RERF update RERF

News & Views from the US–Japan Radiation Effects Research Foundation
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Health Effects Reported at IPPNW Congress

Summarizing health effects data accumulated during some 40 years of follow-up in Hiroshima and Nagasaki, RERF researchers opened the colloquium segment of the first Asian meeting of the International Physicians for the Prevention of Nuclear War (IPPNW), held in the two cities 5–12 October. About 3,000 doctors and 2,000 medical students from 76 countries attended the organization's ninth congress.

Choosing Hiroshima and Nagasaki as the meeting venues was intended to focus on the human dimensions of the first use of nuclear weapons in 1945. The IPPNW, awarded the 1985 Nobel Peace Prize, is renowned for its efforts to increase public awareness of the aftermath of nuclear warfare.

IPPNW co-presidents **Bernard Lown**, a Harvard cardiology professor, and **Mikhail Kuzin**, director of the First Moscow Medical School's Surgical Clinic, stated in a joint message: "Although we will continue to study the medical consequences of nuclear war in scientific sessions. . . , this congress will place great emphasis on the experience of Hiroshima and Nagasaki, and on those who were the victims of the atomic attacks. Congress sessions will emphasize the moral and spiritual aspects of the nuclear arms race, for too often we see the issues only as scientific and political."

The opening session, "Radiation effects update: the Hiroshima/Nagasaki experience," was moderated by RERF Chairman **Itsuzo Shigematsu**, who explained that the binational RERF program—upon which the session's reports were based—consists of the follow-up of a fixed cohort of atomic-bomb survivors which was established in 1950.

Research Associate **Yukiko Shimizu** of RERF's Epidemiology Department spoke about cancer mortality and cancer incidence among participants in the long-term Life Span Study. Specifically, she related that leukemia mortality among A-bomb survivors peaked 5–6 years after the bombings but has decreased with time; that the incidence of leukemia and multiple myeloma, as well as the incidence of cancer of the lung, breast, esophagus, stomach, colon, thyroid, ovary, and urinary tract increases with dose; and that factors appearing to modify radiation effects include age at the time of exposure and sex, i.e., radiation sensitivity in terms of cancer induction appears to be greater for persons who were young at the time of the bombings.

RERF Genetics Department Chief **Akio A. Awa** discussed evaluations of the genetic effects of atomic radiation, based on the frequency of untoward pregnancy outcomes, deaths among live-born children, chromosome abnormality frequency, and the frequency of an altered protein among children. Although no statistically significant effects have emerged for these indicators, genetic damage may have been produced in parental germ cells by ionizing radiation exposure. Taking the present data at face value, however, it has been postulated that humans may be less sensitive to radiation than previously has been assumed.

In a summary of cancer risk among the children of A-bomb survivors, RERF Epidemiology Research Associate **Yasuhiko Yoshimoto** focused on children who were exposed to A-bomb radiation in utero and the so-called F_1 population, or those conceived after the bombings whose parents (one or both) survived the event.

Since an increased risk of cancer proportional with dose has been observed among A-bomb survivors, a similar occurrence among the in utero-exposed could perhaps be attributed to somatic mutation. However, only 18 cancer cases of any kind were identified from 1950–1985. It did appear that cancer risk increased with an increased maternal uterine dose, but since the number of cases is inadequate for a site-specific analysis, such an increase can not definitely be attributed to A-bomb radiation.

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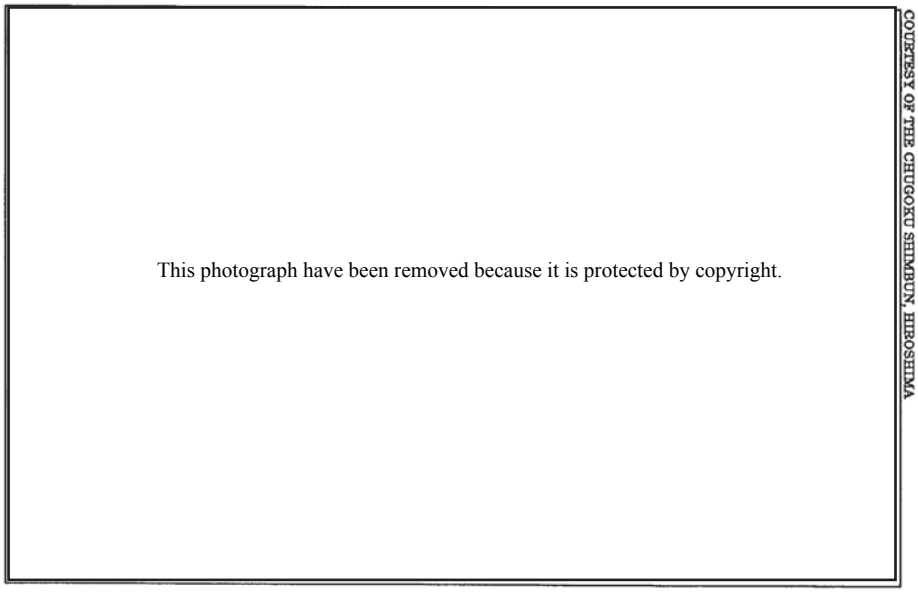

COURTESY OF THE CHUGOKU SHIMBUN, HIROSHIMA

Above, RERF Research Associate Kazuo Neriishi draws blood from Soviet firefighter Leonid Telyatnikov for use in chromosome aberration studies. Telyatnikov, who helped extinguish the fire caused by the Chernobyl nuclear power plant accident, attended the ninth annual IPPNW meeting with a Soviet delegation. The meeting attracted to Hiroshima and Nagasaki thousands of physicians, who had a chance to listen to numerous radiation-exposed persons, including fellow IPPNW members who survived the aftermath of the first use of nuclear weapons.

Perspectives

An Eye towards the Future

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

This issue concludes the first volume of *RERF Update*. Judging from the letters you have written, it appears to have been received well, which provides us with a strong stimulus to continue on our present course. But nothing made by man cannot be improved upon, so we will try to further develop the newsletter with respect to readability and scientific quality. One change we would like to see is more input from people outside RERF.

In this issue, you will find two articles that begin to realize that goal: one by **William H Ellett** from the National Research Council and one by **James V. Neel** (who is not exactly an outsider, of course), professor emeritus of human genetics and internal medicine at the University of Michigan Medical School. In future issues, you will see more of these invited contributions. But we would be delighted if readers of *Update* would feel the urge to contribute even though they have not explicitly been invited to do so.

Another new feature in this issue is the start of what promises to be a long series of articles on the history of the Atomic Bomb Casualty Commission and the Radiation Effects Research Foundation. We will make particular efforts to have major players in the historical events that shaped our organization give an eyewitness account, especially covering the *histoire humaine* rather than just the facts.

We have always been, in fact if not de jure, a binational organization, and the 40-year-long cooperative program between American and Japanese nationals has stimulated some interesting events along the way. In the early days, ABCC found itself in a completely Japanese environment, amidst the rubble of total devastation, where military governmental regulations influenced the vagaries of everyday life. There must have been a tremendous contrast between this outside world and inside ABCC where, notwithstanding the large number of Japanese employees, the environment was definitely Western, with compromises to the Japanese way (and tempo) of life where necessary. As one author of a 1953 book tells it, "All this appeared to make [ABCC] a so-called 'little foreign country' entirely different from Hiroshima." This peculiar nature of our operations created tensions, some temporary and resolved by adaptation, some of a deeper and therefore more extended character, some still present today.

