are involved with DOE-related epidemiology, were **Carl Quong**, Lawrence Berkeley Laboratory—comprehensive epidemiologic data resource; **Shirley Fry**, Oak Ridge Institute for Science and Education—health and mortality studies; **Laurie Wiggs**, Los Alamos National Laboratory—health and mortality studies; **Ethel Gilbert**, Pacific Northwest Laboratory—health and mortality studies; **Richard Stevens**, Pacific Northwest Laboratory—role of metabolism and free radicals; and **Ronald Kathren**, Washington State University—uranium and transuranium registries. ❑

Shigematsu Begins Fourth Term as RERF Chairman

At the 27th meeting of the RERF Board of Directors, held 10–12 June at the Hiroshima Laboratory, **Itsuzo Shigematsu** (below, third from left in the front row) was reappointed RERF chairman for an unprecedented fourth four-year term. He became the third RERF chairman in July 1981. ❑

Attending the 27th RERF Board of Directors meeting were (back row, from left) Ei Matsunaga, Charles Edington, Tomoyuki Kono, Donald Harkness, Yutaka Hasegawa, Catherine Berkley, and Milton Eaton. Middle row, from left: David Williams, Richard Sperry, Joseph Rall, Akira Shishido, Kazuaki Arichi, Mortimer L Mendelsohn, Seymour Abrahamson, Katsutaro Shimaoka, and Yasukiyo Hirano. Front row, from left: Teruhiko Saburi, Seymour Jablon, Itsuzo Shigematsu, JW Thiessen, Tsutomu Sugahara, and Warren Sinclair.

In This Issue

Perspectives

Radiation and Menopause

by Seymour Abrahamson, RERF Chief of Research & Update Editor in Chief

In this issue **Midori Soda** and **John Cologne** present unequivocal data showing a dose-related earlier onset of menopause in Nagasaki women exposed to atomic-bomb radiation. This may be the first study clearly demonstrating that radiation does indeed have an effect on the aging process, an issue that has been contentious over the years. Life Span Study Report 11, Part 3 (Y Shimizu et al, *Radiat Res* 130:249–66, 1992; RERF Technical Report 2-91) and the various reports of the Adult Health Study (AHS) also have clearly demonstrated the influence of radiation on noncancer mortality, particularly on cardiovascular disease in postmenopausal women exposed to atomic-bomb radiation in Hiroshima before the age of 40 years. The interaction of radiation with the brain, pituitary, and ovary feedback system certainly appears to be part of the process; ie, the advancement of menopause advances the onset of other physiological factors associated with diseases of the cardiovascular system and other aging-related diseases.

New RERF publication policy

In this issue of *RERF Update*, we announce a major change in RERF publication policy with respect to the Technical Report (TR) Series, begun in 1959. The TRs, the cornerstone of the ABCC/RERF in-house publication program, have included both reports published only by RERF and most research papers published elsewhere, eg, in peer-reviewed journals, books, and conference proceedings. In recent years, however, it has become obvious that publication of TRs involved considerable duplication of effort for both research departments and the Publication and Documentation Center. Converting journal articles into TRs frequently required much reformatting, with no substantive changes in content. After the TRs approved in 1992 are processed, *the TR Series will be terminated.* The primary mechanisms for disseminating RERF research results will be publication in the scientific literature and the distribution of journal-article reprints, which generally will be provided to the same institutions that received the TRs, eg, government agencies and libraries. Reprints of journal articles will be made available to individuals *on request*. Listings of new publications will continue to appear in *RERF Update* and in RERF's Japanese-language newsletter.

Research papers—usually those involving the Life Span Study and Adult Health Study programs—that might contain more tables and figures than can be accommodated in most journals or other reports not suitable for journal publication will be issued as "RERF Reports" and distributed essentially in the same way as the journal reprints. No changes are presently contemplated to the research protocols. Possible changes to the Commentary and Review Series are now being considered.

This new publication policy was developed following discussions between representatives of the scientific staff and the Scientific Reports Review Committee, chaired by **JW Thiessen**. He initiated several important publication policies during his 6 years as vice chairman of RERF, culminating in this, his last official recommendation before retirement on 30 June. ❑

News Briefs

✓ Chairman To Be Decorated by Royal Swedish Academy

The Royal Swedish Academy of Sciences has announced that it will award to RERF Chairman **Itsuzo Shigematsu** a gold medal from the Academy's Radiation Protection Fund. Shigematsu will be presented with this award in January 1994 at the International Congress of Radiology to be held in Singapore.

✓ Recent RERF Appointments

At the 27th RERF Board of Directors meeting, 10–12 June, the following new appointments were announced. **Mortimer L Mendelsohn** was named RERF vice chairman, replacing **JW Thiessen,** who retired to Somers, Montana, on 30 June. Permanent Director **Yutaka Hasegawa** was reappointed for a second term and will oversee the Nagasaki Laboratory and the Hiroshima Laboratory's departments of Epidemiology and Epidemiologic Pathology. Newly appointed RERF Board of Directors member **Toshiyuki Kumatori** will be replaced on the Scientific Council by **Hiromichi Matsudaira**, director of the National Institute of Radiological Sciences. Replacing **Kunio Aoki** as a member of the Scientific Council is **Tomio Hirohata**, a professor of public health at Kyushu University School of Medicine.

✓ Harkness Appointed RERF Permanent Director

On 1 July, **Donald R Harkness** became one of RERF's six permanent directors. Formerly professor and chairman of the University of Wisconsin Department of Medicine, Harkness will oversee the Department of Clinical Studies and the radioisotope facilities. His research specialties are the biochemical basis of hemolytic anemia, the regulation of hemoglobin function, and interspecies variation. Harkness attended high school at the American School in Tokyo from 1947 to 1950.

✓ Shimomura Receives Imperial Citation

On 26 May at a ceremony in New York City, **Seiichi Shimomura**, a physician in the ABCC Department of Medicine from 1951–54, was presented with an imperial Japanese award, known as the Fourth Order of Merit with the Small Cordon of the Rising Sun, for his dedication to the medical care of Japanese-Americans and for his contributions to Japan–US medical exchanges. Born in Seattle, Shimomura returned to Japan with his family in 1935 and later graduated from Okayama Medical College.

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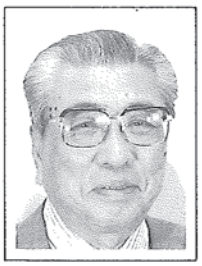

Shigematsu

Harkness

Radiation-accelerated Age at Menopause

The authors describe the key results of a study to measure the impact of radiation exposure on age at menopause in women exposed to the atomic bombing of Nagasaki.

by Midori Soda, Departments of Clinical Studies and Epidemiologic Pathology, RERF, Nagasaki, and John Cologne, Department of Statistics, RERF, Hiroshima

Deterioration of female reproductive function begins in the middle of the fourth decade of life, and menopause—permanent cessation of menstruation—is considered to be the end of reproductive function. Many studies have explored the relationship between age at menopause and environmental factors, but most have been cross-sectional or have relied on subjects' recall of age at menopause. Little cohort-based research, with follow-up to incident menopause, has been reported.

