RERF update RERF

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

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Thousands Join in Commemorative Ceremonies

The annual August pilgrimage to Hiroshima and Nagasaki by tens of thousands reawakens the world to the events of 45 years ago and to the destructive potential of today's vast nuclear arsenal.

Marked by innumerable private and informal memorial services, the anniversaries of the bombings are internationally recognized for the large officially sanctioned ceremonies held in the Peace Parks of Hiroshima and Nagasaki on 6 and 9 August, respectively.

This year, for the first time since 1976, the Japanese prime minister attended both events. Prime Minister **Toshiki Kaifu** called for the abolition of nuclear arms and pledged the nation's commitment toward that goal.

The mayors of both cities also appealed for nuclear disarmament.

"The leaders of the United States and the Soviet Union concurred this June on the first real reduction ever in their arsenals, and agreement has been reached on negotiating further nuclear disarmament," remarked Hiroshima Mayor **Takeshi Araki**. "...Hiroshima has the highest regard for this tide of disarmament, which changes the fate of mankind from annihilation to survival. All nuclear powers should heed this global call and move immediately to ban nuclear tests and abolish nuclear weapons."

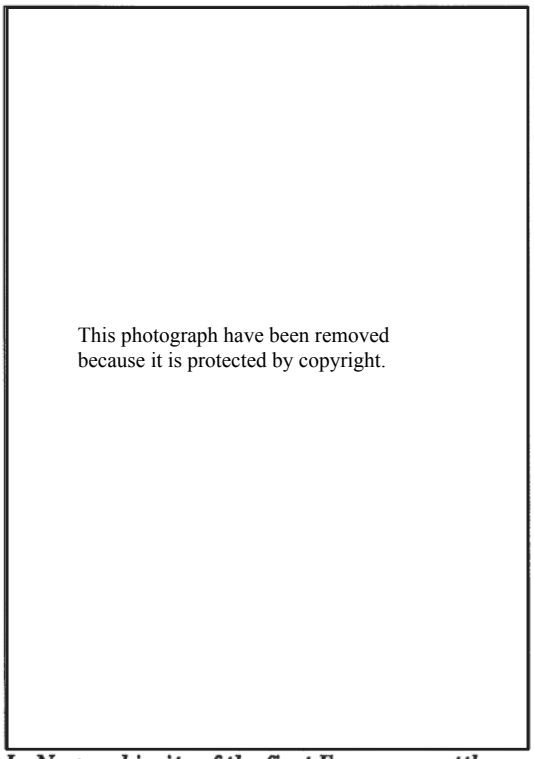

PHOTO COURTESY OF NISHI NIPPON SHIMBUN

In Nagasaki, site of the first European settlement in Japan, a processional wends its way from Urakami Cathedral the evening before the anniversary of the atomic bombing.

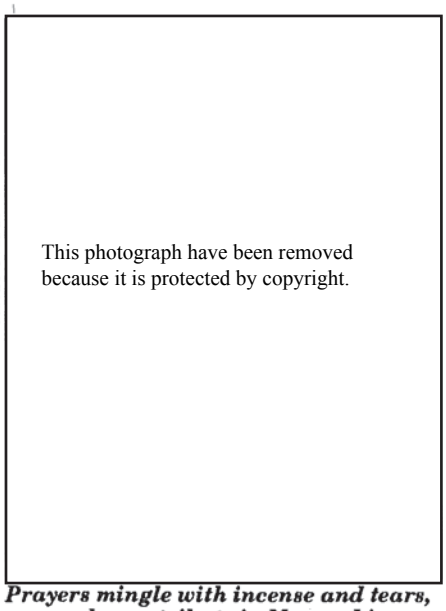

PHOTO COURTESY OF NAGASAKI SHIMBUN

Prayers mingle with incense and tears, as people pay tribute in Nagasaki.

Noted for his outspoken criticism of Japan's role in World War II, Nagasaki Mayor **Hitoshi Motoshima**, who survived a near fatal attempt upon his life earlier this year, said:

"The nuclear states, however, have not abandoned their strategy of nuclear deterrence nor desisted from nuclear tests. The development of nuclear weapons—and the potential for nuclear war—continue as before. In particular, the situation in the Asia–Pacific region, where ocean-based nuclear missiles are concentrated, can be regarded with little optimism. What is necessary now is leadership and diplomatic initiatives on the part of the Japanese government for the establishment of a nuclear-free zone in the Asia–Pacific region."

Calling attention to the circumstances leading up to the bombings, citizens and public officials alike have recently begun to voice their opinions on formerly unspoken topics.

"War can be prevented only by facing our painful past and learning what caused the war," remarked 66-year-old **Suzuko Numata**, who was quoted in a nationwide English-language newspaper. But, as she can attest, facing the past can be very difficult.

Numata, who lost a leg in the bombing of Hiroshima and has never attended the official memorial ceremony, started to publicly recollect her painful days only seven years ago. A city-appointed storyteller, the former teacher now relates her experiences to schoolchildren visiting Hiroshima.

Regarding apologizing and extending assistance to non-Japanese A-bomb survivors, Nagasaki Mayor Motoshima stated, "Our moral responsibility towards these people is great indeed. This is particularly true for the people of Korea and China who were forced to come to Japan under the cruel system of colonial rule, who were subjected to inhuman treatment, and who perished in the atomic bombings far from their homes. Many survivors in these countries are now facing old age with the mental and physical torments caused by exposure to the bombings. It is imperative that we take immediate steps to offer apologies, to conduct investigations, and to provide assistance for these people."

Although the ceremonies provide an annual focus for international discourse on nuclear warfare and its effects, some feel the events are only a "festival," and are thus unable to properly convey the sobriety of the bombs' aftermath. Instead, some call for a national holiday so all the people of Japan can pray for the souls of the A-bomb victims and think about the circumstances of war.

As Mayor Motoshima put it: "Peace is the greatest treasure we can pass on to future generations." ❑

Perspectives

Sadako and the paper cranes—science and symbolism

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

Last year in this column, in the autumn issue of *Update,* I addressed the question: "What is a survivor?" Since then, I have learned of the stories of two survivors, both described in the *Hiroshima Signpost* (a local monthly English-language magazine). These stories illustrate how generalizations of the type that I discussed last year can result in wrong conclusions. In these cases, fatal radiation effects were ascribed on the basis of the generalization that survivors are more likely to develop cancer than those who were not exposed to A-bomb radiation. The only indication, however, that the disease resulting in their deaths was A-bomb-related was the fact that they were in the city at the time of the bombing, but simple matters such as distance from the explosion (and therefore, degree of exposure) were disregarded.

The two persons involved have become powerful symbols for the plight of the survivors, and I feel a certain reluctance to take the chance that this little exposé will be misinterpreted as an attack on this symbolism for peace and against the horror of nuclear weapons. On the other hand, I consider that it is important to stress scientific values, "truths," if you want, even though they may contradict popular beliefs. As I said last year, I have no intention to diminish the real suffering, in the past or present, of many survivors, nor, I add, the sincerity of those who strive for peace and see Hiroshima and Nagasaki as the focal points for their efforts.

Thousands of multicolored folded paper cranes are sent to Hiroshima from all over the world to honor the children who perished as a result of the atomic bombing.

The first of my two examples, described in the July 1990 issue of *Signpost* ("A rainbow of cranes," p. 15) concerns the well-known story of "Sadako and the thousand cranes." Sadako, according to the *Signpost*, was two years old on 6 August 1945. Her house was badly damaged, but no one in her family was hurt. Ten years later, Sadako developed leukemia, by many then known as "the atom-bomb disease."

A Japanese legend says that if a sick person folds 1,000 paper cranes the illness will go away. Sadako started to fold cranes from brightly colored paper, but she died after she had folded only 644 of them. When this happened, friends finished folding the cranes to complete the 1,000. This touching story has become known worldwide, and has resulted in the folding of enormous numbers of stringed paper cranes by children all over the world, who send them to

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News Briefs

✓ RERF to Assist International Efforts to Treat Radiation-Exposed

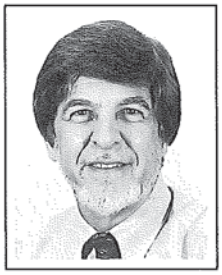
RERF will be one of 10 organizations taking part in a proposed Study Council for International Cooperation in the Medical Treatment of Exposed People. Hiroshima Prefecture's Governor **Toranosuke Takeshita** has announced that the prefecture will establish the organization to coordinate research efforts providing international assistance, to establish a system and facilities for training foreign physicians, and to develop a cohesive way of making available the information gained from the treatment of A-bomb survivors and the study of the health effects of radiation exposure.