We hope to be able to shed some light on the binational aspects of our work also, both from an American as well as a Japanese perspective. Dr. Neel's article is an excellent beginning, and we hope that it sets a standard for future historical contributions. In our next issue, readers can look forward to a piece by **Koji Takeshima**, who is mentioned in Dr. Neel's article.

During the upcoming year, we heartily encourage reader participation in our letters to the editor column, "Feedback." By doing so, we are endeavoring to make *Update* a forum for exchanging and even debating the important and sometimes controversial issues inherent to radiation effects research. We will consider part of our mission accomplished if the kind of material published in *Update* evokes enough of a reaction to stimulate exciting feedback—or even just static—from our readers.

Finally, send your suggestions and recommendations. There is an abundance of material that will eventually see the light, but it would help us to know about particular desires among our readership. *Update* is for you, so keep your letters coming! ❑

IPPNW Congress

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The F_1 population is being followed up to determine if these subjects have an increased cancer risk due to the presence during fertilization of radiation-induced mutations of sperm cells or ova. A study of cancer among F_1 subjects who were under the age of 20 from 1946–1982 showed no significant increase in the cancer risk related to parental gonadal dose.

Professor **Michito Ichimaru** of Nagasaki University's Atomic Disease Institute described special features of possible radiation-induced leukemia and discussed the leukemogenic mechanisms of A-bomb radiation.

Although leukemia risk peaked in 1951, the risk of chronic myelogenous leukemia (CML) still remains slightly elevated in Hiroshima. The threshold for CML development may be less than 0.5 Gy in Hiroshima, whereas statistical analyses indicate the threshold for acute leukemia may be about 1 Gy. With doses in excess of 1 Gy, no promyelocytic or monocytic leukemia has been observed.

Research Associate **Masaharu Hoshi** of Hiroshima University's Research Institute for Nuclear Medicine and Biology explained continuing efforts to refine dose estimates which are used with the results of epidemiological studies of cancer among survivors to calculate radiation exposure risk estimates. The comprehensive reassessment that resulted in the DS86 system reviewed: 1) weapons yield, 2) radiation energy spectra, 3) radiation air transport, 4) house shielding, and 5) organ dose. After reappraisal of components 1–3, in Hiroshima at a typical location 1.5 km from hypocenter, the neutron dose was reduced to one-tenth and the gamma dose was increased twofold. In Nagasaki, the neutron and gamma doses were reduced to about 50% and 75%, respectively. Consideration of components 4 and 5 produced a maximum change to about one-half. (See page 3 for a discussion of continuing efforts to verify neutron activation in both cities.) ❑

News Briefs

✓ RERF Department Chief in IPPNW Panel Discussion

In early October, **Kiyohiko Mabuchi**, who is concurrently serving as chief of the Departments of Epidemiology and Epidemiologic Pathology, spoke about the acute and long-term effects of radiation as part of an IPPNW discussion session titled, "After the war." (See related story on page 1.)

✓ Soviet Scientists Apprised of Foundation's Research

Valentin Pokrovsky and **Leonid Ilyin**, president and vice president, respectively, of the Soviet Academy of Medicine, and **Nicolai Bochkov**, director of the Soviet Institute of Genetic Medicine, visited the Hiroshima and Nagasaki laboratories of RERF in October. Department chiefs summarized ongoing research projects, in a further effort to cooperate with Soviet scientists who are in the early stages of following up the population affected by the Chernobyl nuclear power plant accident.

✓ Present Status of DS86 Reviewed

Dean Kaul, **William Woolson**, and **Steven Egbert** of Science Applications International Corporation (SAIC) visited RERF for two weeks in early November to discuss the current status of and obtain additional information needed for enhance-

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New Risk Estimates for Trisomy Induction by Radiation Exposure

Recent mouse radiation experiments and new techniques employing human sperm now permit new approaches to estimating trisomy induction in live-born children.

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

In recent reevaluations of the genetic risks associated with ionizing radiation, neither the UNSCEAR nor the BEIR committees appear to have altered their previous estimates regarding induced aneuploidy. Yet, two rather recent papers have provided pertinent information that can be employed in such a risk assessment. We shall attempt to use this information to estimate the expected outcome of the RERF cytogenetic analysis of the offspring of A-bomb survivors. We will be concerned primarily with the induction of trisomy, i.e., the presence of an additional chromosome in the gametes resulting in 24 chromosomes instead of the normal 23.

For estimating human risk, a recent paper by Griffin and Tease (*Mut Res* 202:209–13, 1988) provided the stimulus to extrapolate from gamma-ray chronically induced trisomy in mouse immature oocytes, and to derive an estimate of the expected number of such cases among the A-bomb survivors' offspring for comparison with the observed values. Prior to this study, no increase in aneuploidy in immature oocytes had been observed after radiation exposure. This cell type occurs at a critical stage in the female germ line, as it is present in the ovary from birth until fertilization—as much as 40 years later—accumulating potential damage in this undivided state. Trisomy occurring in oocytes is therefore extremely important when assessing induced genetic damage.

Martin et al. (*Mut Res* 174:219–25, 1986) examined human sperm chromosomes (which fertilized hamster eggs) from a series of males who received radiotherapy treatment months to years before cytological examination of their sperm. Before irradiation, their sperm was also sampled to serve as controls. The spermatogonial cells were the germ cell stage exposed, the most critical stage for risk assessment purposes in males because of their long-lived stem cell function. Post-gonial stages have a very short developmental life span of about 100 days. Thus, damage induced at the spermatogonial stage can be perpetuated over the entire reproductive life span to many descendant germ line cells.

In the following analysis, we adopt several assumptions that provide for conservative risk estimates.

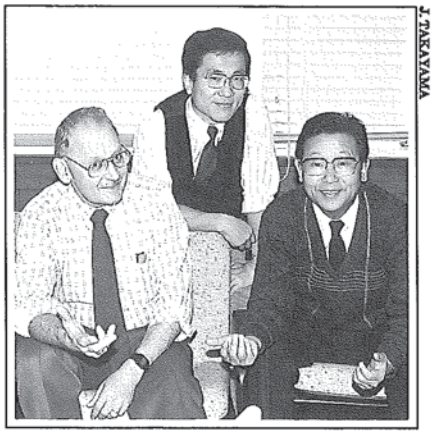
First, the dose-response relationship is assumed to be linear at low doses. This assumption is likely to result in an overestimation of nondisjunction, i.e., the failure of a pair of chromosomes or chromatids to properly separate, since the mechanisms of this class of mutational events are not well understood.

Second, induced aneuploidy events are random with respect to the different chromosome pairs of the human genome. "Spontaneous" events seem to show preferential involvement of some chromosomes.

Third, a dose rate effectiveness factor of 2 is used when extrapolating from chronically delivered doses to acutely delivered doses in the range of 1 Gy.

From Griffin and Tease's 0-Gy, 1-Gy and 2-Gy data, we derive a regression coefficient of 0.01 trisomies per gray per gamete.

In method 1, we assume that the induced rate for humans will be higher because of the larger chromosome number. Adjusting for the increased number, (x/0.01 = 46/40), suggests a human rate of 0.012/Gy ± 0.005.



J. TAKAYAMA

From left, coauthors Abrahamson, Nakamura, and Awa.

The observed spontaneous trisomy rate scored in mouse oocytes in Meiosis II was 0.0032. In humans, the spontaneous trisomy rate, 0.003, is the value derived from Table 2 of the genetics chapter in UNSCEAR 1982 (*Ionizing radiation: sources and biological effects*, Report A/37/45, pp 425–569, 1982) for complete trisomies in 67,000 newborn infants; the inclusion of mosaics would increase the frequency to 0.0038. It is also important to note that about 50% of the trisomies in newborns is of the sex chromosome type.

