26th Scientific Council Deliberates Peer Review Report and F_1 Plans

by Clark W. Heath, Jr., Associate Chief of Research

The 26th meeting of the Scientific Council, which was co-chaired by Drs. Maurice S. Fox, *professor of molecular biology, Massachusetts Institute of Technology,* and Hiromichi Matsudaira, *consultant, Japan Science and Technology Corporation*, was held at RERF in Hiroshima April 7 to 9. The previous year's activities were reviewed, current and planned future research were presented, March's clinical genetics and immunology workshops (*See* Update *10 [1]: 1 and 5.)* were summarized, and attention was directed to the recommendations of the epidemiology peer review (*See* Update *10[1]: 1.*) and plans for the proposed F_1 study (*See story, page 4.)*

RERF Chairman Shigenobu Nagataki opened the meeting, and Vice Chairman and Chief of Research Sheldon Wolff gave a brief review of RERF activities over the past 12 months and invited the council's advice regarding future research directions. The remainder of the first day was devoted to presentations covering recent research and future plans in the Departments of Clinical Studies (Drs.

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放影研 RERF update

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放影研 RERF update

Radiation Effects Research Foundation News and Views
Hiroshima and Nagasaki, Japan

Epidemiology Review Recommendations and F_1 Study Concerns Focus of Board of Directors Meeting in Nagasaki

by Kazumasa Kunitoshi, Chief of the Secretariat

The 33rd meeting of RERF's board of directors was held at the Nagasaki laboratory on 23 and 24 June, its first meeting there in seven years. Recommendations of last November's multinational peer review of the epidemiology program, a report on the signing of a letter of confirmation concerning the "F_1 Health Effects Study Plan," consideration of future policy relating to that study, discussion regarding the current shortage of one American board member, and the presentation and deliberation of various status reports were on the board's agenda. Dr. Richard B. Setlow, a newly appointed RERF visiting director, was introduced, and Drs. Masao Sasaki and Theodore L. Phillips, the two scientific councilors whose terms of office were to expire in this fiscal year, were reappointed.

Board of directors at the main entrance to RERF Nagasaki
From left to right, front to back: Row one: Dr. Masumi Oike, Dr. Kazuaki Arichi, Vice Chairman and Chief of Research Sheldon Wolff, Chairman Shigenobu Nagataki, Dr. Richard B. Setlow, Dr. Patricia A. Buffler, Permanent Director Senjun Taira, and Dr. Itsuzo Shigematsu; ***Row two:*** Secretariat Chief Kazumasa Kunitoshi, Dr. Midori Soda, Dr. Kiyohiko Mabuchi, Dr. Tomio Hirohata, Richard D. Sperry, Mr. David Williams; ***Row three:*** Associate Chief of Research Clark W. Heath, Jr., Dr. Evan B. Douple, Ms.Catherine S. Berkley, Mr. James Hall, Dr. Masazimi Akahoshi, and Mr. Hiromasa Kuroki.

In his opening remarks, Chairman Nagataki commented on the significance of the meeting being convened in Nagasaki, concerns regarding the limited financial support from the U. S. government for the five years up to 2001, and the letter of confirmation signed by the All-Japan Second Generation A-bomb Victims Liaison Council (*Niseikyo*). With respect to the F_1 negotiations, Dr. Nagataki pointed out the gradual improvement in the understanding among the *Niseikyo*. During the meeting, the history up to the letter's signing and the letter's contents were reviewed, and plans were described for establishing third-person scientific and ethical advisory committees later this year.

Reporting on the recommendations of the multinational peer review of the epidemiology program, Scientific Councilor Tomio Hirohata emphasized the need to continue radiation carcinogenesis studies based on the LSS and AHS populations and recommended that analyses of cancer incidence data be a priority. Further evaluation of the interaction of radiation exposure with factors other than radiation, such as smoking and alcohol intake, and of the increase of noncancer diseases, particularly cardiovascular disease, among A-bomb survivors was also recommended.

Scientific Council Chair Hiromichi Matsudaira reported on the recommendations of the 26th Scientific Council meeting held April 7 through 9 in Hiroshima and gave a detailed account of how RERF's five-

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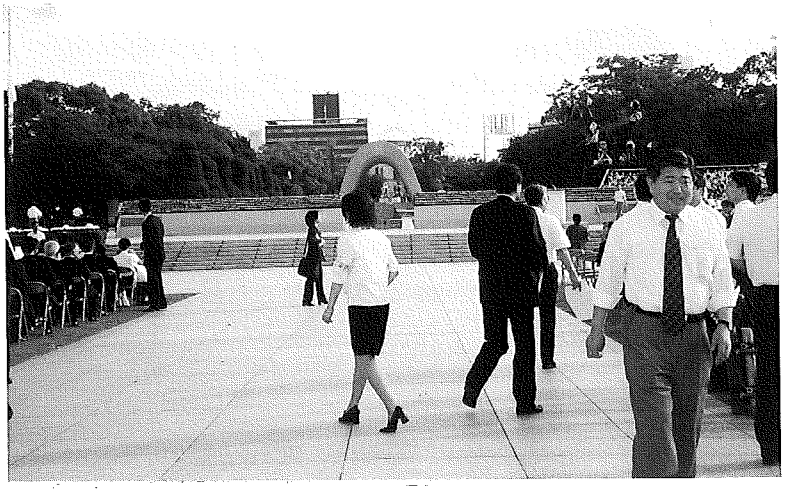
Solemn Ceremonies Mark Hiroshima and Nagasaki Atomic-Bomb Memorial Days



Atomic-Bomb Memorial Day Ceremonies in Hiroshima, August 6, 1999 *An estimated 50,000 people attended commemorative services in Hiroshima's Peace Park, which lies at the site directly under where the A-bomb exploded. Attention was focused on the cenotaph (center, above), under which lies books containing the names of those people known to have died at the time of the bombing or who were survivors and have since died. Delegates of various governments and organizations as well as individuals left memorial wreaths and flowers in front of the memorial during the ceremony and throughout the day. Incense also burns before the memorial, and religious ceremonies were conducted until the late hours. Each year, the cenotaph is opened so that the names of those who have died during the year may be recorded. Invited participants sat in chairs that filled the lawn from the cenotaph to the Peace Memorial Museum (below, left) and the International Conference Center (below, right). (Pictures courtesy of Dr. and Mrs. Wolff)*

Fifty-four years after the atomic bombings of Hiroshima and Nagasaki, annual memorial services in the two cities brought together people from all over the world to remember the events of August 6 and 9, 1945 and to pray that the future holds no more such tragedies for mankind.

On August 6, in Hiroshima, about 50,000 people, including A-bomb survivors and families of those killed by the bomb, attended morning services in the Peace Park. Vice Chairman and Chief of Research Sheldon Wolff and his wife, Frances, and Permanent Director Senjun Taira represented RERF. Hiroshima Mayor Tadatoshi Akiba, in his first speech after inauguration as mayor, made a strong appeal for the elimination of nuclear weapons, using language that would be easily understood by the young people in attendance. In the evening, RERF Chairman Shigenobu Nagataki attended another service in front of the cenotaph in the Peace Park for the members of the Hiroshima City Medical Association and the medical workers killed by the bombings.

On August 9, about 25,000 attended the Atomic-Bomb Victims and Peace Memorial Ceremonies held in Nagasaki's Peace Park. Dr. and Mrs. Wolff, Dr. Taira, and RERF Nagasaki's Assistant Secretariat Chief Yasutaka Ohgushi represented RERF at that ceremony.

In a separate ceremony, a cenotaph was unveiled at the site of a newly discovered air-raid shelter on the slope of a small hill near the Institute of Tropical Medicine of the Nagasaki University. Dr. Nagataki and Nagasaki Department of Clinical Studies Administrative Assistant Chief Hiroshi Ichoda attended the cenotaph unveiling and a memorial service for the Nagasaki Medical College's faculty members and students killed in the bombings, which was held the same morning in the memorial auditorium of Nagasaki University School of Medicine.

At both RERF laboratories, the A-bomb memorial days were marked by the presentation, in Japanese, of Director Keisuke Kinoshita's 1984 film, *Leaving the Children Behind*, based on the autobiography of radiologist, Dr. Takashi Nagai. Dr. Nagai, who suffered from leukemia associated with his previous work with radiation, survived the bombing of Nagasaki but was left a widower with two children. The film is the story of his struggle to raise his two children and instill in them an understanding of the importance of human love and peace as he battled the illness that he knew would soon take his life.

Atomic-Bomb Memorial Day Ceremonies in Nagasaki, August 9, 1999 *This statue in Nagasaki's Peace Park represents a universal prayer for world peace and for the consolation of victims of war. In the foreground, wreaths of flowers have been placed to honor victims of the atomic bombing. (Photo courtesy of Dr. and Mrs. Wolff)*

Hiroshima and Nagasaki Peace Praying Hall Construction Scheduled

We mourn for the lives lost to the atomic bomb and dedicate ourselves to the task of informing future generations. We pledge to widely disseminate the accounts of the inferno this device created so that we might learn from this history and build a lasting peace in a world free of nuclear weapons.

—proposed inscription for the Hiroshima Peace Praying Hall

Construction of the long-anticipated Hiroshima National Memorial Hall to Mourn A-Bomb Victims and Pray for Peace will begin in October in the Peace Park, and its expected opening date is March 2002. A second praying hall in Nagasaki is scheduled to begin construction next July for completion in March 2003.

The project, planned and executed by the Japanese Ministry of Health and Welfare (MHW) in collaboration with Hiroshima's local government and seven atomic-bomb survivors' groups, is the culmination of efforts begun prior to the 50th anniversary of the bombing to establish a place where national condolences might be expressed for those who died as a result of the bombing, prayers might be offered for a lasting peace, and people now and in the future might come to understand better the human toll of the atomic bombing.

The hope for "a project of praying for peace" was expressed in an article of the A-bomb Victims Relief Law passed by the Diet in December 1994, and a resolution was made during the voting that a facility to offer condolences to the A-bomb dead be established as early as possible that would allow survivors and bereaved families to express their sentiments and find consolation, a place for prayer and contemplation. A committee to investigate such a proposal was actually convened in 1991, and several discussions occurred prior to the 1994 law. Various delays have postponed the construction.

The atomic bomb that was dropped on Nagasaki at 11:02 a.m. on August 9, 1945 instantly devastated the city and destroyed countless human lives. Those who managed to survive still carry with them the physical and psychological scars left by the bomb, coupled with radiation damage that can never be repaired.

In memory of those who have been sacrificed and with an awareness of those who are still in pain, we sincerely mourn the A-bomb victims.

We are resolved to proclaim boldly the reality of A-bomb damage to each member of the human race and to pass this understanding on to posterity. We pledge to learn from this history and build a lasting peace in a world free of nuclear weapons.

—proposed inscription for the Nagasaki Peace Praying Hall

The Hiroshima and Nagasaki memorials will serve complementary purposes. While the Hiroshima hall will be focused on the collection and use of A-bomb-related materials and data, the primary focus of the Nagasaki facility will be international cooperation and exchange. The facilities will be available to promote new projects and support ongoing activities. Multipurpose areas will include meeting, library reference, and data access rooms. Permanent and changing exhibitions will educate visitors regarding the aftermath of the bombings.

Among the A-bomb dead are many whose names are unknown, including many foreigners and those who died from late effects of radiation exposure. A mural inside the Hiroshima hall will carry 140,000 dots to record the estimated number of victims of the bombings (±10,000), and a reference system will be developed whereby the names and pictures of those who died may be accessed. In Nagasaki, the estimated 70,000 (±10,000) A-bomb dead will be represented.

The two memorial halls are expected to be managed by local nonprofit organizations, with emphasis to be placed on employment of persons knowledgeable of the bombings and sensitive to the feelings of survivors and bereaved families. MHW will be involved in the oversight of the praying halls and operation funding.

RERF Involvement in Database Construction

In 1991, RERF was entrusted with inaugurating the Committee on A-bomb Materials and Information as part of the MHW project envisioning such a memorial. The committee was chaired by Tokyo University Emeritus Professor Yasuo Yoshizawa and was charged with reviewing 1) methods for collecting, arranging, and preserving materials concerning the bombing damage and the effects of A-bomb radiation as well as methods for inventorying such materials; 2) systems for providing information to interested parties inside and outside Japan about A-bomb-related materials collected or registered in the inventory as well as improvement of the information network linking organizations possessing such materials; and 3) arrangement and editing of materials relevant to A-bomb survivors' healthcare and entitlement programs.

During the seven years in which RERF was engaged in this work,* surveys were conducted to ascertain what organizations inside and outside Japan are repositories of related materials, including identification of those with established data bases and those with plans for database development. Identified among information sources were Hiroshima and Nagasaki hospitals and sanatoria, the National Diet Library, the Diplomatic Materials Museum of the Ministry of Foreign Affairs, The Nishina Memorial Foundation, the U. S. National Archives and Library of Congress, the University of Maryland Library, the Franklin D. Roosevelt and Harry S. Truman presidential libraries, and the public records office and Imperial War Museum in the United Kingdom. The committee drafted a regulation to ensure the confidentiality and proper handling of personal data.

The system developed includes optical and CD-ROM filing of 1965, 1975, and 1985 responses to MHW A-bomb Actual Conditions Surveys; CD-ROM recording of survivors' memoirs of their exposure experiences, a 1995 MHW investigation; construction of a data base for management, retrieval, and shared use of A-bomb-related materials; and preparation of personal computer displays of explanatory notes of A-bomb-related information. RERF's work on the project ended in 1998.

**Editor's Note: The progress of RERF's involvement in database development is recorded in each year's annual report, from 1991-1992 through 1997-1998, and these reports are sources for this article. Additional information on the two projects was provided by the Planning Division of MHW's Health Service Bureau.*

RERF and Niseikyo *Sign Agreement Letters for F_1 Heath Effects Study*

by Senjun Taira, Permanent Director

Editor's Note: As RERF prepares to undertake a health effects study in the F_1 population, a regular column updating the study's progress is planned.

The radiation health effects in atomic-bomb survivors, ranging from acute to late diseases, have been studied for more than 50 years. As a result, a variety of issues have been clarified, including the relationship between radiation and carcinogenesis. The relationship between radiation and noncancer diseases is also being examined.

The genetic effects of radiation remain a constant concern, and though no significant findings have been reported demonstrating a relationship, an association is not necessarily precluded because only limited scientific research has been done on the second-generation (F_1) survivors. Therefore, regardless of possible study results, it is important that a health study be conducted in this population, who have now reached ages at which they are prone to adult diseases.

At a ceremony in RERF's Hiroshima laboratory auditorium May 19, Nobuto Hirano (left), president of the All-Japan Niseikyo, *and RERF Chairman Shigenobu Nagataki exchange letters of confirmation to conduct the F_1 Health Effects Study.*

In May, an agreement was reached between the All-Japan Second-Generation A-bomb Victims Liaison Council (*Niseikyo*) and RERF to facilitate such a study, with the understanding that full attention will be paid to the views of second-generation survivors. Before the study may begin, a scientific committee to develop projects of scientific value and an ethics committee to address privacy issues will be established. We hope, then, to conduct the study in consultation with the two committees.

RERF has identified some 88,000 F_1 persons, including a control population. From this group, we need to establish a study cohort and develop a scientifically reliable study. For this, budgets and workloads are likely to increase, particularly for the Departments of Epidemiology and Clinical Studies. We hope that maintaining the close ties between these research and clinical examination departments will contribute to the further development of F_1 studies.

RERF Dispatches Medical Team after Nuclear Plant Leak in Tokaimura

by Senjun Taira, Permanent Director and Yutaka Ogasawara, Chief, Planning Office, Secretariat

At the Ministry of Health and Welfare's request, RERF was one of three organizations that organized and dispatched a medical team following Japan's first critical radiation accident the morning of September 30, at the Tokai Processing Plant of JCO Co. Ltd., a nuclear fuel processing company, in Tokaimura, Ibaragi Prefecture. Clinical Laboratories Division Chief, Dr. Kazuo Neriishi, Dr. Masayuki Hakoda, Senior Technician Shinsuke Matsuura, and Assistant Chief of Nurses Michiko Kuwamoto, all of the Department of Clinical Studies, left Hiroshima the evening of October 1 to participate in on-site investigations carried out by Ibaragi Prefecture and others. Other teams were dispatched by the Research Institute for Nuclear Medicine and Biology of the Hiroshima University and the Hiroshima International Council for Health Care of the Radiation-Exposed (HICARE), which is sponsored by the Hiroshima Prefecture, the Prefectural Medical Association, and the Red Cross A-bomb Hospital, among others.

Over a four-day period, the team examined and screened the blood and urine of as many as 1,852 local residents in the area. Dr. Neriishi reported that following examinations, there was no "significant decrease in lymphocyte counts," and he further remarked that "[h]eavy exposure is unlikely." "However," he added, "the worries that the residents have over the radiation were quite serious. Their mental care will be important." As of this writing, Dr. Neriishi is scheduled to return to Tokaimura with examination results on October 15.

This most tragic accident, which exposed workers as well as members of the community to high levels of radiation, made headlines nationwide, and the scenes of RERF's medical team leaving Hiroshima Station and answering reporters' questions at the site were televised extensively across Japan.

Radiation Emergencies Discussed in August Meetings

by Kazuo Neriishi, Division Chief, Clinical Laboratories, Department of Clinical Studies, Hiroshima

The Third Meeting of the Japanese Association for the Management of Radiation Accidents and the Third Forum on Medical Management for Radiation Accident Emergencies were held on August 20 in Hiroshima. They were jointly sponsored by the Japanese Association for the Medical Management of Radiation Accidents, RERF, the Hiroshima International Council for Health Care of the Radiation Exposed (HICARE), and the Japan Atomic Energy Research Institute and coordinated by RERF Chairman Shigenobu Nagataki.

To ensure the smooth and effective medical care of radiation accident victims, JAMRA was established three years ago through the efforts of Dr. Yoshio Aoki of the Nuclear Safety Committee and others. Because of the atomic bombings, the health effects of exposure, the relief activities for survivors, and the peaceful use of nuclear energy have been discussed widely in Japan. However, there was previously no forum for discussion of the medical management of radiation accidents.

The meetings provided a place for 151 participants from Japan and

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***Board Meeting**, continued from page 1*

year plan was being promoted. He also talked about the increased interaction between RERF scientists and the international scientific community and the continued development of the F_1 study.

Dr. Taira reported on RERF's FY98 international collaborative activities and the Ministry of Health and Welfare (MHW)-funded international joint studies to be conducted by specialists invited from abroad. There was a further report on projects relating to Chernobyl, Chelyabinsk, and Semipalatinsk. Dr. Taira used slides to make a special detailed report on the September 1998 Second International Meeting on Radiation, Ecology, and Health in Kazakhstan and the situation in the Semipalatinsk area. During the fiscal year, 194 people from overseas visited RERF's Hiroshima and Nagasaki laboratories for briefings and training programs, including those related to the Japanese International Cooperation Agency (JICA) and the Hiroshima International Council for Health Care of the Radiation-Exposed (HICARE). The MHW international activities fund also supported the clinical genetics and immunology workshops in March.

Regarding administrative issues, Secretariat Chief Kunitoshi reported on current personnel status, revision in the FY98 salary scales, and concerns of the labor union. He reported that personnel strength as of 1 April 1999 was 284, the numbers of both research scientists and general employees having decreased by four during the year. The decrease in general employees was basically attributable to not replacing mandatory age retirees, but it was reported that the decrease in general employees has reached its limit and efforts are now to be made to employ new staff members for vacant posts. RERF revised its FY98 salary scales, following its usual practice of using the recommendations of the National Personnel Authority.

Mr. Kunitoshi also reported on FY98 expenditures and described the FY99 draft working budget. His financial report was approved.

Dr. Wolff reported on FY98 research activities, and Supervisor David Williams made the audit report of research activities for absent Supervisor Shudo Yamazaki.

The term of office for visiting directors prescribed in the Act of Endowment is four years, but this has posed problems in terms of continuity and the transfer of duties during the year when all outgoing directors are replaced. To allow for continuity, it is desirable that expiration dates be staggered. To this end, it was proposed and approved that the relevant provision in the Act of Endowment be revised. All visiting directors whose terms of office were to be renewed this year were reappointed with different terms of office.

Revisions in regulations concerning child care and care leave, loans, salaries of directors and the Secretariat chief, and FY98 wages were all approved.

A lively discussion took place concerning ways to approach the Department of Energy regarding the need to restore a second American director. However, no conclusion was reached, and it was agreed to carry this issue over to the next meeting.

It was decided to hold the next board of directors meeting in the U. S., the date to be finalized later.

***Scientific Council**, continued from page 1*

Pictured from left to right, front to back: Row one: Dr. S. Ushigome, Dr. M. Sasaki, Dr. J. W. Gray, Dr. J. M. Brown, Dr. M. S. Fox, Dr. T. Hirohata, Dr. S. Preston-Martin, Dr. H. Matsudaira, Dr. S. Yamazaki, Mr. D. Williams; ***Row two:*** Dr. S. Fujita, Mr. K. Kunitoshi, Mr. R. D. Sperry, Dr. D. L. Preston, Dr. E. Douple, Dr. S. Nagataki, Mr. Y. Takayama, Dr. S. Taira, Dr. S. Wolff, Mr. H. Kuroki, Dr. J. Weiss, Dr. S. Kyoizumi; ***Row three:*** Dr. M. Soda, Dr. S. Fujiwara, Dr. A. A. Awa, Dr. N. Nakamura, Dr. C. W. Heath, Jr., Dr. K. Mabuchi, Dr. M. Akahoshi, and Dr. T. Satoh. *(Photo by Junso Takayama.)*

Saeko Fujiwara and Masazumi Akahoshi), Statistics (Dr. Dale Preston), Radiobiology (Drs. Seishi Kyoizumi and Keisuke Iwamoto), and Genetics (Dr. Nori Nakamura), followed by summaries of two recent research workshops, Clinical Genetics (Dr. Norio Takahashi) and Immunology (Dr. Yoichiro Kusunoki). There was specific discussion in the afternoon about future plans for F_1 studies.