RERF Chairman **Itsuzo Shigematsu** welcomed Governor Takeshita's efforts, noting that "measures should be taken so that Hiroshima's accumulated medical data may be imparted to the world." Shigematsu stated that training doctors was an important step, but that it would also be important to summarize Hiroshima's experiences in treating and studying A-bomb victims. "Although the latest scientific achievements are being reported [at meetings and in journals], an overall picture has not yet been compiled."

Other groups participating in the council are the prefectural and city medical associations, Hiroshima University's Research Institute for Nuclear Medicine and Biology, and the Prefectural Environment and Health Department. Further guidance will be provided by the Japanese Ministry of Foreign Affairs, the Ministry of Health and Welfare, and the Science and Technology Agency.

A Brazilian pediatrician will spend eight months at the Red Cross Hospital, RERF, and other institutions in Hiroshima as the first trainee invited by the prefectural office.

✓ New Chief of Research Arrives



Trosko

In early August, **James E. Trosko,** professor of pediatrics and human development at Michigan State University, was appointed RERF's chief of research and permanent director. He replaces **Seymour Abrahamson,** who has returned to his position as professor of zoology at the University of Wisconsin after a two-year appointment at RERF. Trosko's research interests have included the mechanisms by which radiation causes cancer in genetically predisposed children, the modifying effects of environmental chemicals on radiation damage, and, most recently, the development of biologically based models to predict the risk of radiation and chemical exposures on various human diseases.

✓ WHO Scientific Advisory Committee Will Meet in Hiroshima

RERF will host the World Health Organization's Scientific Advisory Committee on the International Programme on the Health Effects of the Chernobyl Accident (IPHECA) 23–26 October. The meeting will focus upon the design of IPHECA as well as the International Centre for Radiation Health Issues (ICHRI), the identification of priorities in scientific research and medical investigations, and the implementation of IPHECA and establishment of ICHRI.

In addition, attendees will discuss the need for international collaboration in addressing the health problems resulting from the Chernobyl accident, and the role of RERF's expertise in long-term follow-up efforts.

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Time Variations in the Relative Risk of Cancer: Theoretical and Epidemiological Evidence

Is the relative risk of cancer constant or does it decrease with time?

by Mark P. Little and Monty W. Charles, Radiological Protection Branch, Technology Division, Nuclear Electric plc, Berkeley Nuclear Laboratories, UK

In various analyses of the Japanese A-bomb survivors (Preston et al., RERF TR 1-86; Preston and Pierce, RERF TR 9-87), RERF researchers have found that for cancers other than leukemia the radiation-induced excess risk is much better modeled by a relative rather than an absolute risk model. On this basis, excess cancer risk can be evaluated by assuming that, after some latent period, it is a constant multiple of the underlying cancer risk (i.e., by the so-called time-constant relative risk model) rather than by assuming that it is constant (i.e., by the so-called time-constant absolute risk model). The United Nations Scientific Committee on the Effects of Atomic Radiation has seen fit to use the constant relative risk model for calculating radiation-induced population risks for cancers other than leukemia (*Sources, effects and risks of ionizing radiation*, Suppl 45 [A/43/45], New York, UN, 1988). The US National Research Council's Advisory Committee on the Biological Effects of Ionizing Radiation in its BEIR III report (*The effects on populations of exposure to low levels of ionizing radiation*, Washington, D.C., National Academy Press, 1980) has used both time-constant absolute and relative risk models to project population risks to the end of life.

The BEIR IV analysis of radiation effects in miners (*Health risks of radon and other internally deposited alpha particle emitters*, Washington, D.C., National Academy Press, 1988) found that a relative risk model, with relative risk decreasing as a function of time since exposure, fitted the data best, and this model was also used to calculate population radon risks. From the recent RERF analyses of the A-bomb survivors, there have also been indications of a reduced relative risk of cancer over time for the youngest age-at-exposure group (Preston et al., RERF TR 1-86; Shimizu et al., RERF TR 5-88); more general evidence for such a reduction is also apparent in the ankylosing spondylitis patients (S.C. Darby et al., *Br J Cancer* 55:179–190, 1987). The latest analysis from the BEIR committee of these and various other radiation-exposed cohorts (*Health effects of exposure to low levels of ionizing radiation* [BEIR V], Washington, D.C., National Academy Press, 1990) found convincing evidence for reductions in relative risk with increasing time after exposure in three of the five categories of cancer considered. The BEIR committee used relative risk models with the corresponding reductions in time after exposure to calculate general US population risks.

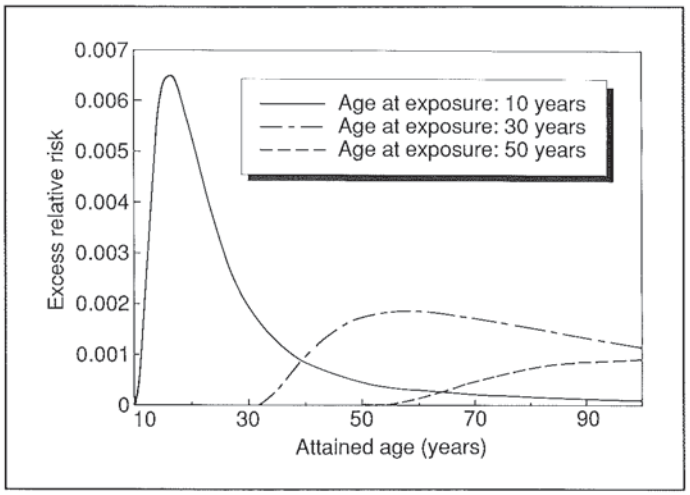

Figure 1. Excess relative risk predicted by the Armitage–Doll model following a single instantaneous exposure for various ages at exposure. The model has six stages, the second of which is assumed to be affected by radiation. The stem cell population is modeled by the Makeham distribution.

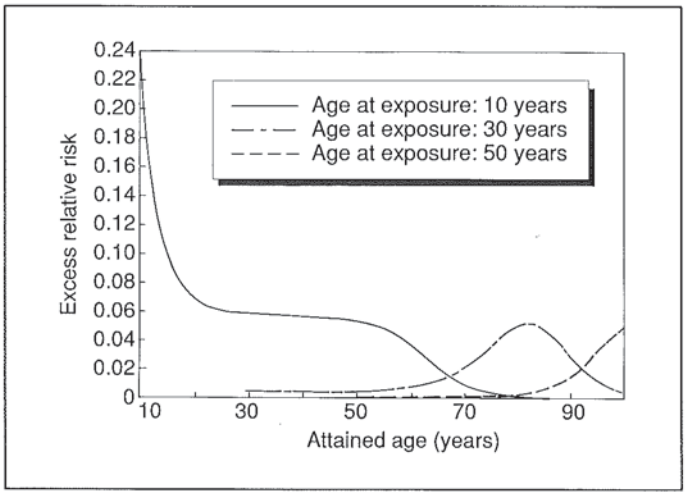

Figure 2. Excess relative risk predicted by the Moolgavkar–Venzon–Knudson model following a single instantaneous exposure for various ages at exposure. Radiation is assumed to modify the rate of transfer of normal to intermediate (premalignant) cells. The stem cell population is modeled by the Makeham distribution.

The problem with calculating population risks from epidemiological data is that few cohorts have been followed up to extinction, and in particular, 40 years after the bombings two-thirds of the Japanese A-bomb survivors are still alive. In attempting to calculate lifetime population cancer risks, it is therefore important to predict how the relative risk might vary as a function of time after radiation exposure, and in turn how assumptions about the possible variation of the relative risk with time will affect population cancer risk estimates.

