

RERF update RERF

News & Views from the US-Japan Radiation Effects Research Foundation
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RERF Expertise Aids International Chernobyl Efforts

During the four years since the Chernobyl power plant accident, international offers to assist Soviet remedial and follow-up efforts have gradually developed under the aegis of international agencies and binational agreements. Uniquely experienced in long-term monitoring of a large radiation-exposed population, RERF is actively participating in endeavors of the International Atomic Energy Agency and the World Health Organization.

Asked in October 1989 by the Soviet government to mobilize an independent international team of experts to assess the health and environmental consequences of the accident, in March the IAEA sponsored a week-long investigative mission to the republics of Byelorussia, the Ukraine, and Russia. After contacting scientific organizations, hospitals, clinics, agricultural groups, politicians, and local citizens, the team reported in mid-April to a multidisciplinary advisory committee chaired by **Itsuzo Shigematsu**, RERF chairman.

Having documented the relevant historical events leading up to the present situation, specialist teams 2-5 are now implementing phases 3 and 4 of the project, as agreed upon by the advisory committee. Implementation will concentrate upon the following issues:

- *Team 2: Corroborating official Soviet data on environmental contamination by cesium, strontium, and plutonium.*

All aspects of instrumentation, sampling methods, analytical procedures, equipment calibration, and statistical evaluation will be reviewed in an effort to verify Soviet radiation fallout maps.

- *Team 3: Validating individual and collective dose assessments.*

Methods and input parameters used to estimate doses will be reviewed. Individual radiation monitors will be distributed to local populations to determine current external radiation doses, and body burdens of Cs-137 will be measured using whole-body counters.

- *Team 4: Evaluating the overall*

regional public health status as well as health effects related to radiation exposure.

Since media reports of severe somatic effects and genetic malformations among the affected populations do not correlate with radioepidemiological data based on the 40-year follow-up of A-bomb survivors, medical specialists, including RERF physicians, will be trying to clarify the health status of people in the affected areas.

Confounding health factors include a regional history of nutritional problems, endemic goiter, deficiency of trace elements in the diet, and the possibility of heavy metal intoxication, particularly from lead.

- *Team 5: Assessing protective measures, intervention criteria, action levels, and countermeasures.*

Past criteria for action up through 1990 will be judged for efficiency and for the residual doses actually received. Criteria and actions for the future will be evaluated.

Concurrently with implementation of phases 3 and 4, specialist meetings are being scheduled involving international and local experts in medical and agricultural fields. A general understanding of the effects of radiation exposure and of criteria for radiological protection is being sought.

RERF involvement

From 9-21 July, RERF Vice Chairman **J.W. Thiessen** will participate in seminars for general practitioners presented under the auspices of the IAEA in Byelorussia, the Ukraine, and the Russian FSSR. He will discuss basic facts about radiation, the consequences of in-utero exposure, the hereditary effects of radiation exposure, and epidemiological methods of studying mortality and morbidity among exposed persons. He will also meet with local administrators.

It is expected that during the summer months, one RERF epidemiologist will be sent to review Soviet data.

In the fall, after children return home from summer camps, IAEA-sponsored medical teams will visit villages to conduct examinations. RERF will dispatch one physician who has extensive ex-

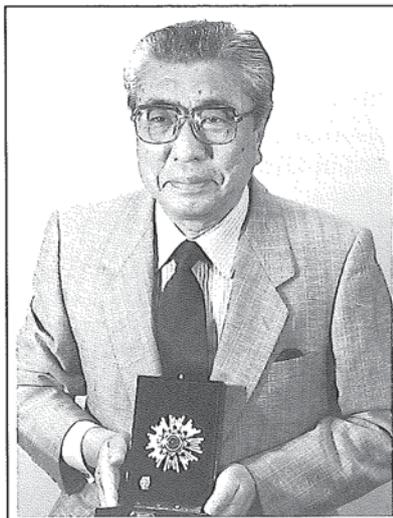
Chairman Receives Imperial Recognition

In late April at the Imperial Palace in Tokyo, RERF Chairman **Itsuzo Shigematsu** was awarded the Second Class Order of the Sacred Treasure by Emperor **Akihito**. Shigematsu received a certificate and medal from Prime Minister **Toshiki Kaifu**. The Emperor congratulated the recipients at an audience after the presentation ceremony.

Now serving his third four-year term as RERF chairman, Shigematsu was commended for "...devoting himself to the public health" for more than 30 years.

A graduate of Tokyo and Harvard universities, Shigematsu was director of the National Institute of Public Health's Department of Epidemiology from 1966-1981, where he is a professor emeritus. He is now a member of the WHO Advisory Panel, and ICRP's Main Commission. Since 1985 he has also served as chairman of the Committee on the National

Survey of A-bomb Survivors, and is chairman of the board of the Japanese Society of Public Health. His scientific publications exceed 500 in number. □



Shigematsu and his award

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The Rites of Spring

by **J.W. Thiessen**
*RERF Vice Chairman &
Update Editor-in-Chief*

Spring at RERF doesn't really begin until the annual Scientific Council meeting, usually in March. The same can be said for summer and the meeting of the board of directors, usually taking place in June. These meetings provide markers in our history, times to look back over the achievements of the previous year and forward to plans for the next. This year in particular was interesting from a number of viewpoints.

The Scientific Council was impressed with the directions the Adult Health Study (AHS) has been taking in the accumulation and evaluation of serial medical data obtained over a

International Efforts

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perience in A-bomb survivor examination, and a staff expert in thyroid diseases will also participate.

"The entire IAEA project is scheduled for completion in late 1990," said Shigematsu. "A report will be published afterwards by IAEA, and open meetings will be scheduled so the results can be discussed."

WHO mitigation program

On 30 April 1990, the USSR Health Ministry and the WHO Secretariat agreed in principle to establish a long-term global program to monitor and mitigate the health effects of the Chernobyl accident. To implement the program, it has been proposed that an international center for radiation health problems be founded in Obninsk, the Russian FSSR.

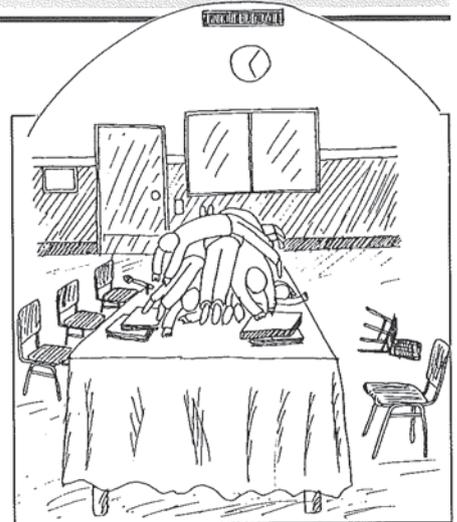
About a month later, representatives of the seven WHO collaborating centers engaged in radiation protection activities, including RERF Permanent Director **Yutaka Hasegawa**, gathered in Leningrad for their third coordination meeting on radiation emergency medical preparedness and assistance. At that time, the USSR-WHO proposal was distributed for comment and review.

First designated in 1979 as WHO's collaborating center for radiation effects on humans, RERF has been advising WHO on follow-up and research related to the health effects of radiation accidents. The Foundation and the other WHO collaborating centers, along with interested governments and institutions, will soon be invited by WHO to participate in the international program with technical and/or financial support. □

period of more than 30 years on (especially) the most highly exposed survivors. Computerization of data and sophisticated statistical analyses have made the AHS data a powerful resource, which has already demonstrated dose responses not obtainable in mortality statistics, such as those concerning hypothyroidism and uterine myoma. The council strongly endorsed the now ongoing development of comprehensive epidemiological approaches which include studies of mortality in the framework of the Life Span Study (LSS), cancer incidence using cancer registry data, and morbidity through the AHS. Applied to the same endpoints, such approaches combine into a very powerful, integrated epidemiological tool. With the next four-year update of the LSS data (through 1989) coming up, it is time to start thinking about incorporating composite analyses into the periodic "mainstay" reports.