In method 2, we assume that the human spontaneous-to-induced ratio will parallel that of the mouse, i.e., if x/0.003 = 0.01/0.032, x = 0.009/Gy.

Thus, both approaches suggest a rate of between 0.9 and 1.2%/Gy/gamete. To be conservative, we use the higher induction rate. Prior information indicates that nearly 90% of this frequency will result in peri-implantation loss and fetal death.

Trisomies involving chromosomes 13, 18, 21, or X and Y are the most frequent among live-born aneuploids. Therefore, the probability of producing these trisomic gametes is $2 \cdot 10^{-3}$ per Gy (0.012 · 4/23), a meaningful contribution to the usual values reported as risks to the first generation following maternal exposures to low doses or low dose rates. About 50% of this frequency, $1 \cdot 10^{-3}$ per Gy, will be viable sex chromosome trisomies (UNSCEAR, loc. cit.). The values cited could be twice as large for high dose and dose rate exposures.

We next examine the data from the human spermatogonial study of Martin et al. (loc. cit.). The mean acutely delivered gonadal dose measured by TLD was 0.86 Gy. From the data presented, there were 5 hyperhaploidy events and 16 hypohaploidy events, counting each chromosome gain or loss as a separate event (the authors did not do so) for a total of 21 events in 149 sperm complements examined for a 0.141 frequency. The authors also stated that the control frequency of hyperhaploidy was 50% of the total aneuploid frequency. Given this information, our calculations for viable hyperhaploid induction are as follows:

A. Total aneuploid (exposed) = 0.141 ± 0.029
B. Total hyperhaploid (exposed) = (0.141 · 5/21) = 0.034
C. Total aneuploid (control) = 0.052
D. Total hyperhaploid (control) = 0.052 · 0.5 = 0.026
E. Total hyperhaploid (induced) = (B – D) = 0.008/0.86 Gy
F. Total hyperhaploid (induced) = $9.3 \cdot 10^{-3}$/Gy

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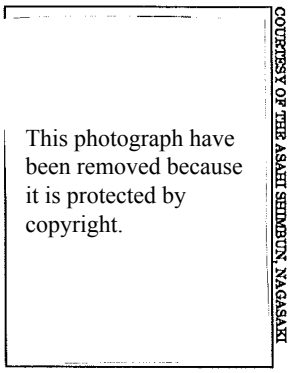
Pediatrician's Book to Focus on Child Survivors

When American-born James Yamazaki arrived in Nagasaki in 1949 to become ABCC's physician-in-charge and pediatrician, the 33-year-old barely spoke the language and was undoubtedly a foreigner in his father's homeland.

This unusual two-year stint in postwar Japan marked the beginning of Yamazaki's life-long involvement in radiation effects research that has included several interdisciplinary studies of the radiosensitivity of the developing brain.



COURTESY OF THE ASAHI SHIMBUN, NAGASAKI

Yamazaki during his recent visit to Japan.

Returning once again to Nagasaki and Hiroshima, Yamazaki rekindled his own memories and those of numerous *hibakusha* (A-bomb survivors) during interviews he recorded this fall. Preparing a book for the University of California Press, Yamazaki will target his work at college students, young parents, and teachers.

"My main purpose is to help the generations that did not experience World War II to understand the scope of happenings during that time period," explained Yamazaki, who is professor emeritus of pediatrics at the UCLA School of Medicine. "Nearly half of the world's current population had not been born yet, and thus these later generations are only peripherally aware of the tragedies that occurred during the Second World War."

A WWII veteran who served in Europe, Yamazaki exhibits a pediatrician's concern for those who at the time of the bombing were children or were in utero. By interweaving scientific data and anecdotal experiences, both the psychosocial and medical aspects of the survivors' lives, as well as the history of relevant radiation research, will be chronicled.

Encouraged to join the ABCC undertaking by a mentor who had spent time in China, Yamazaki was assigned by the National Research Council to study the effects of radiation on fetal development. Already in the mid-1940s, multiple environmental factors were being considered in the etiology of congenital malformation. Thus, after a short tutelage in teratology, Yamazaki found himself in Kyushu providing pediatric support to ABCC's genetics program.

"In Nagasaki, the study design was entirely different from that in Hiroshima," the 73-year-old recalled. "We monitored entire pregnancies—not just malformations at birth.

"In our original report [*Amer J Dis Child* 87:448–63, 1954], we could not conclude that microcephaly, mental retardation or growth impairment were solely due to radiation, because so many factors—directly or indirectly related to the bombing—could have had an adverse effect upon the fetus. Only the continuing studies over four decades by Miller, Woods, Schull, Otake and others at ABCC–RERF have demonstrated conclusively that the developing brain is one of the most radiosensitive tissues in the human."

In some cases eagerly sought out by *hibakusha* during his recent visit, Yamazaki ". . .wanted to know what they've been thinking for the past 40 years, what has gone into their data banks."

"For most, the wound ruptures open again," said Yamazaki, "but not out of bitterness. Instead they expressed a deep grief about the loss of parents. Even after all these years—most being in their 50s and 60s—they still miss their parents very much."

Yamazaki, who hopes to complete his book within a year, also noted that aging *hibakusha* parents of microcephalics and the mentally retarded express great anxiety about the future of their handicapped children—some of whom require full-time care. ❑

Trisomy Induction

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G. Viable trisomies = $(9.3 \cdot 10^{-3} \cdot 4/23)$ = $1.6 \cdot 10^{-3}$/Gy (acute high dose exposure)

H. Viable trisomies = $0.8 \cdot 10^{-3}$/Gy (chronic exposure)

I. Viable sex chromosome trisomies (G · 0.5) = $0.8 \cdot 10^{-3}$/Gy (acute)

J. Viable sex chromosome trisomies (I · 0.5) = $0.4 \cdot 10^{-3}$/Gy (chronic)

Thus, the male contribution to viable induced aneuploidy, while less than the female contribution, was in itself greater than that estimated by most previous national and international reports. But when combined with the female contribution, it is in agreement with recent U.S. Nuclear Regulatory Commission estimates (*Health effects models for nuclear power plant accident consequence analysis. Low LET radiation. Part II. Scientific bases for health effects models,* NUREG/CR-4214, 1989) or the estimates derived in a different manner by Oftedal and Searle, representing an ICRP Task Group (*J Med Genet* 17:15–20, 1980). Moreover, since our extrapolations are derived from studies with small sample sizes, the estimates could easily range over a factor of 2. Collectively, the data for both sexes suggest that a rate of 28 trisomy cases per 10^4 live born per gray may not be an unreasonable estimate. The doubling dose is then estimated as follows for viable trisomies:

$$\text{Doubling dose} = \frac{3 \cdot 10^{-3}\ \text{spontaneous}}{2.8 \cdot 10^{-3}\ \text{induced/Gy}} \cong 1\ \text{Gy (chronic).}$$

The most recent RERF cytogenetic studies on the offspring of exposed parents (Awa et al., RERF TR 21-88) found no increase in sex chromosome abnormalities when compared to the offspring of unexposed parents. In the initial studies, there were 8,322 children of exposed parents—either one or both of whom were exposed to A-bomb radiation—and 7,976 children of nonexposed parents. Now the new DS86 dosimetry program has reduced the number to 6,626 offspring with a parental dose of 0.001 Gy or higher. There were 15 (10–27 lower and upper bounds) sex trisomies in this group for a frequency of $2.3 \pm 1.1 \cdot 10^{-3}$, compared to 18 (9–27 lower and upper bounds) cases in 7,174 children from unexposed parents ($2.5 \pm 1.2 \cdot 10^{-3}$). The remaining group of 1,696 primarily consists of children whose parents can not be assigned doses at present.