A theoretical justification for a reduction in relative risk is provided by the models of P. Armitage and R. Doll (*Br J Cancer* 8:1–12, 1954) and S.H. Moolgavkar, D.J. Venzon, and A.G. Knudson (A.G. Knudson, *Proc Natl Acad Sci USA* 68:820–23, 1971; S.H. Moolgavkar and D.J. Venzon, *Math Biosciences* 47:55–77, 1979). The first of these models can be shown to behave in such a way that, after a sufficiently long time following an instantaneous exposure, the excess relative risk varies by an amount proportional to *time after exposure*$^{-j}$ for some positive j (A.S. Whittemore, *Environmental health quantitative methods*, Philadelphia, SIAM, pp. 72–77, 1977; M. Little and M. Charles, Nuclear Electric Report TD/RPB/REP/0002, 1990). The second

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Science and symbolism

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Hiroshima and Nagasaki as symbols for peace. Even now, one can see these colorful *origami* chains, all year long, near any of the many memorials erected in honor of those who died as a result of the bombing—especially, of course, at the memorial statues honoring the children.

The *Signpost* story mentions that Sadako lived "two miles from the center of Hiroshima," and it describes the state of her house after the explosion. Both data would indicate a considerable distance from the point of explosion. Total destruction of typical Japanese houses occurred up to a distance of 2.5–3 km, so it appears likely that Sadako's house was further away. But even if I assume that the two-mile figure (let's say 3 km) quoted in the *Signpost* is indeed the approximate distance from the epicenter, her bone marrow dose from gamma radiation, assuming no shielding, would have been less than 2 mGy (0.2 rad), with a neutron dose less than 1% of that. With such low exposure, it is extremely unlikely that Sadako's disease was caused by radiation, and it is far more probable that she suffered from a childhood leukemia of unknown cause, as most leukemia cases still are today.

The second story is that of Hiroshima poet Sankichi Toge, described in the *Hiroshima Signpost*'s summer 1989 issue. Sankichi, who is well known here for his poems on the A-bomb experience and his appeals for peace, lived (according to the *Signpost*) at a distance of 3,000 m. He described that he suffered wounds from glass splinters and radiation sickness. Given the distance indicated, the glass splinter wounds appear very likely, but the general malaise that he ascribed to "radiation sickness" is not. At that distance, the doses mentioned above for Sadako apply also to Mr. Toge, and would therefore have been far too low to have caused acute effects from radiation exposure. For that matter, they cannot be considered to have had a significant role in the causation of any malignancy. Nevertheless, as the *Signpost* indicates, Mr. Toge died seven years later from the effects of the atomic bomb.

What worries me is not so much the low scientific-truth content of the stories related here, but the fact that many distant survivors on the basis of such stories still believe that they have been seriously harmed by radiation. Many of them have had more than enough to worry about already. They should enjoy their later years without unsubstantiated fears, based though they may be on tragic and richly symbolic stories. ❑

Time Variations in Cancer Risk

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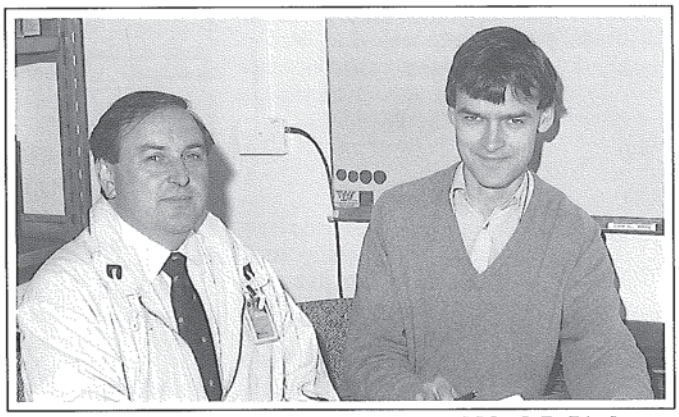
of these models predicts that, after a sufficiently long time following an instantaneous exposure, the excess relative risk would decrease in an exponential fashion (Little and Charles, loc. cit.). In both models, the reduction in relative risk with time after exposure is expected to be particularly marked in the youngest age groups. The variation of relative risk with attained age for various age-at-exposure groups is illustrated for each model in Figures 1 and 2.

The Japanese A-bomb survivors and 12 other cohorts provide epidemiological evidence for a reduction in the radiation-induced relative risk of cancers (other than leukemia) with time following exposure (ibid.). At a sufficiently long time after exposure, our analyses show that for the youngest age-at-exposure groups the excess relative risk varies in proportion to *time after exposure*$^{-j}$ for j between 0.6 and 3.1. This is equivalent to an annual reduction of 4–9% in excess relative risk (depending on the year after which this reduction is assumed to take effect). For the older age groups, there is little evidence for such a reduction in relative risk with time; indeed, there are indications that in this group relative risk might increase with time after exposure. There are indications from the Japanese data that the absolute risk model (with time after exposure adjustment) might fit the non-leukemia cancer data better than the time-adjusted relative risk model. It should be emphasized that the absolute (and relative) risk models used incorporate an adjustment factor proportional to *time after exposure*$^{-j}$.

The implications of reductions in relative risk on calculations of the lifetime population cancer risk estimates 40 or more years after exposure are quite significant, particularly in the youngest age group (those less than 20 years old). We have shown that if the range of observed reductions in relative risk are assumed to operate 40 or more years after exposure, the calculated UK population risk estimates would be reduced by between 15% and 40% compared to those based on a constant relative risk model. Given the indications from the Japanese population that the (time-adjusted) absolute risk model fits better than the (time-adjusted) relative risk model, population risks might be reduced by up to 45% compared with those based on a constant relative risk model.

As a result of the preliminary evidence for reductions in risk in the youngest age-at-exposure groups, the authors (in association with **Roy Shore** of New York University Medical Center, **Mike Hawkins** of the Oxford Childhood Cancer Research Group [Oxford CCRG], and **Nancy Hildreth** of the University of Rochester School of Medicine) have been analyzing the RERF Life Span Study Report 11 cohort (Shimizu et al., loc. cit.) in conjunction with much more detailed information from follow-ups of other radiation-exposed groups of children than that used above. The data are taken from the latest follow-ups of the Rochester thymus-irradiated children, the New York tinea capitis patients, and the Oxford CCRG's childhood cancer cohort. These analyses, if anything, show greater reductions in relative risk than those observed in the above analysis. For these cohorts, an adjustment to the excess relative risk varying between *time after exposure*$^{-2.0}$ and *time after exposure*$^{-3.2}$ fits best overall. This is equivalent to an annual overall reduction of 7–9% in excess relative risk (depending on the year after which this reduction might take effect). ❑



The coauthors, Monty W. Charles, left, and Mark P. Little.

Acknowledgments—The authors would like to thank **Don Pierce**, *Oregon State University, Corvallis, Ore., and* **Dale Preston** *of the RERF Department of Statistics for much helpful correspondence.*

Editor's Note: This paper is published with the permission of Nuclear Electric plc, Berkeley Nuclear Laboratories, Berkeley, Gloucestershire, UK, and represents the opinions of the authors, not necessarily those of RERF.

The LSS Reports: An Evolutionary Process

by Dale Preston, Department of Statistics; and Kiyohiko Mabuchi, Department of Epidemiology and Epidemiologic Pathology

At this time, we are preparing for the production of RERF Life Span Study (LSS) Report 12. In conjunction with this effort, the Epidemiology and Statistics departments are reviewing issues related to the nature of the LSS reports.

After briefly describing several reports on RERF epidemiological studies which should be completed in the next few months, we will describe plans for LSS Report 12 and will outline some of the issues which have been raised in our initial discussions on the evolution of the LSS reports.

We would also like to solicit your opinions on how we can present results from analyses of RERF epidemiological studies in ways which better meet your needs.

Current LSS reports

As exemplified by LSS Report 11 (Shimizu et al., RERF TRs 12-88 and 5-89), the LSS reports have traditionally focused on the mortality follow up of LSS cohort members. As evidenced by the UNSCEAR 88 and BEIR V reports, the LSS reports continue to be the major source of information on long-term radiation risks in humans.

However, improvements in the quality of tumor and tissue registries and the introduction of longitudinal methods for the analysis of the Adult Health Study data are now directing attention toward other aspects of RERF's LSS-based epidemiological studies. Indeed, RERF staff are currently finishing analyses and preparing comprehensive reports on cancer incidence including both solid tumors and leukemia in the LSS (Mabuchi and Soda, *RERF Update* 2(2):5, 1990) and on disease incidence and other data in the AHS (Wong et al., *RERF Update* 2(2):4, 1990).