The past year has also seen considerable progress in laboratory studies with the most modern techniques available, some, according to the council, "... of higher quality than studies carried out in most other laboratories throughout the world." The council was also impressed with the somatic gene mutational methods developed in the Department of Radiobiology. Studies on differential sensitivity among A-bomb survivors have, to date, not shown evidence that exposed survivors are any different from nonirradiated controls. The council felt that these studies might well be complemented with epidemiologic approaches to search for evidence that selective forces may be biasing the radiation risk in survivors.

These are just a few of the subjects discussed during the (very busy) council



meeting, but they illustrate that there is still a lot of important work to be done.

In this issue of *Update*, we will highlight some of the research done in the AHS, particularly with respect to aging, and you will also find information on the cancer registries in Hiroshima and Nagasaki, which have developed into very powerful instruments for the study of cancer incidence among A-bomb survivors. In one of the next issues, we will discuss the DNA and biochemical genetic studies, and will give attention to the comprehensive epidemiologic approaches referred to earlier. As a new recurring item, we include "Facts and Figures," in which we try to highlight some of the research data developed at RERF in well-defined subject areas.

With no dearth of material for this issue, publication of a pair of articles on the beginnings of the genetics program at ABCC by Jim Neel and Jack Schull will be postponed until the next issue. I don't think there is a chance that we will run out of subjects, but I do repeat my appeal to you, our readers, to react to articles in *Update*—or provide one yourself! □

News Briefs

✓ Board of Directors Convened in Hiroshima

The 24th meeting of RERF's board of directors was held from 6-8 June at the Hiroshima Laboratory. The board members resident in Japan are **Itsuzo Shigematsu**, chairman; **J.W. Thiessen**, vice chairman; **Seymour Abrahamson**, chief of research; and permanent directors **Yutaka Hasegawa**, **Sidney Marks**, and **Tomoyuki Kono**. Also attending were visiting directors **Teruhiko Saburi**, Japanese Ministry of Health and Welfare; **Tsutomu Sugahara**, professor emeritus, Kyoto University; **Kikuo Yoshida**, former ambassador to Fiji; **Warren K. Sinclair**, National Council on Radiation Protection and Measurements;

William W. Burr Jr., Oak Ridge Associated Universities; and **Joseph E. Rall**, National Institutes of Health.

✓ A-bomb Research Group Gathered in Nagasaki

The 31st meeting of the Nagasaki A-bomb Late Effects Research Group, 3 June, was kicked off by Hiroshima University's **Kenji Yokoro**, who lectured about experimental research on radiation carcinogenesis. Afterwards the symposium focused on tumors of the hematopoietic organs in A-bomb victims. Among the topics discussed by RERF participants were: M-proteinemia in A-bomb survivors from Hiroshima and Nagasaki; the

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Induced Trisomies 'Revisited'

Amending an earlier discussion of estimating trisomy induction in live-born children, the authors also discuss approaches to developing attributable risks.

by Seymour Abrahamson, Chief of Research; Akio A. Awa, Department of Genetics; and Nori Nakamura, Department of Radiobiology, Hiroshima

We are indebted to Robert L. Brent of Thomas Jefferson University, Philadelphia, Pa., for asking us to develop attributable risks for each type of viable trisomy. In responding to his request, we realized that an error exists in our previous calculations (*RERF Update* 1[4]:3-4, 1989) because we failed to introduce relative viability factors for each potentially viable trisomy type. This correction changes the doubling dose estimate from about 1 Gy to about 3 Gy, as will be explained here. The table introduces the viability frequencies as derived from UNSCEAR 1982 (*Ionizing radiation: sources and biological effects*, Suppl 45 [A/37/45], New York, UN, p 433, 1982). In addition, we will suggest approaches to the attributable risk problem.

For acute exposures in the range of 1 Gy, we again suggest multiplying induced rates under chronic exposure conditions by a factor of 2. Our assumptions are based on the concept that trisomies will be induced randomly among the genome set. If, for example, there is preferential induction of trisomy X or 21, or if induced rates are age-specific, then our estimates may indeed be underestimates. The use of chromosome-specific fluorescent dyes could be employed in studies such as that of Martin et al. (*Mut Res* 174:219-25, 1986) to possibly elaborate on this issue of randomness. There are indications in the cytogenetic studies of Awa et al. (unpublished) that nonrandomness may exist in somatic cell lines for spontaneous trisomy 21 and X, although preferential cell survival may be involved. If gonial cells behave in the same manner, the implications for spontaneous and induced trisomies could be quite significant.

In the table, we give the relative proportions of the four induced trisomic types (column A), their relative viabilities from fetus to live-born (column B), and (in columns C and D) the estimate of induced trisomy frequencies for male exposure and female exposure, respectively, after corrections from columns A and B have been applied. The column heading values of $8 \cdot 10^{-4}/\text{Gy}$ and $2 \cdot 10^{-3}/\text{Gy}$ for the male and female columns, respectively, represent the total induced frequency of aneuploid types before applying the corrections, as developed in our previous *Update* article. Thus, the numbers in the columns represent the expected frequencies of each type of live-born trisomy after male or female exposure. The final column represents the yield expected after exposure to both parents.

Our revised estimates for induced trisomies of about nine cases per 10^6 live-born per 0.01 Gy are still substantially greater than the estimates published in the BEIR V report (*Health effects of exposure to low levels of ionizing radiation: BEIR V*, Washington, D.C., National Academy Press, 1990) or in UNSCEAR 1988 (*Sources, effects and risks of ionizing radiation*, Suppl 45 [A/43/45], New York, UN, pp 375-40, 1988). Also our predicted number of excess

Table 1. Relative proportions of the four induced trisomic types (A), their relative viabilities from fetus to live-born (B), and (C and D) the estimate of induced trisomy frequencies for male exposure and female exposure after corrections from columns A and B have been applied.

A	B	C	D	E
Trisomy type and proportion of induced trisomies	Viability frequency	Induced viable trisomies = original induced male contribution ($8 \cdot 10^{-4}/\text{Gy} \cdot A \cdot B$)	Induced viable trisomies = original induced female contribution ($2 \cdot 10^{-3}/\text{Gy} \cdot A \cdot B$)	Total induced viable trisomies per gray (C + D)
X; 0.25	~1	$2 \cdot 10^{-4}$	$5 \cdot 10^{-4}$	$7 \cdot 10^{-4}$
21; 0.25	0.25	$5 \cdot 10^{-5}$	$1.25 \cdot 10^{-4}$	$1.75 \cdot 10^{-4}$
13; 0.25	0.04	$8 \cdot 10^{-6}$	$2 \cdot 10^{-5}$	$2.8 \cdot 10^{-5}$
18; 0.25	0.04	$8 \cdot 10^{-6}$	$2 \cdot 10^{-5}$	$2.8 \cdot 10^{-5}$
				$\Sigma = 9.31 \cdot 10^{-4}$

$$\text{Doubling dose} = \frac{3.0 \cdot 10^{-4}}{9.3 \cdot 10^{-4}} = 3.2 \text{ Gy}$$

sex trisomies in the children of A-bomb survivors is reduced from five cases to two cases.