There were 4,396 children of exposed mothers whose mean dose was 0.41 Gy. Therefore, we calculate that the expected number of maternally induced sex trisomies would be: $4{,}396 \cdot 0.41\ \text{Gy} \cdot 2 \cdot 10^{-3}$ sex trisomies/Gy (acute exposure) = 3.6 cases.

There were 2,230 offspring born to exposed fathers with a mean dose of 0.52 Gy. The expected number of paternally induced cases is therefore: $2{,}230 \cdot 0.52\ \text{Gy} \cdot 0.8 \cdot 10^{-3}$/Gy (acute exposure) = 1 case.

Thus, it is reasonable to conclude that no more than 5 cases might have been induced based on the above predictions, and about half as many cases if acute high dose conditions are not applicable. It would, therefore, not have been surprising to observe no significant alteration in sex trisomy frequency between the two groups if our risk estimates are valid.

Finally, the estimated number of 28 induced cases per 10^4 live born per gray could increase the present risk estimates by at least 25% for total first generation effects. This suggests that continued research efforts in both humans and the mouse should be directed at extending the studies that served as the springboard for our estimates. Indeed, other mammalian species could also be studied using the general techniques that have been developed. ❑

The Neutron Activation Issue

Neutron activation data, at least in Hiroshima, indicate that estimated activation decreases with distance more rapidly than the measured values do. The author, who has been involved in the dose reassessment from the beginning, discusses the potential impact and resolution of this finding.

by William H Ellett
U.S. National Research Council

When the Senior Dosimetry Committees of the United States and Japan approved the use of DS86 in March 1986, the members were well aware that measurements of cobalt-60 activation made by **Tadashi Hashizume, Takashi Maruyama** and their colleagues in the 1960s indicated a slower decrease of thermal (low-energy) neutrons in Hiroshima with distance than was calculated using the DS86 methodology. Therefore, the Senior Committees recommended new studies of neutron activation in Hiroshima to see if the earlier results could be confirmed.

Today, such a study is extremely difficult because most of the radioactivity induced by neutrons has decayed. For example, cobalt-60 activity is now only 0.3% of its original value. Moreover, Hiroshima has been rebuilt to an extent that only a few structures are available from which suitable samples can be obtained. Nevertheless, results of earlier measurements have been confirmed largely by the efforts of Japanese investigators, particularly the study of cobalt-60 activation by **T. Kimura, N. Takano** and others. Measurements of europium-152 activation by **Masaharu Hoshi** and his colleagues at Hiroshima University and by **Takashi Nakanishi** and his colleagues at Kanagawa University have provided additional information on how the thermal neutron field in Hiroshima varied with distance.

In the U.S., **George Kerr** and his colleagues at Oak Ridge National Laboratory and the Battelle Pacific Northwest Laboratories have made cobalt-60 measurements on duplicate samples which agree very well with Japanese measurements. To supplement this work, **Tore Straume** at Lawrence Livermore National Laboratory (LLNL) has initiated a new study in which long half-life chlorine-36 activation is measured by accelerator mass spectroscopy. This approach opens the way for measurements on concrete samples which are more readily available than iron samples containing cobalt.

In considering implications of the activation measurements, it is important to differentiate between two quite different radiological quantities: kerma and particle fluence. Activation results give a measure of the number of thermal neutrons interacting with the detector, whereas kerma is a measure of the energy imparted to the detector. In the case of the atomic bombs, the low-energy neutrons contributed a negligible amount of energy so that the measured activation is not indicative of the kerma (or the dose) at a given location. Nevertheless, one would expect that the change in neutron activation with distance from the explosion—if not the absolute value—could be calculated with the DS86 methodology. Instead, the calculated activation decreases with distance more rapidly than the measured values. However, some of the approximations in the thermal neutron transport calculations do not enter into calculations for fast neutrons. It is conceivable, therefore, that DS86 adequately predicts the variation with distance of the fast neutron fluence and, hence, the correct kerma—even if it cannot be used to model slow neutron activation.

We have very little information on this point. In general, comparisons of activation measurements made at weapons tests do agree with calculated values, but the neutron spectrum from the Hiroshima bomb is atypical in that it contained relatively few neutrons with energies above 1 MeV. The neutron problem could result from the transport of neutrons having intermediate energies, in which case weapon tests of bombs of the usual Nagasaki type may not be applicable.

Since it is not clear why DS86 calculations do not agree with measurements of neutron activation, considerable effort is being made to determine why this is so. It is important that the credibility of DS86 dose estimates be maintained, since it is possible that the failure of DS86 to calculate activation properly is a symptom of some poor approximations in the source term or in the radiation transport models upon which DS86 dose estimates are based.

As has been the case throughout the current dose reassessment program, a binational effort is being made to resolve the neutron issue. On the Japanese side, plans are underway to provide a documented database on the numerous activation measurements. This is an important operation because these data have been collected over a long period of time with a variety of techniques and instrumentation. At present, interpreting the measurements is difficult because the presence of the structure from which the samples are taken perturbs the neutron flux at the point of measurement. Moreover, neutron absorption by the sample itself, as well as in any overlying materials, must be taken into account to calculate the expected radioactivity. Correcting for these effects is not trivial. The best information may come from comparing results with similar samples from similar locations. It is not possible to do this now and an evaluated database which provides detailed information on the environment where each sample was collected, a description of the sample, and the estimated precision and accuracy of the measurements will facilitate the correct interpretation of the experimental data.

In addition, Japanese scientists are continuing their measurement program including TLD measurements of gamma-ray kerma as a function of distance. These data may provide additional insight into the pattern of neutron attenuation because about 40% of the gamma kerma beyond 1 km or so is due to neutron capture in air. Such data will require very careful evaluation. At great distances, much of the thermal luminescence is due to background radiation not bomb gammas, thus the development of more sophisticated methods for estimating background dose is also urgently required.

On the U.S. side, an effort is being made to verify the fundamental assumptions on which DS86 is based. At the Los Alamos National Laboratory, a formal technical review of the neutron scattering cross sections for oxygen and nitrogen has been initiated. On the experimental side, Straume at LLNL will measure chlorine-36 activation in concrete samples collected in Nagasaki by Japanese collaborators. If the results of these Nagasaki experiments agree with calculations, it will indicate that the calculated neutron source for Hiroshima is in error, not the radiation transport calculations. This will lead to additional calculations of the initial neutron spectrum from the Hiroshima weapon at Los Alamos and probably at LLNL as well.

Investigators at Science Applications International Corp. have initiated two new approaches for analyzing the DS86 neutron transport methodology using experimental data. One is based on a comparison of calculated thermal neutron activation with measurements made at a unique weapons test where only delayed neutrons reached the gold detectors.

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News Briefs

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ments to DS86. Representing the U.S. and Japanese Senior Dosimetry Committees, **William Ellett** and **Eizo Tajima** were involved in many of the discussions.