The second morning was devoted to review of research and future plans in the epidemiology department, particularly with respect to the recommendations offered by the departmental peer review meeting held in November 1998. The discussion, led by Dr. Kiyohiko Mabuchi, continued the first day's focus on F_1 Study plans, followed by comments from Dr. Senjun Taira regarding ongoing dialogue between RERF and the *Niseikyo* (All-Japan Second-Generation A-bomb Victims Liaison Council). In the afternoon, there was further discussion of future interdepartmental research plans, followed by separate meetings between council members and individual departments.

The council used the morning of the third day to write its report. In the afternoon, Cochairmen Fox and Matsudaira presented a summary of the report and its recommendations in its preliminary draft form. The final report was presented to RERF's board of directors when they met in Nagasaki in June. *(See cover story.)* The next meeting of the Scientific Council will take place April 10-12, 2000.

Other council members present included Drs. Tomio Hirohata, *professor emeritus, Kyushu University*, Shinichiro Ushigome, *professor, Department of Pathology, Jikei University School of Medicine*, Masao Sasaki, *professor, Radiation Biology Center, Kyoto University*, Susan Preston-Martin, *professor, Department of Preventive Medicine, University of Southern California,* Joe W. Gray, *professor of laboratory medicine, University of California, San Francisco*, and J. Martin Brown, *professor, Department of Radiation Oncology, Stanford University School of Medicine.* Drs. Yusuke Nakamura, *director, Human Genome Center, University of Tokyo,* and Theodore L. Phillips, *chairman, Radiation Oncology, University of California, San Francisco,* were unable to be present. Observers included RERF Supervisors David Williams and Shudo Yamazaki as well as Mr. Hiromasa Kuroki, Dr. Toshinobu Satoh, and Mr. Yasunobu Takayama, of the Japanese Ministry of Health and Welfare, Dr. Evan Douple, of the U. S. National Academy of Sciences, and Dr. Joseph Weiss, of the U. S. Department of Energy.

Radiation and Noncancer Disease Mortality

by Donald A. Pierce, Senior Scientist, Departments of Statistics and Epidemiology, Hiroshima
Yukiko Shimizu, Assistant Chief, Department of Epidemiology, Hiroshima
Dale L. Preston, Chief, Department of Statistics
Kiyohiko Mabuchi, Chief, Department of Epidemiology, Hiroshima

Can radiation exposure cause increased noncancer death rates many years after exposure? In a forthcoming paper,[1] summarized here, we strongly suggest that it does.

This is not the first RERF publication to suggest such effects,[2] but the previous report was met with strong skepticism. A primary reason is that there is no established mechanism for such effects. Indeed, many have thought such a mechanism implausible. Furthermore, there is a general belief that no other human studies have shown such effects in the dose range of the atomic-bomb survivors. Thus, it is not surprising that many scientists have dismissed the earlier findings as reflective of some kind of bias in the RERF study, such as misclassified cancer deaths or nonradiation differences, e.g., the proportion of smokers, between high- and low-dose survivors.

However, there is increasingly clear evidence of an association, whether causal or not, between A-bomb radiation exposures and late noncancer disease mortality rates. In the new report, we consider biases that might explain such an association and conclude that bias is unlikely to account for the apparent radiation-associated excess risk of noncancer diseases in the survivors. Moreover, we note that associations have been seen in other human studies,[3-5] but in accordance with good epidemiologic practice, investigators have generally chosen not to overemphasize what seem more plausibly to be chance variations than causal effects. However, we believe that many will agree that the time has come for new attitudes toward such findings and that reconsideration may well lead to the elucidation of biologically plausible mechanisms for such effects.

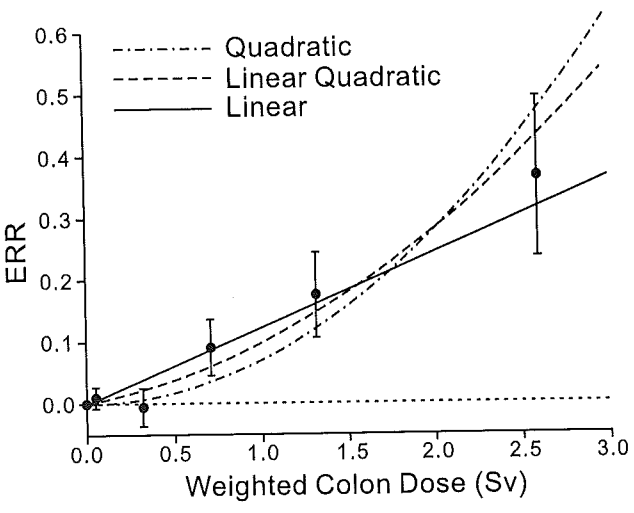
Figures 1 and 2 provide a general overview of the basic findings in our report, which considers more than 27,000 noncancer deaths among almost 87,000 survivors in the Life Span Study cohort between 1950 and 1990. Death rates for the broad categories of heart disease, stroke, digestive diseases, and respiratory diseases exhibit statistically significant trends with dose, with age-specific rates being increased by about nine to 18% following 1-Sv exposure. These categories account for more than 75% of the total noncancer disease deaths. There is no indication of a dose response for the infectious diseases (primarily tuberculosis) or other diseases (typically senility or other ill-defined conditions). Figure 1 presents the dose response in a pooled analysis of deaths in the six noncancer disease groups shown in Figure 2. There is strong evidence of a graded dose response with a fairly clear indication of elevated risks at doses in excess of 0.5 Sv. Noncancer death rates are increased by about 10% following exposure to 1 Sv. There remains uncertainty about the shape of the dose response, as indicated by the three dose-response curves shown in the figure, providing statistically equivalent descriptions. In particular, there is considerable uncertainty regarding risks in the range below 0.2 Sv, of primary interest for radiation protection. Although in the higher dose range, the relative increase in mortality has been fairly constant over the follow-up, the evidence for increased risk in the lower dose range has increased with the passage of time. This is because of an apparent "healthy survivor effect" that results in reduced death rates of proximal survivors during the first decade or so of the follow-up after 1950.

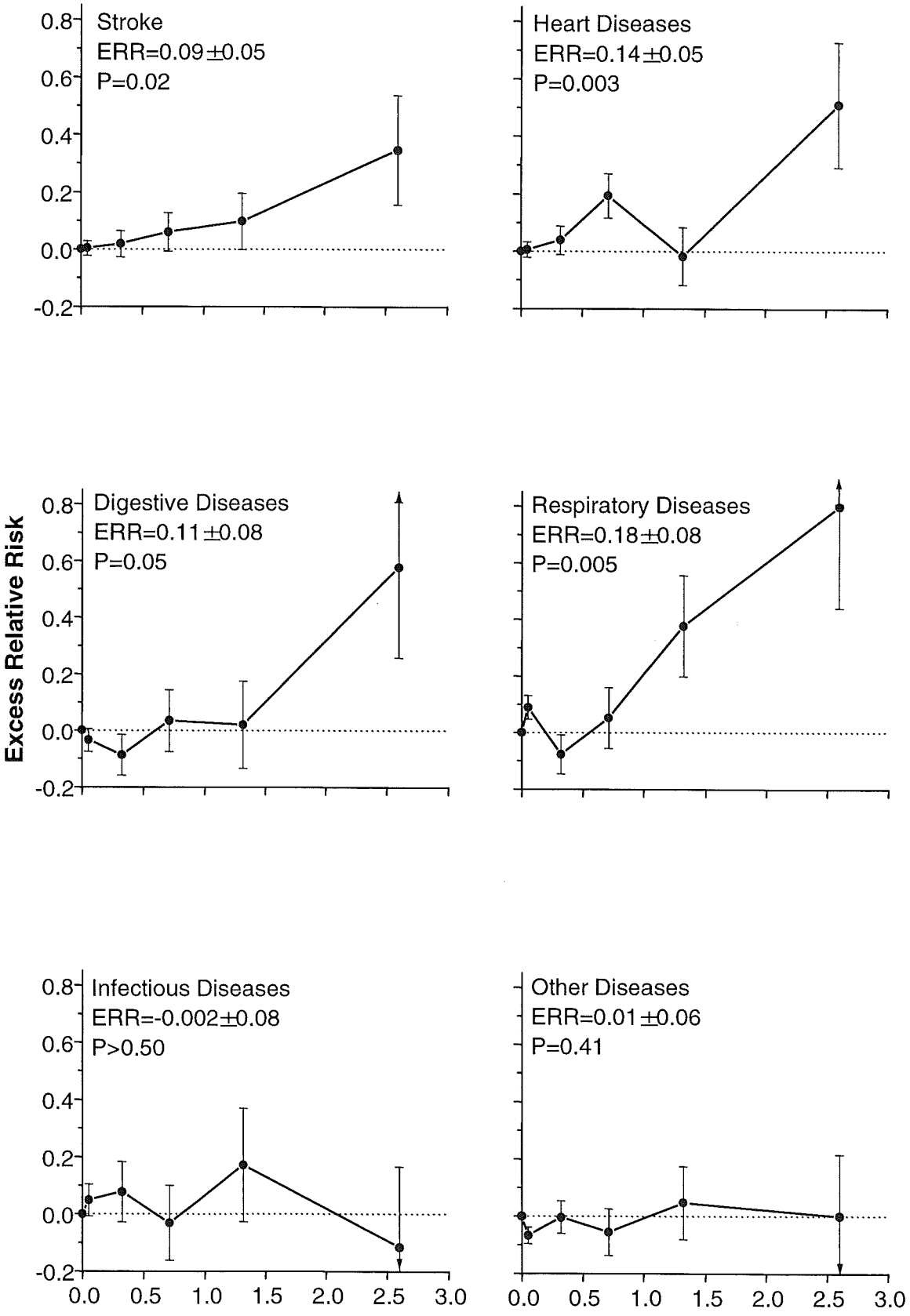
The relative increase in noncancer death rates is considerably smaller than that seen for cancer mortality, which, when averaged over sex, is about 60% per sievert for age at exposure 30. However, because noncancer deaths are much more common than cancer deaths, the absolute increase in noncancer rates is more than half that for solid cancers. Our estimates of the number of radiation-associated noncancer deaths in this cohort for the current follow-up range from 140 to 280, depending on assumptions regarding the shape of the dose response. We estimate that there have been about 340 excess solid cancer and 90 excess leukemia deaths over the same period.

We devote considerable attention to the possibility that the observed association between radiation dose and noncancer risks might be an artifact of some sort of bias or other problems with the data. Several years ago, RERF researchers considered whether or not the noncancer dose response could be explained by plausible misclassification of cancer deaths.[6] Using the data on death-certificate misclassification rates derived from the RERF autopsy program, they found that such errors could not explain the noncancer results. Thus, primary attention turned to the issue of whether there might be large enough differences between high- and low-dose survivors with respect to mortality risk factors other than radiation dose to induce an apparent but spurious association between radiation dose and mortality.

The range of radiation doses and the graded nature of the apparent association with noncancer mortality rates are key considerations in interpreting LSS noncancer findings. If the study were only a two-group comparison of highly- and negligibly-exposed survivors, particularly

*See **Noncancer Mortality**, page 8*





Facing page: **Figure 1.** Dose response for pooled noncancer diseases; the error bars correspond to ± one standard error. ***Above:*** **Figure 2.** Dose response for major noncancer diseases, 1950-1990. ERR estimates and standard errors are given for six dose categories: <0.005, 0.005-, 0.5-, 1.0-, and ≥ 2.0 Sv.

Noncancer Mortality, *continued from page 6*

with an urban-rural distinction between the groups, something like a 10% higher noncancer death rate in the highly-exposed group could be readily dismissed as spurious. However, since the noncancer death rates are increasing gradually with radiation dose, the nature of the evidence is very different from and much stronger than that from a simple two-group comparison. In particular, nonradiation risk factors could cause the observed association only if those factors have a graded relation to radiation dose. When this occurs, the magnitude of the apparent radiation effect would be smaller than the magnitude of the association between the nonradiation factors and death rates.

The nature of the LSS essentially precludes this possibility because radiation doses drop off very sharply with distance from the bombs–decreasing by a factor of 10 for each 600-meter increase in distance from the hypocenter. Thus, survivor doses vary widely within narrow distance bands, and so, there is little scope for nonradiation risk factors to vary in a manner highly correlated with dose. One approach we used to address the question of whether or not the apparent dose effect is spurious involved restricting analysis to survivors who were 900 to 1200 meters from the hypocenters at the time of the bombs. Even within this range, there is a clear and statistically significant association between noncancer death rates and radiation dose.

Over the past decades, RERF has conducted a number of mail surveys of LSS cohort members, which provide information on various potentially important lifestyle and socioeconomic factors that may be related to death rates, such as smoking, alcohol consumption, and occupation. In the report, we used follow-up data on respondents to the surveys carried out in 1965 and 1978 for a direct assessment of the impact of such nonradiation factors. The strength of evidence for an association between radiation and noncancer death rates was not changed appreciably by these adjustments and the estimated magnitude of this association varied by less than 10% for any of the factors considered.

Is there a plausible mechanism for the association? First, consider the differences from a radiation effect on cancer. Although the precise mechanisms for that effect are not known, it is fairly clear that cancers have a monoclonal origin. That is, genetic damage by radiation to a single stem cell can, quite plausibly, increase the chance that the cell will become malignant by a given age. While genetics certainly plays a role in the development and progression of many noncancer diseases, these diseases do not generally appear to have a monoclonal origin. (However, it has recently been suggested[7,8] that some types of arteriosclerosis may involve monoclonal plaque cells.) This nonmonoclonal nature of noncancer diseases suggests that genetic factors affecting noncancer disease rates are likely to be present in all cells of the body, a phenomenon unlikely to be affected by radiation exposure. Thus, it seems reasonable to conjecture that the long-term effects of radiation exposure on noncancer disease rates are not primarily the result of mutations in a single cell but reflect more general systemic effects of the exposure. Such mechanisms could possibly involve the immune system. Recent research indicates that bacterial or viral infections are associated with cardiovascular disease incidence,[9-11] and it is even more clear that viral infections are a major risk factor for chronic liver disease.[12] A substantial whole-body radiation dose, say 0.5 Sv or more, to the bone marrow probably kills a large fraction of the marrow stem cells. The marrow stem cells are largely regenerated from the reduced pool of surviving, but possibly damaged or otherwise atypical stem cells. Thus, it seems plausible that radiation exposure could result in subtle, but permanent, changes in the hematopoietic or immune systems, which could increase the risk of a variety of noncancer diseases. Indeed, there is evidence (in the LSS and elsewhere) that radiation exposure does have long-term effects on these systems, e.g., dose-associated changes in the proportions of certain types of T-helper cells and small increases in various measures of inflammation. These effects are difficult to measure and their consequences uncertain, but it may be that they are larger and of greater consequence than has been thought thus far. The fact that death rates for the class of diseases we termed "infectious" show no association with radiation dose might be taken as evidence against such a theory. However, the theory would not require that all infectious diseases be so affected. The "infectious" disease class consists primarily of deaths due to tuberculosis, and it could be that tuberculosis puts fewer or different demands than other diseases on the immune system.

While we feel that the LSS mortality and clinical data provide convincing evidence of the existence of a radiation effect on noncancer diseases in the atomic-bomb survivors, there are many uncertainties about the nature and implications of this effect. Several steps can be taken to deal with these uncertainties. The RERF clinical data, which also indicate associations between radiation dose and the occurrence of various noncancer diseases, should be used more extensively to help determine specific diseases and disease risk factors that appear to be affected by radiation exposure. Additional follow-up of the LSS mortality data should help determine factors, such as sex and age, that affect the overall level of risk, provide more insight into the shape of the response at low doses, and give us a better idea of the absolute magnitude of the noncancer excess in relation to that for solid cancer. It will also be important to consider the evidence for elevated noncancer risks in other radiation-exposed populations. The RERF noncancer findings should also prompt researchers to seek a better understanding of the biological mechanisms behind the observed effects. The latest findings of noncancer effects in the survivors will certainly be considered by groups concerned with radiation protection, such as UNSCEAR, ICRP, and BEIR; however, uncertainties about the magnitude of low-dose effects and the lack of a biological basis for these effects will tend to limit the impact of current findings.

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See ***Noncancer Mortality,*** *bottom of next page*

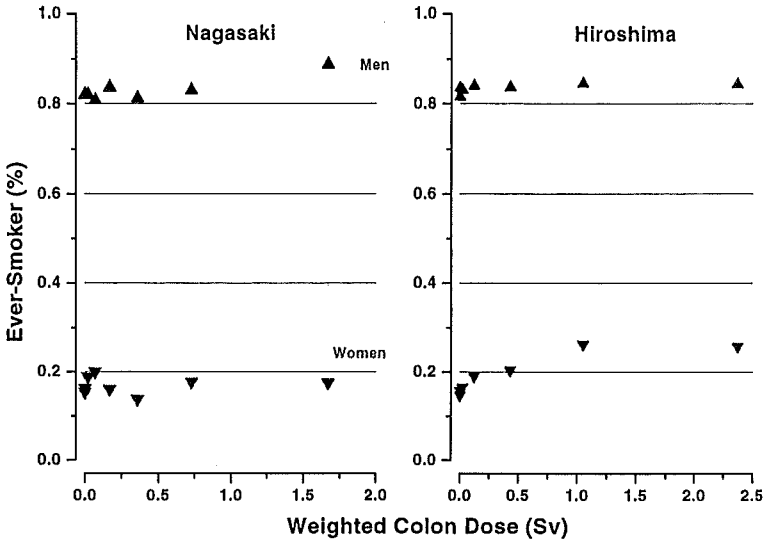
Facts and Figures

Cigarette Smoking and Radiation Dose in the Life Span Study

by Dale L. Preston, Chief, Department of Statistics

There has been a concern that an association between cigarette smoking and radiation dose, for whatever reason, might distort estimates of radiation effects in the Life Span Study (LSS). Here, we describe frequencies of smoking among LSS participants in relation to radiation dose using data from eight LSS mail surveys or interviews carried out between 1965 and 1990. We have smoking information for 63% (54,554) of the 86,572 LSS survivors whose radiation doses are known. The panels in the figure present, by dose categories, the percentage of men and women in each city who indicated they were either current or past smokers (ever smokers). There is no association between smoking and radiation dose other than a modest trend for women in Hiroshima, where rates increase from about 15% to 25%. This probably reflects distance-related urban-rural differences that are more correlated with dose in Hiroshima than in Nagasaki.

The distortion in radiation risk estimates resulting from a failure to allow for smoking in analyses depends on both the magnitude of the smoking effect on relevant disease or death rates and the nature of the association between dose and smoking. For the LSS data, failure to allow for smoking does not greatly distort radiation risk estimates, even when limited to Hiroshima females. Taking solid cancer mortality as an example, age-specific solid-cancer death rates for current or past smokers are 40% higher than for never smokers in the LSS. The proportion of women with doses of 1 Sv who have ever smoked (about 25%) is only ten percentage points higher than for women with very low doses (15%). Thus, adjusting for smoking effectively reduces cancer rates of Hiroshima women at 1 Sv by only about 4% (40% x 10%). Careful analysis of joint effects of radiation and smoking cannot be considered here, but the current estimated radiation effect for women is that those at 1 Sv have 80% higher cancer rates than unexposed women. A 4% adjustment for smoking, therefore, has little effect on radiation risk estimates for solid cancer, even for Hiroshima females. For lung cancer, which is primarily caused by smoking, considerations are different. The joint effects of radiation and smoking should be considered even when there is no relation between smoking and radiation dose since the relationship between smoking and lung cancer is very strong. (An *RERF Report* on this is now being prepared.) It is clear, though, that the weak association between smoking and dose among Hiroshima women does not explain the apparent radiation effect, even for lung cancer.



Noncancer Mortality, *continued from previous page*

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Persistent Inflammation in Atomic-Bomb Survivors

by Kazuo Neriishi, Chief, Division of Internal Medicine, Department of Clinical Studies, Hiroshima and
Eiji Nakashima, Research Scientist, Department of Statistics

In 1986, Sawada *et al.* reported that erythrocyte sedimentation rates, measured in AHS survivors between 1968 and 1980, increased with increasing radiation dose.[1] We recently extended those data by analyzing various laboratory indicators of inflammation measured in 6,304 survivors between 1988 and 1992.[2] Regression analysis, adjusted for age, sex, smoking, and city of residence, showed statistically significant associations with radiation dose for leukocyte counts (71.0/mm^3/Gy, p=0.00151), erythrocyte sedimentation rate (1.58mm/hour/Gy, p=0.0001), corrected erythrocyte sedimentation rate (1.14mm/hour/Gy, p=0.0001), alpha 1 globulin (0.0057g/dl/Gy, p=0.0001), alpha 2 globulin (0.0128g/dl/Gy, p=0.0001), and sialic acid (1.2711mg/dl/Gy, p=0.0001), but not for neutrophil counts (29.9/mm^3/Gy, p=0.1729).[2] Standardized scores combining results from these seven inflammatory tests[3] showed significant associations with radiation dose for both persons with and without inflammatory diseases, and for two inflammatory conditions in particular, chronic thyroiditis and chronic liver diseases (Figure 1).

Since the laboratory indicators of inflammation that we studied are not specific for particular clinical diseases, the implication of their dose-response pattern is hard to interpret. The general occurrence of infectious diseases in survivors is not related to radiation dose.[4] Such a relationship does exist, however, for other diseases in which infection may play an etiologic role. In addition to certain cancers, such diseases include arteriosclerotic cardiovascular disease,[5] where studies elsewhere suggest that inflammatory processes and, possibly, infections with particular infectious agents (e.g., *Chlamydia pneumoniae, Helicobactor pylori*, cytomegalovirus), may underlie the development of atheromatous plaques.[6] In addition, virologic studies in A-bomb survivors have suggested dose-response alterations in immune response to infection with hepatitis B virus and Epstein-Barr virus.[7,8]

Conceivably, such observations may reflect immunologic abnormalities resulting from radiation-induced alterations in T-lymphocyte clones, as suggested in other RERF studies.[9-11] Such alterations might lead in turn to increased susceptibility to certain chronic infections and hence to persistent dose-related increases in inflammation indicators. These changes might also involve autoimmune mechanisms, as suggested by our data regarding chronic thyroiditis. In support of these ideas, preliminary analyses of data from 403 AHS patients, in whom both inflammation indicators and T-cell ratios were measured, suggest that increased inflammation does correlate with decreases in CD4 T-cells (Figure 2).