The issue of attributable risk is complex. Using modern molecular techniques, it is frequently possible to determine the parental origin of the trisomic chromosome. In spontaneous cases, maternal origin is predominant. About 75-90% of trisomy 21, 66% of trisomy XXY, and 90% of the other autosomal trisomies are of maternal origin (T.J. Hassold, in *Aneuploidy, etiology and mechanisms*, New York, Plenum, pp 103-13, 1985).

If the trisomy originated from an unexposed parent, then the attributable risk (AR) to an exposed parent should be zero. If the trisomy origin and exposure were paternal, then the AR would be male in origin, i.e.,

$$\frac{\text{induced male rate}}{\text{spontaneous male rate}} + \text{induced rate.}$$

Male rates seem to be unrelated to paternal age (up to age 55; E.B. Hook, *ibid.*, pp 117-32, 1985), and we estimate the spontaneous male rates as $5 \cdot 10^{-4}$ for XXY, as ranging from 1.3 to $3.2 \cdot 10^{-4}$ for trisomy 21, and as about $1 \cdot 10^{-5}$ each for trisomy 13 and 18. The ARs per gray are then 29% for XXY trisomy, from 14-28% for trisomy 21, and about 44% for either trisomy 13 or 18.

If the exposure and trisomy were maternal in origin, then AR would vary with the age of the mother in some cases by 25-fold or more. The trisomy 21 AR at 1 Gy for a 15-year-old female is about 11% and for a 44-year-old female about 0.5%, because of the age-specific change in the spontaneous rate. Finally, we assume that when parental exposure is known but trisomy origin is not, the AR is:

$$\frac{\text{induced rate of exposed parent}}{\text{age-specific spontaneous maternal rate}} + \text{spontaneous paternal rate} + \text{induced rate (for specific parent).}$$

Thus, AR must be considered on a case-by-case specific basis involving detailed age-specific, chromosome-specific spontaneous rates. □

Vast RERF Database Supplies Aging Clues

Cumulative data collected during three decades of biennial Adult Health Study examinations are an unparalleled resource for exploring the relationship between aging and various health factors, as well as for conducting various prospective studies on the aging process.

by F. Lennie Wong, Department of Statistics; and Kazunori Kodama and Hideo Sasaki, Department of Clinical Studies

As Japan and many other industrialized nations slowly evolve into geriatric societies, aging-related studies have been receiving more attention. In the past, RERF researchers have primarily been examining the possibility of radiation-induced acceleration of the aging process. But, in possessing a 30-year biennially updated database based on medical examinations conducted by the ABCC-RERF clinical staff, RERF is uniquely able to use this abundance of disease incidence, death, laboratory, and physiometric data to portray the lifetime pathological history of 20,000 AHS participants. No other institute in Japan has comparable data.

Utility of the AHS data in the study of nonlethal diseases

Temporal trends for cancers with short survival periods have been well delineated using death certificate information. However, for less lethal and/or curable cancers such as breast or thyroid and, more importantly, for certain noncancer diseases such as hypertension, diabetes mellitus, anemia, cataract, gastric ulcer, and hepatitis, neither temporal trends nor aging effects can be accurately depicted using the death certificate information, as these diseases appear infrequently as

a cause of death. The AHS data can potentially provide the lacking incidence information for these diseases in aging-related studies. Certain diagnostic procedures employed in the AHS exams help to identify occult cases which contribute toward better disease ascertainment, making the overall program a more secure basis for the study of aging-related diseases.

Age and cohort effects on incidence data

Examination of the age-specific incidence rates in the AHS data readily reveals which diseases are associated with aging. The incidence of cardiovascular diseases, cataract, and osteoporosis increases steadily with age, whereas diseases such as duodenal ulcer and hyperthyroidism occur roughly uniformly across different age groups, thus lacking a monotonic relationship with chronological age. When considering these data, how-

ever, it is important to differentiate between age and cohort effects.

An impression of an overall increasing trend in disease incidence with age could arise as an artifact of a difference in cohort response due to a change in environmental condition. When appropriately stratified by birth cohort and other factors, the trend may remain or completely disappear. The typical example is vertebral fracture, which appears to increase with age (Figure 1). However, when incidence is shown by 10-year birth cohorts, a different view emerges. It is immediately recognized that the incidence differs significantly between birth cohorts even at the same age, and there is no increase in the incidence over the follow-up period, particularly in men (Figure 2). Hence, while a misleading picture may result if the cohort is not considered, it is the availability of the different cohorts in the 30-year AHS follow-up that actually enables us to examine the variation in incidence pattern among cohorts over time. This is useful knowledge not only to examine the possibility of radiation-induced acceleration of the aging process but also to incorporate into guidelines for current and future health management of the elderly afflicted with certain disorders.

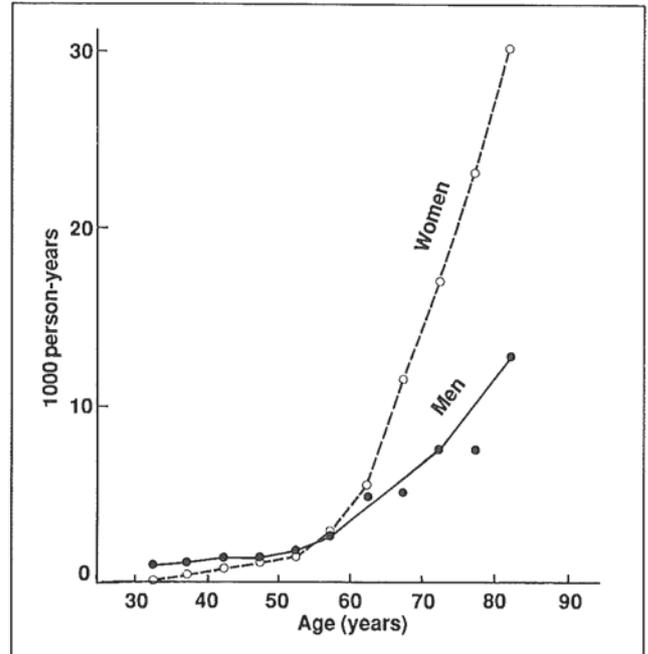


Figure 1. The incidence of thoracic vertebral compression fractures in the AHS cohort (1958-1986) when birth cohort is not considered.

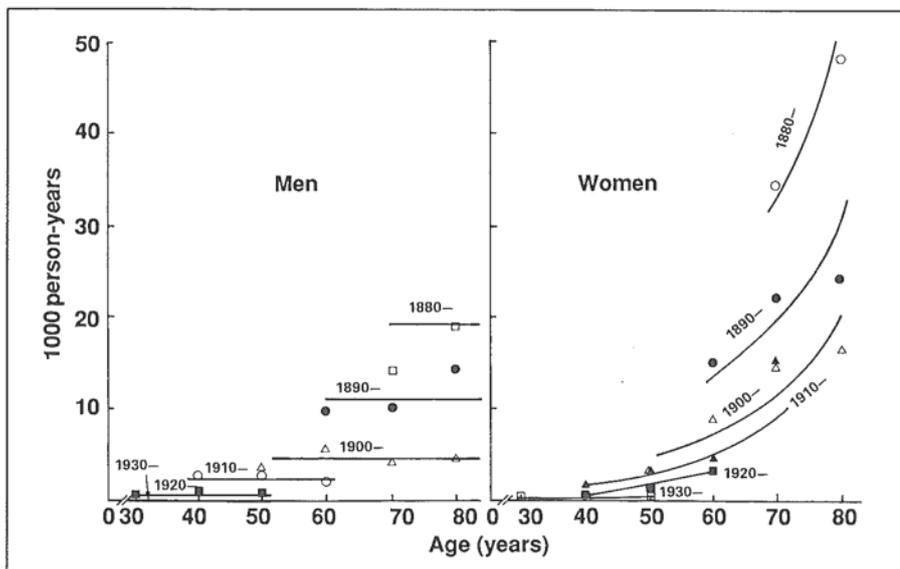


Figure 2. The incidence of thoracic vertebral compression fractures in the AHS cohort (1958-1986), shown by birth cohort.