At the Nagasaki Laboratory of ABCC/RERF, the Adult Health Study (AHS) population has received biennial health examinations since 1958. Because of a policy of avoiding X-ray examinations in women suspected of being pregnant, the answer to the question "When was your last menstruation?" is recorded at each examination. We used this information to investigate the effect of atomic-bomb radiation on the incidence of natural menopause.

In this summary of our analyses we describe the study subjects, the statistical methods used to analyze the incidence data, and our findings concerning age at natural menopause. Briefly, we found that radiation exposure led to accelerated median age at natural menopause. The acceleration was nonlinear in dose; high doses produced proportionately greater acceleration in median age at menopause. The finding should not only stimulate further research into elucidating radiation effects on reproductive function, but more generally lends support to the hypothesis that radiation accelerates aging.

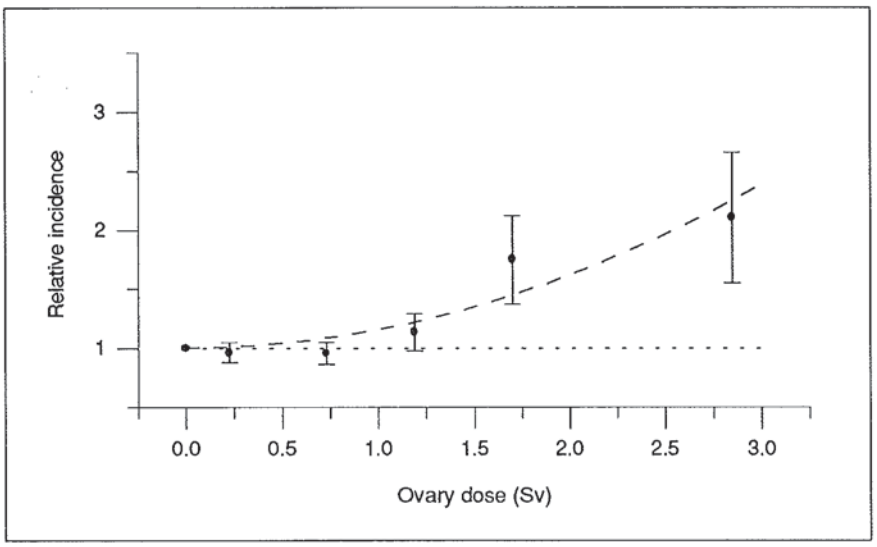

Figure 1. Age- and cohort-adjusted relative risk of natural menopause. Ovary dose is based on the assumption of a relative biological effectiveness of 10. Points are values within dose groups. The dashed line is the fitted quadratic relative-risk model. The dotted line represents a constant relative incidence of 1.

Study subjects

Our analysis was based on 1507 female participants in the AHS in Nagasaki with assigned Dosimetry System 1986 (DS86) doses who were under 40 yr old and in the city at the time of the bombing, were premenopausal as of 1955, and were examined within 3 yr of their latest reported menstrual period. Of these, 1006 were known to be postmenopausal, whereas the remaining 501 were either known to be premenopausal (135) or had been censored due to death, migration, or refusal to attend further AHS examinations (366).

Table. Median age at natural menopause in selected birth-year and exposure categories. We calculated median age from the estimated cumulative age-at-menopause distribution, which was derived from the incidence equation given in the text.

	Ovary dose (Gy)					
Birth year	0	0.001–0.05	0.501–1	1.001–1.5	1.501–2	>2
1915–19	50.8	50.8	50.7	50.7	50.3	49.7
1925–29	51.1	51.1	51.0	50.9	50.7	50.0
1935–39	51.3	51.3	51.2	51.1	50.9	50.3

Calculation of age at menopause

Although menopause is a period of physiological transition spanning several years, in the present study we defined the age at menopause to be the difference between the calendar date at cessation of menstruation and the date of birth. Permanent cessation of menstruation was judged to have occurred in women in whom at least 1 yr had elapsed between their last menstrual period (LMP) and the examination, without intervening pregnancy. If the date of LMP could not be exactly remembered, we used the stated age at which LMP occurred and calculated age at menopause to be age plus 0.5 yr.

Statistical methods

So-called survival methods are most appropriate for the analysis of events occurring in persons observed

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Age at Menopause

continued from page 3

over some period, generally called incidence analyses in epidemiology. For this study, analyses were made by using the Poisson approximation for grouped occurrence data with three-way person-year tables based on attained age, birth cohort (equivalently age at the time of the bombings), and DS86 total kerma dose (in gray). A competing-risks approach was taken to model jointly natural and surgically induced menopause in the cohort. Mean ovary dose (in sievert, using a relative biological effectiveness of 10 for neutrons versus gamma radiation) was calculated for each cell of the person-year table and was used for analyzing natural menopause. Effect of dose (d) on menopause incidence was modeled using the function

$$\lambda_i(d) = \lambda_i(0) \times RR(d) \ ,$$

where $\lambda_i(0)$—the background (unexposed) incidence for age-cohort stratum i—was fit by a log-linear function, and the relative risk $RR(d)$ of menopause due to exposure to dose d was fit by the additive excess-relative-risk function

$$RR(d) = (1 + \beta d + \gamma d^2).$$

Results

Median age at natural menopause in the unexposed women was around 51 yr overall, increasing over time by about 3 months per 10-yr difference in year of birth (Table). This reflects a decrease with birth year in the age-specific incidence that was approximately linear on the log scale (a decrease in age-specific incidence implies a later median age at menopause).

A pure quadratic equation best described the excess relative risk of natural menopause:

$$RR(d) = 1 = 0.058d^2 \ (\pm 0.040)$$

(p = .026; Figure 1). Neither age nor cohort showed a significant interaction with radiation dose. Thus, the proportion of women who have reached natural menopause in any age group and/or birth cohort is higher among the exposed than the unexposed, with the effect most pronounced at high doses. The calculated acceleration of median age at onset of menopause due to radiation exposure was about 0.5 yr at 2 Gy and over 1.5 yr at 4 Gy (Table and Figure 2).

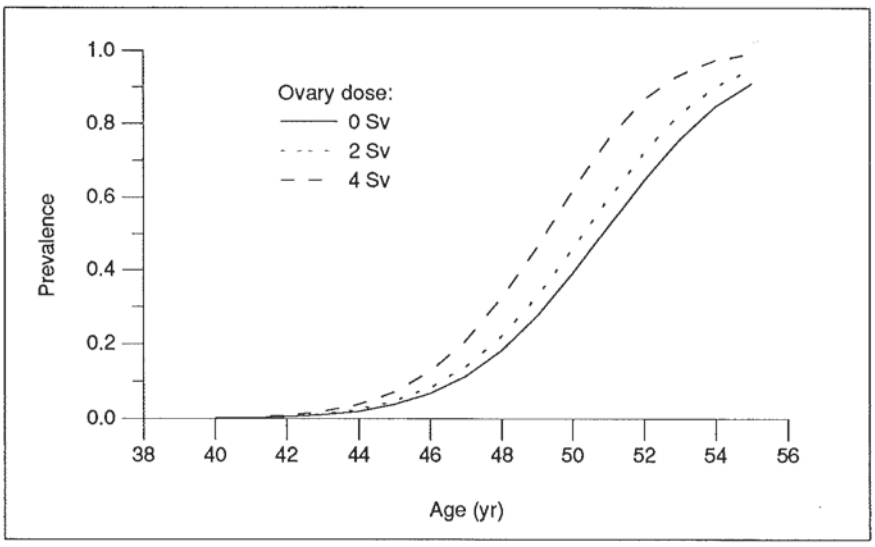

Figure 2. Age-specific prevalence of natural menopause (1920–24 birth cohort) showing acceleration of onset of menopause by radiation