During their visit, the SAIC visitors worked closely with RERF staff on a number of dosimetry-related issues including: steps to allow computing of DS86 doses for some additional groups of survivors or to improve estimates for survivors covered by the current system, the interpretation and use of uncertainty in DS86 estimates, recent efforts to understand more fully the discrepancies between measured and predicted values of thermal and epithermal neutron fluence, and a review of the status of DS86 system documentation. Preliminary revisions of the DS86 system software which included updated procedures and data for the computation of uncertainties in DS86 dose estimates were installed. These changes do not affect current DS86 estimates.

✓ RERF and GSF May Collaborate on Data Analyses

In mid-November, **Wolfgang Jacobi**, director of the Institute for Radiation Protection of the Gesellschaft für Strahlen- und Umweltforschung (GSF) in Munich, discussed lung cancer risk estimates with epidemiology and statistics staff members. Estimates based on RERF Life Span Study data were compared with those obtained in follow-up studies of uranium miners. It was suggested that RERF and GSF collaborate by applying and comparing statistical techniques developed in both laboratories.

✓ Tree Growth Rings Used to Study Residual Radioactivity

At the fifth meeting of an expert committee that is reassessing the extent of "black rain" in Hiroshima and Nagasaki, Hiroshima University Professor and RERF Consultant **Shozo Sawada** recommended adopting the measurement of radionuclides and their isotopes in the annual growth rings of trees found in areas unaffected or heavily affected by black rain, as well as in adjacent areas. Measurements of strontium-90 in persimmon trees are already in progress.

✓ Matsunaga Retires from NIG

RERF Scientific Councilor **Ei Matsunaga,** who retired as director of the Japanese National Institute of Genetics (NIG) in October, has been replaced by **Junichi Tomizawa**, former chief of the Molecular Genetics Branch of the U.S. National Institutes of Health. Matsunaga, now an NIG professor emeritus, will continue as an advisor to RERF.

✓ Shirabe Memorial Unveiled at Nagasaki Laboratory

Family and colleagues of **Raisuke Shirabe**, former RERF visiting director (1975–1983), gathered in October to dedicate a commemorative sculpted portrait of Shirabe that was placed at the main vestibule of the Nagasaki Laboratory.

In his words of welcome, **J.W. Thiessen**, director of the laboratory, gave special recognition to sculptor **Kazukuni Yamazaki** and expressed his expectation that "the sculpture will grace the entranceway of this laboratory to serve as a continual reminder of a great man and a dear friend of our organization."

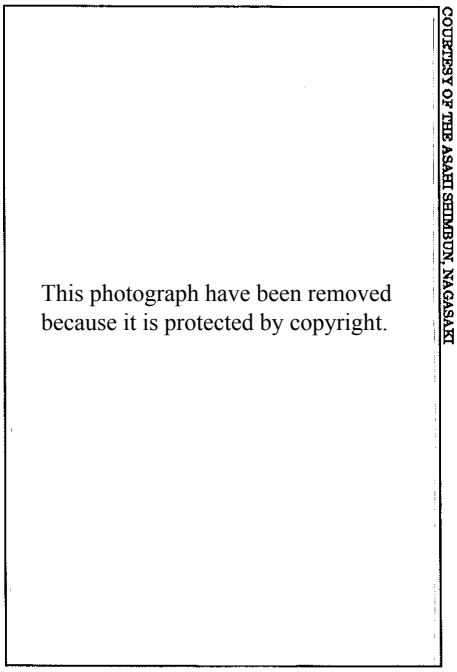
✓ Literary Projects Materialize

Visitors to Nagasaki soon hear the name of Thomas Glover, a Scottish merchant whose Victorian-style home atop Minami Yamate attracts tens of thousands of tourists annually. Few fully realize the contributions Glover made to the modernization of Japan. But Japanese who are curious, now have a new resource: *Blossoms and frost—the Glover family of Nagasaki*, written by **Brian Burke-Gaffney**, Nagasaki Laboratory translator/interpreter. The 154-page book is published in Japanese by Nagasaki Bunkensha Publishing Co., and is available for ¥1,600.

Burke-Gaffney's article about the original tales that evolved into Puccini's opera "Madame Butterfly," appeared in the October issue of *Intersect* magazine, an internationally distributed English-language magazine about Japan published in Tokyo.

William J. Schull, former RERF director, has joined the burgeoning ranks of *gaijin* (foreigners) recording their post-war recollections or personal interpretations of Japan. In February 1990, Harvard University Press expects to publish Schull's book which is tentatively titled *Song among the ruins*, an account of his personal discovery of Japan from 1949–1965.

Recently retired from the University of Texas Genetics Centers, Schull reports that he is slowly writing a scientific history—not so much ". . .an historical account of the [ABCC] or the Foundation as institutions, but rather an effort to trace over time some of the scientific aspects of the studies."



COURTESY OF THE ASAHI SHIMBUN, NAGASAKI

The Raisuke Shirabe Memorial was dedicated at the Nagasaki Laboratory this fall.

✓ Highlights of Lecture Program

On 27 September, **Olga Tsvetkova**, director of the International Scientific Cooperation Department of the All-Union Scientific Center of Radiation Medicine in Kiev, spoke about Chernobyl, three years after the accident.

Three seminars on aging were held in September and October: **K. Hirokawa** of Tokyo Metropolitan Institute of Gerontology's Pathology Department spoke about immunology and aging; **T. Matsuzawa** of Tohoku University's Research Institute for Tuberculosis and Cancer discussed brain shrinkage and aging; and **N. Taniguchi** of Osaka University Medical School's Biochemistry Department focused on sodium oxide dismutase and its implications on aging and cancer.

Kazuo Uemura of the Ryutsu–Keizai University Economics Department on 1 November talked about the development of the International Classification of Diseases.

On 6 November, **Robert MacLennan**, principal research fellow at the Queensland Institute of Medical Research in Australia, discussed a case-control study of oral cancer in Papua New Guinea, and an intervention trial to prevent adenomatous polyps.

Egon J. Hidvegi, scientific director of Hungary's National Research Institute for Radiobiology and Radiohygiene, spoke on 8 November about brain damage and cancer

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Neutron Activation

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Unlike high-energy prompt fission neutrons, these delayed neutrons have a range of intermediate energies that are comparable to the degraded neutron spectrum from the Hiroshima bomb. The other experimental situation involves measurements of neutron kerma made when a replica of the Hiroshima weapon was tested at Los Alamos in 1983. These kerma measurements, which extend over several hundred meters, will be compared with the DS86 kerma calculations based on the well-characterized degraded neutron spectrum from the replica. This will be the first direct comparison of measured and calculated neutron kerma and the results will be of considerable interest.

The continued investigation of the DS86 neutron dose estimates may well make investigators of radiation effects somewhat uneasy. They should not be too alarmed, however, because the neutron dose at Hiroshima was small. If the estimated dose equivalent due to neutrons were doubled, it would have a negligible effect on estimated risks, given their inherent statistical uncertainty. It is of more interest to determine why the discrepancies between measured and calculated activation occur. Even though thermal neutrons did not contribute meaningfully to tissue dose received by A-bomb survivors, the radioactivity these neutrons produced is the only existing record of neutron exposures that occurred in 1945. Dose reassessment will not be complete until questions related to neutron dosimetry are resolved. ❑

Unprecedented Challenges Faced in Early Years

With no comparable project to emulate, the founders of ABCC–RERF ventured into new scientific, administrative and cross-cultural arenas.

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

EARLY PHOTOS COURTESY OF JAMES V. NEEL

The Atomic Bomb Casualty Commission began as a survey team that traveled throughout war-devastated Japan in the 406th Medical General Laboratory—three railroad cars that were picked up on schedule and attached to the Allied Limited train. Above, the author, who is seated on a cot, Tokyo University Surgery Professor Masuo Tsuzuki, Melvin Block and Austin Brues are at work in their mobile laboratory which also doubled as sleeping quarters.