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LSS Cancer Incidence Tracked by Tumor Registries

By outlining the development and use of the Hiroshima and Nagasaki tumor registries, the authors emphasize the critical role these registries play in Life Span Study cancer investigations.

by **Kiyohiko Mabuchi**, Department of Epidemiology and Epidemiologic Pathology, Hiroshima; and **Midori Soda**, Department of Epidemiologic Pathology, Nagasaki



Soda, at left, and Mabuchi.

It is well appreciated that in risk assessment cancer incidence data offer distinct advantages over mortality data. Incidence cases are ascertained at the time of disease onset, thus incidence data can provide a direct measure of cancer risk as it occurs in members of the population—an important feature when studying temporal patterns of cancer. In addition, incidence surveillance is effective in documenting tumors with a favorable prognosis such as cancers of the breast and thyroid which may not appear on death certificates. Furthermore, detailed medical data directly obtained from hospital records provide information needed for accurate and specific diagnosis. Such detailed information is not generally available from death certificate-based studies.

Active approach to cancer registration

The tumor registries are essential in systematically collecting, managing, and analyzing data relating to individual tumor cases on a population basis. More than 30 years ago, population-based registries were established in Hiroshima and Nagasaki under the auspices of each city's medical association. From the outset, ABCC-RERF has been responsible for the day-to-day operations of the registries. On a daily basis, RERF personnel visit the major hospitals in the area and extract necessary information from hospital records. This "active" approach to cancer registration, employed by most of the well-known American tumor registries, results in the high quality of registry data from Hiroshima and Nagasaki.

To evaluate the quality of data and hence the reliability of registration, two numerical indices are commonly used. These are (i) the proportion of cases registered with histologically verified diagnosis (histological verification, HV) and (ii) the proportion of cases registered for which only information from the death certificate is available (death certificate only, DCO). At the present time, the Hiroshima and Nagasaki

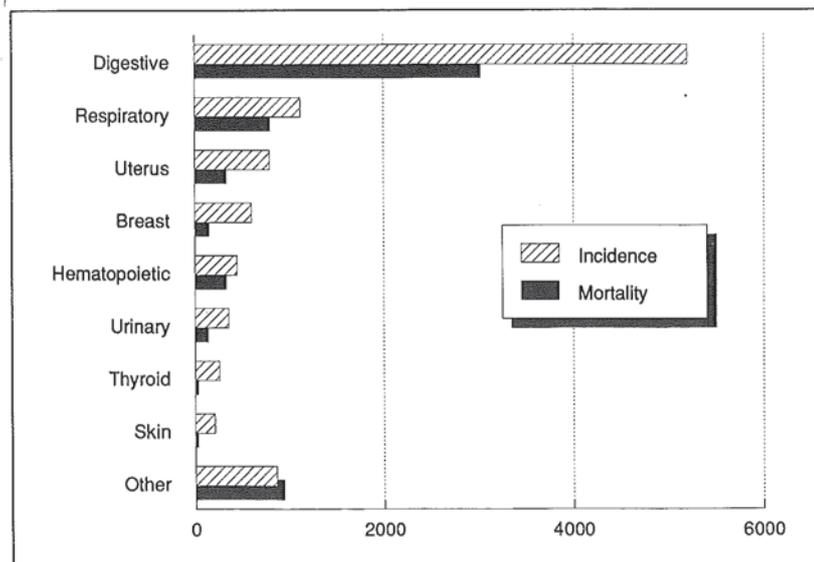
registries have an HV rate in excess of 70% and a DCO rate of less than 9%, which make them among the best in Japan and comparable to many internationally established tumor registries (*Cancer incidence in five continents*, Vol. V, International Agency for Research on Cancer, Lyon, France, 1987).

RERF also supports tissue registries to which tissue-diagnosed tumor cases, both benign and malignant, in the Hiroshima and Nagasaki areas are reported along with tumor tissue slides. The tissue registries serve as a supplemental data source for both case finding and diagnostic confirmation. Recently, a prefecture-wide cancer registry also administered by RERF was started in Nagasaki, adding another source of cancer incidence data.

Incidence data for entire LSS population: a product of registry standardization

It is important to realize that maintaining good population-based tumor registries in Hiroshima and Nagasaki is requisite for attaining a high-quality cancer incidence database for RERF cohorts. Whereas the tumor registries have been instrumental for cancer incidence studies of several specific sites, overall analysis of tumor registry incidence data for the LSS and other cohorts has not been undertaken since Life Span Study Report 9 (Part 3) on Nagasaki for 1959–1978 (T. Wakabayashi et al., RERF TR 6-81). This is partly because of delays in data collection in Hiroshima. Major improvements have taken place during the last several years which make it now possible to generate recent incidence data for the entire LSS sample. Data collection problems in Hiroshima have been resolved and cases from certain major hospitals have been updated.

Together with this, a new effort was initiated jointly by the Hiroshima and Nagasaki registry teams to establish a common tumor registry database for the LSS. The objective was to achieve uniformity and consistency in the handling of registry data from the two cities. A painstaking effort was undertaken by the registry staff from the two cities to standardize diagnostic criteria and data handling procedures. The registry staff reviewed all documents for more than 15,000 cancer patients who have been accessed during the last 30 years. To ensure consistency, staff from the two cities met on a monthly basis to review samples of case materials and to discuss cases presenting difficulty in coding. A common set of coding rules was developed and used under the guidance of the registry physicians and pathologist. Data



The number of cancer incidence cases at major sites occurring in the Life Span Study sample during 1958–1985 is compared with cancer deaths (mortality) for the same time period.

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Aging Clues

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Physiometric determinants and aging

The lifetime pattern of change in certain physiometric variables such as total serum cholesterol, blood pressure, and heart rate can also be examined using AHS data, thus providing another unique view of the aging process.

Although cross-sectional data may be used to assess age-related changes, an association with age may arise as a result of differences between groups rather than as a result of changing patterns for individuals. Thus, as in the case of disease incidence, age and cohort effects may be confounded, which can be avoided by instead using serial measurement data from the same individuals and by using appropriate statistical analysis such as the "growth curve" technique.

Figure 3 shows the difference in the fitted relationship between total serum cholesterol level and age for men and women using the cross-sectional data collected during 1984-1986 and that based on following the patterns of change for individuals beginning in 1958 for those who were 20 years old at the time of the bombing (ATB). While age effect could not be detected in the men from the cross-sectional analysis, there is an obvious age effect based on the follow-up of individuals. Disparate values of age-specific total serum cholesterol levels are indicated as well. Cross-sectional analysis, hence, may provide an incorrect impression of the underlying relationship, and the use of serial data is preferable for characterizing the patterns of individual

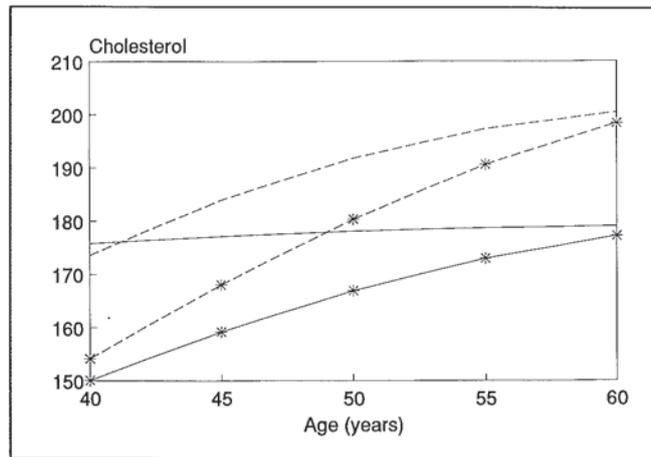


Figure 3. Fitted serum cholesterol level by age in men (solid lines) and women (dashed lines) based on cross-sectional analysis of data from 1984-86 and on growth curve analysis of individuals who were 20 years old at the time of the bombings, assuming a constant body mass index of 0.002 (lines marked by asterisks.)

response and change over time. AHS serial measurement data are available for participants of different birth cohorts (ranging in age from 0 to 70 years ATB), from whom data has been collected at ages ranging from 13 to 98 years. Hence, it is possible to broadly describe changing patterns that may be related to aging.