Discussion

Ionizing radiation destroys germ cells, and the degree of damage is dependent upon age and dose. Rubin and Casarett in 1968 reported that exposure of the ovaries to 6 Gy or more causes sterility in women of all ages. The mechanism underlying menopause is attributed to aging of the ovaries before pituitary aging. Although more than 5 million germ cells are found at the peak (at a fetal age of 20 weeks), no germ cells are evident at the time of menopause. Retrogression and disappearance of ovarian follicles (atresia) are involved to a much greater extent than ovulation in this reduction in germ cells. It has therefore been conjectured from these observations that exposure to atomic-bomb radiation accelerates natural menopause.

Age-specific incidence of natural menopause in the present study was elevated in high-dose subjects, indicating that exposure to atomic-bomb radiation accelerates natural menopause. The degree of acceleration was estimated to be 0.5 and 1.5 yr at 2 Gy and 4 Gy, respectively. The present results therefore suggest that atomic-bomb radiation promotes the aging of the ovaries and support the hypothesis that radiation accelerates the aging process in general. Median age at menopause among the nonexposed subjects was approximately 51 yr, which is similar to the median age reported in other studies. The suggestion that age at menopause has increased in recent years was also supported by our finding that estimated median age at menopause increased by about 1 yr over the 40-yr range of birth years represented in this study.

Most previous studies on age at menopause have been either cross-sectional or retrospective. The accuracy of these studies is limited because all have relied on subjects' memories for data on age at menopause. In contrast, the present study used contemporaneous data, which is expected to be more accurate. It is not exempt, however, from problems associated with imperfect follow-up. To avoid imprecision and recall bias, we excluded the cases in which gaps in attendance at the biennial examinations resulted in a lapse of more than 3 yr between LMP and the day of questioning.

We also investigated the radiation effect on age at surgically induced menopause, but these investigations are not reported here. Further details of these analyses will be provided in a full manuscript that is currently in preparation. A new research program is soon to be initiated to follow the hormonal status of the remaining premenopausal women.

One could speculate that radiation sensitivity among those exposed at prepubescence might differ from the sensitivity of women who had already reached reproductive age at the time of exposure. The majority of women who were young at the time of the bombing were premenopausal at the time of this analysis, so we cannot at present conclude anything about differential sensitivity. Another, similar, analysis should therefore be performed after the entire cohort has reached menopause. ❑

Uses of the Life Span Study Mail Survey Data

Long-term follow up provides the opportunity to examine non-radiation-related risk factors.

by Marc T Goodman, Department of Epidemiology, RERF, Hiroshima, and Yoshisada Shibata, Department of Epidemiology and Biometrics, RERF, Nagasaki

The extended Life Span Study (LSS) comprises approximately 120,000 members, including 93,000 exposed and 27,000 unexposed people who were residents of Hiroshima and Nagasaki in 1950 at the time of the first post-war national census. The original objective of this large, prospective cohort study was to investigate the late effects of atomic-bomb radiation through surveillance of excess mortality. More recently, cancer-incidence data have become available for analysis through the assistance of population-based tumor registries in Hiroshima City and Nagasaki Prefecture.

As has long been known, before the LSS cohort could be used to define precisely the risk of radiation exposure, the cohort had to be well characterized. To meet this requirement, several interview studies and mail surveys have been conducted since 1960 (Table 1). Of particular interest among epidemiologists is the question of whether radiation acts alone or in concert with other agents, such as smoking, to increase the risk of disease.

Radiation is known to induce various biological changes associated with cancer. Radiation-affected or "-transformed" cells may possibly have altered susceptibility or sensitivity to environmental carcinogens (cancer-causing agents). If dietary factors, for example, act as antipromotional (anticancer) agents, these factors may interact with radiation-induced cells to inhibit the carcinogenic process.

Mail-survey items have remained reasonably consistent through the years to provide continuity and to allow analysis of factors, such as reproductive history, that may change with time. Serial information has now been obtained from LSS members on occupation, education, marital status, physical activity at work and elsewhere, tobacco use, alcohol use, height and weight at various ages, diet, and selected medical problems.

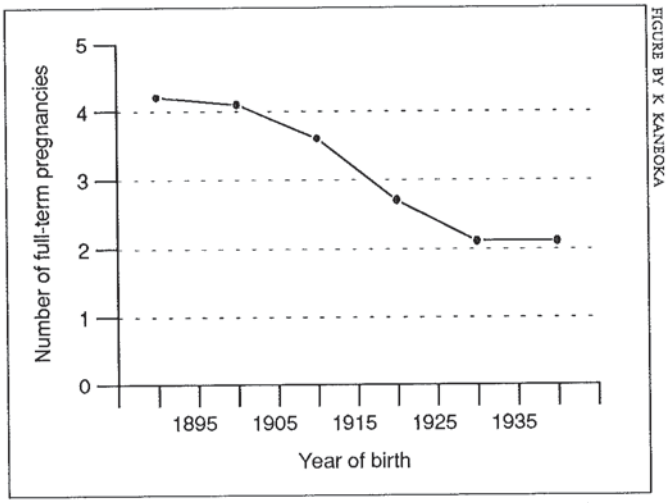

Figure. Number of full-term pregnancies among Life Span Study subjects by birth cohort

Although the mail-survey data have been available for some time, past analyses were hampered by difficulties in managing large data sets and by the unavailability of statistical techniques and computer software to analyze the data properly. With the help of the RERF Research Information Center, accessing computer files and merging data from multiple sources have become increasingly easy. In particular, the recent computerized linkage of the survey data with the tumor registry and the Master File* has facilitated analysis of the data set.

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** The ABCC/RERF Master File contains the names of all persons in the master sample in relation to radiation exposure, laboratory studies, or any study program. This includes all tumor-registry cases before 1985, all autopsies at selected local hospitals up to 1986, and all leukemia-registry cases.*

Table 1. Mail surveys of the ABCC/RERF Life Span Study sample

Survey year(s)	Sex	Research protocol	Age group	Effective sample size	Information collected
1965	Males	9-65	40–69 yr, alive as of 1 Jan 1965	13,065	Occupation, education, marital history, physical activity, tobacco use, alcohol use, height and weight, diet, medical history
1969–70	Females	11-69	All ages, alive as of 1 Sept 1969	20,836	Occupation, education, marital history, reproductive history, lactation history, hormone use, tobacco use, alcohol use, diet, height and weight, medical history
1979–80	Males Females	14-78	All ages, alive as of 1 Sept 1979	40,348	Occupation, education, marital history, reproductive history, lactation history, hormone use, tobacco use, alcohol use, diet, height and weight, medical history
1991–92	Males Females	4-91	All ages, alive as of 1 July 91	45,000	Occupation, education, marital history, reproductive history, lactation history, hormone use, tobacco use, alcohol use, height and weight, medical history, physical activity