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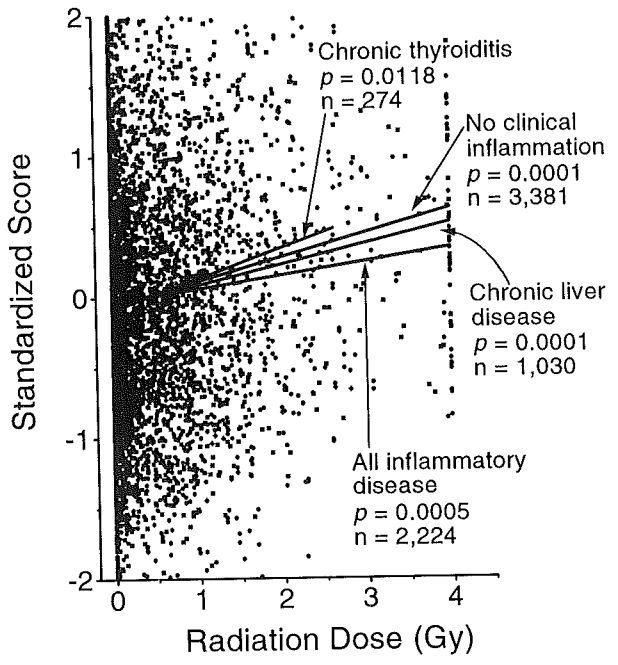

Figure 1. *Standardized scores[3] by radiation dose and inflammatory disease groups*

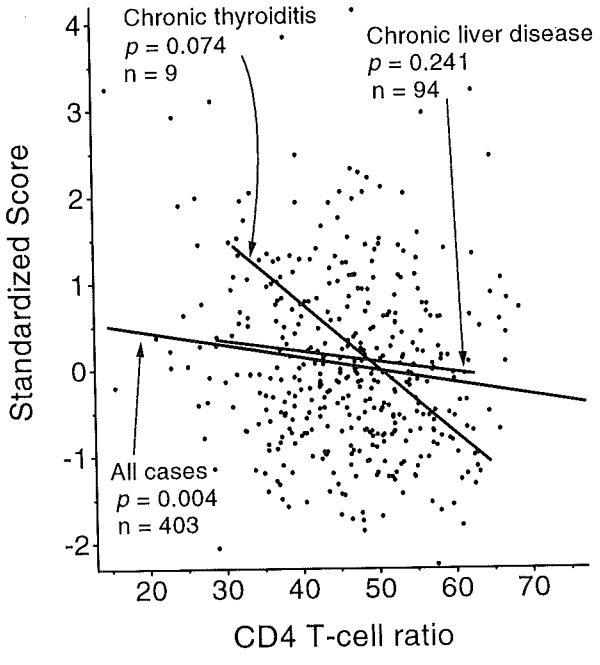

Figure 2. *Standardized scores[3] by CD4 T-cell ratio and inflammatory disease groups*

Thyroid Diseases in Hiroshima and Nagasaki Atomic-Bomb Survivors

by Tan Tominaga, Division of Clinical Laboratories Chief, Department of Clinical Studies, Nagasaki

This summer, RERF's Departments of Clinical Studies in Hiroshima and Nagasaki began a study to evaluate the relationship between atomic-bomb radiation and thyroid disease occurrence in the two cities. The prevalence of such disorders, including thyroid nodules and autoimmune thyroid diseases, will be studied in approximately 5,500 Adult Health Study (AHS) participants. A similar study was conducted in the Nagasaki AHS cohort from 1984 to 1987 (Nagataki S, Shibata Y, Inoue S, Yokoyama N, Izumi M, Shimaoka K. Thyroid diseases among atomic bomb survivors in Nagasaki. *JAMA* 1994; 272(5): 364-370). It found significant relationships between radiation dose and prevalence of solid thyroid nodules, including carcinomas and adenomas, and of autoimmune hypothyroidism.

The new study will therefore give special attention to reassessing the relationship between thyroid diseases and radiation dose in Nagasaki now that more than ten years have passed. In particular, solitary nodules detected in the earlier study will be re-evaluated through precise ultrasound nodule volume measurement. Nagasaki participants will include all surviving persons in whom thyroid nodules or a history of operated nodules were recorded in the previous study. At that time, solid nodules, cysts, or mixed solid/cyst nodules were found in 190 subjects. Postoperative histopathological diagnoses were established in 40 cases, including 21 carcinomas, 16 adenomas, three adenomatous goiters, and 51 nodules were without histologic diagnosis. Ultrasound evaluation, as well as re-evaluation, of long-standing nodules in both cities is important because long-term follow-up has shown an increase in malignant thyroid tumors diagnosed by fine-needle aspiration of thyroid nodules, especially when such nodules present with increased volume, as multinodules, or with intranodular calcification. The development and common use of ultrasound techniques have enabled the diagnosis of more thyroid nodules, thus focusing greater attention on the management of solitary nodules, including "incidentalomas." Since no follow-up data yet exist regarding pathologic outcomes based on precise nodule volume measurements, long-term ultrasound observations can be expected to enhance present guidelines for the clinical management of thyroid nodules.

The new study is expected to require four years in Hiroshima and two-and-a-half years in Nagasaki to complete one or two cycles of AHS examinations. Study participants will include 3,314 Hiroshima and 2,175 Nagasaki AHS cohort members. All participants will undergo palpation of the thyroid gland, thyroid function testing, autoantibody testing, and thyroid ultrasound measurement. A questionnaire will seek information concerning family history of thyroid disorders and personal history of previous thyroid diseases and treatments. The volume of nodular lesions detected on the ultrasound screen will be calculated based on their measured longitudinal and transverse diameters and depths. For persons who had nodules detected in the previous Nagasaki study, an arch-automatic scanning ultrasound instrument (7.5 MHz annular array probe, immersion-in-water method), identical with the one used previously, will be used to scan the thyroid. Subjects with nodular thyroid lesions or thyroid function abnormalities in the present study will be referred to the Nagasaki and Hiroshima University Schools of Medicine to establish precise diagnoses and to provide appropriate clinical management.

Potentially, this prevalence study may lead to cohort-based laboratory investigations regarding possible molecular genetic mechanisms underlying thyroid carcinogenesis. There is particular interest in the potential role of *p53* tumor suppressor gene abnormalities following radioiodine therapy. Although there is no evidence that radioiodine itself induces thyroid neoplasia, poor prognosis has been observed after such therapy in patients whose thyroid cancers harbor *p53* abnormalities. Although no information is available regarding radioiodine uptake at the time of the atomic bombings, it will be of interest to determine the presence of *p53* abnormalities in relation to A-bomb dose among patients with thyroid cancer requiring thyroidectomy. Conceivably, radiation may contribute not only to DNA damage but to avoiding apoptosis of thyroid carcinoma cells by enhancing *p53* dysfunction.

Inflammation, *continued from previous page*

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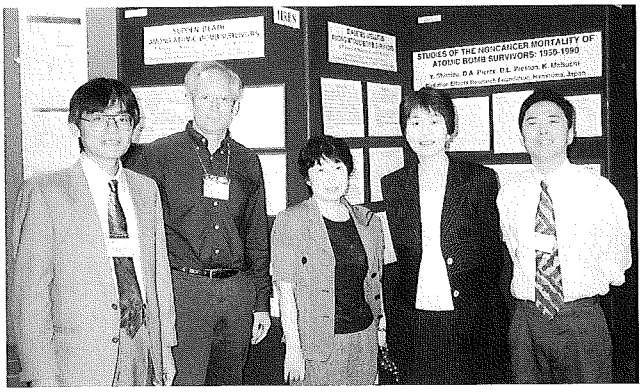
International Congress on Radiation Research
by Dale L. Preston, Chief, Department of Statistics

The International Congress on Radiation Research (ICRR) held its eleventh meeting at University College in Dublin, Ireland July 18-23. The Congress, held once every four years, is one of the major international meetings concerned with radiation research. This year's more than 1,000 registrants included Drs. Ban, Fujiwara, Hayashi, Kasagi, Preston, Sharp, and Shimizu from RERF.

Dr. Ban explained some of his recent work on micronuclei, Dr. Fujiwara described their new analyses of diabetes prevalence in the survivors, Dr. Hayasahi presented new findings on plasma IL-6 levels and radiation dose, Dr. Kasagi outlined results on the incidence of sudden death, Dr. Preston reported on new findings from the Life Span Study analyses of cancer and noncancer risks, Dr. Sharp described recent RERF work on liver diseases, and Dr. Shimizu provided some highlights of our new paper on noncancer disease risks. (*See page 6.*) RERF research was also featured in many of the presentations by non-RERF scientists.

The meeting began after a short talk by Irish President Mary McAleese on the need for scientists to collaborate to solve difficult problems. Sessions on radiation-induced genetic instability and other (potentially) nonmutational radiation effects were followed by epidemiology sessions.

The second day began with a "debate" before a very large audience on the linear nonthreshold model, which forms the basis of radiation protection. The model is based on the idea that radiation's detrimental effects increase in proportion to dose received, even at very low doses. This use of the linear model in the development of radiation protection standards is currently under attack by various groups, represented at this meeting by people who feel that small radiation doses can be safely ignored. RERF data figure prominently in discussions of this issue



Drs. Fumiyoshi Kasagi, Gerald Sharp, Yukiko Shimizu, Saeko Fujiwara, and Tomonori Hayashi in front of poster presentations at Dublin meeting.

Later in the day, radiobiologist Michael Fry, former editor of *Radiation Research*, received an award and gave a special lecture on the past, present, and future of radiation research. Dr. Fry spoke about RERF's continuing important role in the future of radiation research. He highlighted some of our newest results (on noncancer risks) as evidence of the continued relevance of RERF studies and stressed the importance of continued support for RERF work.

The week continued with many interesting lectures and poster presentations. RERF-related participants included Evan Douple, Jim Trosko, John Zimbrick, Elaine Ron, Sarah Darby, Richard Miller, Albrecht Kellerer, Victor Ivanov, and Natasha Shilnikova.

Fortieth A-Bomb Late Effects Meeting
by Sadayuki Ban, Associate Senior Scientist, Department of Radiobiology

The 40th A-bomb Late Effects Research Meeting, sponsored by the Hiroshima A-Bomb Casualty Council, was held in Hiroshima on June 6. RERF Chairman Shigenobu Nagataki served as meeting chairman and Department of Genetics Chief Nori Nakamura chaired the executive committee and gave a special lecture. The program consisted of Dr. Nagataki's opening address and 40 general presentations, including twelve related to atomic-bomb radiation effects and four by RERF researchers. Also on the program were Dr. Nakamura's special lecture, a special report, a symposium, and the closing address made by RERF Director Senjun Taira. Ms. Tomoko Shinohara and Dr. Tomonori Hayashi, from the Department of Radiobiology, Dr. Yoshisada Shibata, formerly from Epidemiology, and Dr. Eiji Nakashima, from Statistics, were the RERF presenters.

Radiobiology Technician Tomoko Shinohara presented work done in collaboration with the Department of Genetics (Ban S, Shinohara T, Itoh M, Nakamura N). Her presentation, "Whole genome amplification to immortalize the DNA extracted from formalin-fixed and paraffin-embedded tissue sections," introduced DNA immortalization (or whole genome amplification), an interesting technique strongly expected to be useful for future genome studies on the late effects of A-bomb radiation. Its basic purpose is to produce a large amount of DNA through polymerase chain reaction (PCR) amplification of short DNA fragments covering the whole genome. This technique has great potential for use at RERF because the various stored biological materials obtained from A-bomb survivors are the sole materials for the retrospective study of the genetic effects of radiation and the amount of DNA extracted from pathological tissues is extremely small. DNA immortalization offers an alternative to using up the valuable DNA in present studies through permanent preservation. Ms. Shinohara related that a group from Nagasaki University reported feasibility test data for DNA immortalization using the Lone-Linker (LL) PCR method and demonstrated the LL-PCR method's effectiveness in immortalizing the DNA extracted from fresh tissues (fresh DNA) but not in immortalizing the DNA extracted from formalin-fixed and paraffin-embedded tissues (archival DNA). Ms. Shinohara indicated that RERF researchers had succeeded in immortalizing fresh and archival DNA using the degenerate oligonucleotide-primed PCR method.

Other RERF talks among the general presentations were those by RERF Radiobiologist Tomonori Hayashi, who presented the collaborative work of the Departments of Radiobiology, Statistics, and Clinical Studies, "Late effects of atomic-bomb radiation on human immune responses: Plasma IL-6 and immunoglobulin levels in atomic-bomb survivors" (Hayashi T, Kusunoki Y, Maki M, Kubo Y, Yamaoka M, Kasagi F, Fujiwara S, Kodama K, Kyoizumi S); Statistician Eiji Nakashima, who spoke on the "Analysis of inflammatory test measurements in atomic-bomb survivors with principal component analysis" (Nakashima E, Neriishi K); and Hiroshima Epidemiology

See ***Late Effects****, bottom of next page*

Ni-Hon-Sea Meeting

by Fumiyoshi Kasagi, Associate Senior Scientist, Department of Statistics

A meeting on senile dementia was held on 5 and 6 April in Honolulu as part of the Ni-Hon-Sea joint comparative study. Drs. Michiko Yamada, of the RERF Department of Clinical Studies, Hiroshima, Fumiyoshi Kasagi, of RERF's Department of Statistics, and Yasuyo Mimori of Hiroshima University, represented Hiroshima at the meeting. Participants from the Hawaii group were Drs. Lon White, Helen Petrovitch, Kamal H. Masaki, and Robert D. Abbott and from the Seattle group, Drs. Eric B. Larson, Amy B. Graves, and Steven D. Edland. The meeting's objective was to search for a consensus on a method of analysis for comparing the incidence of dementia.

Similar to the Ni-Hon-San (San = San Francisco) project, which focuses on circulatory system diseases, the Ni-Hon-Sea study compares subjects with a common Japanese racial background, AHS participants in Japan (Nippon/Ni) and Japanese-American immigrants in Honolulu, Hawaii (Hon) and Seattle, Washington (Sea), for the prevalence or incidence of dementia and ratio of dementia subtypes among subjects from the three locations. The goal of the study, which was undertaken in 1990, is to observe how different cultural and environmental factors affect the prevalence or incidence of dementia and the subtype ratio, and therein lies the study's uniqueness.

Consensus was expected to build on previously published material on the prevalence of dementia among the subjects in the three locations ([1] Yamada M, Sasaki H, Mimori Y, *et al.*: Prevalence and risks of dementia in the Japanese population: RERF's Adult Health Study Hiroshima subjects. *Journal of the American Geriatric Society* 1999; 47[2]: 189-195; [2] White L, Petrovitch H, Ross W, *et al.*: Prevalence of dementia in older Japanese-American men in Hawaii: The Honolulu-Asia Aging Study. *Journal of the American Medical Association* 1996; 276[12]: 955-960; and [3] Graves AB, Larson EB, Edlund SD, *et al.*: Prevalence of dementia and its subtypes in the Japanese-American population of King County, Washington State: The Kame Project. *American Journal of Epidemiology* 1996; 144[8]: 760-771).

First, Dr. Yamada gave an overview of the dementia study of the AHS population and explained the study design in each of the three locations. A question-and-answer session then followed, which focused, in particular, on the different methods used for screening, analysis, and follow-up, and further discussion ensued. Subjects discussed the first day included analytical standardization of dementia, a possible method for incidence estimation utilizing different follow-up techniques, how to deal with the high frequency of deaths due to the old age of subjects, how to deal with dropouts from examination, and using a revised statistical model where possible dementia cases in the dead subjects mentioned above could be taken into calculation for incidence. The second day, issues discussed were neurological and clinical evaluation for vascular dementia regarding diagnostic criteria and neuroimaging, such as CT and MRI.

***Late Effects**, continued from bottom of previous page*

Chief Kiyohiko Mabuchi, who reported on "The significance of long-term epidemiological studies about the health effects of atomic-bomb exposure."

In his special lecture, "Study of the genetic effects of A-bomb radiation-Past, present, and future," Dr. Nakamura explained that, though since 1948 RERF has carried out various large-scale studies to find radiation-related genetic effects among the children of A-bomb survivors, no clear data suggesting genetic effects have been obtained. However, Dr. Nakamura indicated that this does not mean that A-bomb radiation has no such genetic effect, and he expressed his hope that genetic-effect studies will enter a new phase with the introduction of newly developed state-of-the-art genome analysis techniques.

"Study of late A-bomb effects and welfare of A-bomb survivors–Significance, re-examination, and prospects," a symposium moderated by Dr. Shigenobu Nagataki and Nagasaki University School of Medicine Dean Hiroshi Saito, was the highlight of the meeting. Hiroshima University Professor Nanao Kamada spoke from the perspective of medical and biological research and Nagasaki University Professor Sadayoshi Shibata from his experiences in the field of epidemiological studies. MHW Assistant Director Toshinobu Satoh reported on relief measures for A-bomb survivors, and Dr. Chikako Ito, director of the Health Management and Promotion Center of the Hiroshima A-bomb Casualty Council, commented on the welfare and health management of A-bomb survivors. The meeting concluded with Ms. Sakae Ito and Mr. Koichi Wada sharing their horrifying A-bomb experiences, the "terror and misery of the nuclear bombs."

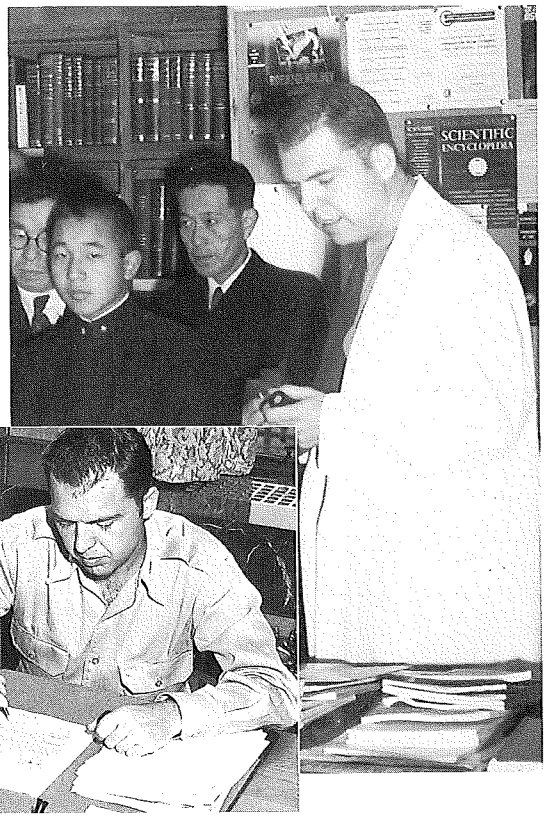
***NCI Meeting**, continued from page 24*

on breast and thyroid cancers, those participating at the informal workshop agreed that colon cancer is also an important cancer to consider because it is one of the high-risk cancers following radiation exposure and perhaps one of the most studied tumors with respect to the multiple stages involved for the transition of a normal cell to one that is malignant. Since normal, benign tumor, and malignant tumor tissues from the A-bomb survivors should be available, a colon cancer study may be a very logical step in understanding the step-wise mechanisms of radiation carcinogenesis. And, considering the limited Department of Radiobiology personnel resources at present and the fact that breast and thyroid will be the main studies focused on here, a colon study would be a worthwhile collaborative endeavor.

During the three-day meeting and visit to the NCI labs, the RERF scientists were impressed by the high level of research conducted in many areas of special interest to the NCI group, and they felt strongly that future collaborations with NCI would be tremendously beneficial to RERF. Similarly, it was understood that the unique resources available at RERF would be of great importance in advancing NCI interests. Therefore, it was a consensus that more frequent discussion between RERF and NCI would be essential in developing specific collaborative plans and that NCI scientists should be invited to RERF and vice versa for periods of a week to a few months. There was also a strong sense of the limited size and, therefore, capabilities of the current RERF molecular biology group in comparison to the NCI group and the need for more effort in finding ways to develop external collaborations with NCI as well as other institutes for RERF to be competitive in this rapidly growing area.

Carl F. Tessmer, ABCC's First Director, Pays April Visit to RERF

by Michael E. Rappaport, Honorary Consultant and former ABCC Administrator



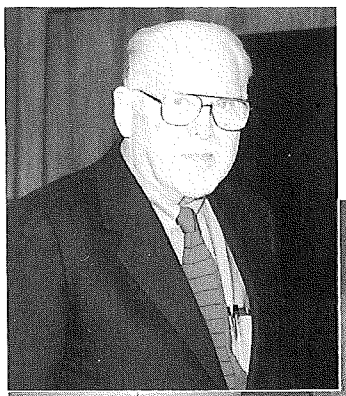
Dr. Carl F. Tessmer, first director of ABCC, made a brief visit to RERF April 27. He was in Japan with his wife, Shizue, on a hastily arranged trip to attend memorial rites for Mrs. Tessmer's brother in Hongo, in eastern Hiroshima Prefecture. Although he was scheduled to return directly from Hiroshima International Airport, near Hongo, Dr. Tessmer felt he just had to look in on RERF, which he had last seen in March 1988, when he gave an address at ABCC-RERF's 40th anniversary celebration.