Our preliminary analyses using the growth curve technique have so far been able to depict lifetime patterns for total serum cholesterol, for diastolic and systolic blood pressures in relation to age, and additionally the influence of sex, city, birth cohort, and radiation exposure on these lifetime patterns. Efforts are underway to examine such relationships for other physiometric determinants.

Disease incidence and physiometric data

Long-term AHS follow-up data enables detection of incident cases for various diseases, and in the study of diseases related to the aging process,

serial data on certain physiometric variables can be incorporated as possible risk factors. Other useful information is collected from the AHS subjects including alcohol consumption, dietary habits, tobacco use, parity, and occupation, all of which may be combined in designing studies to identify risk factors for certain diseases in relation to aging.

Opportunities for prospective aging research

Researchers in the Department of Clinical Studies are now conducting separate studies on aging-related diseases, such as cardiovascular disease and osteoporosis, with support from staff members of the departments of Statistics and Epidemiology. Prospective studies on aging-related conditions, such as senile dementia and cataract, are being planned, because the AHS participants have reached an average age of 61.2 years, thus providing unique opportunities for conducting such studies. □

Tumor Registries

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were entered into a new database system, developed with the assistance of the RERF Research Information Center, and various data quality assurance measures including intensive logical checks were implemented.

A brief inspection of the incidence data suggests the potential power of this data set. The figure on page 5 shows the number of incidence cases among members of the LSS population for 1958-1985 as compared with cancer deaths for the same period. Noteworthy is the number of incidence cases which total nearly 10,000 (excluding those who were not in the cities at the time of the bombings). This is almost twice the number of mortality cases, which total about 5,800. Proportional excesses in incidence over mortality cases are striking for such sites as the breast, thyroid, skin, uterus (mostly cervix), and urinary

tract (mostly bladder). There also is a marked increase in the number of cases (almost 2,000) for cancer of the digestive system, reflecting the high background incidence of cancer of the stomach and liver in Japan. How the increased number of cases together with improved precision in diagnosis affects risk assessment is of special interest to all those who are concerned with radiation carcinogenesis.

Outmigration still a concern

While incidence data have many advantages, it should be noted that cancer incidence data are not free of problems. The major problem, which is already being addressed, results from the considerable number of LSS subjects who have over the years migrated out of the Hiroshima and Nagasaki area. An estimated 20% of the surviving LSS subjects no longer reside in areas covered

by the tumor registries, and migration rates are inversely related to age at exposure. Cancers among the migrants are ascertained by the nationwide mortality surveillance but not by the Hiroshima and Nagasaki registries. An address database project was initiated last year and is being vigorously pursued to acquire and maintain information on residence history for individual cohort members.

Meanwhile, our analytical strategy will be to adjust for migratory movement using methods similar to those employed in a previous breast cancer incidence study (M. Tokunaga et al., RERF TR 15-84). Since migration has not been found to differ by radiation dose, relative risk estimates are not expected to be biased by such adjustment. Analysis of this incidence data set for the LSS sample is currently being undertaken jointly with the Department of Statistics and is expected to be completed soon. □

A-bomb Survivor Deaths Surveyed 40 Years after Bombings

An additional 12,000 A-bomb survivor deaths through the end of 1985 have now been confirmed in a survey conducted by the Japanese Ministry of Health and Welfare. Almost 80% of the 361,000 A-bomb health handbook holders who received questionnaires responded with information about the deceased, based on memories of family members, friends, coworkers, or neighbors who had died. It was the first time such recollections were solicited from the survivors.

About 440,000 deaths were reported, revealing an additional 5,551 deaths in Hiroshima and 6,378 deaths in Nagasaki after eliminating duplication. When the deaths of these newly identified persons are added to total deaths (including those due to accidents and illnesses unrelated to the bombing) derived from surveys conducted by Hiroshima and Nagasaki cities, the revised death tolls up through 1988

are 201,990 for Hiroshima and 93,966 for Nagasaki. It is estimated, however, from other studies that the acute deaths due to the atomic bombings (that is, from blast, heat, and radiation) by the end of 1945 totaled 90,000–120,000 for Hiroshima and 60,000–80,000 for Nagasaki.

"Based on RERF studies, about 2% of the total deaths after 1946 in both cities can probably be attributed to exposure to A-bomb radiation (10 mSv or more)," commented RERF Chairman **Itsuzo Shigematsu**, who served as chairman of the survey committee.

Although an additional 25,000 deaths were also reported, the exact identity of these persons remains uncertain.

"Based on the memories of survivors, it is almost impossible to identify the people whose entire families were killed in the bombings," added Shigematsu. □

News Briefs

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reanalysis of leukemia among A-bomb survivors using recent leukemia classifications and DS86; leukemia among A-bomb survivors during the 1980s; cancer incidence in the Adult Health Study (1958–1986); recent findings on multiple myeloma incidence; a high frequency of TCR α β^+ CD4 $^+$ 8 $^-$ T cells in the peripheral blood of one A-bomb survivor; the inactivation of antigen receptor genes in mature T lymphocytes after exposure to A-bomb radiation, radioactive substances, and chemotherapeutic agents; measurement of HPRT-deficient mutant cell frequency in A-bomb survivors using a modified method for cloning T lymphocytes; and age at menopause in Adult Health Study subjects.

✓ Japanese Agency Sponsors Fellowships for Foreigners

"Promising young researchers from overseas" will be given a chance to work at Japan's national laboratories and at selected nonprofit institutes, such as RERF, as part of a Japanese Science and Technology Agency fellowship program started in 1988. One hundred sixty annual fellowships, ranging from six months to two years, are offered. Applicants must have a doctoral degree or equivalent certification in a scientific or engineering field. For more information, contact: JISTEC, Port One Building 6F, 1-7-6 Minato-machi, Tsuchiura City, Ibaraki Prefecture, 300 Japan.

✓ Projections for Future Human Radiation Research

Stimulated by recent UNSCEAR and BEIR reports summarizing current interpretations of human radiation effects data, a March 1991 workshop in Schloss Elmau, Federal Republic of Germany, will provide a chance for international experts to focus on the future of epidemiological and experimental approaches to radiation effects research, rather than reporting on current work. Limited primarily to human studies, with animal experiments serving only as a secondary topic of discussion, nine half-day sessions will concentrate on the carcinogenic effects of radiation in humans. Session chairmen will seek to achieve a consensus on the direction of future research planning, and will delineate any areas of disagreement. The workshop, scheduled for 4–8 March, is cosponsored by RERF, the Commission of the European Communities, the US Department

of Energy's Office of Health and Environmental Research, and the International Agency for Research on Cancer. Inquiries should be directed to: **G.B. Gerber**, CEC, DG XII.D.3, rue de la Loi 200, B-1049 Brussels, Belgium. Fax: (0)2 236-2006

✓ Boundaries of A-bomb Affected Area To Be Reassessed

Nagasaki Prefecture will survey residual plutonium levels in the city to reassess the official boundaries of the A-bomb affected area. Current boundaries were based mainly on administrative, not scientific, criteria. Plutonium levels in soil samples from 70 locations outside the now designated affected area will be compared with plutonium levels from the Nishiyama district, 3 km east of hypocenter, where readings 10 times higher than those in unaffected areas have been found.