Uses of the LSS Mail Survey Data

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Researchers in the RERF Epidemiology Department have focused much of their recent effort on the effects of tobacco smoking on disease and on the potential joint effects of smoking and radiation dose on cancer risk. In Japan, where rapid economic and social changes occurred after World War II, age-dependent differences in life-style characteristics among the cohort are likely. For example, age at the time of the bombings (age ATB) has been found to modify the association of radiation dose with the risk for various malignancies (D Thompson et al, RERF Technical Report 5-92; *Radiat Res*, in press). However, among the LSS subjects, associations that influence the risk of disease also exist between age ATB and tobacco and alcohol use, body-mass index, reproductive factors, and other characteristics. For example, the reproductive histories of women in the LSS are strongly related to the survivor's age ATB (Figure). These data suggest that the modifying effects of age ATB on the association of radiation with breast-cancer risk may be biased by differences in parity by birth cohort (C Land and M Tokunaga, *RERF Update* 5(1):3–4, 1993). Age-dependent variation in exposure to agents known to be related to disease development must be considered when greater radiation susceptibility is hypothesized among younger people.

In a recent analysis, we examined the influence of smoking, drinking, and dietary habits on the rate of liver cancer among the LSS cohort, using data from the third mail survey (RERF Research Protocol 14-78). The risk of liver cancer among smokers was twofold greater than the risk among those who had never smoked. Also, a significantly increased risk of liver cancer was found among men who had quit drinking at the time of the survey. After categorizing the ex-drinkers by years of abstinence, we found a stronger association of alcohol use with the risk of liver cancer among men who had recently quit compared with cohort members who had abstained for 16 years or longer at the time of the survey (Table 2). This finding might be explained by an effect of preclinical disease on the relation between alcohol drinking and liver cancer. Persons may stop drinking because of cirrhosis or other conditions that result in higher risk for liver cancer. Other risk factors for liver cancer included a history of radiation therapy and a history of diabetes.

In addition to these completed and ongoing analyses, several other uses of the data are planned. Besides being useful for elucidating cancer endpoints, mail-survey information can be used to conduct correlational analyses, such as an examination of the association between reproductive factors and radiation dose effects, and survival analyses, such as an evaluation of the effect of exercise, tobacco use, and alcohol use on the risk of death.

Several disease genes have recently been discovered using sophisticated genetic techniques, which has led to increased interest in identifying the markers of disease susceptibility. Of special interest among the cohort of atomic-bomb survivors is whether people respond uniformly to radiation exposure and, if not, what factors modify the effects of radiation on disease. The LSS cohort provides a unique opportunity to collect and analyze family data systematically. In combination with the mail surveys, the determination of family ties will enable us to assess patterns of familial aggregation of specific biological outcomes— ranging from possible chromosomal radiosensitivity to clinical measurements, such as blood pressure, serum cholesterol and cancer—and to provide clearer distinctions between the independent and interactive contributions of environmental (eg, radiation exposure or tobacco smoking) and genetic factors to the aggregation.

Important byproducts of the mail surveys are the frank comments and questions from the respondents. Respondents to the most recent survey suggested the need for a survey that focuses on the unique psychological problems of atomic-bomb survivors. Furthermore, they suggested that more efforts are needed to publicize the activities of RERF in Japan. Beginning with *RERF Update*, and through our ongoing analyses and other outreach efforts, we hope to do just that. ❑

Table 2. Alcohol consumption and the relative risk of liver cancer in men

Years since drinking stopped	Relative risk	95% confidence interval
<11	7.9	3.9–16.0
11–15	2.1	0.9–4.7
>15	1.0	0.3–2.8

News Briefs

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While at ABCC, Shimomura conducted health examinations of atomic-bomb survivors and also examined the crew of the *Lucky Dragon* tuna-fishing vessel, which was contaminated by fallout from the 1954 Bikini-atoll nuclear test (see related story in this issue, pp 8–10).

✓ International Advisory Committee Participation

RERF Department of Statistics Chief **Dale Preston** attended a meeting of the United Nations Scientific Committee on the Effects of Atomic Radiation, held in Vienna, 19–27 May. He contributed to discussions of epidemiologic studies of radiation carcinogenesis.

RERF Department of Epidemiology Chief **Kiyohiko Mabuchi** has been appointed to Committee I of the International Commission on Radiological Protection (ICRP).

RERF Chairman **Itsuzo Shigematsu** retired this year from the Main Commission of the ICRP. After more than 15 years of service, respectively, RERF Chief of Research **Seymour Abrahamson** and **William J Schull**, long-time RERF scientific collaborator, will retire from ICRP Committee I.

✓ Research Staff News

Hiroshima

Department of Clinical Studies: **Kazunori Kodama**, chief, is concurrently serving as acting chief of the Division of Radiology after **Sachiko Kawamura** resigned on 30 June.

Department of Radiobiology: On 1 May, **Seishi Kyoizumi** was promoted to associate senior scientist.

✓ Highlights of the RERF Lecture Program

On 28 June, **Soren M Bentzen**, Danish Cancer Society, Århus, Denmark, spoke about intra- and interpatient variability in the normal-tissue response to radiotherapy and its relation to in-vitro radiosensitivity.

Fumihiko Matsuda, Kyoto University, discussed the organization and evolution of the human immunoglobulin heavy-chain locus on 9 July. ❑

Preliminary Report of the 1991 Life Span Study Mail Survey

by Yoshisada Shibata, Department of Epidemiology and Biometrics, RERF, Nagasaki

Via the most recent Life Span Study (LSS) mail survey, conducted from September 1991 until November 1992, information on epidemiologic factors that might affect the assessment of health effects associated with atomic-bomb radiation, as well as the addresses of members of the extended LSS cohort, have been updated.

The survey recipients were 17,110 male and 28,017 female members of the LSS cohort, who were assumed to be alive at the start of the survey, excluding those not in the city (NIC) at the time of the bombings.

The subjects were divided into Group I, the respondents of the 1979–80 mail survey (in this issue, see also M Goodman and Y Shibata, pp 5–6), and Group II, the nonrespondents to the last mail survey, plus the Nagasaki distal survivors (ie, those more than 2500 m from hypocenter at the time of the bombing), who had been added to the LSS cohort in 1980. Classifications of subjects by group, city, sample class, sex, and Dosimetry System 1986 category and their age distributions are shown in the Table.

The Group I questionnaire requested information about (a) the subject's name and address and the identity of the person completing the questionnaire (if not the subject), (b) present and past health status, (c) present living conditions, (d) obstetric and gynecologic history (females), (e) smoking and drinking habits, (f) exercise, and (g) occupation. The Group II questionnaire was an extended version of the questionnaire sent to Group I.