Our current plans call for LSS Report 12 to cover cancer and noncancer mortality from 1950 through 1989. As in the past, the report will include a review of the current status of the cohort and will summarize mortality risks by cause. The population to be used in the analyses will include about 87,000 people with DS86 dose estimates who were in the city at the time of the bombings. This population includes 11,000 survivors not included in the Report 11 analyses for whom DS86 doses were computed as a result of the 1989 extensions to the DS86 system (Fujita, *RERF Update* 1(2):3, 1989). We plan to have a draft on cancer mortality ready for internal review by the end of 1991.

A subtle but important change will be made in determining the follow-up period for each individual in the study population. For the first time in RERF studies, person-year computations will use the date of last known vital status or "loss to follow up" as the exit date if this date is before the study cutoff date. This change is being made to minimize problems arising from the three-year cycle for collecting mortality data and to provide a more consistent method for handling people lost to follow up due to emigration from Japan.

Evolution of the LSS reports

Turning to general issues raised in discussing the evolution of the LSS reports, we will focus on two areas: 1) the scope of the reports, and 2) the way risk estimates are presented and how summaries and the relevant data can be made available to interested users.

Undoubtedly, the LSS reports will continue to be a major source of descriptions and summaries of knowledge accumulated from the cohort experience to date. It is also clear that as better data from the tumor and tissue registries and the AHS cohort become available, we must broaden the scope of the LSS reports. However, there is a feeling that in some ways too much is expected from the reports.

There has been a de facto tradition that analyses of RERF data should not extend beyond the period covered by the most recent LSS report. This tradition inhibits production of more detailed topical reports on subjects addressed to some extent in the previous LSS report. Thus, those who are writing the current report feel pressure to include more detail, thereby lengthening the time spent preparing the report. In addition, when a specific topic is presented in some detail in an LSS report, it is unlikely to receive the critical review it would receive if reported separately.

The scope of the LSS reports

In response to issues related to the scope of the LSS reports, we have decided to put more emphasis on the production of short, topical reports on specific diseases or other issues related to radiation risk in the LSS. To encourage this, the mortality data set being prepared for LSS Report 12 will be made available for concurrent analyses by RERF staff. Procedures are being developed to update these data on an annual basis. We have also identified several areas requiring more detailed studies, and we are taking steps to see that progress is made in some of these areas, including:

- assessing cancer risks among those under age 20 at the time of exposure;
- comparing risks observed among the in-utero population with risks seen in the youngest survivors;
- reporting in detail on specific sites including stomach, lung, and thyroid, as well as skin cancers; and
- carrying out cause-specific analyses designed to look for common risk patterns across cancer types.

Risk estimate considerations

As noted above, another general topic arising in our discussions concerns presenting and summarizing risk estimates. Model-based methods have been used extensively in analyses of the LSS data since LSS Report 10 (Preston et al., RERF TR 1-86). These methods provide us with powerful tools to describe the levels and patterns of excess risk, but the methods used for summarizing these results are not satisfactory.

In most LSS reports, the emphasis has been on sex, age-at-exposure, and time-averaged relative or excess risks which are easy to compute and relatively easy to use for many purposes. However, the fact that these single-number summaries reflect an implicit weighting based upon the sex and age distribution of the LSS cohort (see Facts & Figures, p. 10) is often ignored.

We feel that discussions of the consistency between current risk estimates and those in earlier reports are inadequate. For example, in each recent LSS report, it is noted that leukemia risk estimates are lower than those in the previous report. However, in view of the decreasing trend in excess leukemia as time passes, this result is not unexpected. A potentially more useful summary of the risk should indicate how risk can be expected to change over time, in conjunction with a discussion of whether the change in risk is consistent with the predictions of the models used in earlier reports.

The solution to the problem of summarizing risks is not obvious. One type of summary which could be used more extensively in RERF reports is the lifetime risk estimate.

Lifetime risk estimates are appealing because they are a single-number summary which, if the underlying assumptions, computational methods, and base populations are clearly specified, can provide a basis for comparing current risk estimates with estimates in earlier reports or other populations. Presenting the detailed mathematical expressions for the models used is necessary, but translating these

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The Very Early Years of the ABCC Genetics Program, 1946–1954

by James V. Neel
Professor Emeritus of Human Genetics and Internal Medicine, University of Michigan Medical School

In a previous article (*RERF Update* 1(4):7–8, 1989), I have described the beginnings of the ABCC, and also the origins of its genetics program. The reader may recall how in the summer of 1947, after having spent some seven months in Japan attempting to develop a plan for a genetics program, I returned to Washington, D.C., to present a protocol for a genetics study to an advisory committee of the National Academy of Sciences. Having received its endorsement and having recruited a team of three American associates for the program, I returned to Japan in the fall of 1947 to initiate the study under the auspices of the fledgling ABCC.

Our task was to learn as much as possible about the children being born in Hiroshima and Nagasaki. As I have related earlier, the key to this was the special ration system for pregnant women which was in effect in Hiroshima and Nagasaki during the immediate postwar years. We developed a questionnaire to be administered when for ration purposes the women registered their pregnancies at the completion of the fifth lunar month of pregnancy. Registration occurred at the various city health centers. The plan was to obtain identifying information and radiation histories when the women registered, then information on the children at birth. We began to register pregnant women in Hiroshima in February 1948 and in Nagasaki in July of the same year. The information to be collected following the birth of a child included the sex of the child, viability at birth, presence of congenital malformation, birth weight, and survival through the neonatal period.

Early scientific expectations

It seems important at this point to describe the scientific expectations with which this study was approached.

In the early postwar years, the chief information concerning the genetic effects of radiation was based on the fruit fly, *Drosophila*. Data on the genetic effects of radiation on the mouse (which would have been more appropriate when thinking about human risks) were limited, consisting primarily of the results of studies by Dr. **Donald Charles** at the Rochester, N.Y., branch of the Manhattan Engineering District (the military's cryptic term for the US atomic bomb project). From these data and what was known about the amounts of radiation received by survivors and the numbers of children they would probably have, we really did not expect to observe a statistically significant increase in malformed children in the offspring of irradiated survivors. On the other hand, there were some scientists who did have that expectation, and the popular presses of both the US and Japan carried many wild speculations. The level of these rumors was such as to create serious problems when a survivor exposed as a child reached marriageable age. The NAS advisory committee mentioned earlier agreed with our assessment, but felt there was no choice but to proceed with a study, despite the fact that statistically significant effects of radiation would probably not be observed.

One thing was clear: the study had to be as complete as possible, i.e., we had to obtain data on all the babies, not just some of the babies.

Posts of importance

Four jobs were critical to the program in those early days. First, there were young Japanese physicians—many just out of medical school and internship—working with the ABCC while they were establishing a practice. Many of these have gone on to be important members of the medical communities of Hiroshima and Nagasaki. The second very critical type of personnel was the midwives of the two cities. They were requested after a woman's delivery to complete the questionnaire which had been initiated when the mother-to-be had registered her pregnancy. Finally, there were clerks and nurses—the clerks to administer the questionnaires at the various city health centers and to process the data from the questionnaires, and the nurses to assist the doctors in their home visits and clinic examinations. Ultimately, in the two cities, about 15 clerks were employed. Many of the readers will remember Mrs. **Jean Okumoto**, who so skillfully supervised the clerical operation during those early days, and **Kiyoko Minato**, **Chiyoko Watanabe**, and **Setsuko Hanazono**, "genetics" nurses who, like Mrs. Okumoto, stayed on with ABCC (and RERF) for many years after the clinical genetics program was terminated.