✓ South American Hibakusha to Receive Medical Care

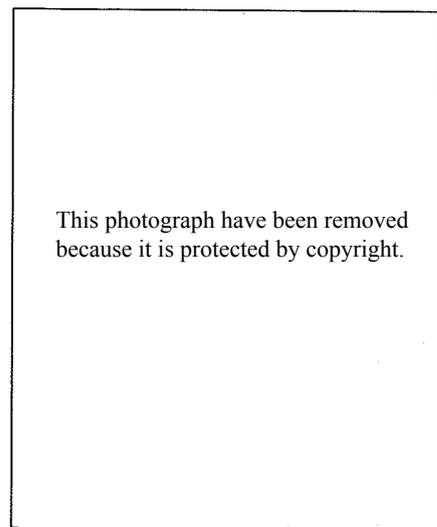
Trips to Hiroshima and Nagasaki by South American A-bomb survivors who need medical treatment are being budgeted for by the respective city governments. Of the 188 A-bomb survivors now living in South America, a maximum of three per year will be invited by the Hiroshima Prefectural Medical Association, while Nagasaki will fund one trip during 1990. Since 1988, doctors from Hiroshima and Nagasaki, as well as from the Japanese Foreign Ministry and the Welfare Ministry have traveled to South America to consult with these survivors.

✓ Chinese Scientists Visit RERF

Ren Tianshan, Laboratory of Industrial Hygiene, Beijing, visited the Hiroshima Laboratory and lectured on China's high- and low-background radiation areas. In August, Tianshan's colleague, visiting research associate **Sun Quanfu** will finish a year's stay in RERF's Department of Statistics. Sun has been expanding his knowledge of epidemiological and statistical techniques in studies of spleen shielding and thyroid cancer.

✓ RERF Director Visits Beijing

In mid-May, RERF Permanent Director **Sidney Marks** visited the Laboratory of Industrial Hygiene in Beijing to conduct preliminary discussions on joint studies, and also lectured on radon epidemiology at the Institute of Radiation Protection in Taiyuan.



This photograph have been removed because it is protected by copyright.

COURTESY OF THE MAINichi GRAPHIC

Video footage was shot at RERF for Soviet TV programs. Shown above, RERF Clinical Studies Department Chief Kazunori Kodama, at left, draws blood from Robert Semenovitch Tilles, a member of the Soviet delegation, who was exposed to radiation at Chernobyl. Various tests for biological dosimetry will be performed at RERF.

✓ Soviet TV Shows Include Interviews of A-bomb Survivors

Two Soviet television shows focusing on radiation effects included interviews with A-bomb survivors from Hiroshima and Nagasaki. In late spring, eight representatives of Soviet national TV visited RERF while in town to tape interviews with survivors to be included in a 24-hour fund-raising telemarathon for those affected by the Chernobyl accident.

In May, TV studios in Hiroshima and in the republic of Kazakhstan, where the Semipalatinsk nuclear test site is located, were linked by satellite for discussions. From Hiroshima, 100 A-bomb survivors and experts on radiation exposure, including RERF Chairman **Itsuzo Shigematsu**, exchanged views with an equal number of Soviet citizens.

✓ Chilean IAEA Fellow at Hiroshima Laboratory

Juana Ines Lopez, a specialist in nuclear safety and radioprotection at the Comisi3n Chilena de Energia Nuclear in

continued on page 10

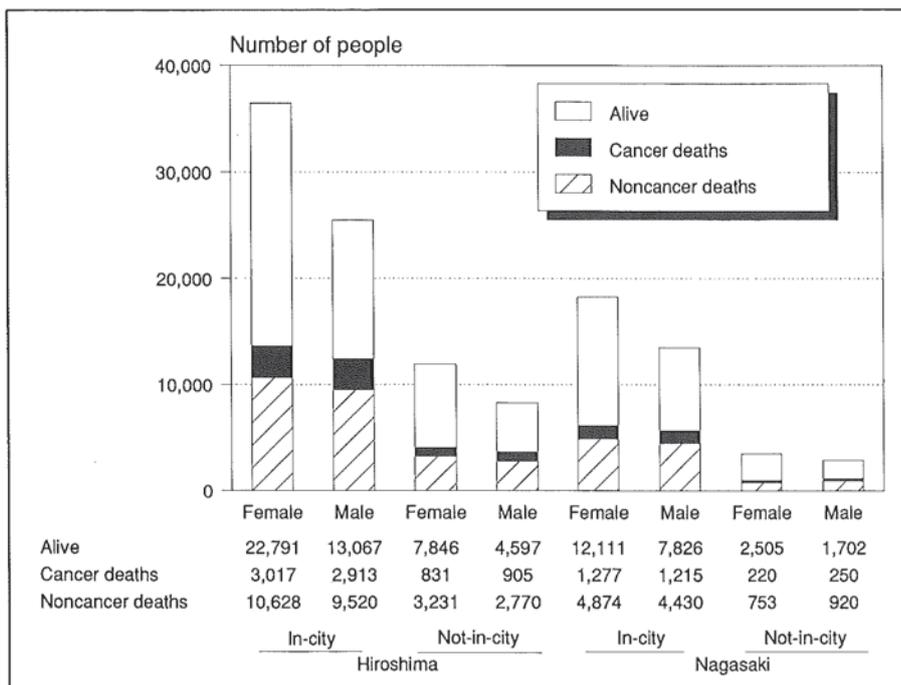
Facts & Figures

The RERF Life Span Study Cohort: Status 1950–1989

Editor's note: "Facts & Figures" will present brief, easy-to-grasp summaries extracted from RERF studies—information that may not be readily accessible in comprehensive technical material elsewhere.

The RERF Life Span Study (LSS) cohort, upon which the RERF epidemiological mortality follow-up study is based, consists of 120,321 exposed and nonexposed subjects. To date, only 122 of the cohort members have been lost to follow-up.

The accompanying figure is based on 120,199 people with complete follow-up whose data set will be used in RERF's LSS Report 12. This data set will include information on mortality in the LSS collected through the end of 1989. However, unlike the data used for earlier LSS reports, it is not assumed that complete follow-up information is available for cohort members for whom no record of death has been received. Rather, information about the date of last contact is used in the computation of person-years. The accompanying figure summarizes the current data on cancer and noncancer mortality. Among exposed "in-city" members of the cohort, about 6% of the cancer deaths are estimated to be excess cancers caused by exposure to A-bomb radiation. ("In-city" includes those exposed at far distances whose dose can be con-



sidered low or negligible.)

Since 1985, an additional 3,640 deaths have been recorded, with 2,788 occurring among exposed survivors. The table at right shows the distribution of newly recorded deaths by city, exposure status, and sex. □

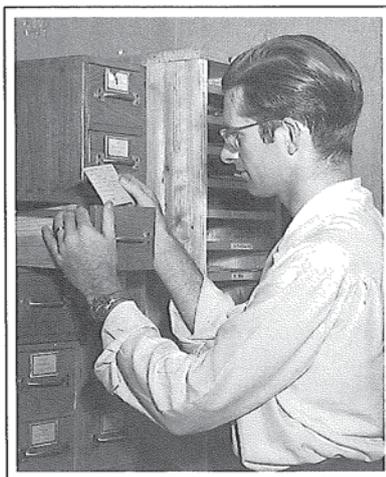
	Deaths in the Life Span Study since 1985			
	In-city		Not-in-city	
	Female	Male	Female	Male
Hiroshima	1,199	797	400	279
Nagasaki	435	357	94	79

Book Review

Song among the Ruins by William J. Schull;
Harvard University Press, 1990; 294 pp, \$25.