Those who currently work at or visit RERF, and who came to know its various resources and smoothly functioning programs, would have great difficulty in visualizing its early days. Unfortunately, to my knowledge, all of the original Japanese employees and associates of the then-ABCC have now retired; no one is left with firsthand knowledge of the challenges faced in developing the present program.

The first organized attempt to follow up on the effects of the atomic bombings was in September 1945, when teams from the U.S. Army, Navy, and Air Force joined with a Japanese team to evaluate the immediate aftereffects of the exposures. This group, usually referred to as the Joint Commission, issued a report in mid-1946 which included a recommendation that some provision be made for long-term follow-up. It was further suggested that the most suitable agency from the U.S. side for this involvement would be the National Academy of Sciences. The Academy was and is a quasi-governmental agency, a link between civilian and government science, and so was in a unique position to coordinate such an undertaking. This recommendation was ultimately accepted by President Harry S Truman, and the Academy—as the first step in meeting this new responsibility—decided to send several consultants to Japan.

My own contacts with the undertaking began in November 1946. I was then in the Medical Corps of the U.S. Army; suddenly I was assigned to accompany two civilian consultants selected by the Academy, Dr. **Austin Brues** and Dr. **Paul Henshaw**, on their mission, as were two other young medical officers, First Lt. **Melvin Block** and Lt. (j.g.) **Frederick Ullrich**. My assignment was in part based on the fact that I was the only medical officer in the U.S. Army with a Ph.D. in genetics, and it was understood from the outset that I had particular responsibilities related to possible genetics studies.

Arriving in Japan in late November, our group of five was directed to conduct its activities within the Public Health and Welfare Section of General Headquarters (GHQ), Supreme Commander of the Allied Powers. Every activity in the Occupation had to have a proper title; it is my recollection that Dr. Henshaw first suggested we be called the Atomic Bomb Casualty Commission.

In its earliest days, the ABCC consulted with a wide spectrum of Japanese scientists who were interested in radiation effects. Shown at a 1946 Tokyo meeting are: from left, seated, Drs. Nakahara, Henshaw, Sasaki and Brues; and from left, standing, Drs. Neel, Murati, Tsuzuki, Higashi and Ullrich.

Our little group spent about six weeks meeting with Japanese scientists in Tokyo, Osaka and Kyoto. We surveyed the situation in Hiroshima and Nagasaki, and in January 1947, the civilians and Lt. Ullrich returned to the States, leaving Block and me in a somewhat undefined situation. We decided to return to Hiroshima, where he, a surgeon-to-be, would try to determine some of the factors responsible for the keloid scars so prominent in some of the survivors, and I, in collaboration with another young medical officer—Lt. (j.g.) **Frederick Snell,** who had been released from duty at the naval base in Yokosuka—undertook to determine the hematological status of school children who had suffered epilation at the time of the bombing. I believe that the report by Snell, myself and **K. Ishibashi** on our findings was the first published under the ABCC imprimatur (*Arch Int Med* 84:569, 1949). During this period, I was also busy trying to develop a plan for a satisfactory genetics study.

In June 1947, I was ordered back to Washington to report to the Academy's newly-formed Committee on Atomic Casualties. There followed a very busy three months, during which I submitted the plan for a genetics program to a special committee convened by the Academy. They accepted it, and I set to work to recruit my team. But I was also asked by the Academy to return to Hiroshima as the pro tem. director of the ABCC, and this meant many conferences to decide upon the best way to proceed in occupied Japan. By the end of the summer, I had assembled a group of three: Dr. **Masuo Kodani**, a cytogeneticist; **Richard Brewer**, a data processor; and First Lt. **Ray Anderson**, a pediatrician, as the

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Early Years of ABCC

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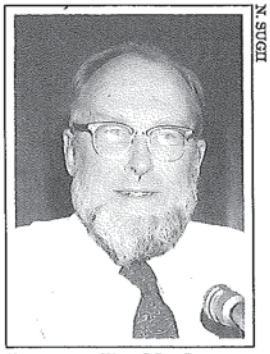
nucleus of the American genetics group.

Returning to Japan in September, I had dual responsibilities: On the one hand to begin to generate the physical facilities necessary for the program, and on the other hand, to begin to implement the necessary scientific program and to recruit Japanese personnel. It is important to recognize that there simply was no precedent for a long-range epidemiological study of this nature; we had no model to emulate.

At that time, GHQ policy required that any U.S. activity work in close liaison with some corresponding Japanese organization. Col. **Crawford Sams,** chief of the Public Health and Welfare Section, GHQ, directed us to affiliate with the newly organized Japanese National Institute of Health, which then formed a Section on Atomic Bomb Effects. Of course, the JNIH had no previous experience with this type of research either.

It is difficult today to grasp the magnitude of the challenges we faced in 1947. The devastation of the bombings had left no suitable physical facilities for the study. Transportation and communication were difficult, for both survivors and staff, so that the ease of patient contact and scheduling that we take for granted today simply did not exist. But far more important, from the scientific standpoint, was the fact that this would be a study without scientific precedent, which had to be organized so that it would be in keeping with Japanese culture and tradition—otherwise it could not succeed.



N. SUGII

In 1946, Jim Neel never dreamed he would still be involved in ABCC work 43 years later. Above, the author lecturing at RERF in 1983.

With respect to the physical facilities, I had to obtain both temporary space and begin to plan for more permanent facilities. Because it was thought that more than twice as many survivors had received significant amounts of radiation in Hiroshima as in Nagasaki, circumstances dictated that the major effort be mounted in Hiroshima. With respect to the temporary needs in that city, I negotiated for space in the *Gaisenkan*, on the Ujina waterfront. A former military assembly hall, it was far enough away from the hypocenter that it had escaped serious damage. It provided office facilities and an unused auditorium where we could stockpile material for the building ultimately to be constructed. It also could be accessed by sea, by rail, or by road, and had adjacent space for a motor pool. During this same time period, I also enlisted the help of the city administration in finding a suitable place for a permanent facility. Our first choice was a former military area near the heart of the city. In this solution, I was later overruled by the consulting architect to the Academy, **Sigmund Pfeiffer**. The present location of RERF, atop Hijiyama, was certainly a more picturesque site than my selection of a "working class" area, but it presented both psychological and practical problems in those days of poor transportation facilities.

Shown after a luncheon hosted by the mayor of Hiroshima on 6 December 1946, ABCC's early cast of characters included: front row: a city official, Drs. Ullrich, Neel, and Tsuzuki; standing: Dr. Saida, a city official, Col. Johnson, Drs. Henshaw, Brues, Volk, Matsubayashi, and Block, as well as Dr. Omura, the official Japanese Welfare Ministry representative. Johnson and Volk were GHQ-assigned escorts.

With respect to the research program, it was understood I would concentrate on getting a genetics program under way, while the Academy recruited personnel for medical studies on the survivors. Very early, we made contacts with Dr. **Koji Takeshima,** a young *nisei* (American-born) surgeon at the Red Cross Hospital, who was to be very important not only in helping us understand Japanese ways but in our recruiting of Japanese physicians. The plan I had developed, in collaboration with Dr. **I. Matsubayashi** of the Hiroshima City Health Department, required that we enroll all pregnant women in the two cities in our study when they registered their pregnancy with the city for ration purposes. When the pregnancies terminated, the midwives and/or physicians who attended the deliveries gave us a preliminary report on the outcome, whereupon one of our own staff physicians would visit the mother and examine the baby. I have long since forgotten how very many meetings I had with the midwife associations to enlist their cooperation and instruct them in the necessary procedures.

