

**International Dosimetry
Reassessment Forum
Hosted by RERF**
*by Shigenobu Nagataki,
Chairman, and
Shoichiro Fujita, Assistant
Chief, Department of Statistics*

On 13 and 14 March, more than 60 participants from Japan, the United States, and Germany, and including RERF Hiroshima and Nagasaki researchers, met at the ANA Hotel in downtown Hiroshima for the U.S.-Japan Joint Dosimetry Workshop, the largest meeting ever hosted by RERF. The workshop was co-chaired by Tatsuji Hamada, permanent director of Japan's Nuclear Safety Research Association, who headed the Japanese dosimetry group, and Warren K. Sinclair, former RERF director and president emeritus of the U.S. National Council on Radiation Protection and Measurements, who heads the National Academy of Sciences (NAS) Dosimetry Committee and who headed the U.S. working group.

RERF's mission is to conduct research to ascertain the human health effects of radiation and to disseminate research findings for use by the international community, including the numerous bodies that establish international radiation protection stan-

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**放影研
RERF update**

Volume 11, Issue 1, Spring 2000

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**放影研
RERF update**

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

**Peer Review Generates 13 Recommendations
Autumn Genetics Review Third in Cycle**

In accordance with the 1996 recommendations of the Blue Ribbon Panel for the external evaluation of RERF's research departments, from November 1 to 3, 1999, the Department of Genetics was reviewed by an international panel of genetics experts. Dr. John Evans, professor in the MRC Human Genetics Unit of Western General Hospital at Edinburgh University in Scotland, chaired the panel. This third peer review followed reviews of the Departments of Radiobiology and Epidemiology in 1998 and took place in the auditorium of RERF's Hiroshima laboratory. The review resulted in 13 recommendations that will be addressed at the April 2000 Scientific Council meeting, when the recommendations and RERF's responses are presented for consideration.

After greetings by RERF Chairman Shigenobu Nagataki, an overview of RERF by Vice Chairman and Chief of Research Sheldon Wolff, and an overview of the department by Genetics Chief Nori Nakamura, the review proceeded with the following presentations: Norio Takahashi, *Cell lines, DGGE, Southern blot, and DNA chips*; Jun-ichi Asakawa and Mieko Kodaira, *Two-dimensional DNA electrophoresis in mice and in offspring of the survivors*; Mieko Kodaira, *Minisatellite mutations*; Norio Takahashi, *Future plans in molecular genetics*; Yoshiaki Kodama, *Overview of cytogenetics studies*; Nori Nakamura, *See Peer Review, page 5*



U.S. Ambassador and Osaka Consul General Visit RERF

U.S. Ambassador to Japan Thomas S. Foley (center) and Osaka Consul General Robert Ludan (right) visited RERF the morning of 23 February 2000. Ambassador Foley spoke to RERF staff upon his arrival, toured some of the facilities guided by Chairman Shigenobu Nagataki, and met with directors and researchers to ask questions about research activities. Ambassador Foley was in Hiroshima 21-23 February to speak at an economic seminar sponsored by the Hiroshima Chamber of Commerce. Consul General Ludan and his wife, who is also a foreign service officer, had also visited RERF 1 December 1999. Pictured at left is Ms. Jane Heller, ambassadorial aide.

ABCC Geneticist James Neel Succumbs to Cancer at 84 in Ann Arbor

by Jun-ichi Asakawa,
Senior Research Scientist,
Department of Genetics

Dr. James Van Gundia Neel, RERF consultant emeritus and professor emeritus of human genetics at the University of Michigan Medical School, died of cancer February 1 at his home in Ann Arbor, Michigan. He was 84 years old.

In 1947 and 1948, Dr. Neel came to Japan as chief of the first field survey team the U.S. National Academy of Sciences' National Research Council organized for the Atomic Bomb Casualty Commission (ABCC). Until his death, he continued to be deeply involved in the ABCC-RERF program. He played a key role in the establishment of the Biochemical Genetics Laboratory, which was inaugurated in 1976. Once a year until 1991, he visited Hiroshima with his wife, stayed at Hijiya Hall for one to two months, and provided us with scientific guidance.

Dr. Neel was born in Hamilton, Ohio and received his bachelor's degree from the College of Wooster (Ohio). After becoming the first doctor of science (Ph.D.) in Dr. Curt Stern's human genetics department at the University of Rochester (New York), in 1944, he acquired his M.D. from Rochester. While serving as an instructor of vertebrate anatomy there, Dr. Neel counted as one of his students Howard B. Hamilton, who later served as ABCC's chief of the Department of Clinical Laboratories. For two years from 1946, Dr. Neel served in the U.S. Air Force, during which time he became involved in the ABCC program. After retiring from the service, he joined the University of Michigan, where he inaugurated the Department of Human Genetics in the university's medical school and served on staff for 39 years.