William J. (Jack) Schull has written a marvelous "personal history" of his encounters with Japan and the Japanese. His book covers a period of more than 40 years, beginning with his arrival in Hiroshima for his first two-year stint with the Atomic Bomb Casualty Commission in 1949 and ending with his return from Hirado in 1964, but with a last chapter, called "Retrospect" that brings us (nearly) up to date. In these pages, he reminisces, discusses, and sometimes philosophizes on the basis of his experiences—scientific and personal. The book contains not so much an account of ABCC's history—a work still to be written—but, beyond that, the reflections of a man continuously challenged to understand, if not to explain, a world so different from the one he came from and eventually returns to.

To a Western analytical mind, Japan is a country full of contradictions, and the Japanese, at times, a riddle



Schull in August 1949 at ABCC.

wrapped in an enigma. Generalizations, however, are not the prime product of an understanding man, and Schull is careful not to entertain too many of them. Instead, the book is full of sensitive descriptions of friendships developed and colleagues met. These passages are, to me, the real delight of the book. There is a lot more to enjoy, though: for anybody who has ever worked at ABCC or RERF, it is enlightening, to say the least, to hear about the way we were. In that respect also the book is a joy to read. And finally, there are a lot of curious facts worth knowing by anyone with an interest in this country.

Like a delicate wine, the book is to be enjoyed at a slow pace. It is one of those few books that get better upon rereading, and as the narrative is secondary, it is ideal for browsing. Above all, it is a must for everyone with an interest in the how and why of Japan. It is, of course, far from a textbook on the Japanese soul, but it certainly helps one to begin to develop an understanding of this fascinating subject.

I hope that Schull, who must have a lot more material than that covered in this book, e.g., on his experiences since 1964, will see fit to write a follow-up. But even without it, he has done a lot of us a favor already, and he is to be congratulated on a fine piece of literature and history.

—J.W. Thiessen

Recent Scientific Publications

Approved Technical Reports

Isolation and partial characterization of peripheral blood CD4⁺ T cell clones expressing $\gamma\delta$ T cell receptors. S Kyoizumi, M Akiyama, Y Hirai, Y Kusunoki. **RERF TR 5-90.**

Rare T cell clones bearing both CD4 and T cell receptors (TCR γ and TCR δ) were obtained from human peripheral blood by cell sorting using anti-CD4 and anti-TCR δ 1 antibodies. All the clones established were reactive with anti-TCR $\gamma\delta$ 1 antibody, whereas only about 20% of the clones showed reactivity with anti-STCS1 antibody. Unlike CD4⁺ T cells bearing TCR $\alpha\beta$, all the clones tested were lectin-dependent and showed CD3 antibody-redirected cytolytic activity. About 60% exhibited natural killer cell-like activity. Immunoprecipitation analysis of TCR $\gamma\delta$ showed that each clone expressed either a disulfide-linked or nondisulfide-linked heterodimer consisting of 37–44 kilodalton TCR γ and TCR δ chains. Southern blot analyses of TCR γ and TCR δ genes revealed some identical rearrangement patterns, suggesting the limited heterogeneity of CD4⁺TCR $\gamma\delta$ ⁺ T cells in peripheral blood.

Radiosensitivity of skin fibroblasts from A-bomb survivors with and without breast cancer. S Ban, RB Setlow, MA Bender, H Ezaki, T Hiraoka, M Yamane, M Nishiki, K Dohi, AA Awa, RC Miller, DM Parry, JJ Mulvihill, GW Beebe. **RERF TR 6-90.**

Fibroblasts were established in vitro from skin biopsies obtained from 55 women and one man with or without breast cancer and with or without exposure to radiation from the atomic bomb explosion in Hiroshima. The radiosensitivity of these cells was evaluated by clonogenic assays after exposure to X rays or to fission neutrons from a Cf-252 source. Data were fitted to a multitarget model,

$$\frac{S}{S_0} = A[1 - (1 - e^{-AD})^N],$$

for both X-ray and neutron dose-survival curves. A single-hit model,

$$\frac{S}{S_0} = Ae^{-AD},$$

fits the neutron dose-survival responses as well. There was no difference in the means or variances of radiosensitivity between exposed and nonexposed groups, or between patients with or without breast cancer. Hence, although the sample is not large, it provides no support for the hypothesis that A-bomb radiation preferentially induces breast cancer in women whose cells in vitro are sensitive to cell killing by radiation.

Estimating the magnitude of random errors in the DS86 dosimetry using data on chromosome aberrations and severe epilation. R Sposto, DO Stram, AA Awa. **RERF TR 7-90.**

An analysis of the proportion of cells with chromosome aberrations (CA) in cultured blood lymphocytes from A-bomb survivors in Hiroshima and Nagasaki revealed (1) that

the dose-response relationship using DS86 assigned dose is significantly steeper in the subsample of individuals who reported severe epilation after the bombings than among those who did not report severe epilation, and (2) among individuals exposed at higher doses there is substantially more variation in the proportion of cells with CA than would be expected if there were no heterogeneity in dose response among individuals. Since to some extent these effects are due to random errors in the DS86 dose assignments, one might envision using them to estimate the magnitude of random errors in the DS86 dosimetry. However, such an attempt is complicated by the fact that these effects could also be due to individual differences in sensitivity to radiation, so that at a given level of exposure individuals who are more sensitive to induction of severe epilation are also more prone to induction of CA.

In this paper, working within a class of dosimetry error models, we estimated the magnitude of random dosimetry errors which would be required to account for all of the difference in the observed dose response between persons who did and did not report severe epilation, and for all of the overdispersion in the proportion of cells with CA, under the assumption that random dosimetry error is the only cause of these effects. By performing analyses of these data over a range of dosimetry error models, we conclude that random dosimetry errors in the range 45% to 50% of true dose are necessary to explain completely the difference in dose response between the two epilation groups. This level of dosimetry error also accounts for the overdispersion in the proportion of cells with CA. Random dosimetry errors as small as 40% are consistent with the assumption that there are no differences in radiation sensitivity among individuals. We compare these dosimetry error figures with those obtained independently by others. We also discuss evidence that the contribution of differences in radiosensitivity may be quite small, so that random dosimetry errors may be the most likely cause of these effects. Additional analyses of the type we have undertaken, using different endpoints, could lead to a better understanding of the amount of random dosimetry error associated with the DS86 dosimetry, and thus more accurate estimation of dose-response relationships based on RERF data.

Approved Research Protocol

Breast cancer incidence study among A-bomb survivors, Hiroshima and Nagasaki, 1950–1985. M Tokunaga, CE Land, S Tokuoka, I Nishimori, M Soda, S Akiba. **RERF RP 1-90.**

We propose to extend through 1985 the study of breast cancer incidence among members of the RERF Life Span Study (LSS) sample. This will be the fourth in a series of similar surveys, which previously covered the periods 1950–1969, 1950–1974, and 1950–1980, respectively. As in previous studies, the proposed investigation will be aimed at completely ascertaining breast can-

cer cases from locally available sources, including the tumor and tissue registries of Hiroshima and Nagasaki, public and private hospitals in the two cities, and death certificates routinely made available to RERF through the *koseki* [family register] system. Whenever possible, breast cancer cases among LSS participants no longer residing in or near Hiroshima or Nagasaki will be ascertained by record linkage with tumor and tissue registries in other population centers. Cases will be selected after reviewing all collected diagnostic materials, and whenever possible histological subtyping will be done after reviewing tissue samples.