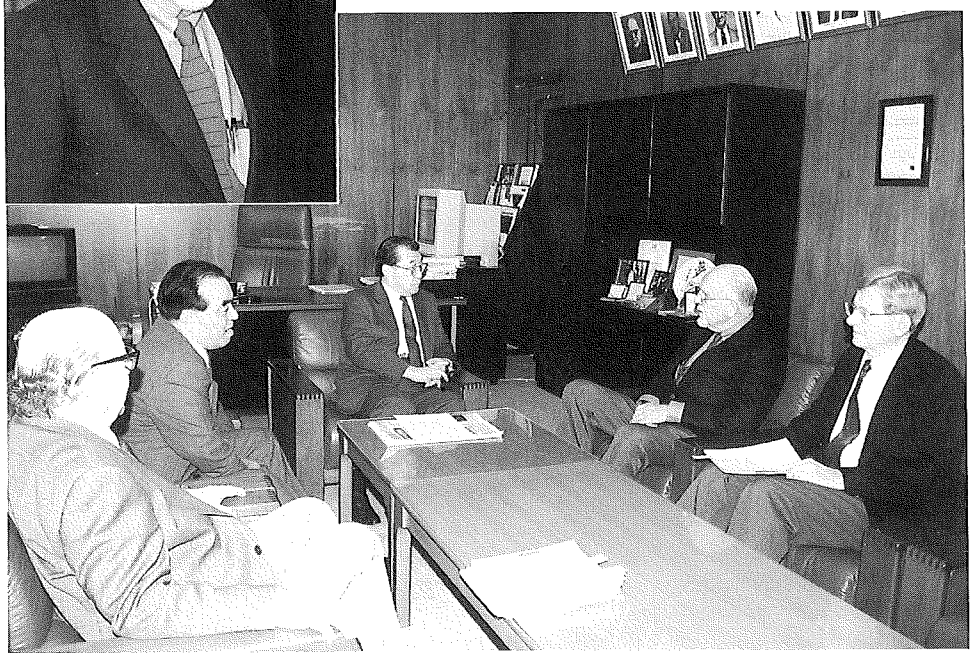
Dr. Tessmer was received in the chairman's office by Chairman Shigenobu Nagataki and Permanent Director Senjun Taira. Administrative Advisor Richard D. Sperry and Honorary Consultant Michael E. Rappaport were also present.

Dr. Nagataki briefly described the present RERF situation. Dr. Tessmer reported that he maintains his interest in ABCC-RERF affairs through publications, news articles, and contacts with colleagues with news of the organization. He said that he also regularly visits the RERF home page and finds it thoroughly interesting and useful.

Dr. Tessmer then met with Secretariat Chief Kazumasa Kunitoshi in his office, which in the early days was the director's office and Dr. Tessmer's office from December 1950, when he moved from the ABCC temporary facilities in Ujina to the newly completed Hijiyama Laboratory, until the end of his tenure in February 1952. Mr. Kunitoshi brought out a Japanese version of early ABCC history, and Mr. Sperry, some early annual reports to the National Academy of Sciences. A brief, nostalgic review of these papers concluded Dr. Tessmer's visit.

Even a partial listing of Dr. Tessmer's efforts and achievements as ABCC's first director would merit an extended second article. On the occasion of this visit, it is appropriate to recall that he took a leading role in selecting the Hijiyama site for ABCC laboratories and in negotiating the acquisition of the area with Hiroshima Prefecture, the Japanese government, and especially with Hiroshima City. In a series of meetings with Mayor Shinzo Hamai, Dr. Tessmer described ABCC's objectives and needs and obtained the mayor's understanding in obtaining the release of the present site. Upon approval of Hiroshima's City Council, the property was assigned to the Finance Ministry of the Japanese government, which then leased it to ABCC. Mayor Hamai remained a lifelong supporter of the Commission.



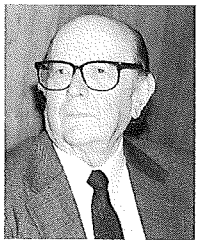


Photos: Upper right: *April 6, 1949, Dr. Tessmer with ABCC visitor, Crown Prince Akihito, at the Commission's first study facilities at the Gaisenkan (Hall of Triumphant Return) in Ujina; Associate Director Hiroshi Maki stands between the two. The man to the prince's right is unidentified. In his comments on the occasion of ABCC-RERF's 40th anniversary, Dr. Tessmer described the visit as "one of the national honors bestowed on ABCC and me personally." (*RERF Newsletter *14 (special edition): 67.* ***Upper inset:*** *July 27, 1949, Lieutenant Colonel Tessmer at his desk. (ABCC file photos).* ***Lower left, left to right:*** *Mr. Michael Rappaport, Dr. Senjun Taira, Dr. Shigenobu Nagataki, Dr. Carl Tessmer, and Mr. Richard Sperry in the chairman's office during Dr. Tessmer's April 27 visit. Hanging above them on the wall are photographs of all the previous chairmen; Dr. Tessmer's photo is at the far left and out of photo shot at the other end is Dr. Shigematsu's portrait.* ***Lower inset:*** *Dr. Tessmer, at 87, during his April visit to RERF. (Photos by Kiyoko Yamayoshi)*

ABCC's Early Days: Planning and Building on Hijiyama

by Michael E. Rappaport, Honorary Consultant and Former ABCC Business Administrator

Editor's Note: The following was prepared as a panel presentation for NAS's commemorative ceremony on the occasion of the 50th anniversary of ABCC-RERF in June 1997. At that time, Mr. Rappaport joined Drs. Gilbert Beebe, Robert Miller, Hiroshi Maki, and James Neel on a panel representing ABCC. (See Update 9[1], cover story and picture, page 6.) *Mr. Rappaport's talk has been adapted for* Update.



I have often been introduced to ABCC-RERF newcomers and visitors as one who has been with the organization since day one. Actually, when I joined ABCC in March 1949, there were perhaps 400 employees working busily in Hiroshima, Nagasaki, Kure, and Tokyo.

I was hired as associate engineer in ABCC's construction department, which was headed by Homer Pfeiffer, architect-in-charge. Pfeiffer and Associate Engineer George Friend gave me a short briefing on the scope of construction, to consist of a clinic and laboratory in Hiroshima, a virtually identical facility in Nagasaki, and two more laboratories of the same design in Kure and Sasebo intended for control studies. Each of the four designs comprised five two-story reinforced concrete buildings sheathed in specially manufactured Quonset huts as well as connecting corridors and reception areas.

The construction of the first of these, at Hijiyama, was to start in June 1949, and in the meantime, research and supporting activities proceeded in Hiroshima in a former Japanese army building in Ujina and a temporary clinic in Kure. In Nagasaki, ABCC rented a building from the Nagasaki Prefectural Maintenance Association and fitted it out as a temporary laboratory. (*See* Update *10[1], Nagasaki cover story and picture, p. 7.)* We called it Nagasaki Kaikan, or just Kaikan.

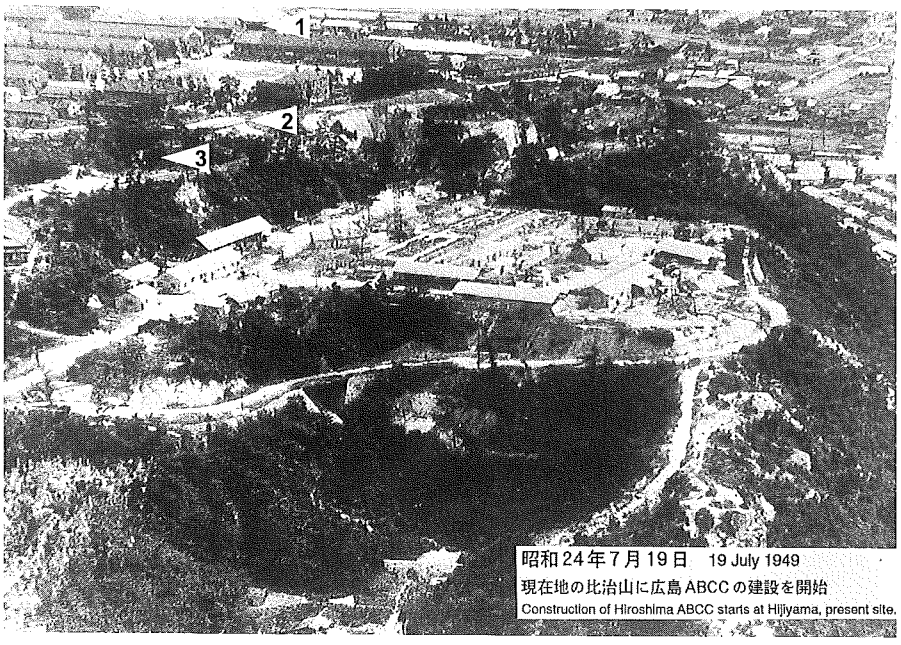
Of the four new clinics envisioned, only the one on Hijiyama was constructed. The Kure and Sasebo projects were abandoned when it became possible to identify and examine control populations in the two bombed cities. The Nagasaki project, which was to be built on the site of a prison destroyed by the bomb, was canceled when it was found that research needs could be met in the renovated Kaikan.

The construction of the Hijiyama laboratory was a major highlight in our early efforts to provide research space. It was completed as designed in 1950, in contracted time and within the budget provided. It brought to Japan the latest American building materials and hospital and laboratory equipment, and it won the Contractor-of-the-Year award for the builder.

To this success can be contrasted our failure to foresee the space needs at Hijiyama and Nagasaki Kaikan. It took several more years to obtain funds for and to construct additional buildings needed to accommodate all operations in the two cities. Incidentally, by the time the Kure phase was canceled, materials had already been ordered and were on their way to or arriving in Japan. We had considerable difficulties storing them and even more trouble accounting for them.

Other difficulties were numerous but never insuperable. The procurement of local materials, such as cement, piping, pipe fittings, and even lumber and gravel, was time-consuming in a country that had only begun to recover from the turmoil of war and its aftermath. Access to adequate utilities was a constant problem, especially water, electric power, and telephone lines. We managed because in both Hiroshima and Nagasaki, the city authorities were cooperative and helpful. On one occasion, the mayor of Hiroshima, Shinzo Hamai, personally intervened and ordered the water board to expedite reconstruction of a pumping station supplying water to Hijiyama.

We were fortunate in the early stages in recruiting a staff of engineers and architects who proved competent, energetic, and dedicated to the project. Some of them chose to remain at ABCC after the major construction was finished and served effectively in various technical and supervisory positions.

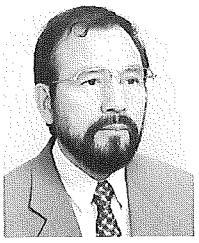


Aerial photo of construction site of Atomic Bomb Casualty Commission, Hijiyama Hill, July 19, 1949 *Arrow 1: Japanese wartime buildings on the current site of the Hiroshima Medical School; arrow 2: building occupied by Buddhist nuns who moved before the construction of Hijiyama Hall; and arrow 3: future site of Hijiyama Hall, which was completed in the spring of 1953. Temporary construction sheds are apparent on the site as well as trenches for the foundations of Buildings A, B, C, D, and E. (ABCC file photo)*

Thoughts on Retirement

Pathological Studies: from Beginning to End, A Project that Will Stay in My Mind Forever

Torao Sasaki, advisor and former assistant chief, Secretariat, Hiroshima



I retired from RERF under the age limit last December. In my 38 years and four months at ABCC-RERF, I worked for the first 22 years personally contacting A-bomb survivors outside of the office, and for the last 16 years, I engaged in fiscal work in the accounting section of the Secretariat. During those years, I received guidance and support from many to whom I would like to express my sincere gratitude.

Before I began to work for ABCC, I worked for a construction company and came to ABCC as a foreman for bringing fresh material concrete; I was involved in the construction of the present "Unit I" building. At ABCC, I saw for the first time unique surroundings that exuded American culture, and that attracted me. When I learned that ABCC was recruiting new employees, I applied for a position.

I was employed as a contactor in the clinical contacting section (later the pathology contacting section) of the Department of Medical Sociology in September 1960. With the introduction of the pathological study program, 14 men were employed in a span of a couple of years. This operation also started in Nagasaki about a year later. My job was to approach the surviving family for permission to perform an autopsy on the family member who just died. I had not encountered death in my own family or relatives, so when I came to ABCC at the age of 22, I often felt lost, not knowing what to say.

In those days in Hiroshima, I recall having daily meetings about issues like how we could get information on deaths in the city or what we should do before we could come to the stage of asking for the dead bodies. My seniors, who already had some experience in autopsy work done in test cases, guided me. We divided the city into four blocks, north, south, east, and west, and assigned each area to a person, who would go the rounds there in the morning and afternoon. We canvassed every kind of place and person for death information–major hospitals, clinics, city halls, city branch offices, funeral homes, district welfare offices, crematories, and ad pages in papers. We were constantly thinking about how to acquire death information more quickly, to the point that whenever we saw a group of women in white aprons [dress frequently seen as women helped out bereaved families or assisted in some other way in the community] on the street, we automatically thought something must have happened. Collecting death information went on 24 hours a day, 364 days a year (only New Year's Day was off), until we could finally collect information in the city and its vicinities 100% and more. Inevitably, the surgeons and technicians in the pathology department were obliged to follow the 24-hour schedule as well.

When we received information on the death of someone eligible for ABCC autopsy (ST-100), we would go and ask for permission of the family. Normally, autopsy permission was requested from a family by a physician who had treated the deceased, and they would agree. However, in the case of ABCC, a clerk unknown to the family, who was neither a physician of the deceased nor a physician at all, visited the family out of the blue and started negotiating for an autopsy. This was a difficult task, with no precedent at all. Since we had little knowledge of the names of diseases, we were given lectures by pathologists and read medical books day after day. Because of the large number of Buddhists called the "aki-monto," for whom Hiroshima is known, we invited Buddhist monks to teach us the point of contact of Buddhism with medicine or autopsy. We also studied the manners of tea ceremony and engaged in simulation training, dividing into groups representing the family of the deceased and the contactors approaching the family and trying to cultivate the tenacity to ask again and again after being rejected a few times. Nevertheless, we would cower when we had to go through the imposing gate of the home of some business tycoon or when we faced the corpse of an elderly A-bomb survivor lying all alone in the mortuary with no relations. There were times we could not hold back our tears feeling a deep sorrow I am unable to describe.

Unlike today, there was strong anti-American sentiment running through the city, and because of anti-ABCC feeling, we were unwelcome guests at wakes. People in sorrow and anger they could not suppress would lash out at us, "You are vultures smelling death!" How helpless we were before such words, and we felt immeasurable pain. Nevertheless, the 14 of us gave our duties our best efforts, firmly believing that our work would some day prove beneficial to A-bomb survivors and all humankind.

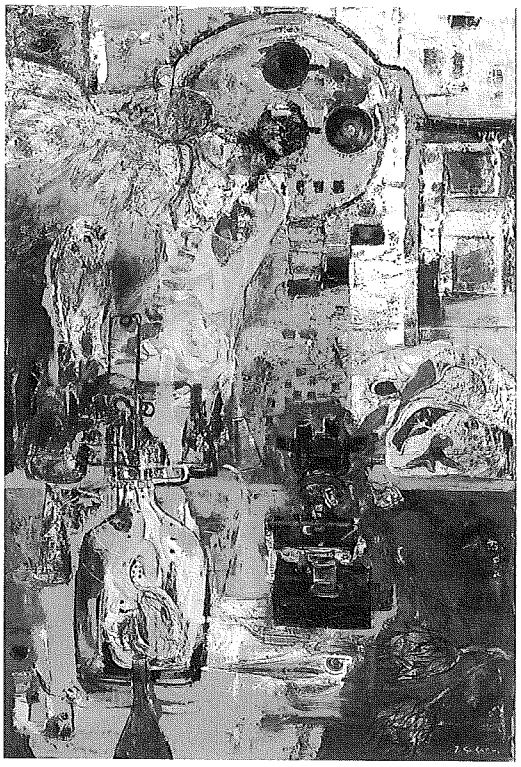
Around the same time, the remains of hundreds of A-bomb victims were discovered in the playground of the junior high school on Ninoshima Island (Minami-ku, Hiroshima). They had managed to escape from the inferno and had been carried to the island. My colleagues and I could not help rushing to the site, where we laid flowers, prayed for the victims' souls, and helped unearth the remains. From them, we began to understand the aftermath of the A-bombing. Families still awaiting the return of their loved ones spoke tearfully when we contacted them concerning the remains. Feeling a strong resolve to also give our best to ABCC's work for these people, we renewed our efforts.

Our duties at ABCC could not have been accomplished without the great support of physicians from the city's private clinics and major hospitals. At that time, autopsies were being eagerly performed at hospitals including Hiroshima University Hospital, Hiroshima Red Cross A-bomb Hospital, City Hospital, and Prefectural Hospital. As a result, more and more people started to take interest in autopsies, but this worked against ABCC. "If someone in our family dies, the ABCC people will come to us. What shall we do?" Thus, cases of deciding in advance at family

meetings to reject our requests increased. Although the autopsy rate reached about 45% at its peak in 1962-63, it started to decrease, a trend which was unstoppable. Each time a new chief arrived, we at the front line gave our ideas on how to halt the decreasing autopsy rate, but the chief's two-year term was too short to produce meaningful results, and the autopsy program steadily declined. The autopsy operation of the pathological study program, then one of ABCC's three major study programs, along with the Adult Health Study (AHS) and Life Span Study (LSS), was finally officially discontinued by the decision of the board of directors at their 1978 meeting.

The beautiful hiking paths of yesteryear at Hijiyama are also heavy-laden with a sad history, in which about 3,900 corpses, including those not included in the autopsy program, were carried up by hearses. Did we provide sufficient aftercare to the surviving families who agreed to the autopsies of those dear to them? When I reminisce about some of the families I contacted, I cannot feel all too sure.

The next job I held was related to the Adult Health Study ME-200, that is, identifying those who had refused to come to ABCC ("no contact" cases, so to speak) and approaching them again to improve AHS participation. Unlike the autopsy contacting work, I could talk directly with those individuals who made the choice not to come to ABCC. Neither was there a time limit like that for delivering cadavers for autopsy. So, I felt confident that with time and persuasion, the survivors would open up. It was most gratifying when, after I could have a heart-to-heart talk with them, people who previously refused to come to ABCC finally agreed to participate and later expressed their appreciation, saying, "Receptionists, nurses, and doctors were all kind." Such memories abound. I was on this job for two years.



From Mr. Sasaki's "Laboratory" series, this painting, which was exhibited in May at the Hiroshima Prefectural Art Museum, is entitled Mercy Flight. *It speaks of the good that can arise from the sorrow and sacrifice (mercy) of many. Mr. Sasaki received the prestigious Hisashi Tsuji Memorial Award for this work.*

For the last 16 years, I worked in the accounting section of the Secretariat. I was transferred there at the middle age of 45, and though I tried to shift gears, I had to struggle, starting from scratch. English was also needed, which added to my pains. Year by year, the budget got tight and RERF was in financial straits. Particularly from 1994 on, we struggled to cut costs, cornered by the decline in the dollar rate against the yen. One conspicuous action at that time was the closing of the cafeteria at Hijiyama Hall. There were also a number of years in succession in which there were quite a few mandatory retirements, and we had to penny pinch to find funds to pay termination allowances. Japan and the U. S. both worked desperately (including negotiations between the Japanese Ministry of Health and Welfare and the Department of Energy [DOE] and simultaneous telephone sessions among RERF, the National Academy of Sciences [NAS] and DOE), and we finally managed to pull ourselves through. We sighed with relief as if we had just come through a steep, narrow road. In such a time of difficulty, I cannot help recalling the words of a jeep driver. I arrived at ABCC full of hope, but whenever we went out on a contacting job, he would say, "Why did young people like you decide to work here? This place won't last another two years." We were stunned and perplexed, but as it turned out, the study results at ABCC/RERF came to be duly recognized. There is much left for RERF to do now and in the future because it is an important institute unparalleled in the world.

Another piece of my memory as a young employee is that I proposed to the hospital staffs an interhospital ping pong tournament in the hope of establishing good relations among hospitals and clinics and thereby smoother operations. Two annual tournaments (spring and fall) are still held today in which, among others, Hiroshima Red Cross A-bomb Hospital, Citizens' Hospital, Toyo Kogyo Hospital (presently Mazda Hospital), Prefectural Hospital, Chuden (Chugoku Electric) Hospital, and JR Hospital participate. The tournaments provide a forum for exchanging friendship among those in the medical profession.

"Laboratory" is the theme of the paintings I have done off duty. I have painted not a few works (80 pieces of F100 size) on this theme, based on the anxiety of A-bomb survivors, and they have been recognized as unique efforts in the painting world. These paintings are my personal history. The starting point of my serial paintings was the sight of the remains of A-bomb victims unearthed at Ninoshima Island, and then, the Chernobyl nuclear power plant accident later on inspired more in the series. This motif, however, found its way into my paintings for the sole reason that I worked at RERF, which gave me the opportunity to hear the outcry of A-bomb survivors and become well aware of RERF's mission. When I think about it, I cannot help being deeply moved.

Thirty-eight years and four months at ABCC-RERF passed away in one blink. Although I retired under the age limit as of the end of last year, RERF will live on in the world forever.

In closing, I want to wish RERF, led by the wisdom of its directors and staff, further prosperity as it enters step by step into the future. Thank you very much.

Editor's Note: Mr. Sasaki retired from RERF at the end of December 1998. He reminisced about his almost 40 years with ABCC-RERF in the Japanese-language RERF Newsletter *(18 March 1999; 25(2)).*

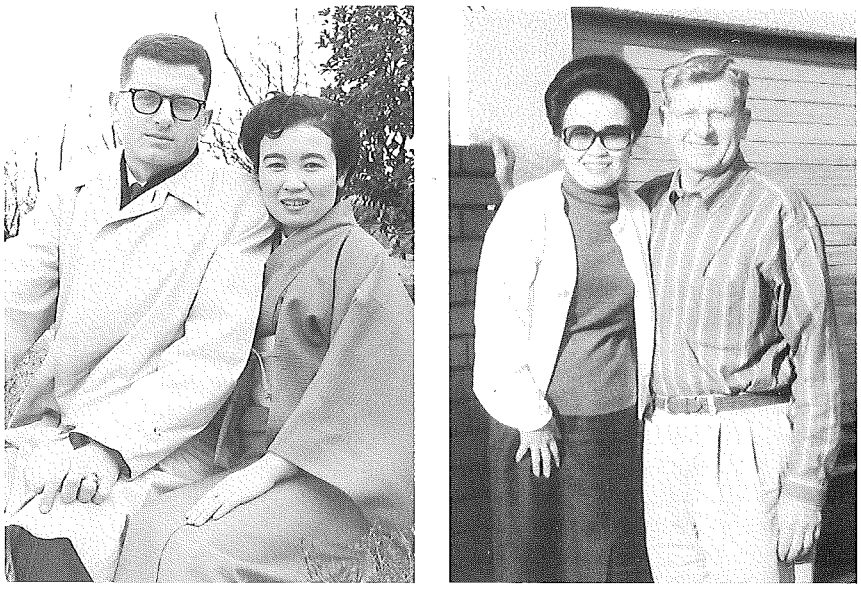
Richard Sperry's Four Decades with National Academy of Sciences Recognized in June Ceremony in Washington, D. C.