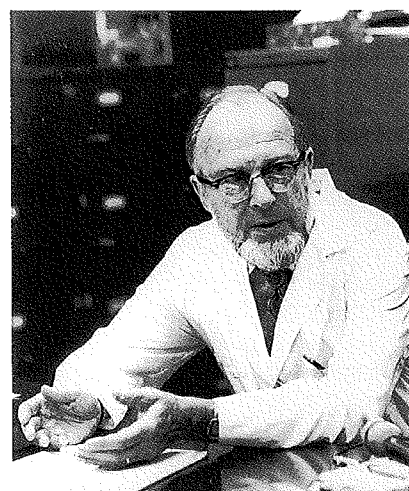
For 25 years, Dr. Neel chaired that department, and from 1966 until his retirement in 1985, Dr. Neel served as UM's Lee R. Dice university professor of human genetics. During those years, he pioneered studies concerning the relationship between diseases and heredity and accomplished not a few outstanding achievements. From late 1940 through early 1950, Dr. Neel studied thalassemia, and he gained worldwide

attention when he provided genetic evidence that the sickle cell disease was inherited as a simple Mendelian autosomal recessive trait. As a result, despite his young age, he was elected a member of the U.S. National Academy of Sciences (NAS), and a portrait of the young Neel is permanently displayed at the Academy in Washington.

In his more than 60-year scientific career, Dr. Neel studied the genetic effects of the atomic bomb on the children of A-bomb survivors and engaged in a wide variety of other research activities. Among them, he studied genetic polymorphism in the Yanomama tribe, natives living in the upper reaches of the Amazon. Dr. Neel also discovered rogue cells, which he related to JC polyoma virus infection, recently establishing a causal relationship between the virus and the development of cancer. In recognition of these achievements, Dr. Neel received various honors, including the William Allen Human Genetics Society Award, the Albert Lasker Award for Medical Research, and the Smithsonian Medal. He was one of the founders of the U.S. Human Genetics Society, and together with Dr. William J. Schull (RERF director), Dr. Neel contributed to the progress of human genetics in Japan and trained many Japanese geneticists.

To me, Dr. Neel has been not only a teacher, but a father figure. Last May 27, I received a sad personal letter from him, in which he said, "Regrettably, the prostate cancer I have been affected with for several years has worsened, and I may not be able to live long." Although I was prepared, I did not expect the day to come so early. While waging battle with his disease, Dr. Neel never once forgot his research or his commitment to our Laboratory, continuing to offer advice. December 15, Dr. Rork Kuick, Department of Genetics expert advisor, and I called on Dr. Neel at his home in Michigan, where he was receiving medical care. We were seeking his continued scientific advice and wishing him well. Even at that time, he brought up a number of points for finishing up our joint study and encouraged us to follow through. We understood that this would be our last meeting.

Dr. Neel will remain in my



Dr. Neel described his experiences in two early articles for RERF Update, which feature ABCC historical photos. The first (1[4; Winter 1989-90]: 7-8) is entitled "Unprecedented Challenges Faced in Early Days," and the second (2[3; Autumn 1990]: 6-9) is a "Looking Back" piece by Drs. Neel and Schull that describes the early genetics program. In two later issues, Drs. Neel and Schull were highlighted on the Update cover (3[4; Winter 1991-2]: 1) after receiving the 1991 Conte Award and Dr. Neel joined the many celebrants of ABCC/RERF's Golden Commemoration (9[1; Spring 1998]: 1, 6-7). Other historical information may be found on RERF's web site: www.rerf.or.jp. (Photo courtesy of University of Michigan)

memory as a scientist dedicated to the pursuit of truth until the end of his life. I would like to express my genuine appreciation to Dr. Neel for his various great achievements and pray that his soul rest in peace. I would also like to offer my heartfelt condolences to Mrs. Priscilla Neel and her family, who devotedly cared for Dr. Neel until the end. Dr. Neel is survived by his wife, three children, three grandchildren, and a sister. Lastly, I would like to extend my sincere appreciation to the large number of present and former employees of ABCC-RERF who have kindly contributed to the James V. Neel Fund at the University of Michigan, which was established out of respect for the wishes of Dr. Neel.

Publications, continued from p. 21
Journal of Radiation Biology 1999 (November); 75(11): 1449-1458.

Little MP (National Radiological Protection Board [NRPB], UK), Muirhead CR (NRPB), Haylock RGE (NRPB), Thomas JM (NRPB). *Relative risks of radiation-associated cancer: comparison of second cancer in therapeutically irradiated populations with the Japanese atomic bomb survivors*. Radiation and Environmental Biophysics 1999(December);38(4): 267-283.

Dosimetry Workshop, from page 1 dards. The atomic-bomb dosimetry system we currently employ for our studies was adopted in 1986 and is referred to as the DS86 system. It replaced an earlier system—established in 1965—as better methods of calculating radiation dose were developed. In the almost 14 years since the 1986 methods were introduced, new published observations and calculations have led to a questioning of the usefulness of the DS86 system, but no consensus has been reached as to how to interpret the new information.