The purpose of the proposed study, like that of its predecessors, is to characterize the LSS sample in terms of breast cancer risk, particularly in relation to radiation dose, age at exposure, calendar time, sex, and age at observation. But, this study will differ from previous investigations of this sample in the following ways: 1) ascertainment will be based on the LSS-extended 1985 sample, which includes distally exposed Nagasaki survivors not in the sample at the time of the earlier surveys, 2) the DS86 dosimetry system will be used rather than the T65D system, and 3) greater attention will be paid to problems of underascertainment of cases due to migration of sample members from the Hiroshima and Nagasaki areas. 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.

Publications in the Open Literature

Frequency of variant erythrocytes at the glycophorin-A locus in two Bloom's syndrome patients. S Kyoizumi, N Nakamura, H Takebe, K Tatsumi, J German, M Akiyama. *Mutat Res* 214:215–22, 1989. (RERF TR 8-89)

The LD₅₀ associated with exposure to the atomic bombing of Hiroshima. S Fujita, H Kato, WJ Schull. *J Radiat Res (Tokyo)* 30:359–81, 1989. (RERF TR 17-87)

Prenatal exposure to atomic radiation and brain damage. M Otake, H Yoshimaru, WJ Schull. *Cong Anom* 29:309–20, 1989. (RERF TR 16-87, 2-88, 3-88, 13-88)

Improved methods for obtaining colonies of human peripheral blood lymphocytes in vitro for radiation dose-survival studies. N Nakamura, J Kushihiro, M Akiyama. *Mutat Res* 234:15–22, 1990. (RERF TR 15-89)

Prenatal exposure to ionizing radiation and subsequent development of seizures. K Dunn, H Yoshimaru, M Otake, JF Annegers, WJ Schull. *Am J Epidemiol* 131:114–23, 1990. (RERF TR 13-88)

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Recent Scientific Publications

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Radiation-related posterior lenticular opacities in Hiroshima and Nagasaki atomic bomb survivors based on the DS86 dosimetry system. M Otake, WJ Schull. *Radiat Res* 121:3-13, 1990. (RERF TR 4-89)

Studies of the mortality of A-bomb survivors. 9. Mortality, 1950-1985: Part 2. Cancer mortality based on the recently revised doses (DS86). Y Shimizu, H Kato, WJ Schull. *Radiat Res* 121:120-41, 1990. (RERF TR 5-88)

An improved method for the detection of genetic variations in DNA with denaturing gradient gel electrophoresis. N Takahashi, K

Hiyama, M Kodaira, C Satoh. *Mutat Res* 234:61-70, 1990. (RERF TR 3-90)

Report on the results of the seventh medical examination of A-bomb survivors resident in North America. C Ito, K Kodama, H Sasaki, S Ishibashi, K Dote, T Watanabe, K Hirata, S Sugimoto. *Hiroshima Igaku-J Hiroshima Med Assoc* 43:175-221, 1990 (bilingual).

Congenital malformations, stillbirths, and early mortality among the children of atomic bomb survivors: A reanalysis. M Otake, WJ Schull, JV Neel. *Radiat Res* 122:1-11, 1990. (RERF TR 13-89) □

News Briefs

continued from page 7

Santiago, spent a 5-week International Atomic Energy Agency fellowship working in the RERF Cytogenetics Laboratory, where she learned about techniques for culturing blood and for analyzing stable chromosome aberrations in lymphocytes.

✓ In Memoriam: Yasuyoshi Nisimaru and Kaoru Urabe

Yasuyoshi Nisimaru: Instrumental in establishing the ABCC technical report series, Nisimaru joined ABCC as an editor after retiring as dean of the Hiroshima University School of Medicine in 1960. He founded the Foundation's monthly newsletter and introduced a section devoted solely to ABCC research in the Hiroshima Medical Association's journal as a way of informing local physicians of ABCC's findings. Nisimaru passed away in mid-May at the age of 93.

Kaoru Urabe: A former bacteriologist at Hiroshima University, Urabe served as ABCC editor from 1970-75 and as an RERF consultant until 1978. He passed away at the age of 83 on 10 March.

✓ Research Staff News

Hiroshima

Department of Radiobiology: Toshio Seyama was appointed chief of the Division of Cell Biology. He previously worked with the Research Institute for Nuclear Medicine and Biology, Hiroshima University. Takashi Ito has joined the Division of Cell Biology as a research associate. Visiting research student Yasuko Fukuda, from the Mayo Medical School, Rochester, Minn., is spending four months studying T-cell receptors in the Immunology Laboratory.

Research Support Center: Research Associate Michael A. Edington has joined the Editorial Section as an English-language editor. He was previously an editor at the National Academy Press, National Academy of Sciences, Washington, D.C.

Research Information Center: Acting Department Chief Jill Ohara has returned to RERF after a 20-month sabbatical in Seattle, Wash. She divided her time between the Statistics and Epidemiology Research Corporation and the Fred Hutchinson Can-



From left: Ohara, and Akahoshi.

cer Research Center, where she focused upon statistical programming and database management systems.

Nagasaki

Department of Medicine: Masazumi Akahoshi, formerly chief of the Department of Clinical Studies, is now chief of the Department of Medicine.

Department of Clinical Studies: Naokata Yokoyama, research associate, Division of Medicine, is concurrently serving as chief of the Division of Clinical Laboratories. Yasuko Amasaki is now chief of the Division of Radiobiology.

Department of Epidemiologic Pathology: Hiroyuki Miyaji is now section chief of the Tumor & Tissue Registry Office.

✓ Highlights of Lecture Program

Suketami Tominaga, Aichi Cancer Center Research Institute, Nagoya, lectured on the epidemiology of biliary tract cancer on 17 April.

On 14 May, Kenneth J. Kopecky, Fred Hutchinson Cancer Research Center, Seattle, Wash., discussed the Hanford environmental dose reconstruction and thyroid disease studies.

Eiichi Soeda, Institute of Physical and Chemical Research, Tsukuba, presented a lecture on the human genome project in Riken on 18 May.

O.E. Barndorff-Nielsen, Division of Theoretical Statistics, the University of Aarhus, Aarhus, Denmark, lectured on modified signed log likelihood ratios on 27 April.

On 25 May, R.H. Berk, Department of Statistics, Rutgers-The State University, New Brunswick, N.J., discussed distribution-free tests in linear models. □

International Oral Presentations

The 2nd Congress of the Asian Association of Endocrine Surgeons, Okayama, Japan, 24-25 April 1990.

◆ *Prevalence of thyroid diseases in autopsy cases of A-bomb survivors, Hiroshima.* H Ezaki, T Hiraoka, Y Yoshimoto, R Etoh, S Akiba.

The 13th Scientific Meeting of the International Society of Hypertension, Montreal, Canada, 21 June-1 July 1990.

◆ *A review of blood pressure trend and left ventricular hypertrophy.* M Akahoshi, T Matsuo, K Shimaoka, Y Shibata, K Kodama, S Seto, K Hashiba.

◆ *Longitudinal analysis of blood pressure in diabetics and its relation to obesity—26 years of follow-up study.* M Akahoshi, S Seto, T Matsuo, K Shimaoka, K Kodama, K Hashiba.

The 2nd International Congress: Advances in Management of Malignancies, Ascoli Piceno, Italy, 28 May-1 June 1990.

◆ *Malignancies in A-bomb survivors in Hiroshima and Nagasaki.* K Shimaoka. □

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.

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