To obtain a higher response rate, reminder letters and additional copies of the questionnaire were sent to nonrespondents at least twice. Supplementary mail or telephone interviews were conducted when the returned questionnaire included incomplete or contradictory answers to key questions. Response rates for the two groups differed, and an association with age was suggested. The response rates increased with subject age, reaching a maximum at about 60 to 70 years old, and then decreased. The reminder contacts significantly effected the response rate, which suggested that setting the maximum number of reminder letters at two was appropriate (Figure). The response rates for the two cities and for males and females differed little, whereas response rates were lower for subjects with radiation exposures of 1.0 Gy or higher in each age class for the two groups. ❑

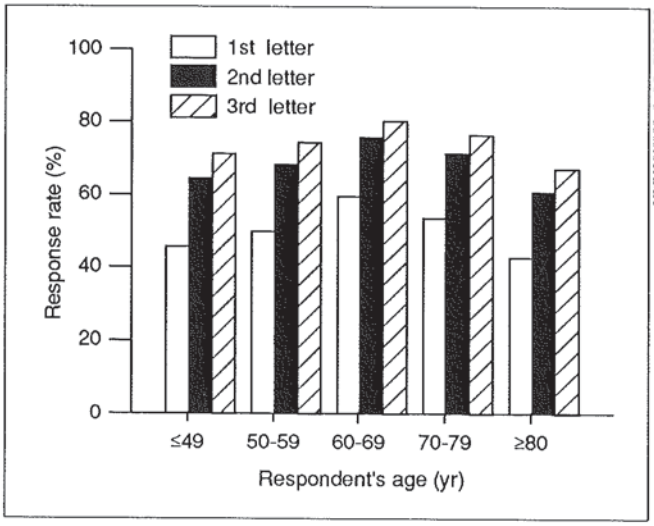


FIGURE BY Y KATAYAMA

Figure. Response rates by age and number of letters sent

Table. Age distribution and classification of subjects by group, city, sample class, sex, and Dosimetry System 1986 category

Group[a]	City	Sample class	Sex	Total	Age distribution (yr)[b]	Estimated dose (Gy) <0.01	0.01–0.99	≥1.0	UNA or UNK[c]
I	Hiroshima	Extended LSS	Males	7401	(50, 58, 65)	2936	4001	93	371
			Females	12,891	(55, 64, 74)	5203	6735	155	798
			Total	20,292					
I	Nagasaki	Extended LSS	Males	2568	(51, 58, 62)	796	1251	67	454
			Females	4008	(54, 61, 69)	1319	2019	84	586
			Total	6576					
II	Hiroshima	Extended LSS	Males	3412	(50, 55, 61)	1417	1770	73	152
			Females	5491	(53, 63, 74)	2261	2792	109	329
			Total	8903					
II	Nagasaki	Extended LSS	Males	1177	(50, 55, 61)	370	614	27	166
			Females	1711	(52, 60, 67)	545	853	39	274
			Total	2888					
II	Nagasaki	Distal	Males	2552	(50, 55, 59)	2479	41	0	32
			Females	3916	(52, 60, 72)	3757	88	0	71
			Total	6468					

[a]Group I subjects consisted of those who had responded to the last mail survey. Group II subjects consisted of those who did not respond to the last mail survey, plus Nagasaki distal survivors, ie, those who had been more than 2500 m from the hypocenter at the time of the bombing; [b]the triplet represents the 25th, 50th, and 75th percentiles; [c]Dosimetry System 1986 estimated dose is unavailable (UNA) or unknown (UNK).

The *Lucky Dragon* Incident and ABCC: Part II

Within 2 weeks, the magnitude of the fallout resulting from the nuclear detonation on Bikini atoll and the radiation sickness of the crew of the Japanese fishing vessel the Lucky Dragon *had become matters of international concern.*

Excerpts from Merril Eisenbud's book* An Environmental Odyssey, *published by the University of Washington Press

Editor's note: The following concludes a condensed account of the Lucky Dragon *incident and the involvement of RERF's predecessor organization, the Atomic Bomb Casualty Commission (ABCC). Part I appeared in* RERF Update *5(1):10–12, 1993. The author served with the US Atomic Energy Commission (AEC) for many years and at one time was the contract administrator for ABCC.*

PHOTO COURTESY OF MERRIL EISENBUD

***The group that traveled to Yaizu to view the* Lucky Dragon *included, from left, Wataru Miyagawa, an administrative official from the Ministry of Foreign Affairs; Harumi Takeuchi, chief of the European-American Section, Ministry of Foreign Affairs; the author; John Lewis, ABCC hematologist; Hiroki Kakehi, Tokyo University medical professor; Eizo Tajima, St Paul's University professor; Fumio Yamazaki, director of the Radiation Section, Institute of Physical and Chemical Research; John Morton, ABCC director; and one unidentified man. In the author's right hand is a board wrapped in newspaper that he found atop the cabin of the* Lucky Dragon.**

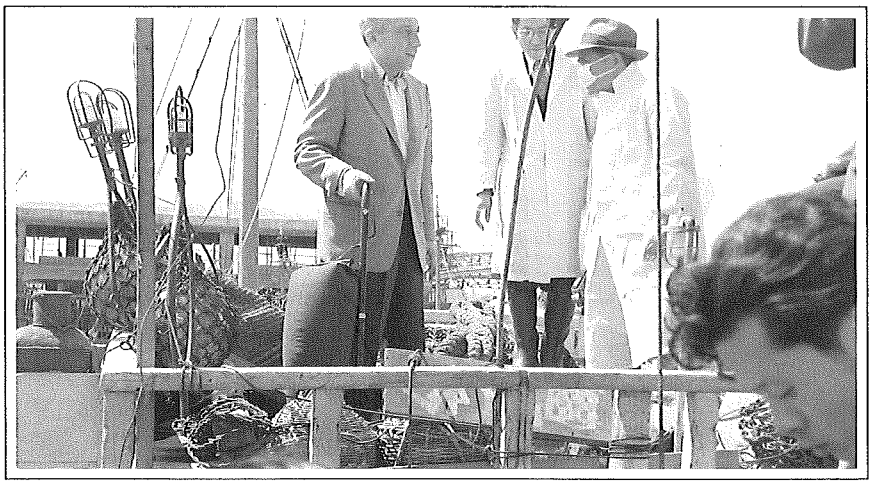
I was anxious to visit the *Lucky Dragon*, and the [Japanese] committee [investigating the incident] not only arranged for this, but suggested that while we were in Yaizu we should pay a courtesy call on the twenty-one fishermen who were hospitalized there. On March 26, [**John**] **Morton** [ABCC director], Dr [**John**] **Lewis**, who was an ABCC hematologist, and I, accompanied by several Japanese physicians and physicists, flew to Yaizu, ninety minutes southwest of Tokyo, in a C-47 provided by the US Air Force.

When we arrived, we were welcomed impassively by the school children of Yaizu, who were lined up along the short airstrip. We proceeded to the hospital followed by a few carloads of reporters, who had also met us at the field. The visit to the patients was only a courtesy call; they were evidently glad to see us. They were resting on mats, surrounded by their families, who, in the Japanese [fashion], were preparing food for them on hibachis within the room. The reporters were not allowed into the hospital, but since the windows were at ground level and wide open, the photographers had no trouble taking all the photographs they needed. I had broken the Geiger-Mueller tube of one of the two radiation detectors I had brought with me, but with the remaining instrument I was permitted to scan the bodies of some of the fisherman. Although it was now nearly four weeks since the accident, their thyroids still contained readily measurable amounts of iodine-131. The information I obtained was very scanty because there was not time for more systematic measurements. Many of the men had skin burns, particularly on their scalps and along the line of their trouser belts where the fallout particles had become lodged as they stood shirtless on deck when the fallout was occurring.