On 11 June, RERF Administrative Advisor Richard Sperry was recognized in Washington for his 40 years of service to the National Academy of Sciences (NAS). He was unable to attend formal ceremonies but was given a gold watch to commemorate the event in a private ceremony in NAS executive offices. The award was presented to Mr. Sperry by National Research Council Executive Officer William Colglazier. Also participating in the presentation were Assistant Executive Officer Myron Uman, Executive Director of the Commission on Life Sciences Warren Muir, Director of the Board on Radiation Effects Research Evan Douple, Administrative Associate Catherine Berkley, Confidential Assistant to the Executive Officer Judy Justusson, and other board staff, including Doris Taylor and Bridget Edmonds.

Prior to coming to ABCC, Mr. Sperry served in the army in Korea, received his degree in business management from the University of Illinois, and held positions in organizations in the U. S. and Japan. He began his NAS career when he joined the staff of the Atomic Bomb Casualty Commission as an administrative assistant in August 1958, and he served successively as accountant and supply officer, fiscal and supply officer, and assistant business administrator. Dick continued in this position after ABCC was reorganized into RERF in April 1975. During the transition and reorganization period, he provided leadership in restructuring NAS accounting practices and procedures so that RERF, a Japanese juridical entity, could meet the budgetary, disbursing, and auditing requirements of the two sponsoring governments. In January 1976, Mr. Sperry returned to Washington to work in the NAS offices, where he served as supervisor of the accounts payable and payroll sections of the NAS accounting office, as budget analyst in the comptroller's office, and finally as budget officer of the National Research Council. He returned to RERF in April 1988 to serve as business administrator, and following RERF mandatory-age retirement in July 1994, he continued his work in the capacity of administrative advisor. He is by a wide margin the longest serving member of the Operating Committee and sits with the Executive Committee.

Mr. Sperry's dedication to ABCC-RERF and the National Academy of Sciences has been greatly appreciated over the past four decades. His understanding of the organization and its history and mission accumulated over time, 41 years as of this writing, has proved invaluable, and his financial and budgetary expertise have aided the organization through some foreboding times. In addition to his regular duties, Dick Sperry has welcomed new NAS employees to RERF and guided them through the process of adjusting to life in Japan, a task often demanding and complex due to language and cultural differences and an unfamiliar working environment.

The commitment reflected by Dick Sperry's continued presence and dedication to the work of the National Academy of Sciences and, more specifically, to ABCC-RERF is truly admirable.



Left: *Dick Sperry and his future wife, Toyoko, in Hijiyama Park, in February 1957 and* ***right:*** *Dick and Toyoko Sperry this spring. (Photos courtesy of Dick Sperry)*

From left to right: *William Colglazier, National Research Council executive officer; Dick Sperry, holding the watch presented to him by NAS; Warren Muir, Commission on Life Sciences executive director; and Evan B. Douple, Board on Radiation Effects Research director. (Photo courtesy of NAS)*

Dr. Akio Awa Honored with National Academy of Sciences Plaque

Drs. Clark W. Heath, Jr. (far left) and Sheldon Wolff (far right) look on as Dr. Evan Douple presents Dr. Akio A. Awa with his NAS plaque. (Photo by Kiyoko Yamayoshi)

Dr. Akio Awa's 32 years of dedicated service to ABCC-RERF and his contributions to the National Academy of Sciences were acknowledged with a plaque presented by Dr. Evan Douple, director of the Board on Radiation Effects Research of the Commission on Life Sciences of the National Academy of Sciences at an award ceremony in RERF's auditorium on 21 June. Dr. Awa, who retired from RERF at the end of March, joined many others, including Former Chairman Itsuzo Shigematsu, who have been honored by the Academy.

In his presentation speech, Dr. Douple recognized Dr. Awa's great part in the scientific program through the years, sentiments reiterated by RERF Vice Chairman and Chief of Research Sheldon Wolff, who pointed out Dr. Awa's stature as a world-renowned cytogeneticist who has brought recognition to the Foundation's work and provided support in many less conspicuous ways to many people. Dr. Wolff was especially appreciative of the role that Dr. Awa played over the last two years as associate chief of research, a role he took on after retiring as head of the genetics department. In addition to highlighting Dr. Awa's *"leadership in cytogenetics and radiobiology research,"* the plaque's inscription addressed the very unique qualities that characterize Dr. Awa's most special gifts: *"Your thoughtfulness, keen wit, extensive knowledge, personable nature, and sense of humor have made you a* sensei [teacher] *to whom many have turned for advice."*

Dr. Awa emotionally accepted the plaque, remarking about his work, "I cannot say positively whether our cytogentics studies have been performed adequately, [but] some day in the future, our results will be critically reviewed and the relevance of the studies will be objectively evaluated by other scientists." He thanked the Academy and all those who have assisted him in his various endeavors. Chairman Shigenobu Nagataki thanked Dr. Douple and the Academy for paying such tribute to Dr. Awa, and he added his own congratulations on this special occasion.

Editor's note: Dr. Awa retired 31 March 1999 to accept a much smaller role with RERF as part-time consultant. He joined ABCC in 1967 after graduating in 1956 from Hokkaido University, where he completed his doctoral work in 1963 in the world-famous cytogenetics laboratory headed by Professor Sajiro Makino and later worked as a research fellow and research assistant. Dr. Awa has been involved in both biodosimetric and genetic studies at ABCC and RERF, and he founded the current cytogenetics laboratory. From 1985 until 1993, Dr. Awa served as chief of RERF's Department of Genetics. In January 1994, he became associate chief of research, a position he maintained until March. When he retired in 1995, he assumed the position of consultant and continued his role as associate chief of research.

The Spring 1999 issue of RERF Update *featured a farewell tribute to Dr. Awa written by Dr. Nakamura (10[1]: 23).*

Seymour Abrahamson Receives Imperial Award in May Conferment

On May 12, Seymour Abrahamson, former RERF permanent director, vice chairman, chief of research, and associate chief of research, traveled to Tokyo to be awarded the Third Order of the Sacred Treasure, the highest imperial recognition for non-Japanese. He was presented with a letter of commendation and a medal by the Japanese Minister of Health and Welfare and was later received by Emperor Akihito in the Imperial Palace. Former Chairman **Itsuzo Shigematsu** and his wife and Former Director and Chief of Secretariat **Tomoyuki Kono** and his wife hosted a dinner for Dr. Abrahamson, his wife, Shirley, and his son, Dan, in the evening, and the three reminisced about their experiences at RERF.

Dr. Abrahamson received this national recognition for his long involvement with RERF and genetics and radiation studies. As reported in the last issue of *RERF Update* (10[1]:2), Seymour Abrahamson retired from RERF last December 31, after serving intermittently for more than six years over a ten-year period in the above-cited positions. During his tenure with RERF, he was particularly concerned with the studies on atomic-bomb survivors' health, the Life Span Study, genetic studies, and the study of radiation exposure. Dr. Abrahamson was also instrumental in

See ***Abrahamson Award,*** *page 23*

Dr. Abrahamson wearing his award medal on May 12. (Photo by Akiko Enami)

Administration

At the June 26 to July 2 meeting of the Health Physics Society in Philadelphia, Pennsylvania, U.S.A., RERF Chairman **Shigenobu Nagataki** was presented with the 1999 G. William Morgan Award. In accepting the award, Dr. Nagataki spoke on the "Prospect for RERF Studies to Influence Radiation Regulations in the Next Millennium." Dr. Nagataki joined Harvard University Public Health Professor **Richard Monson** in receiving this year's awards. Dr. Monson chaired last year's peer review panel for RERF's Department of Epidemiology.

This was the 44th meeting of the society, which was established to conduct research on the atomic bombings. Though the presentations were of a scientific nature, they reflected the social circumstances surrounding the research reported. Many of the meeting presentations were related to RERF activities. U.S. Department of Energy representatives spent a full day reporting on Mayak study results, work with which **Dr. Preston** is involved. Other RERF-related topics included neutron issues in Hiroshima and Nagasaki and Dosimetry System 86. Members of the U.S. Nuclear Regulatory Commission, Department of Energy, and Environmental Protection Agency were among many presenters at the one-week meeting.

Hiroshima

Department of Clinical Studies

Saeko Fujiwara, assistant department chief was released from her concurrent assignment as chief of the Division of Clinical Laboratories, effective June 1.

Dr. Masayuki Hakoda was employed as chief of the Division of Clinical Laboratories, effective June 1. Dr. Hakoda graduated from Hiroshima University School of Medicine in 1981, completing his internal medicine training at Hiroshima University Hospital. From 1983 to 1988, he served as an RERF research scientist in the Department of Radiobiology. Dr. Hakoda has also served on the medical staff and as an associate professor at the Institute of Rheumatology of Tokyo Women's Medical College.

Masaharu Nobuyoshi, research scientist, was released from his concurrent assignment in the Immunology Laboratory of the Department of Radiobiology, effective October 1.

Department of Epidemiology

Hiroko Moriwaki, was promoted from acting chief to chief of the epidemiologic analysis laboratory, effective 1 October 1998 (*not previously reported in* Update).

Gerald B. Sharp was promoted from research scientist to associate senior scientist, effective July 1.

Department of Genetics

Dr. Inaho Danjo was employed as a research scientist in the biochemical genetics laboratory, effective August 1. Prior to coming to RERF, Dr. Danjo worked as a postdoctoral fellow in the Department of Neurogenetics of the Max-Planck Institute for Psychiatry, Munich, Germany (1998-1999), and the Department of Human Genetics of the National Institute of Genetics, Mishima (1995-1998). She received her Ph.D. in Genetics from the Graduate University for Advanced Studies of the National Institute of Genetics in Mishima in 1995 and her B. S. in biochemistry from Saitama University. Prior to her doctoral studies, she was employed by Hayashibara Biochemical Corporation Ltd., in Okayama. Her primary research interests are radiation biology, signal transduction, and genome science.

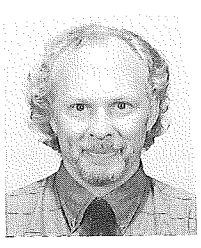
Department of Radiobiology

Dr. Donald G. MacPhee joined the RERF NAS staff as department chief September 21, filling the vacancy left by Toshio Seyama, who left in June 1998. Dr. MacPhee came to RERF from LaTrobe University in Melbourne, Australia, where he has been teaching and researching in the Departments of Genetics and Microbiology since 1970. He has also been active as a consultant to parliamentary committees and as an advisor to Australian government ministers on issues involving radiation and chemical mutagenesis for the last 25 years. Dr. MacPhee received his Ph.D. (1967) and B.S. from the University of Edinburgh.

Department of Statistics

Dr. **Harry M. Cullings** returned to RERF as a visiting research fellow, effective September 21, and will join RERF's National Academy of Science staff October 18 as a research scientist. (*Dr. Cullings' earlier visit in 1998 was reported in* RERF Update *10[1]: 25.)* In 1998, Harry left the University of Colorado Health Sciences Center, where he worked for 15 years as a health physicist, to enter a postdoctoral fellowship program in the radiation sciences at the University of Pittsburgh. While there, Dr. Cullings first became involved in the RERF dosimetry project through NAS's Board on Radiation Effects Research. While at Pittsburgh, he also



New staff, pictured from left to right: *Dr. Masayuki Hakoda, Clinical Studies, Hiroshima; Dr. Inaho Danjo, Department of Genetics; Dr. Donald MacPhee, Radiobiology; Dr. Harry Cullings, Statistics; Ms. Margaret Irwin, PDC; and Dr. Ayumi Hida, Clinical Studies, Nagasaki.*

worked on the application of micro- and mini-satellite assays as indicators of radiation mutagenesis, in the genetics laboratory of Dr. **Bob Ferrell**, who worked at ABCC in the early 1970's. At RERF, Harry will be continuing his work on issues related to dose reassessment while also working on other consulting and research projects.

Dr. Cullings received a B.S. in physics and biophysics from Lehigh University in Bethlehem, Pennsylvania, an M.S.B.A. with a concentration in management information systems, from the University of Northern Colorado, and an M.S. in radiological (medical) physics and a Ph.D. in biostatistics, both from the University of Colorado Health Sciences Center in Denver. Harry's doctoral dissertation involved modeling temporal patterns in lung cancer screening tests in a cohort of uranium miners. Harry's doctoral advisor at Colorado, Dr. **Phil Archer**, worked as a statistician at ABCC in the years 1965-1968. Dr. Cullings also worked for five years as a nuclear medical scientist in the U. S. Army.

Fumiyoshi Kasagi, associate senior scientist, was promoted to senior scientist, effective July 1.

Information Technology Department

Tsuneyuki Isaka, administrative assistant department chief, retired June 30.

Hiroaki Katayama, chief of the Systems Technology Section and concurrently Systems Administrative Unit supervisor, was promoted to administrative assistant department chief, while maintaining his role as chief of the Systems Technology Section, effective July 1.

Publication and Documentation Center

Margaret A. Irwin was appointed information specialist in the Administrative and Support Section of the Publication and Documentation Center, effective October 1. Ms. Irwin will engage in archiving activities, collecting, preserving, organizing, and cataloguing documents and photographs related to ABCC-RERF.

Prior to coming here, she served as special collections librarian and coordinator of the ABCC Collections in the John P. McGovern Historical Collections and Research Center of the Houston Academy of Medicine-Texas Medical Center Library (HAM-TMC). Ms. Irwin visited RERF in March 1997 (*See* Update *9[1]: 16.)* to examine materials housed in Hiroshima to assess how they might best be preserved and utilized, and her long history with the ABCC Collections will help her perform those duties here. Those collections now comprise 17 major manuscript collections, a number of smaller contributions, thousands of photographs, and serials and monographs published by and ABCC-RERF. At HAM-TMC, Ms. Irwin has produced print and electronic records of materials for better user access and communicated with other repositories housing ABCC-RERF-related materials. Just prior to her arrival in Hiroshima, she was engaged in the creation of a web page for the ABCC Collections; work on that project is on-going.

Nagasaki

Department of Clinical Studies

Masazumi Akahoshi was promoted from acting chief to chief of the department, effective July 1.

Ayumi Hida was employed as a research scientist in the Division of Medicine, effective 1 April 1999. Dr. Hida came to RERF from the First Department of Internal Medicine at the Nagasaki University School of Medicine, where she was engaged in the clinical examination and studies of diffuse collagen diseases. She was earlier a research student in the same department, and she worked at Tomie Hospital, Sasebo Central Hospital, Koseikai Hospital, Nagasaki Prefectural Saiseikai Hospital, Showakai Hospital, and Nagasaki Kita Hospital. She is a graduate of the Nagasaki University School of Medicine.

Department of Epidemiology

Akihiko Suyama was appointed chief of the Department of Epidemiology, effective 1 October. After graduating from Tottori University School of Medicine in 1980, Dr. Suyama joined the university's Second Department of Internal Medicine, and after being affiliated with the group presently studying hepatitis C, he moved to the Hygiene Department and worked there for 18 years. Initially, he studied medical information engineering.

Dr. Suyama was later entrusted with the Tottori Prefecture cancer registry and shifted his research theme to cancer epidemiology. He then studied the cancer cohorts of those with impaired glucose tolerance and low serum lipids and carried out a case-control study of low-dose radiation effects at Misasa Spring. Dr. Suyama also worked on several other research activities, including a project to predict the prevalence of childhood infectious diseases as a method to facilitate their prevention, another to assess medical economy, and one to develop an RDBMS (Relational Database Management System).

In 1997, Dr. Suyama received his doctorate in medical science from the Tottori University School of Medicine with his thesis, entitled "Epidemiological study on characteristics of cancer incidence observed among a group of examinees in a standard health examination." Dr. Suyama holds medical and engineering licenses.

Radioisotope Facility

The Nagasaki Radioisotope (RI) Facility was closed and the Nagasaki RI Safety Committee was abolished, effective March 31.

Errata

In the Spring issue of RERF Update *(10[1]) several errors were made:*

- *On page one, in the article on the epidemiology review, the names of the review panelists on the far left and right of the photo were reversed. So, the first man on the left is Dr. Hiroyuki Shimizu, and the man on the far right is Dr. Tsutomu Hashimoto.*
- *On page 25, under "RERF Staff News," in the entry for Dr. Harry Cullings, under "Department of Statistics," Dr. Takeshi Maruyama should be Dr. Takashi Maruyama.*
- *In the publications listings, on pages 31 and 32, the heading for the Mizuno publication for RP 5-90 and 2-94 (Cell Biology) should read "Special Cancer Studies" rather than " Special Clinical Studies."*

In the autumn 1998 issue (9[2]):

- *On the back page (24), under meetings, the oral presentation by Iwamoto et al. listed for RP 4-94 should be 2-94, a cell biology study.*

Dr. Iwao Moriyama, Former Department of Epidemiology and Statistics Chief, Welcomed to RERF by Dr. Mabuchi and Chairman Nagataki during July Visit

Friends and former associates welcomed Dr. and Mrs. Iwao Moriyama and their son, daughter-in-law, and two teenaged grandchildren,when they visited RERF July 5. It was a first visit to Japan for the younger family members.

Guided by Department of Epidemiology Chief Kiyohiko Mabuchi, Dr. Moriyama met with Chairman Shigenobu Nagataki, Vice Chairman and Chief of Research Sheldon Wolff, and Associate Chief of Research Clark W. Heath, Jr. He then visited his old domain in the Department of Epidemiology and exchanged greetings and reminiscences with the staff.

A lunch at Hijiyama Hall followed. Organized by Dr. Yukiko Shimizu, assistant chief, Department of Epidemiology, it brought together about 20 of the Moriyamas' friends, including some who had retired from RERF. The Moriyamas spent some time with each participant and exchanged news and recollections of their previous stays.

Dr. Moriyama served as chief of the Department of Epidemiology and Statistics from July 1971 through June 1973 and again from September 1975 through August 1978. He was able to provide counsel in initial planning of reorganization of ABCC and again in helping resolve the complexities of the early transition to RERF. At ABCC and RERF, among many projects, he took a leading role in producing the *Japanese National Institute of Health (JNIH)-ABCC Life Span Study, Report 7*, the *ABCC-JNIH Pathology Studies, Report 3*, and the *RERF Pathology Studies, Report 4*.

Dr. Moriyama has had a distinguished career in statistics and epidemiology. He graduated from the University of California and obtained his M.P.H. and Ph.D. degrees from Yale University. After several years of academic research, he joined the U. S. Department of Health, Education, and Welfare, now Health and Human Services, where he has continued to hold various appointments, including chief of Mortality Analysis, director of the Office of Health Statistics, and associate director of International Statistics. He also served as a consultant to government and private organizations in South America, Europe, and Asia. Dr. Moriyama said he has been trying to cut down on his consulting activities although he continues with some commitments in Central America.

Pictured from left to right, front to back: Row one: Mrs. Moriyama, Dr. Moriyama, Mrs. C. Maki (widow of Hiroshi Maki); ***Row two:*** Mrs. K. Katagami, Dr. Moriyama's granddaughter, daughter-in-law, son, and grandson, Mr. M. Kurisu, Mr. Y. Kanemitsu; ***Row three:*** Mr. K. Joji, Dr. H. Kato, Dr. S. Fujita, Dr. T. Imada, Mr. T. Anamura, Mr. S. Inoue, Dr. K. Mabuchi, Dr. Y. Shimizu, Mr. M. E. Rappaport, Mr. R. D. Sperry, Mrs. M. Kato, Mr. T. Miyagawa. *(Photo courtesy of Mrs. K. Katagami)* ***Inset:*** Dr. Moriyama in March, 1977. *(RERF file photo)*

RERF Medical Team Visits U.S. for Twelfth Biennial Examination Cycle

by Saeko Fujiwara, assistant department chief, Department of Clinical Studies, Hiroshima

Four employees of the Radiation Effects Research Foundation (RERF) joined the medical teams participating in the twelfth biennial health examination of atomic-bomb survivors residing in North America conducted during May and June. This program has been carried out since 1977, when it was established as a collaboration between the Hiroshima Prefectural Medical Association and RERF with the support of the Ministry of Health and Welfare as a humanitarian effort. From the fourth examination, Hiroshima Prefecture, the city of Hiroshima, and the Atomic-bomb Casualty Council have also provided financial support. Four hundred and fourteen survivors were examined during this year's cycle.

Two teams conducted the health examinations—the first in San Francisco, California and Seattle, Washington between 20 May and 2 June, and the second in Los Angeles, California and Honolulu, Hawaii, between 9 and 23 June. From RERF, Dr. Saeko Fujiwara of the Department of Clinical Studies and Tadaaki Watanabe of the Secretariat joined the first team, and Dr. Kojiro Koyama of the Department of Epidemiology and Issei Yamanaka of the Information Technology Department were attached to the second.

Owing to the great efforts of many people in the U. S., arrangements were made to allow Japanese doctors without U.S. medical licensure to examine A-bomb survivors during the examination period under the supervision of American doctors and with the approval and cooperation of the local medical associations. In 1986, the program was legally recognized in a rider attached to the Medical Act of the State of California.

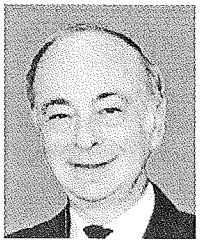
The current population of A-bomb survivors in the U.S. is approximately 1,100, of whom 139 in San Francisco, 46 in Seattle, 136 in Los Angeles, and 93 in Honolulu were examined. Their background histories have a wide variety: some were born in the U.S. and exposed to the atomic bombings when they visited Japan for educational reasons; some emigrated to the U.S. after the A-bombing; and some visited the U.S on business and stayed. Their median age at the time of the bombings was 15 to 19; hence, many examinees' current ages range from the late 60s to the 70s.