The undertaking required a major training program for physicians and clerks. And how many times we met with the midwives to explain the study and to discuss the types of findings we expected them to report (see the accompanying

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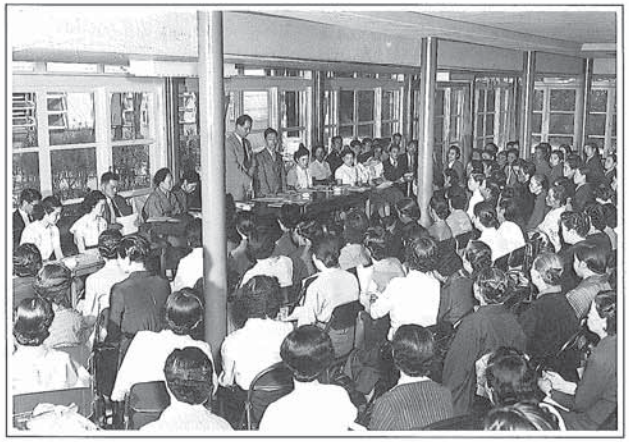

In postwar Japan, midwives were present at more than 90% of births, and thus in Hiroshima and Nagasaki they were able to notify ABCC of most births occurring in the two cities from 1948–1953. Above, the ABCC genetics staff is shown meeting with a small portion of the several hundred midwives upon whom the collection of data depended. At left, Dr. Yasumitsu Tachino and Head Nurse Kiyoko Minato are shown making a postnatal house call, as a follow-up to information provided by the attending midwife. Of the more than 76,000 children seen up through 1953, ABCC pediatricians were able to reexamine about 30% at the age of about nine months. A subsequent drastic drop in the live birth rate led to discontinuation of the physical exams in 1954, although data on sex ratio and survival of newborns were still collected.

Role of Japanese Midwives Critical to Birth of Genetics Program

by William J. Schull
Director, Genetics Centers, University of Texas Health Science Center

During the 40-odd years that stu(of the atomic-bomb survivors and their offspring have been underway, many local contributors have gone largely unrecognized. This is the story of two such individuals—**Setsuko Yamamoto** and **Tei Murakami**.

To understand their importance and contributions, one must bear in mind the design of the early genetics studies and the nature of the obstetrical practices of the time.

In the immediate postwar period and for some years thereafter, most Japanese infants were born at home. Since less than 10% of these births were attended by a physician, the cooperation of the midwives was essential to a successful ABCC genetics program.

At the outset of the genetics studies in 1948, several hundred women were practicing midwifery in each of the two cities. When a pregnant women registered her pregnancy with the municipal authorities and with the ABCC, a form was completed in duplicate that identified her and her husband, detailed their exposure experiences and previous reproductive performance, and provided space for a description of the termination and the physical status of the infant. One copy was given to the registrant to give to the [illegible]ndant at the birth of her child, and the [illegible]er was retained by the Commission. The midwife completed a portion of this form to notify us of a terminated pregnancy and whether the infant was stillborn or died prematurely, to aid us in obtaining the body for postmortem examination. Each midwife was remunerated for the births she reported to the program, but—beyond weighing the infants with portable scales we provided—the midwives could not be expected to carefully describe congenital malformations. This was the function of our staff physicians who, accompanied by one of the Commission's public health nurses, would call upon the family after we had been notified of a birth.

As with medical or paramedical groups worldwide, the midwives had organized an association with a president, a vice president, and a council charged with administering the association's affairs. During the roughly six years of clinically surveying births in Hiroshima and Nagasaki, Mrs. Yamamoto and Mrs. Murakami served as presidents of the respective associations and through them most of our interactions with the midwives occurred. These periodic meetings with the entire association included explanations of proposed changes in the research program and discussions of problems or findings. Social gatherings, such as the open house and barbecue held in 1950 when the Commission began to operate out of its new facilities on Hijiyama, were usually attended only by the association officers.

Inevitably, in a study of this scope involving countless individuals, misunderstandings arose. Commonly, these took the form of an ill-considered remark by the staff physician to the family while examining a newborn. Such comments were communicated to the attending midwife who understandably took offense. These conflicts were never reported directly to us, but nonetheless we promptly learned of the damaged feelings through Mrs. Yamamoto or Mrs. Murakami to whom the midwife had complained.

A ritual evolved to resolve these matters, and each of us soon learned our parts in the unwritten script. If the incident occurred in Hiroshima, I or whoever happened to be the resident head of the genetics program, accompanied by Dr. **Koji Takeshima**, would call upon Mrs. Yamamoto.

When we reached her home, we were always cordially welcomed and invited to the pleasant second-floor room she used whenever we visited. As soon as we were seated, she served us tea, and after the customary pleasantries and inquiries into health had been exchanged, she began to explain what had happened as it was reported to her by the offended midwife. It was evident that whether the physician had or had not been correct, he had committed a tactical error that we could not ignore—the cooperation of the midwives was too central to our whole program.

I would tell Mrs. Yamamoto that the physician was a young man, recently employed, but whom I knew to be considerate and not given to deliberately insensitive statements. I was sure that he meant no slight. These were truthful,

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Genetics Program

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article by Dr. Schull)! We planned that all newborns would be examined by a physician. If the midwife had observed some abnormality in the child, she was to notify us at once, and one of the doctors would make an immediate house call. If the child appeared normal, the midwife still notified us of the birth but on a more leisurely schedule—and the doctor still made a house call, accompanied by a nurse. All this required a small fleet of jeeps plus their drivers. In one way or another, when the program was in full swing, at least 200 persons were involved in the genetics program in the two cities. When this clinical program was terminated, these people were all reassigned if they wished to stay with ABCC. Two former "genetics drivers" who were with ABCC and RERF for many years were **Masaru Nakagawa** and **Minao Kurisu.**

The ABCC genetics department staff meeting with the Hiroshima Midwives Association in the early 1950s. Standing are Genetics Department Chief Duncan McDonald (left) with Dr. Koji Takeshima, whose services as interpreter and advisor to the American staff were indispensable. At McDonald's right is Midwives Association President Setsuko Yamamoto.

Observing Japanese custom: a key goal

It was a great stroke of good fortune during the early survey stages of the study to make contact with Hawaiian-born Dr. **Koji Takeshima**, then a young surgeon at the Hiroshima Red Cross Hospital (see *RERF Update* 2(1):7, 1990). During the very early days, when the genetics program was housed in the Red Cross Hospital, Dr. Takeshima was the right-hand man, first of myself and then of successive directors of the genetics program. In 1948, after he became associate director and chief Japanese National Institute of Health (JNIH) representative, Dr. **Hiroshi Maki** was to assume this same role. Needless to say, the developing genetics program was also closely scrutinized by the appropriate JNIH personnel.

In this study, we were determined to observe Japanese custom as far as possible; Dr. Takeshima was our principal advisor. Our deep commitment to the question of congenital defect forced us to intrude upon people in times of sorrow and, since we needed to know if there was a pertinent family background, we had to ask very personal questions. It was necessary that we be both very professional and very sympathetic. I would like to believe that if we occasionally caused embarrassment, it can be excused on the grounds that our failure to demonstrate a striking increase in congenital defects removed a great barrier to the prospects of a good marriage for many of the younger survivors—and even their children.

I also need to remind the reader that although this study was initiated during the US occupation of postwar Japan, and of course required the concurrence of General Headquarters, it was in no way official "policy." Its success depended on the voluntary cooperation of the Japanese people, just as the program of RERF does today. It is to me a tribute to the intelligence of the Japanese people and to the tact of the ABCC staff that cooperation was so high.

Largest early ABCC program

On the US side, there was also a need for additional and continuing personnel. I was in and out of Japan during those early years, but there were others who came for periods of two or more years. The original team of three Americans consisted of Dr. **Ray Anderson**, a pediatrician–geneticist; Dr. **Masuo Kodani**, a cytogeneticist; and **Richard Brewer**, the data processor. Ray, then in the army, returned to the US as soon as his tour of duty ended (and subsequently became a pediatric cardiologist). The other two stayed on, but replacing Ray was urgent, especially since we had not been able to recruit a Japanese geneticist.

At this juncture (1949), I was fortunate enough to attract Dr. **W.J. Schull** to the program. He had just completed his doctorate in genetics at Ohio State University. When he completed his two-year ABCC contract, I was delighted to recruit him for the University of Michigan human genetics program, from which base, like myself, he continued his involvement in the follow-up studies. At ABCC, Dr. Schull was replaced by **Duncan McDonald** and **Newton Morton**.

On the pediatric side, ABCC was by now interested in building up strength in this area, and during this early period we had a string of very able associates: Drs. **John Wood**, **James Yamazaki** (see *RERF Update* 1(4):4, 1989), **Wayne** and **Jane Borges**, **Frank Poole**, **Robert Kurata**, **Stanley** and **Phyllis Wright**, and **George Plummer**. This pediatric strength enabled us to reexamine about 30% of all live-born infants registered in the genetics program when they were 8–10 months old. To obtain the most accurate information possible on congenital defects, an autopsy program was initiated under the direction of **William Wedemeyer** in Hiroshima and **Naomasa Okamoto** in Nagasaki.