For some reason I never understood, the American [news] media carried reports that I was not permitted to examine the fishermen because I [was] neither an MD or PhD. The fact was that the Japanese scientists [asked] me to visit the fishermen when we visited Yaizu. Unreliable media reports can be very troublesome. . . .

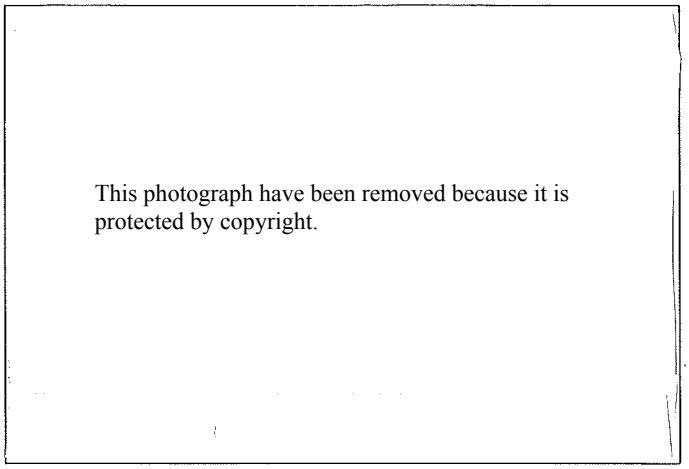
After our lunch we visited the fishing boat, where the Japanese scientists who accompanied us donned lab coats and gauze masks before boarding. We Americans brought no protection, nor did I believe it was necessary for the type of contamination we were to encounter. However, when we saw our pictures in the Tokyo papers next morning, I did regret that, compared to the Japanese, we seemed so cavalier in our attitude towards radioactivity. Before leaving Tokyo I had requested that the embassy provide me with a household vacuum cleaner, and this I used to collect fallout particles from some of the less accessible exterior surfaces of the boat that I thought might have escaped the pickings of the many Japanese scientists who preceded me. On the roof of the cabin I found a loose piece of wood about eighteen inches long that was coated with many white grains about 0.2 mm in diameter. With the permission of the Japanese, I took the board back to HASL [the Health and Safety Laboratory] as a souvenir of my visit. The dust collected by the vacuum cleaner was divided for

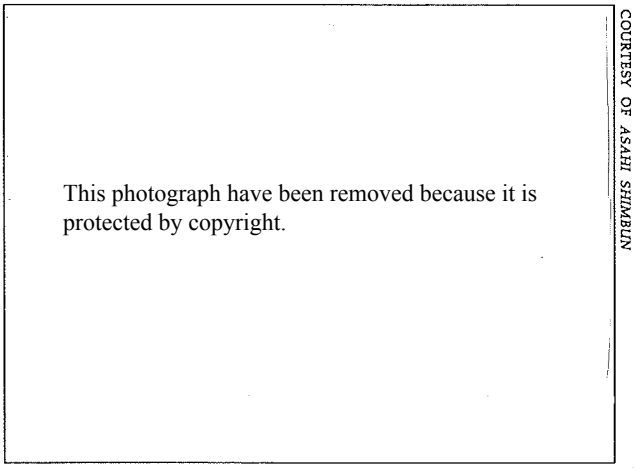
PHOTO COURTESY OF MERRIL EISENBUD



Top left, impromptu snapshot of Eisenbud, left, with Japanese scientists. The vacuum cleaner held by Eisenbud was used to collect particles from the deck of the* Lucky Dragon *for use in studies by US and Japanese scientists. Bottom left, artist's rendering of ABCC Director John Morton and Japanese scientists aboard the contaminated fishing vessel. Bottom right, Eisenbud (denoted by circles), equipped with Geiger-Muller counter, is accompanied by military representatives and Japanese officials in this artist's recreation of the scene.

COURTESY OF *ASAHI SHIMBUN*





COURTESY OF *ASAHI SHIMBUN*

study by several laboratories in Japan and the US.

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During the last week in March, nearly one month after their exposure to the fallout radiation, the white blood counts of most of the fishermen were continuing to decrease, and alarm increased over the possibility that some of them would not survive. In one case the count dropped to 800 cells per cubic millimeter and others hovered just above 1000. This is a dangerous phase of the acute radiation syndrome, in which the body is less able to resist infection. If infection can be prevented for a few weeks, the damaged bone marrow, which produces a reduced number of blood cells, will gradually repair so that recuperation of the white blood count can begin. The ABCC physicians were of the opinion that they could possibly make practical suggestions that would reduce the probability of infections, but the Japanese doctors continued to decline their assistance, and neither Morton nor his American assistants were ever consulted concerning medical management of the cases. Fortunately, the blood counts began to return to normal after four to six weeks, and the men returned to normal health after one year, except for the radio operator who developed jaundice in June (about three months after exposure) and died in September. The cause of death has been attributed to serum hepatitis, probably a consequence of the large number of blood transfusions he received. It was accepted practice in Japan at that time to transfuse only about 100 cc at a time. This required a great number of transfusions, with a proportionate increase in the risk of infection by the hepatitis virus. Although the radio operator did not die directly from radiation injury, his death was clearly a secondary result of his exposure.

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What was happening in Washington?

During my stay in Japan I had excellent rapport with the AEC in Washington as well as with HASL in New York. There was hardly a day when I didn't cable for information, copies of literature requested by the Japanese scientists or, in some cases,] equipment. I had excellent support, and all my requests were answered promptly.

My greatest concern with Washington was the near absence of official statements. A terse statement that a new test series had begun in the Pacific was issued to the press immediately following the BRAVO detonation, but no other information was given at that time despite the fact that it was already known that unexpectedly high levels of fallout had occurred. No further information was released for many days. The evacuation of the [inhabitants] and the dispatch of a team of medical specialists all took place without public announcement. But JTF-7 [Joint Task Force 7] was a task force of many thousands of personnel, and the magnitude of the event was such that it was impossible to keep rumors of the disaster from reaching the public. It was not until March 10 that the AEC issued its second report in which it announced that 236 Marshallese had been evacuated from their home atolls according to plan as a precautionary measure. This was a clear understatement of the facts. The

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The *Lucky Dragon* Incident: Part II

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statement said nothing about the early effects of the heavy radiation exposures that were already evident.

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The magnitude of the fallout became known everywhere in the world on March 16, when the Japanese newspapers announced that the *Lucky Dragon* had returned to its home port of Yaizu with twenty-three fishermen suffering from radiation sickness. The news created a sensation throughout the world, but no immediate statement was issued by Washington. In the absence of information from the US, newspapers in western countries, including the United Stated, were forced to rely on reports from Japan, which were in many cases exaggerated.

By March 31 there were no additional announcements from Washington, and Ambassador **Allison** decided it would be necessary for me to conduct a background briefing for the American members of the Tokyo press corps. . . .