We were most impressed with the U. S. survivors' great anticipation for the health examinations and the willingness of the volunteer staff to help with the examinations. We realized beyond our expectations what a relief it was for the aging survivors living in the U.S. to be able to express their health conditions in Japanese and hear the doctors' answers in Japanese. The medical teams

See ***Health Examination****, bottom of next page*

Dr. Alvin G. Lazen, Former Science Council Observer

Editor's Note: The following is adapted from obituary information released by the National Academy of Sciences.



On July 26, former National Academy of Sciences Commission on Life Sciences (CLS) Director Alvin G. Lazen died in Baltimore. Dr. Lazen was a NAS staff member for 22 years, serving as a member and chair of the National Research Council's Human Subjects Committee, helping with the development and contributing to the Program Officers' Workshop, and helping to organize the Japanese Human Frontier Program. He served as study director on numerous important reports, including Science and Creationism, Trends in Early Research Careers, and a number of studies on radiation effects. In his many leadership roles, he represented NAS with dignity and commitment to the highest standards of quality and integrity. He was a regular observer at RERF's Science Council and board of directors meetings.

Dr. Lazen was the CLS executive director from 1981 to 1988, a position now held by Warren Muir and recently vacated by Paul Gilman. He was active as the NAS contact during the early stages of the Japanese Human Frontier Science Program, which was originally proposed by the Japanese government in late 1986 and early 1987 to solicit advice from foreign scientists and academies to promote international cooperation for basic research in molecular biology and neurobiology.

In 1993, Dr. Lazen received NAS's Individual Staff Award (also awarded to Seymour Jablon in 1975), which recognizes high quality of and dedication to service to the Academy, its programs, and vision. He will be remembered for his kind generous manner, keen sense of humor, and dedicated service, and he will be sorely missed.

Two Hiroshima Maidens Surgeons, Drs. Bernard E. Simon and Tomin Harada

On August 1, **Dr. Bernard E. Simon** died in New York at 87. Dr. Simon was one of the team of American plastic surgeons who operated on the 25 young Japanese women who came to be known as the Hiroshima Maidens. In 1955, the women went to the U. S. for treatment of the injuries they suffered in the atomic bombing of Hiroshima. Dr. Simon and several other American physicians volunteered to perform the numerous multiple surgeries at New York's Mount Sinai Hospital, where he worked for more than four decades and where he died. Simon and the other surgeons provided care to the women and instruction in plastic surgery techniques to the Japanese surgeons who accompanied them to the U.S. At that time, plastic surgery was a relatively new field of medicine in Japan.

Another member of the Maidens' project, **Dr. Tomin Harada,** one of the first team of accompanying Japanese physicians who observed the American surgeons' work, died in Hiroshima June 25. A Hiroshima surgeon known for his concern for peace, Dr. Harada served as the first chairman of Hiroshima's World Friendship Center and remained an active presence in the organization. In the report of his death in June 26's *Chugoku Shimbun*, former Hiroshima Mayor Takashi Hiraoka remembered Dr. Harada as "a person of rare quality who truly loved and practiced peace, . . . an irreplaceable person for Hiroshima."

The January death of **Helen Yokoyama**, a former ABCC employee who served as chaperone and surrogate mother for the Maidens, was reported in the last issue of *Update* (10[1]: 26).

Abrahamson Award, *continued from page 19*

bringing about the international evaluation of RERF by the so-called Blue Ribbon Panel. He has been a leader in the field of genetics in Japan since 1968 and further contributed to the studies of radiation effects on human health through the Japan Radiation Research Society.

On May 14, a celebration was held at Hijiyama Hall in Dr. Abrahamson's honor. More than 80 RERF employees and retirees joined in the festivities to thank Seymour for his years of friendship and hard work and to share with him in this glorious moment of recognition for all of RERF.

Other former American and Japanese staff members have been privileged to receive imperial honors. **Dr. Shigematsu** received the Second Order of the Sacred Treasure in the spring of 1990 (*See* Update *2[2]:1);* Board Member **Seymour Jablon**, RERF directors, Mr. **Chiaki Miyata**, Drs. **William J. Schull**, **Mortimer Mendelsohn**, and **Fumihiko Munakata**, and Department of Epidemiology Chief **Hiroo Kato** received the same distinction as Dr. Abrahamson, in 1987, 1992, 1992, 1994, 1995 and 1997, respectively; and **Mr. Kono** was honored with the Third Order of the Rising Sun in the spring of 1998 (*See* Update *9[2]: 2*), a distinction shared by Chairman **Hisao Yamashita** in 1991 and Chairman **Masao Tamaki** in 1985. Other recipients have included Board Member **Sadahisa Kawamoto**, who received the Fourth Order of the Rising Sun in 1991, and finally, Chief of Medicine **Hisao Sawada** and Chief of Pathology **Tsutomu Yamamoto**, who were recognized with the Fourth Order of the Sacred Treasure in 1991 and 1993, respectively.

Health Examination, *continued from previous page*

were heartily welcomed as if they were old friends of the examinees, who eagerly prepared home-made dishes and desserts in the early morning for the team members. The support of the survivors and the many volunteers in the U.S. enabled the smooth operation of the examinations. Volunteers made use of their days off to help us work efficiently from early in the mornings, with examinations conducted mainly on weekends, when hospitals were closed, in areas temporarily prepared for the occasion. All of us of the medical teams greatly appreciated the efforts of all involved.

Children of A-bomb survivors accounted for 13% of the total examinees. It was clear from conversations with the examinees that the survivors themselves were very much concerned about A-bomb effects on their children's health. We were swamped with questions about the health effects on second-generation A-bomb survivors and realized how eagerly they were awaiting the F_1 study. Even though we keep in close contact with the survivors living in Hiroshima, it was refreshing to come in touch with survivors living in such completely different circumstances from those in Japan.

Scientists Discuss Future of RERF Molecular Oncology/Epidemiology at NCI

by Keisuke S. Iwamoto, Senior Scientist, Department of Radiobiology

The fast-paced world of molecular biology does not wait for stragglers. However, the field is critical for investigating the still largely unknown mechanisms of radiation carcinogenesis–a phenomenon well documented in the A-bomb survivor population. Only through greater understanding of the process will improved methods for prevention and treatment become available. Molecular biological studies established at RERF to address such problems require eventual collaborations for the foundation to keep up with the accelerating pace of progress in the field. The exchange of ideas and resources in collaborative investigations has the potential for vastly widening the scope of studies and answering questions that cannot be accomplished by individual laboratories. In hopes of creating such potentially fruitful partnerships, five RERF researchers visited the U. S. National Cancer Institute (NCI), one of the world's premier cancer research institutes.

From February 17 to 19, 1999, Drs. Sadayuki Ban, Kiyohiro Hamatani, Keisuke S. Iwamoto, and Terumi Mizuno, of the Department of Radiobiology, and Department of Genetics Chief Nori Nakamura visited NCI's Division of Cancer Epidemiology and Genetics (DCEG). The trip was coordinated by Hiroshima Department of Epidemiology Chief Kiyohiko Mabuchi, who was on sabbatical leave at NCI at that time. The RERF scientists presented an overview of current RERF molecular studies in an informal workshop. They also met with several individual NCI researchers, mainly from the Genetic Epidemiology Branch headed by Dr. Margaret Tucker, to discuss specific projects, including breast and skin cancer studies as well as others, and visited the Laboratories of Population Genetics (LPG) for further discussion with Dr. Ken Buetow, the labs' director. Dr. Tucker outlined the various research activities in her branch, and the group discussed possible future collaborations between RERF and NCI. Dr. Margaret Karagas, an epidemiologist at the Dartmouth Medical College, also participated in the individual discussions on skin and breast cancer. The RERF group also met with Dr. James Fagin from the University of Cincinnati, who was in the Washington area for an NIH Study Section meeting, and discussed molecular studies of thyroid cancer.

In anticipation of future collaborative research, it was felt that it would be important to establish techniques to "immortalize" DNA from paraffin-embedded tissues and to develop a DNA bank for research use. This is a technique by which the limited amount of A-bomb-survivor DNA can be amplified *ad infinitum*, which will obviate the additional effort to re-collect the blocks and cut sections, and it will facilitate research collaborations. The current techniques to immortalize DNA being tested at RERF need to be carefully reviewed. The portion of the genome amplified (or not amplified) needs to be determined and ways must be found to improve the technique to maximize faithful amplification of the entire genome (so that artificial mutations are not introduced).

Once the immortalization technique has been established, a research protocol must be developed to establish DNA banks to immortalize DNA for various cancer studies. The research protocol should define the criteria for accepting proposed studies using stored DNA, such as the scientific rationale and significance, research priorities (high priority cancer sites) at RERF, estimated costs, and technical staff support needed.

NCI has a vested interest in breast cancer and a great deal of available resources for studying the disease. In accordance with the recommendations of the 1998 peer review of RERF's Department of Radiobiology, it was felt that it would be important to get the early-onset breast cancer project at RERF off the ground as soon as possible. Although the frequency of mutations in the breast-cancer-related genes *BRCA1* and *BRCA2* in Japanese breast cancer patients has been found to be lower than in their Western counterparts, the RERF LSS breast cancer cases may represent a uniquely radiosensitive subset. Furthermore, DNA collected from this project will provide broader and more innovative research that can be undertaken in collaboration with NCI and other investigators. This project will provide an impetus for addressing technical and other issues needed for future studies, such as procurement of tissues and biological specimens, DNA immortalization and storage, ethical considerations, and development of research collaboration.

During the visit, RERF's results on skin cancer, such as the apparent low frequency of pyrimidine-pyrimidine mutations of the *p53* gene in ultraviolet-exposed parts of the body and the *patched* gene data stimulated much discussion and interest. The *patched* gene may play an important role in radiation-induced carcinogenesis, as evidenced by studies on nevoid basal cell carcinoma (NBCC) patients who have germline mutations of this gene and who show an elevated risk of basal cell carcinoma (BCC) within the radiation field following radiotherapy.

Liver cancer is another disease of mutual interest to the NCI and RERF groups. Dr. Buetow's labs have been studying *p53* mutations in hepatocellular carcinomas (HCCs) from aflatoxin-exposed populations. They are also interested in identifying polymorphisms in genes that may increase susceptibility to such HCCs. Suggested collaborative areas briefly discussed include studies on the hepatitis viruses and techniques for detecting gene deletions.

Dr. Fagin is one of the leading investigators of thyroid cancer in the United States. Exchanges of research data between his lab and RERF's provided a good deal of fruitful discussion. One topic that currently interests him is the nuclear orientation of chromosomes and the importance of such structures in determining the type of the *ret* fusion gene. Dr. Fagin encouraged continued work on identifying *ret* fusion genes in the A-bomb survivor tissues and on investigating some of the mechanisms.

Other promising cancer sites discussed at the meetings were colon cancer and neurilemmoma, which are currently being studied at the NCI. Interest in these cancers were expressed by the investigators because of the high relative risks of these tumors, especially neurilemmomas, in ionizing-radiation-exposed populations. The *NF2* gene was suggested as one candidate gene to study in neurilemmomas. The NCI is currently conducting a study to investigate the *NF2* gene and neurilemmoma in an irradiated population in Chicago, and RERF should await results of the NCI study before initiating a new project in the atomic-bomb survivors. Even though the radiobiology peer review suggested that RERF molecular research be focused

See ***NCI Meeting****, page 13*

RERF Lecture Series, 1 April to 30 September

Editor's Note: All of these presentations were given in the auditorium of RERF's Hiroshima laboratory.

14 April, **Carmel Mothersill, Ph.D.**, director, Radiation Science Centre, Dublin Institute of Technology, Dublin, Ireland: *Radiation-induced genomic instability in normal human epithelial tissue*

17 May, **P. S. Chauhan**, head, Cell Biology Division, Bhabha Atomic Research Center, Department of Atomic Energy, Government of India, Mumbai, India: *Genetic risks of environmental agents: Role of human epidemiology with radiation as a model (Cytogenetic, malformation, and mini- and microsatellite analysis on Kerala population)*

2 June, **Dr. Tony Hayter**, associate professor, Department of Industrial Engineering, Georgia Institute of Technology, (currently visiting researcher at National Institute of Agro-Environmental Sciences in Tsukuba: *An introduction to multiple comparisons data analysis with examples*

28 June, **Dr. Song-Feng Wang**, secretary general, Republic of China Atomic Energy Commission, Taiwan: *Mitigation and prevention of the ^{60}Co-contaminated Rebar incident*

22 September, **Jacob A. Brody, M.D.**, professor, University of Illinois at Chicago School of Public Health, Chicago, Illinois, U.S.A.: *Age-associated diseases and conditions: Implications for decreasing late life morbidity*

30 September, **Dr. Shankar Menon**, programme coordinator, Organization for Economic Cooperation and Development/Nuclear Energy Agency, Nykoping, Sweden: *The regulation of recycling of radioactively contaminated material*

Hiroshima Statistics Study Group Lecture Series, 1 April to 30 September

28 May, **Akira Asano, Ph.D.**, associate professor, Division of Mathematical and Information Sciences, Faculty of Integrated Arts and Sciences, Hiroshima University: *Texture analysis using mathematical morphology*

25 June, **Donald Pierce, Ph.D.**, Senior Scientist, Departments of Statistics and Epidemiology, RERF: *Development of multistage models for cancer*

RERF PR Video Nears Completion

Japanese- and English-language versions of a new RERF promotional video are in their final stages of preparation for release in time for the November open houses in Hiroshima and Nagasaki. The new film has been undertaken to provide an up-to-date overview of the foundation and its research activities for visitors to the two laboratories. It is intended to be easily understood by the wide range of visitors that pass through RERF throughout the year, from researchers and diplomats to junior high school students. The Knack Images Production Company in Hiroshima has been contracted to do the work.

***Accident Meeting**, continued from page 4*

abroad to meet and share information. Representatives of the Japanese Ministry of Health and Welfare and the Science and Technology Agency joined representatives of the World Health Organization and the International Atomic Energy Agency in contributing to the program.

Editor's Note: As of June, RERF Chairman Shigenobu Nagataki is heading a group appointed by the Japanese Ministry of Health and Welfare, who are charged with preparing a manual for use by local emergency personnel and hospitals in the event of radiation emergencies. Currently, all that is available is a handbook for use by employees of nuclear plants, which has been prepared by nuclear scientists and not physicians. The importance of this project is underlined by the fact that in the recent incident in Tokaimura, local rescue teams were exposed to radiation when they rushed into the accident site without taking proper precautions.

***Pubs. Using RERF Data**, continued from page 34*

Little MP (National Radiological Protection Board, UK [NRPB]), Muirhead CR (NRPB), Charles MW (School of Physics and Space Research, University of Birmingham, UK). *Describing time and age variations in the risk of radiation-induced solid tumour incidence in the Japanese atomic bomb survivors using generalized relative and absolute risk models.* Statistics in Medicine **1999**; 18: 17-33.

Little MP (National Radiological Protection Board, UK [NRPB]), Weiss HA (London School of Hygiene and Tropical Medicine, UK), Boice JD (International Epidemiology Institute, Maryland, USA), Darby SC (Clinical Trial Service Unit, University of Oxford, UK), Day NE (Institute of Public Health, University Forvie Site, UK), Muirhead CR (NRPB). *Risks of leukemia in Japanese atomic bomb survivors in women treated for cervical cancer and in patients treated for ankylosing spondylitis.* Radiation Research **1999**; 152: 280-292.

Luebeck EG (Fred Hutchinson Cancer Research Center, Washington, USA[FHCRC]), Moolgavkar SH (FHCRC). *Response to the letter of Dr. Sherman and correction of error in* Radiation Research *148, 348-358 (1997).* Radiation Research **1998**; 149(3): 309. ***(Correction of Kai M, et al., above)***

Prentice RL (Fred Hutchinson Cancer Research Center, Washington, USA). *Binary regression using an extended beta-binomial distribution, with discussion of correlation induced by covariate measurement errors.* Journal of the American Statistical Association **1986**; 81(394): 321-327.

Sherman CD (Department of Mathematics, San Francisco State University). *Modeling cancer incidence in A-bomb survivors: A perspective.* Stochastic Environmental Research and Risk Assessment **1999**; 13: 48-65.

RERF Hosts IAEA Director General

On April 15, Dr. Mohamed El Baradei, director general of the International Atomic Energy Association, visited Hiroshima and paid a courtesy call to RERF. Dr. El Baradei met with Chairman Nagataki and Vice Chairman Wolff during his visit and toured the Hiroshima facilities.

Scientific Publications, 1 April to 30 September

Following are listings of the 57 manuscripts reported published by RERF staff members between 1 April and 30 September 1999 and any others not previously reported for the 1998-1999 fiscal year. Publications are arranged in reverse order by research protocol (RP) number by study program. Publications not directly related to a given RP are listed separately after these as collaborative and institutional publications and include RERF director-authored and edited publications. A separate section also follows for Chernobyl-related collaborative research.

Investigators' and authors' names are followed by their affiliations in parentheses. Abstracts are included for those articles bound in RERF Report *covers. The following codes are used to identify RERF departments in publications and the section on meeting participation and oral presentations (See page 31.):*

Clinical Studies, Hiroshima	*CH*	*Clinical Studies, Nagasaki*	*CN*
Epidemiology, Hiroshima	*EH*	*Epidemiology, Nagasaki*	*EN*
Genetics	*G*	*Radiobiology*	*R*
Statistics	*S*	*Information Technology*	*IT*
RERF Director	*D*	*Secretariat*	*Sec*

***(Japanese)** after an entry indicates that the original article is in Japanese; **(J)** after an entry listed with an* RERF Report *number indicates that a Japanese translation is available.*

Those publications designated as RERF Reports *have undergone internal review prior to journal submission. Following acceptance and publication by a peer-reviewed journal, reprints are purchased from the publisher and bound with a Japanese summary in* RERF Report *covers.*

Life Span Study

RP 1-75

Shimizu Y (EH), Pierce DA (S), Preston DL (S), Mabuchi K (EH). *Studies of the mortality of atomic bomb survivors. Report 12, Part II. Noncancer mortality: 1950-1990.* Radiation Research 1999 (October); 152(4): 374-389. (*RERF Report* 11-98) **(J)**

Abstract: This report updates the data on noncancer mortality for 86,572 atomic bomb survivors with dose estimates in the Radiation Effects Research Foundation's Life Span Study cohort. The primary analyses are based on more than 27,000 noncancer disease deaths that occurred in the cohort between October 1, 1950, and December 31, 1990, 30% more than in the previous report. The present analyses strengthen earlier findings of a statistically significant increase in noncancer disease death rates with radiation dose. Increasing trends are observed for diseases of the circulatory, digestive and respiratory systems. Rates for those exposed to 1 Sv are elevated about 10%, a relative increase that is considerably smaller than that for cancer. However, estimates of the number of radiation-related noncancer deaths in the cohort to date (140 to 280) are 50 to 100% of the number for solid cancer. The data do not yet clarify the shape of the dose response. There is no significant evidence against linearity, but the data are statistically consistent with curvilinear dose-response functions that posit essentially zero risk for doses below 0.5 Sv. Similarly, while the data are consistent with substantial variation in the excess relative risk with age at exposure or attained age, there is no statistically significant dependence on these factors. In view of the small relative risks and the lack of understanding of biological mechanisms, we emphasize consideration of whether the findings could be explained by misclassification, confounding or selection effects. Based on available data, we conclude that such factors are unlikely to fully explain the observed dose response. A significant dose response is also seen for deaths from blood diseases with an excess relative risk that is several times greater than that seen for solid cancer. Particular attention is paid to the possibility that this apparent effect is a consequence of the attribution of leukemia or other cancer deaths to noncancer blood diseases. We find that misclassification does not explain this excess risk. As in earlier reports, suicide rates tend to decrease with increasing dose.

Immunology Studies

RP 1-93

Kusunoki Y (R), Kyoizumi S (R), Yamaoka M (R), Maki M (R), Hirai Y (R), Kasagi F (S), Kodama K (CH), Seyama T (R). *Effects of atomic-bomb radiation on human immune responses: (14) Relationship between decrease in the ratio of peripheral blood CD4 T cells and the development of myocardial infarction.* Nagasaki Igakkai Zasshi (Nagasaki Medical Journal) 1998 (December 25); 73: 332-335. (Proceedings of the 39th Late A-bomb Effects Research Meeting, 1998). **(Japanese)**

RP 2-90

Kyoizumi S (R), Hirai Y (R), Shibata Y (ABDI/NUSM), Fujita Y (EH). *A-bomb survivor blood cell bank.* FY-1998 Report of A-bomb Disease Research Teams. Tokyo: Nippon Koshueisei Kyokai (Japan Public Health Association); 1999 (March), pp 9-10. **(Japanese)**

RP 7-89

Iwamoto KS (R), Mizuno T (R), Seyama T (R), Kyoizumi S (R). *Mutant* p53*: Epigenetic mutator of the T-cell receptor via induction of methylation.* Molecular Carcinogenesis 1999 (June); 25(2): 113-121. (*RERF Report* 6-98)

Abstract: The mechanism and effects of epigenetic alterations in human carcinogenesis are not well understood, except that cancers often have alterations in the methylation status of their genomes. Additionally, human cancers, including aggressive T-cell leukemias and lymphomas, have a high frequency of *p53* mutations, particularly missense mutations, which raises the possibility of gain-of-new-function proteins, but the new proteins' oncogenic functions are mechanistically ill-defined. To investigate the mechanisms behind the high prevalence of *p53* tumor suppressor gene mutations in aggressive or relapsed T-cell leukemias, we transfected Jurkat cells null for p53 protein with a temperature-sensitive *p53* mutant. We showed that this mutant p53 abrogated expression of the T-cell antigen receptor (TCR) by affecting the methylation of an at least 20-kb region of DNA, 5' to the *TCR* beta-chain gene enhancer region, which includes *TCR beta C1* and *beta C2*.

Expression of the TCR is restored when the temperature is reduced to 32 degrees Centigrade, at which temperature the mutant p53 regains wild-type function. The TCR, a common site of dysfunction in T-cell malignancies, is the principal signal transduction moiety controlling both T-cell activation and activation-induced apoptosis. These results suggest a new role for mutant p53—as an epigenetic mutator, bridging p53, methylation, and transcriptional silencing—and suggest novel mechanisms in immunosuppression and cancer progression.