The National Academy of Sciences (NAS) Dosimetry Committee has been deliberating the issues surrounding DS86, and they are scheduled to make a final report in September 2000. This U.S.-Japan Dosimetry Workshop was convened to solicit the input of an international spectrum of scientists before the NAS report is finalized. The specific goals of the workshop were to provide a forum for Japanese, American, and European investigators to discuss openly the latest research results, any unresolved issues, and methods to solve any problems, to help decide the need for a revised dosimetry system and reach agreement between Japan and the U.S., to establish where future Japanese- and U.S.-funded work is going based on the observations of the Japanese and U.S. working groups and the NAS committee, and to provide a summary report of the conclusions and recommendations emanating from the two-day workshop.

For the greater part of the first day, the workshop participants reviewed the measurements of fast and thermal neutrons and of gamma rays, which had been obtained in Japan, the U.S., and Germany. In Hiroshima, there has been a discrepancy between DS86 calculations and actual measurements of the radioactivity induced by thermal neutrons in exposed rock, iron, and concrete (Eu-152, Co-60, and Cl-36). The measurements become greater than the DS86 calculations as the distance from the hypocenter increased. This issue of neutron discrepancy has been examined in the U.S. and Japan for about ten years. The tendency is clear, and it is considered that we already have enough measurement data. With regard to the neutron activation measurements, some presentations and considerable discussion addressed the issue of background levels that might be produced by cosmic rays or other unidentified

sources and the related issue of the depth profiles of measured values in core samples from massive bodies of material. Although it is generally thought that there is no such systematic discrepancy in Nagasaki, data suggest its presence. Therefore, measurements are still underway in Nagasaki.

Recently, it has become possible to measure very low radioactivity induced by fast neutrons in exposed copper samples (Ni-63), and several copper samples are being measured now. Since fast neutrons constitute a large portion of the neutron dose, it is expected that these measurements will be a key to solving the neutron problem. The number of available well-documented copper samples is quite small, and collection of more samples is urgent.

Gamma doses are measured by a method called thermoluminescence dosimetry (TLD). Measurements are slightly higher than DS86 calculations (by about 10%), but their correspondence is quite good. For the assessment of total radiation dose, the contribution of gamma dose is considered to be larger than that of neutrons. Thus, gamma doses are important. It is considered that we already have enough measurement data.

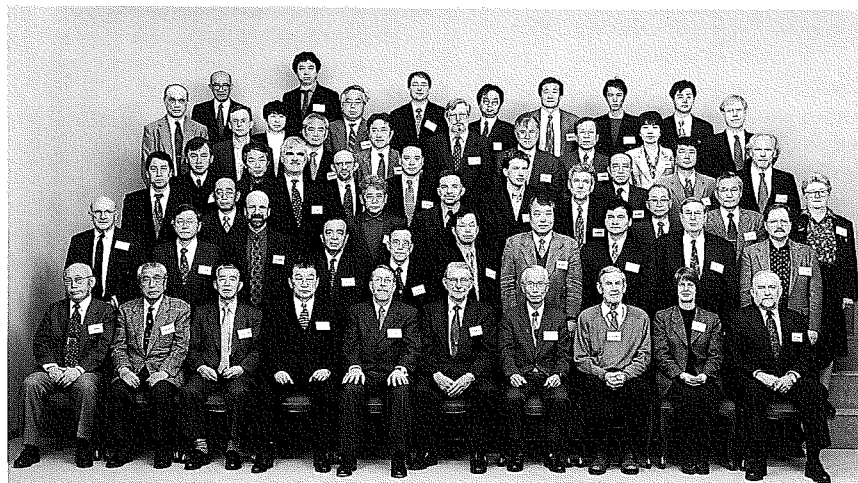
An RERF data base containing about 600 measurements of exposed materials was explained in outline form. The data base is elaborate and includes detailed information on the

characteristics of each data set, and it is expected to be useful in a comprehensive assessment of measurement information and dose uncertainty.

Theoretical dose calculations were discussed towards the end of the first day, and examples of calculation aimed at achieving consistency with the existing measurements were presented. At this stage, it is extremely difficult to match calculations with measurements perfectly. Valuable data from the Tokaimura accident, which showed the credibility of the theoretical calculations of neutron dose, were also presented.

Workshop participants also considered how to achieve a more active exchange of information on survivor location and shielding as well as the role biological dosimetry should play in dose assessment.

Most of the second day was spent discussing current problems and their solutions, which were the key workshop issues. At the end of the workshop, the co-chairmen read a statement that not only emphasized the importance of the collection and measurement of exposed copper samples but also described the need to complete comprehensive assessment of radiation dose, including neutrons, within the next year. It was confirmed that DS86 would continue to be used until a new system was completed and approved jointly by senior dosimetry groups in the U.S. and Japan.