What I could not explain to the reporters, because I did not know, was why our government had released so little information. It was now a full month since the fallout occurred, and about two weeks since the *Lucky Dragon* had returned to Yaizu. The Japanese scientists were making statements that were being reported in the world press. The statements they were making were frequently inflammatory, which was understandable under the circumstances. Sensational stories were being published in the US newspapers as well. The ambassador and his staff were puzzled that so little information had been released.

The press briefing took place during the afternoon of March 31, Tokyo time, which was early on March 30 in Washington. Unknown to me, President **[Dwight] Eisenhower** had scheduled a televised press conference for the following day and had invited Admiral **Lewis L Strauss**, chairman of the AEC, to join him and to make a statement about the BRAVO fallout. I believe that it was a coincidence that the briefing in Tokyo coincided with Strauss' statement. The president was responding to the same pressure for information that caused the ambassador to arrange the briefing. When the Strauss statement, which was made in the presence of the president, was received in Tokyo, it came as a shock to Morton and myself as well as to senior officials at the embassy. The statement said the fishermen "must have been well within the danger area," which could not be supported by any evidence of which I was aware, but was a convenient assumption from the point of view of the liability of the US for damages sustained by the fishermen and the owner of the *Lucky Dragon*.

The statement then went on to say that the skin lesions "are believed to be due to the chemical activity of the converted material in the coral, rather than to radioactivity. . . ." In other words, the burns were due to the fallout of corrosive particles of calcium oxide produced by the action of the great heat of the fireball on coral. This was particularly painful to read since it was not so, and because, in the same paragraph that contained that statement, Strauss mentioned that the commission was represented in Japan by Morton and myself. There was every reason why the Japanese scientists, whose confidence we were struggling to develop, should have believed that the misinformation originated with us.

On April 9 Morton and I decided that our usefulness was at an end in Japan and arranged to leave for what I thought would be brief visit to Eniwetok to meet our colleagues who were ministering to the needs of the Marshallese. The ambassador issued a press release in which he reviewed what we had accomplished, and the foreign minister delivered a note of thanks to us together with gifts of appreciation.

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During those few days [at] Eniwetok I had time to reflect on what had happened in the previous weeks. I speculated on why the AEC had taken so long to announce what had happened, and why the press releases were so misleading. I have never learned what happened, but I can only assume the AEC was unable to obtain the required agreements of other agencies such as the departments of Defense and State. The fallout episode must have caused consternation at the Defense Department because they learned that it would be necessary to shelve the plans which, in the event of war with the Soviets, called for destruction of eastern European air bases with megaton bombs that would create giant craters when exploded at ground level. They were building bombs they couldn't use! That is, unless they wanted to cover western Europe with lethal levels of fallout! The North Atlantic Treaty Alliance (NATO) had only recently been formed and was depending on the US nuclear shield to defend western Europe. What would be the effect on the NATO alliance of the knowledge that thermonuclear bombs could produce such heavy levels of fallout?

"Nuclear weapons were abhorrent to me, as they still are, but they existed, and it was important that the effects be understood."

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Nuclear weapons were abhorrent to me, as they still are, but they existed, and it was important that their effects be understood. Our studies were adding to that understanding, and perhaps the prospect that extensive areas of land would be blanketed with radioactive dust would be one more reason why nuclear weapons would never be used in war.

In early May 1954, after an absence of nine weeks, I returned to New York to assume my new responsibilities as manager of the AEC's New York Operations Office. . . . At the age of thirty-nine, I was being promoted into one of the more important positions within the AEC. I would be involved in the administration of large-scale government research and development contracts and would have the opportunity to participate in the application of nuclear energy to civilian needs such as the production of energy and exploration of outer space. ❑

Recent Scientific Publications

Editor's note: The reports listed have been approved and will be distributed as soon as they are printed. Wording of the titles and summaries may be slightly altered before final printing.

Approved Technical Reports

Variations among Japanese of the factor XI gene (*F9*) detected by PCR-denaturing gradient gel electrophoresis. C Satoh, N Takahasi, J Asakawa, K Hiyama, M Kodaira. **RERF TR 21-92.**

In the course of feasibility studies to examine the efficiencies and practicalities of various techniques for screening for genetic variations, the human coagulation factor IX (*F9*) genes of 63 Japanese families were examined by polymerase chain reaction–denaturing gradient gel electrophoresis (PCR-DGGE). Four target sequences with lengths of 983–2891 base pairs (bp) from the *F9* genes of 126 unrelated individuals from Hiroshima and their 100 children were amplified by PCR, digested with restriction enzymes to approximately 500-bp fragments, and examined by DGGE—a total of 6724 bp being examined per individual. GC-rich sequences (GC-clamps) of 40 bp were attached to both ends of the target sequences, as far as was feasible. Eleven types of new nucleotide substitutions were detected in the population, none of which produced restriction-fragment-length polymorphisms or caused hemophilia B. By examining two target sequences in a single lane, approximately 8000 bp in a diploid individual could be examined. This approach is very effective for the detection of variations in DNA and is applicable to large-scale population studies.

Accurate and rapid detection of heterozygous carriers of a deletion by combined polymerase chain reaction and high-performance liquid chromatography. J Asakawa, C Satoh, Y Yamasaki, S Chen. **RERF TR 22-92.**

We have developed a technique to detect accurately heterozygous carriers of a deletion. Specific target sequences were amplified using the polymerase chain reaction (PCR) and the products were subsequently analyzed by high-performance liquid chromatography. Examples from four loci demonstrated that 24–27 cycles of amplification for a single-copy DNA, based on 50-ng genomic DNA results in excellent quantitation, which readily permits the detection of heterozygous carriers of a deletion. We have demonstrated that triplex PCR (three targets in a single PCR) entails no loss of precision. We have also demonstrated that this method could accurately differentiate the heterozygous carriers of a deletion from normals in four family studies, three for Duchenne muscular dystrophy patients and one for a hemophilia B patient.

Immune responses to Epstein-Barr virus in atomic-bomb survivors: study of precursor frequency of cytotoxic lymphocytes and titer levels of anti-Epstein-Barr–related antibodies. Y Kusunoki, S Kyoizumi, Y Fukuda, H Huang, M Saito, K Ozaki, Yuko Hirai, M Akiyama. **RERF TR 23-92.**

Precursor frequencies (PF) of cytotoxic lymphocytes to autologus Epstein-Barr-virus–transformed B cells and serum titers of anti-Epstein-Barr-virus–related antibodies were measured in 68 atomic-bomb (A-bomb) survivors to clarify the immune mechanism controlling Epstein-Barr-virus (EBV) infection. The PF was negatively correlated with the titer of anti-early antigen IgG, which is probably produced at the stage of EBV reactivation. A positive correlation between the PF and titer of anti-EBV-associated nuclear antigen (EBNA) antibody was also observed, indicating that the PF reflects the degree of in-vivo destruction by T cells of the virus-infected cells. These results suggest that T-cell memory specific to the EBV controls the virus and that the PF assay is useful for the evaluation of immune responses to EBV. However, no significant effect of A-bomb radiation on the PF was observed in the present study, probably due to the limited number of subjects.