Special Clinical Studies

RP 5-92

Mimori Y (Hiroshima University School of Medicine [HUSM]), Ikeda J (HUSM), Nakamura S (HUSM), Yamada M (CH), Sasaki H (Health Management and Promotion Center, Hiroshima A-bomb Casualty Council). *Prevalence of dementia and its subtypes in the Japanese and Japanese American population: Comparison between Hiroshima, Honolulu and Seattle.* Ronen-ki Chiho (Journal of Senile Dementia) 1999 (April); 13(2): 173-179. **(Japanese)**

Yamada M (CH), Mimori Y (Hiroshima University School of Medicine [HUSM]), Sasaki H (CH), Kasagi F (S), Ikeda J (HUSM), Nakamura S (HUSM). *Study of cognitive function disorder among A-bomb survivors.* Nagasaki Igakkai Zasshi (Nagasaki Medical Journal) 1998 (December 25); 73: 228-231. (Proceedings of the 39th Late A-bomb Effects Research Meeting, 1998). **(Japanese)**

RP 3-90

Wong FL (CH), Yamada M (CH), Sasaki H (CH), Kodama K (CH), Hosoda Y (CH). *Effects of radiation on the longitudinal trends of total serum cholesterol levels in the atomic bomb survivors.* Radiation Research 1999 (June); 151(6): 736-746. (*RERF Report* 17-97)

Abstract: The effects of radiation on the long-term trends of the total serum cholesterol levels of the Hiroshima and Nagasaki atomic bomb survivors were examined using data collected in the Adult Health Study over a 28-year period (1958-1986). The growth-curve method was used to model the longitudinal age-dependent changes in cholesterol levels. For each sex, temporal trends of cholesterol levels were characterized with respect to age, body mass index, city, and birth year. We then examined whether the temporal trends differed by radiation dose. We showed that the mean growth curve of cholesterol levels for the irradiated subjects was significantly higher than that for the unirradiated subjects, and that the increase was greater for women than for men. No difference in dose response was detected between Hiroshima and Nagasaki. An increased mean level of cholesterol was evident for irradiated women in general, but a notable increase was apparent in males only for the youngest birth cohort of 1935-1945. The difference in the mean cholesterol levels between the irradiated and unirradiated subjects diminished past 70 years of age. It is not known whether this is due to natural progression or is an artifact of nonrandom variation in the rate of participation in the examinations. The maximum predicted increase at 1 Gy for women occurred at age 52 years for the 1930 cohort: 2.5 mg/dl (95% CI 1.6-3.3 mg/dl) for Hiroshima and 2.3 mg/dl (95% CI 1.5-3.1 mg/dl) for Nagasaki. The corresponding increase for men occurred at age 29 years for the 1940 cohort: 1.6 mg/dl (95% CI 0.4-2.8) for Hiroshima and 1.4 mg/dl (95% CI 0.3-2.6) for Nagasaki. Controlling for cigarette smoking did not alter the dose-response relationship. Although the difference in the mean growth curves of the irradiated and unirradiated groups was statistically significant, there was a considerable overlap in the individual growth curves of the two groups. The significant sex difference and the greater magnitude of radiation effects in women suggest that hormonal changes resulting from radiation exposure, such as accelerated menopause, is an area worth investigating to delineate the mechanisms underlying the increased cholesterol levels of the irradiated female subjects. This increase may also partially explain the increased rate of coronary heart disease seen in the atomic bomb survivors.

RPs 3-91 and 3-89

Fujiwara S (CH). *Epidemiologic study on osteoporosis in the Adult Health Study cohort.* Kodama K (CH), ed. Textbook of methods and application of epidemiology and public health. Hiroshima, Japan: The Third British Epidemiology and Public Health Course; 1998 (November 29), pp 263-266. (Proceedings of the Third British Epidemiology and Public Health Course).

Fujiwara S (CH). *Epidemiology of osteoporosis.* Rinsho Seikei Geka (Clinical Orthopaedic Surgery) 1999 (March 25); 34(3): 291-297. **(Japanese)**

Fujiwara S (CH). *Epidemiology of osteoporosis and fracture risk.* Matsumoto T, ed. Kotsu Soshosho (Osteoporosis) (Pratical Internal Medicine Series 4). Tokyo, Japan: Nankodo; 1998, pp 17-22. **(Japanese)**

Fujiwara S (CH). *Epidemiology of spine fracture.* Orimo H, Suda T, Inoue T, Morii H, Morita R, Fujita T, eds. Osteoporosis Update. Tokyo, Japan: Life Science Pub.; 1999, pp 24-27. **(Japanese)**

Fujiwara S (CH). *Incidence of spinal fracture.* Osteoporosis Japan 1999 (January); 7(1): 18-19. **(Japanese)**

Fujiwara S (CH). *Osteoporosis and bone fractures.* Sanfujinka Chiryo (Obstetrical and Gynecological Therapy) 1999 (March); 78(3): 289-292. **(Japanese)**

Fujiwara S (CH). *Osteoporosis and diet, exercise, and life style.* In: Nishizawa Y., *et al.*, eds. Calcium, its basic, clinical, and nutritional aspects. Tokyo: Iyaku Journal Publishing; 1999, pp 174-181. **(Japanese)**

Fujiwara S (CH). *Population demographics and trend of aged population.* Nakamura T, Matsumoto T, eds. Handbook for Osteoporosis Therapy. Tokyo: Iyaku Journal; 1998, pp 34-36. **(Japanese)**

Fujiwara S (CH). *Relationship between life-style and spinal fracture.* Clinical Calcium 1998 (June); 8(6):745-748. **(Japanese)**

Fujiwara S (CH). *Risk factor of osteoporosis.* In: Nakamura T, Matsumoto T, eds. Lifestyle: Handbook for osteoporosis

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therapy. Tokyo: Iyaku Journal Publishing; 1998, pp 63-65.

Fujiwara S (CH), Kodama K (CH), Yamada M (CH), Kasagi F (S), Masunari N (CH), Nagataki S (D). *Effects of past dietary pattern on bone density and the rate of change of bone density of the middle- and advanced-aged persons.* Osteoporosis Japan 1998 (October 9); 6(3): 607-611. **(Japanese)**

Cell Biology Studies

RP 2-94

Iwamoto KS (R), Fujii S (R), Kurata A (Osaka National Hospital [ONH]), Suzuki M (ONH), Hayashi T (R), Ohtsuki Y (Kochi Medical School), Okada Y (Matsuyama-Shimin Hospital), Narita M (Kamo Hospital, Toyota), Takahashi M (Tokushima Central Prefectural Hospital), Hosobe S (Akita Red Cross Hospital), Doishita K (Fukui Prefectural Geriatric Center), Manabe T (Kawasaki Medical School, Kurashiki [KMS]), Hata S (KMS), Murakami I (Iwakuni National Hospital), Hata S (Nagano Red Cross Hospital), Itoyama S (Yaizu Municipal General Hospital), Akatsuka S (Urawa Municipal Hospital), Ohara N (Okayama University Hospital), Iwasaki K (Sasebo City General Hospital), Akabane H (Yokosuka Kyosai Hospital, Kanagawa), Fujihara M (Hiroshima Red Cross Hospital and Atomic Bomb Survivors' Hospital), Seyama T (Yasuda Women's University, Hiroshima), Mori T (National Institute of Radiological Sciences, Chiba). *p53 mutations in tumor and non-tumor tissues of Thorotrast recipients: a model for cellular selection during radiation carcinogenesis in the liver.* Carcinogenesis 1999 (July); 20(7): 1283-1291. (*RERF Report* 10-98)

Abstract: Concerns over cancer development from exposure to environmental sources of densely ionizing, high linear energy transfer (LET) radiation, such as alpha-particles from radon, is a current public health issue. The study of tumors attributable to high -LET irradiation would greatly augment our insights into the biological mechanisms of carcinogenesis. Chronic low-dose-rate internal exposure to alpha-radiation from thorium dioxide deposits following intravascular administration of the radiographic contrast agent Thorotrast is known to increase the risk of cancer development markedly, especially that of hepatic angiosarcomas and cholangiocarcinomas. Although the mechanism is hypothesized to be via cellular damage, DNA being a major target, wrought by the high-LET alpha particles, the specific genes and the actual sequence of events involved in the process of transforming a normal cell into a malignant one are largely unknown. To shed some light on the molecular mechanisms of cancer development during a lifetime exposure to alpha radiation, we analyzed the most commonly affected tumor suppressor gene in humans, *p53*, in 20 Thorotrast recipients who developed cancer, mostly of hepatic bile duct and blood vessel origin. Of the 20 cases, 19 were found to harbor *p53* point mutations. Moreover, the accompanying non-tumor tissues from these patients also had *p53* mutations, albeit at lower frequency. The distribution pattern of the point mutations was significantly different between the non-tumor and tumor tissues, with most mutations in malignant tissues located in the highly conserved domains of the *p53* gene. Our results support the idea that *p53* mutations are important in the genesis of Thorotrast-induced tumors but that these point mutations are a secondary outcome of genomic instability induced by the irradiation. Additionally, non-tumor cells harboring *p53* mutations may gain some survival advantage *in situ,* but mutations in the domains responsible for the formation of structural elements critical in binding DNA may be necessary for a cell to reach full malignancy.

Iwamoto KS (R), Mizuno T (R), Tokuoka S (EH), Mabuchi K (EH), Seyama T (R). *Development of radiation-induced cancers in humans: Molecular lessons from the atomic-bomb survivors.* Nagasaki Igakkai Zasshi (Nagasaki Medical Journal) 1998 (December 25); 73:185-188. (Proceedings of the 39th Late A-bomb Effects Research Meeting, 1998). **(Japanese)**

Biochemical Genetics Studies

RP 7-85

Asakawa J (G). *High resolutional two-dimension electrophoresis of DNA by using a vertical giant gel system.* Seibutsu Butsuri Kagaku (Japanese Journal of Electrophoresis) 1998; 42(3): 145-154. **(Japanese)**

Asakawa J (G). *Search for germinal mutation by two-dimensional electrophoresis of DNA fragments.* Hiroshima Igaku (Journal of the Hiroshima Medical Association) 1999 (March); 52(3): 281-282. **(Japanese)**

Asakawa J (G), Kodaira M (G), Nakamura N (G), Satoh C (G), Fujita M (G). *Chimerism in humans after intragenic recombination at the haptoglobin locus during early embryogenesis.* Proceedings of the National Academy of Sciences of the United States of America 1999 (August 31); 96(18): 10314-10319. (*RERF Report* 12-98)

Abstract: The human haptoglobin (HP) *HP*2* allele contains a 1.7-kilobase (kb) intragenic duplication that arose after a unique nonhomologous recombination between the prototype *HP*1* alleles. During a genetic screening of 13,000 children of survivors exposed to atomic-bomb radiation and 10,000 children of unexposed persons, two children suspected of carrying *de novo* mutations at the haptoglobin locus were identified (one in each group). DNA analyses of single-cell-derived colonies of Epstein-Barr virus-transformed B cells revealed that the two children were mosaics comprising *HP*2 / HP*2* and *HP*2 / HP*1* cells at a ratio of approximately equal to 3:1. We infer that the latter cells are caused by reversion of one *HP*2* allele to *HP*1* through an intramolecular homologous recombination between the duplicated segments of the *HP*2* allele that excised one of the segments. Because the mosaicism is substantial (approximately equal to 25%), this recombination must have occurred in early embryogenesis. The frequency of finding these children and the extent of their mosaicisms corresponds to an *HP*2* to *HP*1* reversion rate of 8×10^{-6} per cell during development. This leads to the prediction that the HP*1 allele also will be represented, although usually at a very low frequency, in any HP2-2 person. We tested this prediction by using PCR for a single individual

and found the *HP*1* allele at frequencies of 4 x 10^{-6} and 3 x 10^{-6} in somatic and sperm cells. The *HP*1* allele was detected by PCR in all four other HP2-2 individuals, which supports the regular but rare occurrence somatically of homologous recombination within duplicated regions in humans, in agreement with previous observations in mouse and *Drosophila*.

Kodaira M (G). *Genetic effects of atomic-bomb radiation: Analysis of minisatellite loci detected by DNA fingerprint probes.* Hoshasen Seibutsu Kenkyu (Radiation Biology Research Communications) 1999 (June); 34(2): 205-212. **(Japanese)**

Ohshima T (Kanazawa University School of Medicine), Takayasu T (Yamagata University School of Medicine), Fujita M (G), Satoh C (G). *A transferrin D variant (D_{HR5}) identical with D_{Saga} by polyacylamide gel isoelectirc focusing was found in a disputed paternity case.* Japanese Journal of Legal Medicine 1998; 52: 253-256.

Takahashi N (G). *Overview of DNA-chip technologies and their application for the study on the potential genetic effects of atomic bomb radiation.* Hoshasen Seibutsu Kenkyu (Radiation Biology Research Communications) 1999 (June); 34(2): 232-242. **(Japanese)**

Cytogenetics Studies

RP 8-93

Kodama Y (G), Nakano M (G), Itoh M (G), Ohtaki K (G), Kusunoki Y (R), Hirai Y (R), Kyoizumi S (R), Nakamura N (G). *Origin of clonal chromosome aberrations in atomic-bomb survivors.* Hoshasen Seibutsu Kenkyu (Radiation Biology Research Communications) 1999 (June); 34(2): 213-222. **(Japanese)**

Nakamura N (G). *Is micronucleus derived from chromosome breakage?* Hoshasen Seibutsu Kenkyu (Radiation Biology Research Communications) 1999 (June); 34(2): 251-258. **(Japanese)**

Ohtaki K (G). *Clonal chromosome aberrations in atomic-bomb survivors: Deletion 5q and inversion 14, characteristics of leukemia-related changes.* Hiroshima Igaku (Journal of the Hiroshima Medical Association) 1999 (April); 52(4): 388-390. **(Japanese)**

Ohtaki K (G). *Clonal chromosome aberrations in atomic-bomb survivors: Deletion 5q and inversion 14, characteristics of leukemia-related changes.* Hoshasen Seibutsu Kenkyu (Radiation Biology Research Communications) 1999 (June); 34(2): 223-231. **(Japanese)**

Ohtaki K (G), Nakamura N (G), Awa AA (G). *Chromosome aberration: Inv(14)(q11q32) in lymphocytes from A-bomb survivors.* Nagasaki Igakkai Zasshi (Nagasaki Medical Journal) 1998 (December 25); 73: 340-342. (Proceedings of the 39th Late A-bomb Effects Research Meeting, 1998). **(Japanese)**

F_1 Studies

RP 4-75

Hayakawa N (Research Institute for Radiation Biology and Medicine, Hiroshima University), Ito C (Health Management and Promotion Center, Hiroshima A-bomb Casualty Council), Satow Y (Hiroshima Bunka Women's Junior College), Takahashi N (G), Asakawa J (G), Yamada M (CH), Akahoshi M (CN). *Genetic effects of radiation: Summary report.* FY-1998 Report of A-bomb Disease Research Teams. Tokyo: Nippon Koshueisei Kyokai (Japanese Public Health Association); 1999 (March), pp 20-24. **(Japanese)**

Special Cancer Studies and Tissue Registry

RP 5-90

Cologne JB (S), Tokuoka S (EH), Beebe GW (National Cancer Institute, USA), Fukuhara T (Hiroshima Prefectural Hospital), Mabuchi K (EH). *Effects of radiation on incidence of primary liver cancer among atomic bomb survivors.* Radiation Research 1999 (October); 152(4): 364-373. (*RERF Report* 6-99)

Abstract: We describe the radiation risk for primary liver cancers between 1958 and 1987 in a cohort of atomic bomb survivors in Hiroshima and Nagasaki, Japan. The analysis is based on a comprehensive pathology review of known or suspected liver neoplasms that generated 518 incident, first primary cases, mostly hepatocellular carcinoma. Excess relative risk from atomic bomb radiation was linear: 0.81 per sievert weighted liver dose (95% CI [0.32,1.43]; $P < 0.001$). Males and females had similar relative risk so that, given a threefold higher background incidence in males, the radiation-related excess incidence was substantially higher in males. Excess risk peaked for those with age at exposure in the early 20s; there was essentially no excess risk in those exposed before age 10 or after age 45. Whether this was due to a difference in sensitivity or possible confounding by other factors could not be addressed retrospectively in the full cohort. A paucity of cholangiocarcinoma and hemangiosarcoma cases suggested that they are not significantly associated with whole-body radiation exposure, as they are with the internal alpha-particle-emitting radiological contrast medium Thorotrast. Because most of the radiation-related excess cases occurred among males, it is important to ascertain what factors put men at greater risk of radiation-related liver cancer.

RP 29-60

Oda K (Hiroshima Citizens Hospital; Research Institute for Radiation Biology and Medicine [RIRBM], Hiroshima University [HU]), Kimura A (RIRBM/HU), Matsuo T (Nagasaki University Hospital), Tomonaga M (Atomic Bomb Disease Institute, Nagasaki University School of Medicine), Kodama K (CH), Mabuchi K (EH). *Increased relative risk of myelodysplastic syndrome in atomic bomb survivors.* Nagasaki Igakkai Zasshi (Nagasaki Medical Journal) 1998 (December 25); 73:174-179. (Proceedings of the 39th Late A-bomb Effects Research Meeting, 1998). **(Japanese)**

Atomic-Bomb Dosimetry Studies

RP 1-92

Nakamura N (G). *Comparison between radiation dose estimates from tooth enamel using ESR and DS86 dose*

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estimates. FY-1998 Report of A-bomb Disease Research Teams. Tokyo: Nippon Koshueisei Kyokai (Japan Public Health Association); 1999 (March), pp 48-49. **(Japanese)**

Nakamura N (G), Miyazawa C (Ohu University School of Dentistry), Sawada S (Research Institute for Radiation Biology and Medicine, Hiroshima University), Akiyama M (R), Awa AA (G). *Validation of electron spin resonance studies of tooth enamel to estimate gamma-ray exposure in atomic bomb survivors.* Mendelsohn ML, Mohr LC, Peeters JP, eds. Biomarkers: Medical and Workplace Applications. Washington, D.C., USA: Joseph Henry Press; 1998, pp 65-69.

RP 18-59

Preston DL (S), Mabuchi K (EH), Kodama K (CH), Fujita S (S). *Relationship of epilation to distance from hypocenter.* Nagasaki Igakkai Zasshi (Nagasaki Medical Journal) 1998 (December 25); 73: 251-253. (Proceedings of the 39th Late A-bomb Effects Research Meeting, 1998). **(Japanese)**

Watanabe T (Sec), Yamashita T (EN), Fujita S (S). *Collection of materials exposed to atomic bomb radiation in Hiroshima and Nagasaki (FY 1998).* FY-1998 Report of A-bomb Disease Research Teams. Tokyo: Nippon Koshueisei Kyokai (Japan Public Health Association); 1999 (March), pp 34-36. **(Japanese)**

Not Emanating from Specific Protocols

Kusunoki Y(R), Hayashi T (R), Kyoizumi S (R). *Immunity polarization in atomic-bomb survivors: From the viewpoint of the Th1/Th2 paradigm.* Hiroshima Igaku (Journal of the Hiroshima Medical Association) 1999 (May); 52(5): 509-511. **(Japanese)**

Nakamura N (G). *Future directions of low dose-low dose rate studies.* Hoshasen Seibutsu Kenkyu (Radiation Biology Research Communications) 1999 (June); 34(2): 243-250. **(Japanese)**

Nakamura N (G) *Genetic effects of atomic-bomb radiation: Past, present and future (Review).* Hoshasen Seibutsu Kenkyu (Radiation Biology Research Communications) 1999 (June); 34(2): 153-169. **(Japanese)**

Chernobyl-related Research

Shirahige Y (Nagasaki University School of Medicine [NUSM]), Ito M (NUSM), Ashizawa K (NUSM), Motomura T (NUSM), Yokoyama N (NUSM), Namba H (NUSM), Fukata S (Kuma Hospital [KH]), Yokozawa T (KH), Ishikawa N (NUSM), Mimura T (NUSM), Yamashita S (NUSM), Sekine I (NUSM) I, Kuma K (KH), Ito K (Ito Hospital), Nagataki S (D). *Childhood thyroid cancer: comparison of Japan and Belarus.* Endocrine Journal 1998 (April); 45(2): 203-209.

Collaborative/Institutional/Directors' Publications

Abrahamson S (D). *Lauriston Taylor lecture. 70 years of radiation genetics: Fruit flies, mice and humans.* Health Physics 1996; 71(5): 624-633.

Forrow L (Beth Israel Deaconess Medical Center, Boston), Sidel VW (Montefiore Medical Center; Albert Einstein College of Medicine, New York) (Supervised and commented by Nagataki S (D)). *Medicine and nuclear war—from Hiroshima to mutual assured destruction to abolition 2000.* JAMA (Japanese version) 1999 (April 15); 4: 103-111. **(Japanese)**

Ichinose Y (National Ureshino Hospital, Saga), Eguchi K (Nagasaki University School of Medicine [NUSM]), Migita K (NUSM), Kawabe Y (Nagasaki University Hospital), Tsukada T, Koji T (NUSM), Abe K (NUSM), Aoyagi T, Nakamura H, Nagataki S (D). *Apoptosis induction in synovial fibroblasts by ceramide:* in vitro *and* in vivo *effects.* Journal of Laboratory and Clinical Medicine 1998 (May); 131(5): 410-416.

Inai K (Hiroshima University School of Medicine [HUSM]), Yamashita S (Nagasaki University School of Medicine [NUSM]), Tanaka H (Research Institute for Radiation Biology and Medicine, HU), Dohi H (Hiroshima Red Cross Hospital and Atomic Bomb Survivors' Hospital), Takamura N (NUSM), Naito S (NUSM), Fujita Y (EH), Kyoizumi S (R), Hirai Y (R), Shibata Y (Atomic Bomb Disease Institute/ NUSM). *Storage of biological samples: Summary report.* FY-1998 Report of A-bomb Disease Research Teams. Tokyo: Nippon Koshueisei Kyokai (Japan Public Health Association); 1999 (March), pp 4-6. **(Japanese)**

Kawasaki E (Nagasaki University School of Medicine [NUSM]), Yamaguchi Y (NUSM), Nagataki S (D). *Insulitis in an autoimmune-mediated patient originally classified as having type 2 diabetes.* Diabetes Care 1999 (April); 22(4): 541-542.