U.S.-Japan Joint Dosimetry Workshop

From left to right, front to back: Row one: Dr. Shozo Sawada, Dr. Itsuzo Shigematsu, Dr. Hiromichi Matsudaira, Dr. Shigenobu Nagataki, Dr. Evan Douple, Dr. Warren K. Sinclair (U.S. chair), Dr. Tatsuji Hamada (Japanese chair), Dr. Robert F. Christy, Dr. Sue B. Clark, Dr. Robert W. Young; *Row two:* Dr. Sheldon Wolff, Dr. Toshisou Kosako, Dr. David Thomassen, Dr. Senjun Taira, Dr. Tokushi Shibata, Dr. Kiyoshi Shizuma, Dr. Masaharu Hoshi, Dr. Zhaksibay S. Zhumadilov, Dr. Donald MacPhee, Dr. Tore Straume; *Row three:* Dr. Gen Suzuki, Dr. Kazuo Iwatani, Dr. Kazuhisa Komura, Dr. Alfredo Marchetti, Dr. Albrecht M. Kellerer, Dr. Takashi Maruyama, Dr. Shoichiro Fujita, Dr. Naomi H. Harley; *Row four:* Dr. Kazuo Kato, Dr. Seishi Kyoizumi, Dr. Dean C. Kaul, Dr. Joseph F. Weiss, Dr. Yasumasa Fukushima, Dr. Georg Rugel, Dr. Masao Sasaki, Dr. Tetsuji Imanaka, Dr. Harry Cullings; *Row five:* Dr. Harold L. Beck, Dr. Werner Ruehm, Dr. Yukiko Shimizu, Dr. Norihiko Hayakawa, Dr. Nori Nakamura, Dr. Kenneth J. Kopecky, Dr. Takamitsu Oka, Dr. Seiichi Shibata, Dr. Saeko Fujiwara, Dr. Stephen D. Egbert; *Row six:* Dr. Yutaka Okumura, Dr. Jun Takada, Dr. Masazumi Akahoshi, Dr. Jeffrey McAninch, Dr. Kouichi Takamiya, Dr. Tatsuya Shimasaki, Dr. Satoru Endo, Dr. Masayori Ishikawa (photo by Ikonaga Photo Studio, Hiroshima).

About the author

Dr. Gen Suzuki became RERF's new chief of Clinical Studies effective January 1. Dr. Suzuki came to RERF from his position as chief of the Second Laboratory of Radiation Health of the National Institute of Radiological Sciences (NIRS), in Chiba, a role he had played for almost four years. Prior to joining NIRS in 1985, Dr. Suzuki was affiliated with the Third Department of Internal Medicine of the University of Tokyo, was a visiting fellow at the U.S. National Institutes of Health, and served as a hematologist at the (Japanese) National Hospital Medical Center. Dr. Suzuki earned a D.M.Sc. from the University of Tokyo, where he completed a postdoctoral fellowship in immunology.

Dr. Suzuki is a member of the Japanese Society for Immunology, Japanese Cancer Association, Japanese Society for Internal Medicine, Japan Hematological Society, Japanese Society for Clinical Immunology, Japanese Society for Radiation Effects, Japanese Association of Medical Management of Radiation Accidents, and Japan Society of Blood Transfusion. He also leads a subcommittee of the Radiation Emergency Exposure Medical Committee of the Nuclear Safety Research Association, is a consultant in nuclear safety tactics for the Nuclear Safety Bureau of the (Japanese) Science and Technology Agency, and served as nuclear power advisor for Shizuoka Prefecture during 1999.

Dr. Suzuki is interested in physiological, including immune and inflammatory, responses to radiation and the long-term impact of acute radiation on innate as well as acquired immunity, immunities that may relate to nonmalignant disorders in A-bomb survivors. In addition, he is interested in the establishment of a radiation emergency network in the Chugoku area, an area comprising Hiroshima, Okayama, Yamaguchi, Shimane, and Tottori Prefectures in western Honshu, Japan's main island.

RERF Dispatches Radiation Emergency Specialists to Thailand at Request of IAEA

by Gen Suzuki, Chief, Department of Clinical Studies, Hiroshima

On the morning of February 24, the International Atomic Energy Agency (IAEA) in Vienna contacted RERF Chairman Shigenobu Nagataki requesting that he dispatch a team of medical experts in emergency radiation exposure to Samat Prakan, Thailand following an accident involving exposure to ^{60}Co due to improper disposition of telecobalt treatment equipment. RERF serves as a collaborating center for the Radiation Emergency Medical Preparedness and Assistance Network (REMPAN) of the World Health Organization (WHO). In response, Dr. Minako Otani, professor of emergency medicine at the Hiroshima University School of Medicine, Dr. Sakae Tanozaki, chief researcher at the Department of Radiation Health of the National Institute of Radiological Sciences in Chiba, and Dr. Gen Suzuki, chief of RERF Hiroshima's Department of Clinical Studies, left for Thailand on the morning of February 26.

On January 24 and 25, four junk dealers sneaked into a parking space where three units of the telecobalt treatment equipment had been left for "storage" by an import agency, and they proceeded to disassemble and steal two of the units. They removed a radiation source and its stainless steel and lead shield from one of the units and dismantled it. When they could take it apart no further, they took it to a junk shop on February 1, where they resumed their efforts, cutting the stainless steel with a gas torch and allowing the cobalt radiation source to drop from the shielding vessel to the ground, where it remained exposed until February 19. In the course of these events, the four people who stole the cobalt, two junk shop workers, a housekeeper, and six family members of the junk shop owner were heavily exposed. While stealing and carrying the equipment, the four thieves suffered whole-body exposure as well as partial exposure at the hands, buttocks, and knees. Those at the junk shop were exposed repeatedly to the uncovered cobalt. Admitted to hospitals one after another from February 16 through 21, the ten individuals complained either of vomiting, diarrhea, fatigue, bleeding, or burns. According to newspapers in Thailand, three victims died on March 9, 14, and 25, respectively, because of radiation syndrome.