To put this plan in effect required developing a complex recordkeeping system. All this was finally in place by March 1948, and I returned to my position at the University of Michigan, having been relieved of my directorial responsibilities by Lt. Col. **Carl Tessmer.** You may be sure I had no thought at the time that the concerns of the genetics program would still be bringing me back to Japan in 1989. ❑

Dr. Neel has promised to discuss the beginnings of the genetics program in a future issue of Update.

International Oral Presentations

The 66th Meeting of the American Thyroid Association, San Francisco, Calif., 6–9 September 1989.

➪ *Aging influenced thyroid volume in men, and circulating thyrotropin and triiodothyronine concentrations.* S Inoue, H Hirayu, M Izumi, K Shimaoka, S Nagataki.

The 1st Joint Meeting of the International Conference on Calcium Regulating Hormones and the American Society for Bone and Mineral Research, Montreal, Canada, 9–14 September 1989.

➪ *High prevalence of hyperparathyroidism among A-bomb survivors.* S Fujiwara, H Ezaki, R Sposto, S Akiba, K Neriishi, K Kodama, Y Hosoda, S Inoue, K Shimaoka.

International Workshop on Risk Estimates for Radiation Carcinogenesis, Köln, Federal Republic of Germany, 28–29 September 1989.

➪ *Risk estimates for radiation carcinogenesis (Epidemiological studies at RERF).* Y Shimizu

International Symposium on Chromosome Aberrations: Basic and Applied Aspects, Essen, Federal Republic of Germany, 5–7 October 1989.

➪ *Chromosome aberrations in A-bomb survivors.* AA Awa.

The 1st International Stroke Congress, Kyoto, 15–19 October 1989.

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

Recent Scientific Publications

Approved Technical Reports

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

Of all data sets pertinent to estimating the genetic risks to humans after exposure to ionizing radiation, potentially the most informative is that consisting of the cohort of children born to A-bomb survivors. We present here an analysis of the relationship between parental exposure history and "untoward pregnancy outcomes" (UPO) within this cohort, using to the fullest extent possible the recently revised estimates of the doses received by the parents—the so-called DS86 doses. Available for study are 70,073 pregnancy terminations, but DS86 doses have not been or presently cannot be computed on 14,770 of these. The frequency of UPOs, defined as a pregnancy terminating in a child with a major congenital malformation, and/or stillborn, and/or dying in the first 14 days of life, increases with combined (summed) parental dose, albeit not significantly so.

Under a standard linear model, when the sample of observations is restricted to those children whose parents have been assigned the newly established DS86 doses (n = 55,303), ignoring concomitant sources of variation and assuming a neutron RBE of 20, the estimated increase per sievert in the predicted frequency of untoward outcomes is 0.00354 (±0.00343). After adjustment for concomitant sources of variation, the estimated increase per sievert in the proportion of such births is 0.00422 (±0.00342) if the neutron RBE is assumed to be 20. A one-hit model with adjustment for concomitants results in an almost identical value, viz., 0.00412 (±0.00364).

When the sample is extended to include parents lacking the full array of dose parameters necessary to calculate the DS86 dose, but sufficient for an empirical conversion of the previously employed T65DR dose system to its DS86 equivalent, we find under the linear model that the estimated increase per sievert in UPOs is 0.00264 (±0.00277) at an RBE of 20, after adjustment for concomitants. (Now n = 69,706; for 367 of the 70,073 outcomes, neither a DS86 nor an ad hoc dose can be calculated.) The corresponding value with the one-hit model is 0.00262 (±0.00294). The former value is some 31% higher than that published previously.

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

Using stored serum samples collected from 1970–72 and/or from 1977–79, serum ferritin, transferrin, and ceruloplasmin levels were immunologically determined for 233 stomach cancer and 84 lung cancer cases diagnosed from 1973–1983 and for 385 matched controls from a fixed population of Hiroshima and Nagasaki A-bomb survivors. Elevated stomach cancer risk was associated with low serum ferritin levels, with more than a threefold excess among those in the lowest quintile as compared to the highest ferritin quintile. The average serum ferritin concentration was 8% lower in the stomach cancer cases than in the controls. Risk did not vary with the time between blood collection and stomach cancer onset, remaining high among those with low ferritin levels five or more years before cancer diagnosis. Low ferritin combined with achlorhydria, diagnosed about 10 years before the blood collection and up to 25 years before cancer diagnosis, was an exceptionally strong marker of increased stomach cancer risk. No effect of transferrin or ceruloplasmin independent of ferritin was observed on gastric cancer risk. Lung cancer risk was not related to these three serum proteins.

Is variation in human radiosensitivity real or artifactual? A study by colony formation method using peripheral blood T lymphocytes. N Nakamura, J Kushiro, R Sposto, M Akiyama. **RERF TR 15-89.**

Two methods of producing human T-lymphocyte colonies in vitro are described, as well as dose-survival experiments using these methods for the investigation of possible differential radiosensitivity among individuals. In one method, the cloning efficiency (CE) of nonirradiated lymphocytes was between 10% and 40% (method 1), whereas subsequent improvement in assay conditions (method 2) resulted in a CE greater than 30%. In vitro X-irradiation of colonies produced using method 1 revealed that the dose required to kill 90% of the cells (D_{10}) was 2.87 ± 0.28 Gy (mean ±SD, n = 18) for repeated examinations of lymphocytes from one reference individual. Using method 2, the D_{10} values were greater, viz., 3.66 ± 0.21 Gy for 28 repeated tests of the same reference individual and 3.58 ± 0.19 Gy for 31 different individuals. Analysis of variance to compare the data from repeated examinations of one person versus data from single examinations of different persons showed that variation in the D_{10} value was not significantly greater in the latter group. These results support the hypothesis that individual variation in human radiosensitivity is quite small, if it exists at all, as far as can be determined by the loss of colony-forming ability of irradiated G_0 lymphocytes.

Radiosensitivity of CD4 and CD8 positive human T lymphocytes by an in vitro colony formation assay. N Nakamura, Y Kusunoki, M Akiyama. **RERF TR 16-89.**

The recent development of an in vitro lymphocyte colony assay provides a new opportunity to examine possible variations in human radiosensitivity of humans using peripheral blood lymphocytes (PBL) in place of the hitherto used skin fibroblast assay. Our recent study showed that most of the colonies consisted of lymphocytes bearing CD4 or CD8 antigens. Since the fraction of $CD4^+$ and $CD8^+$ cells in PBL differs among individuals, it was suspected that individual radiosensitivity might be biased by the different subset frequencies if the dose-survival curves of the $CD4^+$ and $CD8^+$ cells differed.

In the present study, $CD4^+$ lymphocytes (helper/inducer T cells) and $CD8^+$ lymphocytes (suppressor/cytotoxic T cells) were isolated from PBL and their dose-survival curves were determined. The results showed that the D_{10} (the dose required to reduce the surviving fraction to 10%) was quite similar for these two types of cells (3.13 ± 0.10 Gy [mean ±SD] for $CD4^+$, 3.34 ± 0.50 Gy for $CD8^+$ and 3.07 ± 0.05 Gy for the unsorted cells), supporting the use of a whole PBL population for screening of individuals with altered radiosensitivity.