Nagataki S (D). *Atomic bomb survivors population.* Thomas G, Karaoglou A, Williams ED, eds. Radiation and Thyroid Cancer. Singapore: World Scientific Publishing Co. Pte. Ltd.; 1999, pp 35-40. (Proceedings of an International Seminar on Radiation and Thyroid Cancer)

Nagataki S (D). *Thyroid cancer in atomic bomb survivors.* Thomas G, Karaoglou A, Williams ED, eds. Radiation and Thyroid Cancer. Singapore: World Scientific Publishing Co. Pte. Ltd.; 1999, pp 189-193. (Proceedings of an International Seminar on Radiation and Thyroid Cancer).

Nagataki S (D), Kasuga M. *A talk on research and its background.* Diabetes Frontier 1999 (June); 10(3): 377-386. **(Japanese)**

Nakao YK (Nagasaki University School of Medicine [NUSM]), Motomura M (NUSM), Suenaga A (NUSM), Nakamura T (NUSM), Yoshimura T (School of Allied Medical Sciences, NU), Tsujihata M (Nagasaki Kita Hospital), Mori M (Nagasaki Chuo National Hospital), Ito M (Eiken Chemical Co. Ltd., Otawara), Nagataki S (D). *Specificity of omega-conotoxin MVIIC-binding and -blocking calcium channel antibodies in Lambert-Eaton myasthenic syndrome.* Journal of Neurology 1999 (January); 246(1): 38-44.

Nakashima T, Sasaki H, Tsuboi M, Kawakami A, Fujiyama K, Kiriyama T (Nagasaki University School of Medicine

[NUSM]), Eguchi K (NUSM), Ichikawa M, Nagataki S (D). *Inhibitory effect of glucocorticoid for osteoblast apoptosis induced by activated peripheral blood mononuclear cells.* Endocrinology 1998 (April); 139(4): 2032-2040.

Pierce DA (S), Peters D (Department of Statistics, Oregon State University). *Improving on exact tests by approximate conditioning.* Biometrika 1999 (June); 86(2): 265-277.

Sera N (Nagasaki University School of Medicine [NUSM]), Ashizawa K (NUSM), Namba H (ABDI/NUSM), Yokoyama N (NUSM), Izumi M (NUSM), Nagataki S (D), Yamashita S (ABDI/NUSM), Eguchi K (NUSM). *A study of usefulness of quantitative analysis of ultrasonographic features among thyroid diseases.* Nagasaki Igakkai Zasshi (Nagasaki Medical Journal) 1998 (December 25); 73: 263-265. (Proceedings of the 39th Late A-bomb Effects Research Meeting, 1998). **(Japanese)**

Tamura M (Nagasaki University School of Medicine [NUSM]), Kimura H (NUSM), Koji T (NUSM), Tominaga T (CN), Ashizawa K (NUSM), Kiriyama T (NUSM), Yokoyama N (NUSM), Yoshimura T (School of Allied Medical Sciences, NU), Eguchi K (NUSM), Nakane PK (NUSM), Nagataki S (D). *Role of apoptosis of thyrocytes in a rat model of goiter. A possible involvement of Fas system.* Endocrinology 1998 (August); 139(8): 3646-3653.

Tamura M (Nagasaki University School of Medicine [NUSM]), Yokoyama N (NUSM), Abe Y (NUSM), Sera N (NUSM), Tominaga T (CN), Ashizawa K (NUSM), Ejima E (NUSM), Kiriyama T (NUSM), Uetani M (NUSM), Kuwayama A (National Nagoya Hospital), Nagataki S (D). *Preoperative treatment of growth hormone-producing pituitary adenoma with continuous subcutaneous infusion of octreotide.* Endocrine Journal 1998 (April); 45(2): 269-275.

Tsujino A (Nagasaki University School of Medicine [NUSM]), Nakamura T (NUSM), Furuya T (NUSM), Goto H (NUSM), Nishiura Y (NUSM), Shirabe S (NUSM), Nakane S (NUSM), Motomura M (NUSM), Nagataki S (D). *Elevated serum levels of soluble E- and L-selectin in patients with human T-cell lymphotropic virus type I-associated myelopathy.* Journal of the Neurological Sciences 1998 (February 18); 155(1): 76-79.

RERF Research Presented at Meetings, 1 April to 30 September (and presentations not previously reported for the fiscal year)

RERF researchers reported attending ten meetings outside of Japan at which they made 21 presentations and 12 meetings in Japan at which they made 19 presentations from 1 April through 30 September 1999. As with publications, research presentations are listed by research protocol number under the appropriate study program. Meetings are listed chronologically under RP. The same department codes used for publications are used to identify investigators' affiliations.

Life Span Study

RP 1-75

Izumi S (S), Ohtaki M (Research Institute for Radiation Biology and Medicine, Hiroshima University). **Multiple regression analysis of survival time data using Weibull-gamma model.** Joint Annual Meeting of the Biometric Society of Japan and the Japanese Society of Applied Statistics, FY1999, 6-7 May 1999, Tokyo, **Japan**

Mabuchi K (EH). **The significance of long-term epidemiological studies about the health effects of atomic-bomb exposure.** The Fortieth Late A-bomb Effects Research Meeting, 6 June 1999, Hiroshima, **Japan**

Preston DL (S). **Radiation effects on the atomic-bomb survivors.** The Eleventh International Congress of Radiation Research, 18-23 July 1999, Dublin, **Ireland**

Shimizu Y (EH), Pierce DA (S), Preston DL (S), Mabuchi K (EH). **Studies of the noncancer mortality of atomic-bomb survivors: 1950-1990.** The Eleventh International Congress of Radiation Research, 18-23 July 1999, Dublin, **Ireland**

Shimizu Y (EH). **Epidemiological study on health effects of atomic-bomb survivors.** The Eleventh International Conference of Women Engineers and Scientists, 24-27 July 1999, Chiba, **Japan**

Pierce DA (S). **On the relation between frequency inference and likelihood.** The Fifty-second Session of the International Statistical Institute, 15-18 August 1999, Helsinki, **Finland**

Nagataki S (D). **Thyroid cancer in atomic-bomb survivors.** The Twenty-sixth Annual Meeting of the European Thyroid Association, 28 August-1 September 1999, Milan, **Italy**

Mabuchi K (EH). **Epidemiological characteristics of the cancer risks in atomic-bomb survivors.** The Forty-second Annual Meeting of the Japan Radiation Research Society, 1-3 September 1999, Hiroshima, **Japan**

Shimizu Y (EH), Pierce DA (S), Preston DL (S), Mabuchi K (EH). **Noncancer disease mortality among atomic-bomb survivors, 1950-1990.** The Forty-second Annual Meeting of the Japan Radiation Research Society, 1-3 September 1999, Hiroshima, **Japan**

Nakamura N (G). **Molecular mechanisms of cancer deduced from data of A-bomb survivors.** The Fifty-eighth Annual Meeting of the Japanese Cancer Association, 29 September-1 October 1999, Hiroshima, **Japan**

Adult Health Study

RP 2-75

Nakashima E (S), Neriishi K (CH). **Analysis of**

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inflammatory test measurements in atomic-bomb survivors with principal component analysis. The Fortieth Late A-bomb Effects Research Meeting, 6 June 1999, Hiroshima, **Japan**

Fujiwara S (CH), Nakashima E (S), Kodama K (CH). **Diabetes mellitus among atomic-bomb survivors.** The Eleventh International Congress of Radiation Research, 18-23 July 1999, Dublin, **Ireland**

Kasagi F (S), Kodama K (CH), Fujiwara S (CH), Yamada M (CH). **Sudden death in the atomic-bomb survivors, Hiroshima.** The Eleventh International Congress of Radiation Research, 18-23 July 1999, Dublin, **Ireland**

Neriishi K (CH). **Clinical laboratory test of atomic-bomb survivors.** The Nineteenth Meeting of Summer Seminar of the Japanese Association of Clinical Chemistry, 28-30 July 1999, Hiroshima, **Japan**

Kodama K (CH), Kasagi F (S), Fujita Y (EH), Yamada M (CH), Fujiwara S (CH). **Case-control study of short and long lives in the population of atomic bomb survivors.** The Fifteenth Scientific Meeting of the International Epidemiological Association, 31 August-4 September 1999, Florence, **Italy**

Neriishi K (CH), Tominaga T (CN), Nakashima E (S). **Analysis of inflammatory tests for chronic thyroiditis among atomic-bomb survivors using principal component analysis.** The Forty-second Annual Meeting of the Japan Radiation Research Society, 1-3 September 1999, Hiroshima, **Japan**

Neriishi K (CH), Nakashima E (S). **Persistent inflammation in atomic-bomb survivors and possible mechanisms.** International Conference of Free Radical Processes: Ecological, Pharmacological and Clinical Aspects, 9 September 1999, St. Petersburg, **Russia**

Immunology Studies

RP 1-93

Hayashi T (R), Kusunoki Y (R), Maki M (R), Kubo Y (R), Yamaoka M (R), Kasagi F (S), Fujiwara S (CH), Kodama K (CH), Kyoizumi S (R). **Late effects of atomic-bomb radiation on human immune responses. (15) Plasma IL-6 and immunoglobulin levels in atomic-bomb survivors.** The Fortieth Late A-bomb Effects Research Meeting, 6 June 1999, Hiroshima, **Japan**

Hayashi T (R), Kusunoki Y (R), Kasagi F (S), Kodama K (CH), Kyoizumi S (R). **A dose-dependent increase of plasma IL-6 level in atomic-bomb survivors.** The Eleventh International Congress of Radiation Research, 18-23 July 1999, Dublin, **Ireland**

Hayashi T (R), Kusunoki Y (R), Kubo Y (R), Maki M (R), Yamaoka M (R), Kasagi F (S), Fujiwara S (CH), Kodama K (CH), Seyama T (R), Kyoizumi S (R). **Late effects of atomic-bomb radiation on cytokine and immunoglobulin production.** The Forty-second Annual Meeting of the Japan Radiation Research Society, 1-3 September 1999, Hiroshima, **Japan**

Kusunoki Y (R), Hayashi T (R), Onishi H (R), Kubo Y (R), Morishita Y (R), Yamaoka M (R), Fujiwara S (CH), Kodama K (CH), Seyama T (R), Kyoizumi S (R). **Hypothesis on the relationship between A-bomb-radiation-induced immunity polarization and disease development.** The Forty-second Annual Meeting of the Japan Radiation Research Society, 1-3 September 1999, Hiroshima, **Japan**

Hayashi T (R), Kusunoki Y (R), Kyoizumi S (R), Seyama T (R). **Reactive oxygen and Bcl-2 in radiation-induced apoptosis.** International Conference of Free Radical Processes: Ecological, Pharmacological and Clinical Aspects, 8-10 September 1999, St. Petersburg, **Russia**

RP 11-89

Kusunoki Y (R), Honma M (Division of Genetics and Mutagenesis, National Institute of Health Sciences), Hayashi T (R), Kyoizumi S (R). **Radiation-induced *in vivo* generation of mutant cells lacking MHC class I alleles and their suppression by NK cells.** The Fifty-eighth Annual Meeting of the Japanese Cancer Association, 29 September-1 October 1999, Hiroshima, **Japan**

Special Clinical Studies

RP 3-89

Fujiwara S (CH), Kodama K (CH), Nagataki S (D). **Checkup for osteoporosis in a cohort study population and its effects.** The Twenty-fifth General Assembly of the Japanese Association of Medical Sciences, 2-4 April 1999, Tokyo, **Japan**

Fujiwara S (CH), Naito K (CH), Masunari N (CH), Kasagi F (S), Kodama K (CH), Nagataki S (D), Fukunaga M (Department of Nuclear Medicine, Kawasaki Medical School), Nakamura T (Orthopedic Surgery, University of Occupational and Environmental Health). **Bone mineral density of the lumbar/femur neck, and spinal fracture risk.** The Seventeenth General Meeting of the Japanese Society of Bone Metabolism, 29-31 July 1999, Osaka, **Japan**

Cell Biology Studies

RP 7-92

Ban S (R), Shinohara T (R), Itoh M (G), Nakamura N (G). **Whole genome amplification to immortalize the DNA extracted from the formalin-fixed and paraffin-embedded tissue sections.** The Fortieth Late A-bomb Effects Research Meeting, 6 June 1999, Hiroshima, **Japan**

Ban S (R), Hirai Y (R), Shinohara T (R), Yoshikawa K (Department of Pathology and Tumor Biology, Faculty of Medicine, Kyoto University [Kyoto]), Takahashi R (Kyoto). **Radiation sensitivity of BRCA1- or BRCA2-defective cultured human cancer cells.** The Forty-second Annual Meeting of the Japan Radiation Research Society, 1-3 September 1999, Hiroshima, **Japan**

Ban S (R), Hirai Y (R), Yoshikawa K (Department of

Pathology and Tumor Biology, Faculty of Medicine, Kyoto University [Kyoto]), Takahashi R (Kyoto). **BRCA1 and RAD51 expression and radiation sensitivity of cultured human breast cancer cells.** The Fifty-eighth Annual Meeting of the Japanese Cancer Association, 29 September-1 October 1999, Hiroshima, **Japan**

RP 18-81
Kyoizumi S (R), Koyama K(R), Hayashi T (R), Morishita Y (R), Tsuyama N (R), Seyama T (R). **Radiation-induced apoptosis and cell cycle changes in epithelial cells in the human small intestine.** The Forty-second Annual Meeting of the Japan Radiation Research Society, 1-3 September 1999, Hiroshima, **Japan**

Biochemical Genetics Studies

RP 1-97
Takahashi N (G), Murakami H (G), Kasagi F (S), Yamada M (CH) , Kodama K (CH), Nishishita T (Vanderbilt University School of Medicine [Vanderbilt]), Inagami T (Vanderbilt). **Association of a polymorphism at 5'-region of angiotensin II type 1 receptor with hypertension.** Gordon Research Conferences, 8-13 August 1999, Oxford, **UK**

RP 7-85
Asakawa J (G). **High resolution two-dimensional electrophoresis of end-labeled genomic DNA fragments.** Meeting of the International Council of Electrophoresis Societies, 1999, 25-28 May 1999, Tokyo, **Japan**

Asakawa J (G), Kodaira M (G), Ishikawa N (Ito Hospital [Ito]), Ito K (Ito), Ito K (Ito), Nagataki S (D). **Search of genome-wide genetic and epigenetic alterations in papillary thyroid cancer by sequential two-dimensional DNA gel analysis.** The Twenty-sixth Annual Meeting of the European Thyroid Association, 28 August-1 September 1999, Milan, **Italy**

Kodaira M (G), Satoh C (G), Shimoichi Y (G), Nakamoto Y (G), Imanaka M (G). **Genetic effects of A-bomb radiation: Reanalysis of minisatellites by DNA fingerprints.** The Forty-second Annual Meeting of the Japan Radiation Research Society, 1-3 September 1999, Hiroshima, **Japan**

Asakawa J (G), Kodaira M (G), Ishikawa N (Ito Hospital [Ito]), Ito K (Ito), Ito K (Ito), Nagataki S (D). **Rapid and accurate detection of tissue-specific gene expression in human papillary thyroid carcinomas by two-dimensional differential display.** The Seventy-second Annual Meeting of the American Thyroid Association, 29 September-3 October 1999, Florida, **USA**

RPs 7-85 and 8-93 (Cytogenetics)
Nakamura N (G). **Genetic effects of atomic-bomb radiation: Past, present, and future.** The Fortieth Late A-bomb Effects Research Meeting, 6 June 1999, Hiroshima, **Japan**

Cytogenetics Studies

RP 8-93
Nakamura N (G). **Somatic mutation in blood cells and human aging.** The Sixth Asia/Oceania Regional Congress of Gerontology, 8-11 June 1999, Seoul, **Korea**

Nakamura N (G), Funamoto S (S), Awa AA (G). **Does the chromosome aberration dose response vary depending on the direction from the hypocenter?** The Twenty-fourth Chugoku-area Local Radiation Research Meeting, 3 July 1999, Hiroshima, **Japan**

Nakamura N (G), Funamoto S (S), Awa AA (G). **Does the chromosome aberration dose response vary depending on the direction from the hypocenter?** The Forty-second Annual Meeting of the Japan Radiation Research Society, 1-3 September 1999, Hiroshima, **Japan**

Special Cancer Studies

RP 14-79
Cologne JB (S), Langholz B (Department of Preventive Medicine, University of Southern California). **Selecting controls for assessing interaction in nested case-control studies.** The Thirty-second Annual Meeting of Society for Epidemiologic Research, 10-12 June 1999, Baltimore, Maryland, **USA**

Special Cancer Studies and Tissue Registry

RP 5-90
Sharp GB (EH), Mizuno T (R), Cologne JB (S), Tokuoka S (EH), Mabuchi K (EH). **Does atomic-bomb radiation increase the risk of hepatocellular carcinoma and cholangiocarcinoma among persons with viral hepatitis?** The Eleventh International Congress of Radiation Research, 18-23 July 1999, Dublin, **Ireland**

Tumor Registry and Tissue Registry

RP 18-61
Soda M (CN), Akahoshi M (CN), Ichimaru S (CN), Soda H (Nagasaki University School of Medicine). **Evaluation of the usefulness of lung cancer screening based on a cohort study.** The Twenty-first Annual Meeting of the International Association of Cancer Registries, 29 September -1 October 1999, Lisbon, **Portugal**

Presentations Not Associated with an RP

Koyama K (EH). **The healthy worker effect in a long-term follow-up population.** The Twenty-second Meeting of the Japanese Society of Cancer Epidemiology, 15 July 1999, Tokyo, **Japan**

Koyama K (EH). **Disease prevention and epidemiology.** The Eighth Japan Preventive Nephrology and Urology Meeting, 16-17 July 1999, Kurashiki, Okayama, **Japan**

Ban S (R). **Mitochondrial genome importance in X-ray-induced apoptosis and apoptotic repair.** The Eleventh International Congress of Radiation Research, 18-23 July 1999, Dublin, **Ireland**

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Fujita Y (EH), Kodama K (CH), Kasagi F (S), Fujita S (S), Yanagawa H (Jichi Medical School), Nose T (Tottori University School of Medicine). **Study of aging level indices based on functional status.** The Fifteenth Scientific Meeting of the International Epidemiological Association, 31 August-4 September 1999, Florence, **Italy**

Nakamura N (G). **Atomic-bomb survivor cancer data and their interpretation.** The Forty-second Annual Meeting of the Japan Radiation Research Society, 1-3 September 1999, Hiroshima, **Japan**

Publications Using RERF Data

Editor's Note: Researchers from outside institutions are able to obtain data sets from RERF, and they sometimes incorporate atomic-bomb survivor data into their own studies. Following is an alphabetical listing (by author) of publications by outside researchers using RERF data. Additional entries may be found back to 1987 on the RERF home page (http://www.rerf.or.jp/eigo/archives/outpub.htm).

Finch SC (Cooper Hospital, New Jersey, USA). *Leukemia: Lessons from the Japanese experience.* Stem Cells **1997**; 15(Suppl 2): 135-139.

Heidenreich WF (GSF-National Research Center for Environment and Health, Germany [GSF]), Jacob P (GSF), Paretzke HG (GSF). *Exact solutions of the clonal expansion model and their application to the incidence of solid tumors of atomic bomb survivors.* Radiation and Environmental Biophysics **1997**; 36: 45-58.

Heidenreich WF (GSF-National Research Center for Environment and Health, Germany [GSF]), Paretzke HG (GSF), Jacob P (GSF). *No evidence for increased tumor rates below 200 mSv in the atomic bomb survivors data.* Radiation and Environmental Biophysics **1997**; 36: 205-207.

Howe GR (National Cancer Institute of Canada, Epidemiology Unit, University of Toronto, Canada). *Lung cancer mortality between 1950 and 1987 after exposure to fractionated moderate-dose-rate ionizing radiation in the Canadian fluoroscopy cohort study and a comparison with lung cancer mortality in the atomic bomb survivors study.* Radiation Research **1995**; 142: 295-304.

Howe GR (Division of Epidemiology, School of Public Health, Columbia University, New York), McLaughlin J (National Cancer Institute of Canada, Epidemiology Unit, University of Toronto, Canada). *Breast cancer mortality between 1950 and 1987 after exposure to fractionated moderate-dose-rate ionizing radiation in the Canadian fluoroscopy cohort study and a comparison with breast cancer mortality in the atomic bomb survivors study.* Radiation Research **1996**; 145: 694-707.

Kai M (Faculty of Medicine, The University of Tokyo), Luebeck EG (Fred Hutchinson Cancer Research Center, Washington, USA [FHCRC]), Moolgavkar SH (FHCRC). *Analysis of the incidence of solid cancer among atomic bomb survivors using a two-stage model of carcinogenesis.* Radiation Research **1997**; 148(4): 348-358. ***(See Luebeck EG and Moolgavkar SH, below, for correction to this article.)***

Kellerer AM (GSF-National Research Center for Environment and Health, Germany [GSF]), Kreisheimer M (Ludwig-Maximilians-Universität München), Chmelevsky D (GSF), Barclay D (GSF). *A hybrid likelihood algorithm for risk modelling.* Radiation and Environmental Biophysics **1995**; 34: 13-20.

Kellerer AM (Radiobiological Institute, University of Munich, Germany), Nekolla E (GSF-National Research Center for Environment and Health, Germany). *Neutron versus gamma-ray risk estimates. Inferences from the cancer incidence and mortality data in Hiroshima.* Radiation and Environmental Biophysics **1997**; 36: 73-83.

Little MP (National Radiological Protection Board, UK). *Comments on "Threshold models in radiation carcinogenesis" by D.G. Hoel and P. Li.* Health Physics **1999**; 76(4): 432-434.

Little MP (National Radiological Protection Board, UK), Boice JD (International Epidemiology Institute, Maryland, USA). *Comparison of breast cancer incidence in the Massachusetts tuberculosis fluoroscopy cohort and in the Japanese atomic bomb survivors.* Radiation Research 1999; 151: 218-224.

See ***Pubs. Using RERF Data****, page 25*

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