Four or five accidents like this one, involving the theft of poorly protected radiation sources, occur each year throughout the world. Equipment with large radiation sources is commonly transported internationally by import agents, and control of that equipment is sometimes unregulated. To treat radiation victims properly, individual countries must develop systems whereby radiation dose is promptly and accurately estimated, appropriate treatment including transplantation of hematopoietic stem cells must be available, and an international cooperation system must be in place to respond. This was the first such accident in Thailand, so the country was little prepared to deal with the situation.

Under the guidance of the WHO, a framework for international cooperation is being established to provide advice and medical assistance in case of a radiation accident. The REMPAN network, which first included only France, Russia, and the United States, has expanded to include additional collaborating centers in Argentina, Australia, Brazil, China, Germany, India, Japan, and the United Kingdom. When an accident occurs, the IAEA organizes an *ad hoc* mission that provides advice and medical assistance. Regular interaction among researchers is essential to make international cooperation in Asian countries effective.

A Brief Note of Farewell

by Rosalyn Vu, Chief Editor, Publication and Documentation Center, and Managing Editor, Update

As I prepare in less than 24 hours to catch a train to Osaka and a plane back to Columbus, Ohio, I wanted to take the opportunity of a little free space in this last issue I will be preparing of *RERF Update* to express my sincere gratitude to all those who have helped me over the last three years to produce five issues of this newsletter and to complete all of my other duties as the only English editor here at RERF. Communicating the research carried out on the health effects of radiation exposure from the atomic bombings is an awesome responsibility. I am grateful for the opportunity I have had to help the Foundation to fulfill its mission to serve mankind. I will carry home with me many wonderful memories of dedicated people, past and present ABCC and RERF employees, who have given the better part of their lives to this work.

Peer Review, continued from page 1

ESR as a validating tool of cytogenetic data, implications for DS86; Kazuo Ohtaki, G-banding analysis of clonal aberrations related to leukemia; Mimako Nakano, Clonal aberrations-Observations; Yoshiaki Kodama, Clonal aberrations-Mechanisms; Masahiro Itoh, Neutron fingerprint (F- and S- value issues); and Yoshiaki Kodama, Future plans in cytogenetics.

On November 3, the last day of the meeting, Dr. Evans related the panel's preliminary findings based on the above presentations. The final report included the following 13 recommendations:

- that the number of blood cells and cell lines derived from F₁ children and their parents be expanded, particularly from those parents exposed at high dose levels;
- that work be discontinued on mutations at micro- and minisatellite loci in radiation-exposed individuals because it is essentially complete;
- that work be discontinued on establishing S and F ratios to define and distinguish between chromosome damage induced by radiations of different LET because of sufficient negative findings;
- that microassay analysis be established for examining submicroscopic chromosomal deletions, which will require interaction with laboratories conducting genome research;
- that "stop work" criteria be established when preliminary study results are negative;
- that more basic studies be pursued related to the origin of clonal chromosomal aberrations;
- that the cytogenetics group not expend its resources in pursuing genetic instability;
- that basic research and collaborative efforts be pursued related to identifying subpopulations of F₁ individuals that will be more likely to harbor radiation-induced changes, such as children of exposed individuals who are susceptible to transmission of germline defects;
- that gene analysis technologies, including denaturing gradient gel electrophoresis (DGGE), minisatellite analysis, two-dimensional gel DNA electrophoresis, and DNA microassay analysis techniques, be reviewed to find the most suitable technique for future large-scale studies;
- that cytogenetic and electron spin resonance (ESR) analyses be continued as needed to support DS86 modification efforts and that the proposed multicolor fluorescence *in situ* hybridization (FISH) analysis of lymphocytes of children born to parents with high doses be supported;
- that breakpoints for some clonal chromosomal aberrations in atomic-bomb survivors be characterized at the molecular level;
- that an advisory committee with expertise in genetics, genomics, and he-

matopoiesis be convened annually to review and discuss RERF's research plans; and

- that research priorities be established and resources redistributed according to the above recommendations.

Chairman Evans was joined on the review panel by: science councilors, Joe W. Gray, professor, Laboratory of Medicine, University of California, San Francisco, USA, and Yusuke Nakamura, director, Human Genome Center, Laboratory of Molecular Medicine, Institute of Medical Science, University of Tokyo, Japan; and A. T. Natarajan, professor, Department of Genetics, Radiation Genetics and Chemical Mutagenesis, Medical Genetics Centre South-West Netherlands, MGC, Leiden University, the Netherlands; Norio Niikawa, professor and chairman, Department of Human Genetics, Graduate School of Medicine, Osaka University, Atomic Disease Institute, Nagasaki University School of Medicine, Japan; Taisei Nomura, professor and chairman, Department of Radiation Biology and Medical Genetics, Graduate School of Medicine, Osaka University, Japan; and Akihiro Shima, Department of Integrated Biosciences, Graduate School of Frontier Sciences and Biological Sciences, School of Sciences, University of Tokyo, Japan. Observers were Dr. Evan Douple, director, Board on Radiation Effects Research, Commission on Life Sciences (CLS), National Research Council (NRC), National Academy of Sciences (NAS), Washington, D.C., USA, and Dr. Michael Clegg, professor and dean, College of Natural and Agricultural Sciences, University of California, Riverside, USA, and chair, CLS, NRC, NAS.