Associated professional and support personnel swelled the ranks devoted directly or indirectly to genetics studies to undoubtedly the largest of the early ABCC programs.

Demographic changes cause end of program

Because so little was known about the radiation histories of the people then living in Hiroshima and Nagasaki in those early days, our first plan included two comparison or "control" cities—Kure for Hiroshima and Sasebo for Nagasaki. In fact, we began registering pregnancies in Kure in March 1948. Later, however, it became apparent that many residents of Hiroshima and Nagaski had either not been in the cities at the time of the bombings (ATB) or, if present, had been well beyond the zone of radiation. So, we decided we had sufficient "internal" controls for our studies. Accordingly, in September 1950, after data had been collected on some 8,391 pregnancy terminations, work was discontinued in Kure. No corresponding operation was ever attempted in Sasebo.

A few years after the genetics program was initiated, the Japanese government, in response to the burgeoning population which had resulted from the extensive repatriation of Japanese from such areas as Manchuria, Korea, and Formosa, greatly

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Genetics Program

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PHOTO COURTESY OF JAMES V. NEEL

The genetics clerical staff administered questionnaires at the city health centers and later processed the data collected. In 1950, clerk Mariko Tai and her co-worker were busy converting parents' stated positions at the time of the bombing to distance from hypocenter.

relaxed the indications for induced abortion, in part at least as a means of reducing the live birth rate. Thereafter, Japan sustained the sharpest drop in live birth rate per 1,000 persons ever observed since nations had instituted a system of vital statistics.

Confronted with these developments, Dr. Schull and I began to wonder how much longer it would be scientifically justifiable to continue the program in its present form. We had been carrying out annual analyses of the accumulated data, and now seemed to be the time for a summary analysis. This analysis, conducted with the assistance of Drs. McDonald and Morton, revealed very little difference indeed between the children of parents presumed to have received significant amounts of radiation ATB and the children of parents who had not been radiation-exposed.

Knowing trends in birth rates and knowing in general how the population of exposed parents would decline year by year, we could in the early 1950s look ahead and ask, "How much will the statistical precision of the results be increased by another 5 or even 10 years of data like these?" We tentatively concluded that there was very little likelihood that statistically significant differences would be obtained with another 5 or even 10 years of this large and expensive program. Under the circumstances, should the program be continued in its present form? We thought not, but the decision to discontinue a program with this momentum was almost as major as the original decision to initiate the program. We consulted with the NAS Committee on Atomic Casualties—then the supervisory body on the American side—and were encouraged (in keeping with our own wishes) to submit the question to a very senior committee of geneticists.

This committee, meeting in 1953 at the University of Michigan in Ann Arbor, concurred and recommended that the program be greatly reduced. (Members of the committee were: Drs. **G.W. Beadle**, **D.R. Charles**, **C.C. Craig**, **L.H. Snyder**, and **Curt Stern**, chairman.) The physical examinations would be discontinued in early 1954, but we would continue to collect data on the sex ratio and survival of newly born infants. These two observations were continued because, on the one hand, a sex ratio effect of borderline significance had been observed and, on the other hand, it could not be precluded that an effect of parental exposure on a child's survival might become apparent during childhood. But there was another reason to continue to accumulate a record of newborns (now through birth registrations): it would provide a continuing roster of children born to survivors, so that if future genetic developments provided new approaches to the genetic effects of A-bomb radiation exposure, the children for study would already be identified.

With this decision, Dr. Schull and I then embarked on the definitive analysis of the results of these six years of study. A total of 76,626 infants had been seen during the course of the program. The results of the preliminary analyses were all confirmed, and the program and its findings then written as a book entitled, *The effect of exposure to the atomic bombs on pregnancy termination in Hiroshima and Nagasaki*, published in 1956 by the National Academy of Sciences–National Research Council.

In those days, it seemed that the most important and appropriate use of the data was to set limits, at specified probability levels, on the effects of the exposure on sex ratio, congenital defects, stillbirths, or neonatal deaths. This we did in the final chapter of the book. It was to be more than 34 years before these same data, combined with the data resulting from later innovations in the genetics program and dramatically revised dosimetry procedures, plus advancing understanding of human genetics, would permit an estimate of that most important of radiation parameters for humans, the genetic doubling dose. (See Neel et al., *Am J Hum Genet* 46:1053–72, 1990.) ❑

Acknowledgment—The author is indebted to Dr. W.J. Schull for refreshing his memory about a number of details.

Japanese Midwives

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if not terribly enlightening, remarks; indeed, they characterized our whole professional staff.

However, if she thought it necessary, we would see that the physician in question apologized to the midwife. Invariably, she would say, with a half-suppressed smile—for she too understood the need to preserve protocol—that she appreciated what we proposed to do, but did not believe so drastic a step was necessary. She would call the midwife and tell her of our visit and concern, and assure her that she, Mrs. Yamamoto, was confident that this would not happen again.

Although different in their manner and appearance, both Mrs. Yamamoto and Mrs. Murakami were obviously respected by the members of their associations for their skill, experience, and diplomacy—particularly concerning the relationship between the associations and the Commission. Mrs. Yamamoto, whom I knew better, was a tiny, wizened woman who usually wore the small-patterned, conservatively colored kimonos seemly for her age; she was in her late sixties. Her hair was drawn sharply back from her face. Her skin, etched with age, was swarthy, and she appeared so fragile one was fearful for her with each movement. Soft-spoken, her speech studded with honorifics, she seemed like everyone's grandmother. But the twinkle lurking in her eye and the vigor with which she managed the midwives and their affairs revealed no frailty.

Mrs. Murakami was a more sturdily built, somewhat younger, round-faced woman who was no less cordial than Mrs. Yamamoto and administered her association just as effectively.

Both Mrs. Yamamoto and Mrs. Murakami are now deceased; however, they are survived not only by the many infants they delivered but also by the genetics program to which they contributed so unstintingly. ❑

News Briefs
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✓ RERF Contributes to *JAMA* Radiation Effects Issue

Three invited articles on the cancer risk among atomic-bomb survivors and their children, written by **Yasuhiko Yoshimoto**; **Yukiko Shimizu, Hiroo Kato** and longtime associate **William J. Schull**; and former ABCC pediatrician-in-charge **James Yamazaki**, appear in the 1 August issue of the *Journal of the American Medical Association*, which focuses upon the health effects of radiation exposure. (For bibliographic details, see page 12 of *Update*.)

Shigematsu and A.N. Yakovlev, member of the Presidential Council of the USSR (Kuramoto in background).

✓ Japanese Team Wants to Begin Chernobyl Medical Aid this Year

After returning from a seven-day visit to the affected areas, members of the Chernobyl Nuclear Power Plant Accident Research Team announced in Moscow on 14 August their desire to begin providing medical support by the end of the year to the Soviet teams assisting victims of the Chernobyl accident. The nine-member group, led by **Yohei Sasakawa**, chairman of the Japan Shipbuilding Foundation, also included RERF Chairman **Itsuzo Shigematsu** and **Atsushi Kuramoto**, director of Hiroshima University's Research Institute for Nuclear Medicine and Biology.

Shigematsu noted that the program, sponsored by the Sasakawa Health Cooperation Foundation, would have a ¥5-billion budget (about US$33 million) over the next five years, and would provide medical equipment, medicines, and reagents for clinical tests to institutions in the exposed areas; donate a number of examination cars; send Japanese medical experts to the affected areas; and bring Soviet medical staff to Japanese institutions for training.

✓ Soviet Scientists Visit RERF

In July, seven Soviet experts in radiation medicine arrived for a four-day visit at RERF and other medical and research institutions in Hiroshima where survivors are treated and radiation effects are studied. Part of a larger group in Japan for a joint Japanese–Soviet seminar on radiation effects held in Tokyo, the visitors were **Anatoly E. Romanenko, Olga A. Tsvetkova**, and **Maria Pilinskaya**, All-Union Scientific Center of Radiation Medicine, Kiev; **Anatoly F. Tsyb** and **Victor K. Ivanov**, Research Institute for Medical Radiology, Obninsk; **Sergey V. Petrenko**, Byelorussian Ministry of Health; and **Gennady N. Sushkevich**, USSR Ministry of Health.