Cancer incidence in atomic-bomb survivors. Part III: The incidence of leukemia, lymphoma, and multiple myeloma among atomic-bomb survivors, 1950–87. D Preston, S Kusumi, M Tomonaga, S Izumi, E Ron, A Kuramoto, N Kamada, H Dohy, T Matsuo, H Nonaka, DE Thompson, M Soda, K Mabuchi. **RERF TR 24-92.**

This paper presents an analysis of data on the incidence of leukemia, lymphoma, and myeloma in the Life Span Study cohort of atomic-bomb survivors from late 1950 through the end of 1987 (93,696 survivors representing 2,778,000 person-years). These analyses add 9 additional years of follow-up for leukemia and 12 for myeloma to that in the last comprehensive reports on these diseases. This is the first analysis of the lymphoma incidence data in the cohort. Using both the leukemia registry and the Hiroshima and Nagasaki tumor registries, a total of 290 leukemia, 229 lymphoma, and 73 myeloma cases were identified. The primary analyses were restricted to first primary tumors diagnosed among residents of the cities or surrounding areas with Dosimetry System 1986 dose estimates between 0 and 4 Gy kerma (231 leukemias, 208 lymphomas, and 62 myelomas).

Analyses focused on time-dependent models for the excess absolute risk (EAR). Separate analyses were carried out for acute lymphocytic leukemia (ALL), acute myelogenous leukemia (AML), chronic myelocytic leukemia (CML), and adult T-cell leukemia (ATL). There were few cases of chronic lymphocytic leukemia (CLL) in this population. There was strong evidence of radiation-induced risks for all subtypes except ATL, and there were significant subtype differences with respect to age-at-exposure and sex effects and in the temporal pattern of risk. The AML dose-response function was nonlinear, whereas there was no evidence against linearity for the other subtypes. Averaged over the follow-up period, the EAR estimates (in cases per 10^4 person-year-sievert) for the leukemia subtypes were 0.6, 1.1, and 0.9 for ALL, AML, and CML, respectively. The corresponding estimated average excess relative risks at 1 Sv are 9.1, 3.3, and 6.2, respectively. There was some evidence of an increased risk of lymphoma in males (EAR = 0.6 cases per 10^4 person-year-sievert), but no evidence of any excess in females. There was no evidence of an excess risk for multiple myeloma in our standard analyses.

Approved Commentary and Review

Report of a workshop on the application of molecular genetics to the study of mutation in the children of atomic-bomb survivors. Report coordinated by JV Neel, C Satoh, R Myers. **RERF CR 5-92.**

In February 1983, the Radiation Effects Research Foundation (RERF) Scientific Council recommended that the feasibility of extending to the molecular level the ongoing studies of the genetic effects of atomic-bomb radiation in the children of survivors be explored. In 1984 a first workshop addressing various aspects of this recommendation was held, following which the staff of the Biochemical Genetics Section of the RERF Department of Genetics began to develop the necessary DNA expertise and to establish the cell lines upon which future studies would be based. This is an account of the second such workshop, organized by a committee chaired by then RERF Chief of Research James Trosko, and held at RERF 12–14 November 1991. The pur-

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pose of this workshop was to evaluate the status of the emerging DNA-oriented techniques for the study of mutation and to discuss possible developments that would bear upon the program. This report attempts to summarize the contents of a lively 2.5-day meeting, presided over by Mortimer Mendelsohn and Toshiyuki Kumatori, co-chairmen of the RERF Scientific Council.

Although the purpose of this workshop was to address the specific genetic follow-up studies of children of bomb survivors, it was clear to the participants that their discussions had much-wider implications. There have been various other situations, in several countries, in which populations have had unusual exposures to radiation—most notably, the Chernobyl accident of 1986—as well as to potential chemical mutagens. The various recent discussions of suitable follow-up studies of these latter exposures all include reference to DNA-oriented investigations. The considerations advanced at this workshop should prove useful in the development of any other studies directed at evaluating the genetic effects of human exposures to potential mutagens.

Publications in the Open Literature

Longitudinal study of the association between ABO phenotype and total serum cholesterol level in a Japanese cohort. FL Wong, K Kodama, H Sasaki, M Yamada, HB Hamilton. *Genet Epidemiol* 9:405–18, 1992 (based on RERF Technical Report 14-91).

Ionizing radiation and health. I Shigematsu. *J Epidemiol* 2:S21–9, 1992.

G-banding analysis of radiation-induced chromosome damage in lymphocytes of Hiroshima A-bomb survivors. K Ohtaki. *Jpn J Hum Genet* 37:245–62, 1992 (based on RERF Manuscript 1-93).

Rapid translocation frequency analysis in humans decades after exposure to ionizing radiation. JN Lucas, AA Awa, T Straume, M Poggensee, Y Kodama, M Nakano, K Ohtaki, H-U Weier, D Pinkel, J Gray, G Littlefield. *Int J Radiat Biol* 62:53–63, 1992 (based on RERF Manuscript 3-93).

Normal age-related alterations on chest radiography. A longitudinal investigation. F Mihara, T Fukuya, H Nakata, S Mizuno, WJ Russell, Y Hosoda. *Acta Radiol* 34:53–8, 1993 (based on RERF Technical Report 16-88).

Variations among Japanese of the factor IX gene (*F9*) detected by PCR-denaturing gradient gel electrophoresis. C Satoh, N Takahashi, J Asakawa, K Hiyama, M Kodaira. *Am J Hum Genet* 52:167–75, 1993 (based on RERF Technical Report 21-92)

Induction of BCR-ABL fusion genes by in vitro X-irradiation. T Ito, T Seyama, T Mizuno, T Hayashi, KS Iwamoto, K Dohi, N Nakamura, M Akiyama. *Jpn J Cancer Res* 84:105–9, 1993.

Study of the titers of anti-Epstein-Barr virus antibodies in the sera of atomic bomb survivors. M Akiyama, Y Kusunoki, S Kyoizumi, K Ozaki, S Mizuno, JB Cologne. *Radiat Res* 133:297–302, 1993 (based on RERF Technical Report 14-92).

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Monoclonal gammopathy in atomic bomb survivors. K Nerishi, Y Yoshimoto, RL Carter, T Matsuo, M Ichimaru, M Mikami, T Abe, K Fujimura, A Kuramoto. *Radiat Res* 133:351–9, 1993 (based on RERF Technical Report 2-92)

A longitudinal study of growth and development of stature among prenatally exposed atomic bomb survivors. M Otake, Y Fujikoshi, WJ Schull, S Izumi. *Radiat Res* 134:94–101, 1993.

Publications of Interest Using RERF Data

Bomb survivor selection and consequences for estimates of population cancer risks. MP Little, MW Charles. *Health Phys* 59(6):765–75, 1990.

Time variations in radiation-induced relative risk and implications for population cancer risks. MP Little, MW Charles. *J Radiat Prot* 11:91–110, 1991.

Pre-conception exposure risks in the Sellafield workforce and the Japanese bomb survivors. MP Little. *J Radiol Prot* 10(3):185–98, 1990

Preconception exposure risks six months prior to conception in the Sellafield workforce and the Japanese bomb survivors. MP Little. *J Radiol Prot* 11(2):77–90, 1991).

Radiation-induced cancer risk in children. MP Little, MM Hawkins, RE Shore, MW Charles, NG Hildreth. *Radiat Res* 126:304–16, 1991. ❑

RERF **update** RERF

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