Department of Genetics Peer Review, November 1 to 3, 1999

Pictured from left to right, front to back: Row one: Dr. Shigenobu Nagataki, Dr. Norio Niikawa, Dr. Akihiro Shima, Dr. Taisei Nomura, Dr. John Evans, Dr. Joe W. Gray, Dr. A. T. Natarajan, Dr. Yusuke Nakamura, Dr. Sheldon Wolff; Row Two: Mr. Kazumasa Kunitoshi, Dr. Michael Clegg, Dr. Evan Douple, Dr. Kiyohiko Mabuchi, Dr. Norio Takahashi, Dr. Donald MacPhee, Dr. Clark W. Heath, Jr., Dr. Senjun Taira, Dr. Masahiro Itoh, Dr. Saeko Fujiwara, Dr. Akihiko Suyama; Row Three: Dr. Akio Awa, Dr. Dale Preston, Dr. Jun-ichi Asakawa, Dr. Nori Nakamura, Dr. Yoshiaki Kodama, Dr. Mieko Kodaira, Dr. Kazuo Ohtaki, Dr. Mimako Nakano, Dr. Inaho Danjo.

25-Year Publications, from p. 24

The number of research protocols sometimes reflects multiple entries under the same number. In 1993, *RERF Reports* replaced the in-house Technical Report series that had been used to date. Reprints of journal articles are purchased from publishers and bound in *RERF Report* covers with Japanese summaries. Reports in the *Commentary and Review Series* are published to rapidly disseminate ideas, discussions, comments, and recommendations on research carried out by RERF scientists.

The Origin of Clonal Chromosome Aberrations

Bone marrow stem cells and mature T cells

by Yoshiaki Kodama, Chief, Cytogenetics Laboratory; Mimako Nakano, Assistant Senior Scientist; Masahiro Itoh, Research Scientist; Kazuo Ohtaki, Research Scientist; and Nori Nakamura, Chief, Department of Genetics, and Yoichiro Kusunoki, Assistant Senior Scientist; Yuko Hirai, Senior Scientist; and Seishi Kyoizumi, Chief, Immunology Laboratory, Department of Radiobiology

Cytogenetic testing using blood lymphocytes is well established for biological dosimetry in humans. During past cytogenetic studies in atomic-bomb (A-bomb) survivors, we found substantial numbers of people with identical chromosome aberrations in three or more cells in the same blood samples. These irregularities are termed clonal aberrations. They are exclusively stable-type aberrations, mainly translocations and inversions, and are repeatedly observed in the same survivors from several to more than ten years. More than 20 survivors are now recognized to carry clonal aberrations, and most of these individuals were exposed to doses greater than one gray.

In one survivor, we identified the bone marrow stem cells as the source of clonal chromosome aberrations.^{1,2} In this survivor, the same double translocations were observed in colonies derived from normal T cells, Epstein-Barr-virus-transformed B-cells, and CD34⁺ cells (characteristics of multipotent stem cells). Further, the T cell receptor genes had undergone different rearrangements from each other among the T cells carrying the clonal aberrations. All findings are consistent with the hypothesis that the clonal aberrations are derived from single bone marrow stem cells.

Blood T lymphocytes can be classified into two major subtypes. One subtype is the naïve T cells that have directly descended from the thymus after maturation and have not yet undergone antigen stimulation. The other subtype is the memory T cells that have undergone cell proliferation following antigen stimulation. These two types of cells can be distinguished by specific surface antigens. The memory T cells remain in our bodies for many years, whereas naïve T cells are considered to be continuously replenished.

Recently, it became possible to isolate specific types of cells using magnetic-beads-conjugated monoclonal antibodies that recognize surface antigens, a technique called "magnetic cell separation." In the present report, we used this new method to isolate naïve and memory T cells to examine the origins of clonal aberrations using fluorescence *in situ* hybridization (FISH).