✓ First IAEA Health Study Team Leaves for USSR

An International Atomic Energy Agency-sponsored health study team departed for the Soviet Union late in August to provide medical care to persons affected by the Chernobyl power plant accident. The six-person team, which included RERF research associates **Hideo Sasaki** and **Shizuyo Kusumi** from the Hiroshima Laboratory and **Naokata Yokoyama** of the Nagasaki Laboratory, spent two weeks in the USSR. At the beginning of October, two more teams were dispatched by the IAEA.

✓ Highlights of Lecture Program

On 10 July, **Joe W. Gray**, Lawrence Livermore National Laboratory, Livermore, Calif., presented a lecture on chromosome painting as a new fluorescence in-situ hybridization technique for detecting chromosomal mutations.

Kazutaka Kogi, International Labour Organization, Geneva, lectured on the ILO's experience in the protection of worker health on 16 July.

James E. Trosko, RERF chief of research, lectured on a new integrative view of carcinogenesis mechanisms on 7 September.

✓ Research Staff News

Hiroshima

Department of Clinical Studies: **Kazuo Neriishi**, chief of the Division of Medicine, has been appointed occupational health physician, replacing **Saeko Fujiwara**, who is an associate senior scientist in the Division of Medicine.

Fujita

Department of Epidemiology: Research associate **Elaine Ron** has begun a one-year stay at the Hiroshima Laboratory, where she will be involved in US National Cancer Institute studies of benign tumors.

Department of Epidemiological Pathology: **Shoji Tokuoka** has been appointed a senior consulting scientist. His activities will include pathological research, lipid pathology, and tumor registry-related studies.

Department of Radiobiology: **Xumin Tu**, Laboratory of Industrial Hygiene, Beijing, will spend one year in the Laboratory of Immunology as a visiting research fellow. He will learn immunology and molecular biology techniques for testing immune function and genetic alterations in radiation-exposed people.

Department of Statistics: **Shoichiro Fujita** has been promoted to senior scientist.

Nagasaki

Department of Clinical Studies: **Kiyosumi Oishi** and **Hiroaki Nonaka** have been appointed research associates in the Division of Medicine. Both were previously at Nagasaki University—Oishi in the First Department of Medicine, Nonaka at the Radiation Institute of Nuclear Medicine. ❑

Errata

✏ In *RERF Update* 2(2):3, 1990, "Induced trisomies revisited," the equation under Table 1 showing the doubling dose should read as follows:

$$\text{Doubling dose} = \frac{3.0 \cdot 10^{-3}}{9.3 \cdot 10^{-4}} = 3.2 \text{ Gy}.$$

✏ In *RERF Update* 2(2):4, 1990, "Vast RERF database supplies aging clues," the *y* axes of Figures 1 and 2 should read: "per 1000 person-years."

International Oral Presentations

International Symposium on Flow Cytometry and Image Analysis for Clinical Applications, Morioka and Hanamaki, Japan, 1–3 July 1990.

➪ *Detection of somatic mutation in atomic bomb survivors by flow cytometry.* M Akiyama, S Kyoizumi, J Kushiro, Y Kusunoki, Y Hirai, N Nakamura.

➪ *Dose-response relationship for chromosome aberrations in Hiroshima atomic bomb survivors.* AA Awa, K Ohtaki.

Advances in Environmental Mutagenesis and Carcinogenesis (US–Japan Joint Conference), Tokyo, 16–17 July 1990.

➪ *Detection of somatic mutations in humans.* M Akiyama, N Nakamura, S Kyoizumi, J Kushiro, Y Kusunoki, Y Hirai.

The 12th Scientific Meeting of the International Epidemiological Association, Los Angeles, Calif., 5–9 August 1990.

➪ *Association of blood pressure and stroke incidence in a Japanese population—a 26-year follow-up, Hiroshima/Nagasaki study.* H Sasaki, K Kodama, Y Shimizu, M Akahoshi.

➪ *Long-term survival rate after the first event of myocardial infarction in a fixed Japanese population—Hiroshima/Nagasaki study.* K Kodama, H Sasaki, Y Shimizu, M Akahoshi, Y Hosoda.

The 15th International Cancer Congress, Hamburg, Federal Republic of Germany, 16–22 August 1990.

➪ *Breast cancer risk among atomic bomb survivors exposed as children: Hiroshima and Nagasaki.* M Tokunaga, S Akiba, CE Land.

➪ *Neuroblastoma with DNA amplification and rearrangement in the N-myc gene region.* E Hiyama, K Hiyama, T Yokoyama.

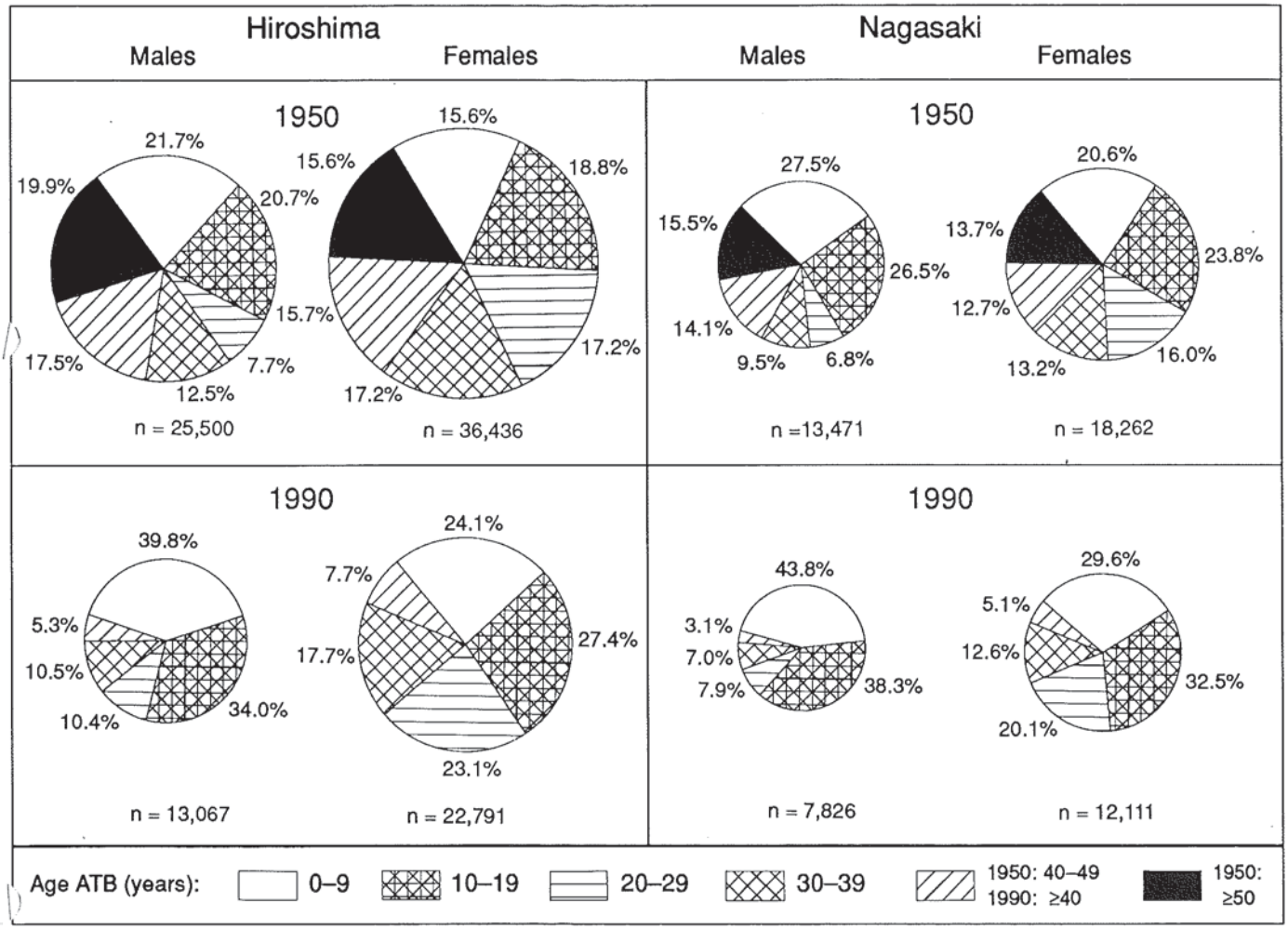
The 5th Congress of the World Federation of Nuclear Medicine and Biology, Montreal, Canada, 26–31 August 1990.