Absence of correlations between the radiosensitivity of human T lymphocytes at G_0 and skin fibroblasts at log phase from the same individuals. J Kushiro, N Nakamura, S Kyoizumi, M Nishiki, K Dohi, M Akiyama. **RERF TR 17-89.**

Matched samples of peripheral T lymphocytes and skin fibroblasts from a total of 22 patients who underwent various surgical procedures were tested for a dose-survival study using loss of colony-forming ability as the end point. The results showed that the mean D_{10} (the dose required to kill 90% of the cells) ±SD was 3.58 ± 0.21 Gy for T lymphocytes irradiated at G_0 and 3.19 ± 0.37 Gy for skin fibroblasts irradiated at log phase. The coefficient of variation was found to be 6% and 11%, respectively. Contrary to expectation, regression analysis of the D_{10} values for the two cell types revealed no significant correlations.

The absence of correlation is most probably derived from the fact that the apparent interindividual variability of dose-survival curves is largely caused by random experimental fluctuations, at least for lymphocytes. Possible reasons for the greater variability observed in the fibroblast assay are discussed.

Approved Research Protocols

Pilot study to examine a new fluorescence in situ hybridization-based method for chromosome aberration frequency analysis and a new method for glycophorin A variant erythrocyte frequency analysis and to determine the utilities of these methods in assessing genetic damage in A-bomb survivors. AA Awa, K Ohtaki, M Akiyama, N Nakamura, S Kyoizumi, JW Gray, JN Lucas, RG Langlois, R Jensen. **RERF RP 10-89.**

The frequencies of stable, structural chromosome aberrations in the lymphocytes of A-bomb survivors will be estimated by visual analysis of metaphase spreads stained for chromosomes 1, 3, 4, and in some cases chromosomes 7 and 15, using fluorescence in situ hybridization with chromosome-specific composite probes developed at Lawrence Livermore National Laboratory (LLNL). These frequencies will be compared with structural aberration frequencies measured at RERF using G-banding and transmission microscopy. The frequencies of erythrocytes

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Recent Scientific Publications

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carrying variant forms of glycophorin A (GPA) will be estimated for these same individuals using a somatic mutation analysis protocol developed recently at LLNL. These frequencies will be compared with GPA variant frequencies using the protocol now in use at RERF.

Individuals included in this study will be of the MN heterozygous blood group with good DS86 dosimetry and little post-A-bomb exposure to other genotoxic agents. Samples from at least 35 individuals exposed to estimated doses ranging from 0 to 4 Gy (5 distally exposed, 10 exposed to doses between 0.5 and 1 Gy, 10 exposed to doses between 1 and 2 Gy, and 10 exposed to doses between 2 and 4 Gy) will be analyzed using all four techniques.

A pilot study for detecting somatic mutations at the HLA-A locus in lymphocytes. J Kushiro, S Kyoizumi, Y Kusunoki, Y Hirai, N Nakamura, M Akiyama. **RERF RP 11-89.**

This pilot study proposes establishing assay methods to detect mutations at the HLA-A locus in peripheral lymphocytes. If successful, this will overcome the limitations associated with both the X-chromosomal hypoxanthine phosphoribosyltransferase (HPRT) locus mutation method for human lymphocytes and the autosomal glycophorin-A locus mutation method for erythrocytes. Use of lymphocytes enables us to grow the mutant cells and extract DNA for molecular analysis. Since an autosomal codominant marker is employed, somatic recombination (which does not occur in X-chromosomal loci) can be detected in addition to gene mutation and deletion.

Two lymphocyte assay methods for detecting somatic mutations at the HLA-A locus will be employed. One, developed by A.A. Morley's group at Flinders University of South Australia, uses monoclonal antibody and complement; the other uses the same monoclonal antibody tagged with fluorescent dye. The mutant cells thus obtained will be subjected to DNA analysis for characterization.

After standardization of the assay methods, a pilot study will be conducted on about 20–50 atomic bomb survivors to evaluate its use in a large-scale survey.

Publications in the Open Literature

X-ray-induced mutations in cultured human thyroid cells. N Nakamura, R Sposto, RC Miller, T Hiraoka, N Takeichi. *Radiat Res* 119:123–33, 1989.

Comment to Dr. Delpla's 'Let us come back to radiation hormesis.' H Kato. *Health Phys* 57:205, 1989 (letter to the editor).

Studies of the mortality of A-bomb survivors. 9. Mortality, 1950–1985: Part 1. Comparison of risk coefficients for site-specific cancer mortality based on the DS86 and T65DR shielding kerma and organ doses. Y Shimizu, H Kato, WJ Schull, DL Preston, S Fujita, DA Pierce. *Radiat Res* 118:502–24, 1989.

New serum indicator of interstitial pneumonitis activity: Sialylated carbohydrate antigen KL-6. N Kohno, Kyoizumi S, Y Awaya, H Fukuhara, M Yamakido, M Akiyama. *Chest* 96:68–73, 1989.

A chromosome study of 6-thioguanine-resistant mutants in T lymphocytes of Hiroshima and Nagasaki atomic bomb survivors. Y Kodama, M Hakoda, H Shimba, AA Awa, M Akiyama. *Mutat Res* 227:31–8, 1989. ❑

News Briefs

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incidence resulting from fission neutron irradiation of the developing mouse embryo.

On 10 November, **Osamu Tokunaga** of Saga Medical College's Pathology Department lectured on vascular endothelial cells and aging.

On 22 November, **Hiroshi Yamasaki** of the International Agency for Research on Cancer in Lyon, France, spoke about oncogene activation in chemically induced carcinogenesis.

Shunsaku Sasaki of the National Institute of Radiological Sciences' Department of Physiology and Pathology on 28 November discussed the topic of life shortening caused by radiation exposure.

Eliezer Huberman, director of the Biological and Medical Research Division at Argonne National Laboratory, on 8 December talked about altered proto-oncogenes in normal tissues from humans exposed to radium.

On 18 December, **William J. Bair** of Battelle Pacific Northwest Laboratories' Life Sciences Center spoke about current revisions of the ICRP lung model.

✓ Research Staff News

Department of Clinical Studies: **Kazunori Kodama**, who was formerly acting chief, is now chief of the department.

Radioisotope Facilities: After reorganization of RERF's research departments, Permanent Director **Yutaka Hasegawa** will now be overseeing the Radioisotope Facilities in addition to his previous responsibilities. **Norio Takahashi** has been appointed chief of the newly formed Radioisotope Facilities Division.

Department of Radiobiology: On 1 December, Research Associate **Seishi Kyoizumi** began a one-year sabbatical at Systemix Research Institute, Palo Alto, Calif. There he will further refine a method of studying the differentiation of human hemopoietic stem cells by transplantation of these cells into severe combined immunodeficient mice.

✓ Two RERF Directors Attend ICRP Meeting

RERF Chairman **Itsuzo Shigematsu** and Chief of Research **Seymour Abrahamson** attended the first meeting of the reconvened International Commission on Radiological Protection, held in Oxford, England, in early October.

✓ Polish Scientist Reviews RERF Radiation Effects Studies

A one-year grant from a Japanese daily newspaper enabled **Marek A. Kubacki**, a Polish internist, to spend a month at the Hiroshima Laboratory this fall collecting information about the long-term health effects of radiation exposure.

✓ WHO Group Discusses Effects of Nuclear War

In mid-November, RERF Chairman **Itsuzo Shigematsu** participated in a meeting to brief the WHO management group on an ongoing project to report on the effects of nuclear war on human health and on worldwide health services. ❑

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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