Materials and methods

Twelve survivors were selected for the study who were previously identified by conventional (nonbanding) staining to carry clonal aberrations with frequencies of three to 12% in blood lymphocytes. Employing G-banding, we identified chromosomes involved in the clonal aberrations using whole blood cultures and found 13 clonal aberrations. Using magnetic cell separation, we separated lymphocytes from these survivors by their surface markers into CD45RA⁺ (naïve T cells) or CD45RO⁺ (memory T cells). Subsequently, we cultured each of the cell fractions for chromosome study. Clonal aberrations were detected by the multi-color FISH technique, in which each of the two chromosomes involved in the clonal aberrations was painted a different color. If the clone was derived from

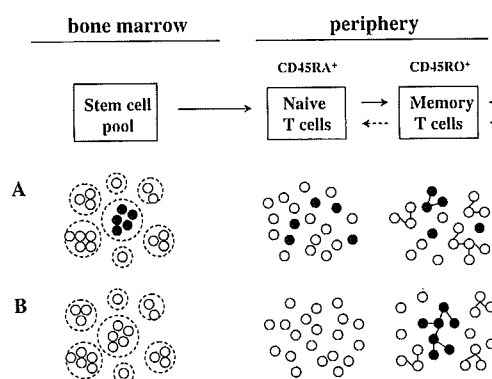
bone marrow stem cells, the clonal aberrations were expected to be found in naïve T cells (and possibly in some memory T cells as well). If the clone was derived from mature lymphocytes in blood, the clonal aberrations would be found mostly in memory T cells (figure).

Results and discussion

Clonal aberrations in naïve and memory T cell fractions showed that the eight clones were most likely derived from bone marrow stem cells in that they were observed in both naïve and memory fractions with essentially the same frequencies. In contrast, the remaining five cases showed clonal aberrations predominantly in memory fractions, suggesting their origin as mature lymphocytes in the blood. Although a few clonal aberrations were observed in the naïve cell fractions of these five cases, these were best explained as derived from contaminating memory T cells in the naïve fraction, which varied from 1.6% to 9.9%.

The results indicate that radiation exposure killed a large fraction of bone marrow stem cells and surviving stem cells rapidly proliferated to overcome the deficiency in the stem cell pool. In the present study, those surviving stem cells that had proliferated but were bearing chromosome aberrations were detected as identical aberrations in both naïve and memory T cell fractions. This is not the whole story, however. Radiation exposure also killed mature lymphocytes through apoptotic death, and surviving lymphocytes should have proliferated somehow to overcome the deficiency. Present results indicate that a single mature T cell has a tremendous capability to proliferate and attain to as much as a few percent of total lymphocytes in

See **Aberrations**, top of next page



Two alternative mechanisms for the clonal expansion of chromosome aberrations observed in peripheral lymphocytes. A. If the clone was derived from bone marrow stem cells, the clonal cells would be observed in both naïve and memory T cell fractions. B. If the clone was derived from peripheral blood cells, clonal cells were expected to be found in only the memory T cell fraction. Open circle: cells without clonal aberrations; closed circle: cells with clonal aberrations. The large circles with dotted lines in the stem cell pool represent the progeny of each stem cell. Only a small fraction of naïve T cells become memory T cells after antigen stimulation. A fraction of memory T cells respond to antigen stimulation and increase in number, but most of these stimulated cells die off at the end of the immunological response to foreign antigens so that a constant memory T cell pool may be maintained.

Aberrations, continued from previous page
the body (estimated to be 10^{11} to 10^{12} in number). This may not be surprising since memory T cells are involved in immunological memory and should effectively increase in number to work against invading foreign antigens.

It is interesting to mention that the clonal aberrations from single mature T cells were not always detectable in past studies using the conventional staining method, which mainly scored 100 cells for each blood sample. This may be partly due to the small number of cells examined and the relatively low frequency of the clone-bearing cells, but it may also be due to the fluctuating nature of the clonal cells in the blood. For example, one donor showed t(2;11) with a frequency of 4.2% in whole blood culture, but the frequency decreased to 0.2% (2/1000) in a test two years later. Therefore, it seems likely that the memory T cell pool undergoes continuous expansion and contraction following stimulation with different antigens, which may be the general feature of clonal aberrations derived from memory T cells.

In this context, Michie *et al.*³ also reported evidence for the rapid turnover of memory T cells *in vivo*. They examined the kinetics of loss of dicentric chromosomes in blood lymphocytes from radiotherapy patients. (In contrast to stable-type aberrations that we examined in this report, the dicentric chromosomes are structurally unstable and are lost once cells divide.) They found that dicentric frequency in memory T cells decreased faster, with a half-life of about one year, whereas the frequency decreased much more slowly in naïve T cells—in fact, the dicentrics persisted even ten years after the radiation exposures—which is consistent with our notion that memory T cells continue expansion and contraction with time. Whether clone size of stem-cell-derived aberrations also fluctuates with time needs further investigation. Additional future examinations of the clonal aberrations in the present

twelve survivors will provide key information on the fate of these clonal aberrations of different origins.

It is important to identify and quantify clonal aberrations so that they may be used in biological dose estimation. Currently, for biodosimetry in A-bomb survivors, we use FISH to score 500 cells as opposed to the past conventional staining method, which scored only 100 cells, and numerous small-sized clones have been detected. Clonal aberrations were reported in soldiers and cleanup workers at the nuclear power plant accident in Chernobyl and ¹³⁷Cs gamma-ray-exposed victims from the Goiania accident, strongly suggesting that clonal aberrations are related to radiation exposures. It is not known, however, if the cells bearing clonal aberrations had acquired growth advantage due to specific genomic rearrangements. Existence of common clonal chromosome aberrations across different individuals (e.g., deletion of 5q and inversion of chromosome 14 in A-bomb survivors; Ohtaki, unpublished observation) indicate that at least some of the clonal aberrations did acquire such an advantage. Thus, molecular characterization of the translocation breakpoints of the clonal aberrations would be important in understanding their biological consequences.