➪ *The prevalence of thyroid disease in the atomic bomb survivors in Nagasaki.* S Nagataki. N Yokoyama, S Inoue, K Shimaoka, H Hirayu, M Izumi. ❑

The LSS Cohort: Distribution of Age ATB

The age distribution for Life Span Study members who were in Hiroshima and Nagasaki at the time of the bombings (ATB) is presented according to city and sex for this population as it was defined in 1950 and includes those assumed to be living at the beginning of 1990. Since more than 99.5% of those over the age of 50 ATB had died by the beginning of 1990, the 40–49 and ≥50 age ATB categories are combined in the 1990 figures.

Because of the age- and sex-matching used in defining the cohort, the age and sex distribution reflects that of survivors who were in the city and near the hypocenter ATB. Thus, there is a deficit of young adult males, particularly in Nagasaki. ❑



The LSS Reports

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often complex equations into patterns of risk is not easy.

In addition, because of the numerous diseases considered in the analyses for LSS reports, a common model is fit and a standard set of tests is used for most diseases. While this helps to avoid overfitting and overinterpretation, it can also lead to neglect of important issues which should be considered for specific diseases. Graphs of dose-response functions or of dose-effect modification for fixed doses are useful, especially if the plots can be used to show how well the fitted model describes the data. Because of the multivariate nature of the LSS data this is generally not easy to do.

In the course of our work on Report 12 and related studies, we plan to make a major effort to improve methods for summarizing and displaying data on disease risk following radiation exposure. The development of better methods for summarizing radiation risks will lead to improvements in virtually all RERF reports. We would appreciate hearing about the types of risk summaries which would be useful in your work with RERF results.

In conclusion, although the LSS reports have done a good job of summarizing the mortality experience of the LSS cohort, it is important to consider how the reports should evolve. This is especially true in view of the increasing importance of tumor registry and AHS data in our understanding of radiation effects.

In particular, we feel that the Epidemiology and Statistics departments should produce more short, detailed topical reports, whereas the major LSS reports should place more emphasis on summarizing and reviewing the important epidemiological findings published since the last report. The LSS reports must also continue to provide basic information on the current status of and recent changes in the LSS cohort including the presentation of cause-specific risk estimates.

It is also important to continue the recent practice of releasing a detailed person-year and case-count tabulation in conjunction with the publication of the major LSS reports (see *RERF Update* 2(1):9, 1990). During the next few years, we hope to develop procedures which will simplify the production of the LSS reports and thus allow RERF's statisticians and epidemiologists to direct their efforts toward producing a broader range of timely reports on specific aspects of the cohort experience. ❑

Recent Scientific Publications

Approved Technical Report

Hyperparathyroidism among atomic bomb survivors in Hiroshima, 1986–88. S Fujiwara, H Ezaki, R Sposto, S Akiba, K Neriishi, K Kodama, K Yoshimitsu, Y Hosoda, K Shimaoka. **RERF TR 8-90.**

During the two-year period from August 1986 to July 1988, the prevalence of hyperparathyroidism (HPT) was determined among A-bomb survivors and unexposed control subjects in Hiroshima. The diagnosis of HPT was determined biochemically, based upon the presence of consistent hypercalcemia and elevated serum parathyroid hormone levels. Among a population of 4,675 individuals (1,527 males and 3,148 females), primary HPT was diagnosed in 22 (3 males, 19 females). Of these, 8 underwent surgery, of whom 6 had a single parathyroid adenoma, and 2 had parathyroid hyperplasia.

HPT was more prevalent among the A-bomb survivors who received higher radiation doses ($p < .001$ for linear trend). The prevalence rates predicted from the model were 0.204% (±0.094%) at 0 Gy and 0.893% (±0.237%) at 1 Gy. The background rate of HPT did not differ significantly by sex or by age at the time of the bombing, although the effect of radiation exposure was greater for individuals exposed at a younger age ($p < .01$).

Publications in the Open Literature

Absence of correlations between radiosensitivities of human T-lymphocytes in G_0 and skin fibroblasts in log phase. J Kushiro, N Nakamura, S Kyoizumi, M Nishiki, K Dohi, M Akiyama. *Radiat Res* 122:326–32, 1990. (RERF TR 17-89)

The children of parents exposed to atomic bombs: Estimates of the genetic doubling dose of radiation for humans. JV Neel, WJ Schull, AA Awa, C Satoh, H Kato, M Otake, Y Yoshimoto. *Am J Hum Genet* 46:1053–72, 1990.

Radiosensitivity of skin fibroblasts from atomic 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. *Cancer Res* 50:4050–5, 1990. (RERF TR 6-90)

Smoking and serum proteins in atomic-bomb survivors in Japan. DO Stram, S Akiba, K Neriishi, RG Stevens, Y Hosoda. *Am J Epidemiol* 131:1038–45, 1990. (RERF TR 3-89)

Cancer risk among children of atomic bomb survivors. A review of RERF epidemiologic studies. Y Yoshimoto. *JAMA* 264:596–600, 1990.

Cancer risk among atomic bomb survivors. The RERF Life Span Study. Y Shimizu, WJ Schull, H Kato. *JAMA* 264:601–4, 1990.

Perinatal loss and neurological abnormalities among children of the atomic bomb. Nagasaki and Hiroshima revisited, 1949 to 1989. JN Yamazaki, WJ Schull. *JAMA* 264:605–9, 1990.

Risk estimates: Past, present, and future. S Abrahamson. *Health Phys* 59:99–102, 1990.

Spontaneous loss and alteration of antigen receptor expression in mature $CD4^+$ T cells. S Kyoizumi, M Akiyama, Y Hirai, Y Kusunoki, K Tanabe, S Umeki. *J Exp Med* 171:1981–99, 1990. (RERF TR 22-89)

Detection of deletions, insertions and single nucleotide substitutions in cloned β-globin genes and new polymorphic nucleotide substitutions in β-globin genes in a Japanese population using ribonuclease cleavage at mismatches in RNA:DNA duplexes. K Hiyama, M Kodaira, C Satoh. *Mutat Res* 231:219–31, 1990. (RERF TR 1-90)

Studies on chromosome aberrations and HPRT mutations in lymphocytes and GPA mutation in erythrocytes of atomic bomb survivors. M Akiyama, S Kyoizumi, Y Hirai, M Hakoda, N Nakamura, AA Awa. In: *Mutation and the Environment. Part C.* Edited by ML Mendelsohn, RJ Albertini. New York, Wiley-Liss, 1990.

Publications of Interest Using RERF Data

Selection effects in the survivors of the atomic weapons explosions in Japan. MP Little, MW Charles. Nuclear Electric Technical Division Report TD/RPB/REP/0001, 1990. *Health Phys* (in press).

Pre-conception exposure risks in the Sellafield workforce and the Japanese bomb survivors. MP Little. Nuclear Electric Technical Division Report TD/RPB/REP/0026, 1990. *J Radiol Prot* (in press).

Theoretical and epidemiological evidence for time variations in radiation-induced cancer risk and implications for population cancer risks. MP Little, MW Charles. Nuclear Electric Technical Division Report TD/RPB/REP/0002, 1990. *J Radiol Prot* (submitted). ❑

Elected Representatives Visit RERF

In early August, five newly elected members of Japan's parliament, the Diet, visited RERF as part of a project that coincided with the 45th anniversary of the atomic bombing. Sponsored by the Hiroshima International Cultural Foundation, the three-day program provided a chance for 15 "freshmen" representatives—most of whom have never personally experienced war—to speak with A-bomb survivors, attend commemorative events, and to participate in a multiparty symposium on the future of Japan's political role in world affairs.

Visitors to RERF's Hiroshima Laboratory were: **Toshiko Hayashi**, Proportional Representation District, House of Councilors; and from the House of Representatives—**Tadatoshi Akiba**, Hiroshima First District; **Yoshito Sengoku**, Tokushima Prefecture District; **Osamu Shibutani**, Tokyo Ninth District; and **Tomiko Okazaki**, Miyagi First District.

More than 200 new representatives won seats during Japan's most recent elections.

"Most of them are of a generation that does not know war," commented **Hiroshi Miyazawa**, a veteran House of Councilors member. "It will be meaningful to have young politicians listen to the voice of Hiroshima and give thought to the world of tomorrow." ❑

RERF **update** RERF

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