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RERF Lecture Series, 1 October 1999 through 31 March 2000

Editor's Note: The following presentations were given in the RERF Hiroshima auditorium unless otherwise noted.

18 October 1999 **Dr. Kiyoshi Miyagawa**, professor, Department of Molecular Pathology, Research Institute for Radiation Biology and Medicine, Hiroshima University, Hiroshima, Japan: *The BRCA/RAD protein complex: Linkage of double-strand break repair to tumor formation*

18 October 1999 **Robert Ullrich, Ph.D.**, Vincent P. Collins distinguished professor, radiation oncology research director, Biology Division, Department of Radiation Oncology, University of Texas Medical Branch, Galveston, Texas, USA: *Radiation-induced genomic instability and radiation carcinogenesis*

10 November 1999 **Dr. Andrew J. Grososky**, Environmental Toxicology Program, University of California, Riverside, California, USA: *Radiation-induced genomic instability*

15 November 1999 **Masahiro Sugawara, M.D.**, professor, Department of Medicine, University of California, Los Angeles School of Medicine, Center for the Health Sciences, Los Angeles, California, USA: *Future aspect of telomerase*

24 November 1999 **Shoichiro Tsugane, M.D.**, chief, Epidemiology and Biostatistics Division, National Cancer Research Institute, East, Chiba, Japan: *A population-based cohort study on diet and chronic diseases: JTHC (a Japanese Ministry of Health and Welfare) Study*

8 December 1999 **Samir M. Hanash, M.D., Ph.D.**, professor, Department of Pediatrics, University of Michigan Medical School, Ann Arbor, Michigan, USA: *Integrating genomic and expression analysis in cancer investigation*

18 January 2000 **Kanehisa Morimoto, Ph.D.**, professor, Department of Social and Environmental Medicine, Course of Social Medicine, Osaka University Graduate School of Medicine, Osaka, Japan: *Lifestyle, chromosome alterations, and immunological potentials*

31 January 2000 **Lee Frank, M.D.**, professor of medicine and pediatrics, University of Miami School of Medicine, Miami, Florida USA: *Development of the antioxidant defense systems of the lung*

10 February 2000 **Catherine Sauvaget, M.D., Ph.D.**, research scientist, RERF Department of Epidemiology, Hiroshima: *Health expectancies in the elderly*

See *Lecture Series*, page 9

Psychological Sequelae in Atomic-bomb Survivors in Hiroshima and Nagasaki 17 to 20 Years after the Bombings

Michiko Yamada, Senior Scientist, Department of Clinical Studies, Hiroshima

Stress response syndromes result from exposure to war, sexual assault, natural disaster, and other types of trauma.^{1,2} Atomic-bomb exposure was an extraordinarily stressful event, and descriptions by physicians of the physical or mental conditions of the survivors often suggest that psychological effects resulted from atomic-bomb exposure. The immediate casualties in the atomic bombings of Hiroshima and Nagasaki were caused by the combined effects of thermal rays, blast waves, and radiation. Most people in Hiroshima and Nagasaki, in particular those within 2,000 meters of the hypocenter, sustained serious physical injuries. People heavily exposed to radiation suffered from acute radiation symptoms. Most buildings were destroyed, and city operations and socioeconomic conditions were greatly disrupted. Many survivors were injured themselves, lost family members, and suffered from the destruction of their way of life.

Little research has been performed on the psychiatric effects of the atomic bombings, and very few reports have covered the period from immediately after the atomic explosions to the present day. Tsuiki reported that psychoneurological symptoms, including weariness, lack of spirit, introversion, and poor memory, became more pronounced with increased severity of acute radiation symptoms.³ Nishikawa studied atomic-bomb survivors who exhibited neurosis-like symptoms during health

examinations at Nagasaki University in 1956 and confirmed that more neurosis-like symptoms were reported in persons who exhibited acute radiation symptoms than in those who did not.⁴ Konuma studied survivors exposed while working as volunteers in Hiroshima and reported that the complaints of those subjects implied autonomic ataxia.^{5,6}

In early 1960, atomic-bomb survivors in ABCC's Adult Health Study (AHS) were seen to manifest increased rates of leukemia, some types of cancer,⁷ cataracts, and thyroid diseases. However, no other diseases, including such psychosomatically related conditions as stomach ulcers, duodenal ulcers, and cardiovascular disease, displayed such increases.⁸ During the third- and fourth-cycle AHS examinations (between 1962 and 1965), 9,421 subjects who visited the clinic for their regular examinations completed a self-administered medical questionnaire patterned after the Cornell Medical Index Health Questionnaire. Most questions dealt with the physical condition of the participants. With the exception of three questions related to the urogenital system, the questionnaire included 118 questions administered equally to both men and women. The participants were asked to reply "yes" or "no" to questions about whether they had certain conditions. In 1990, after analyzing the frequency of physical symptoms re-

See *Psychological Sequelae*, top of next page

Facts and Figures

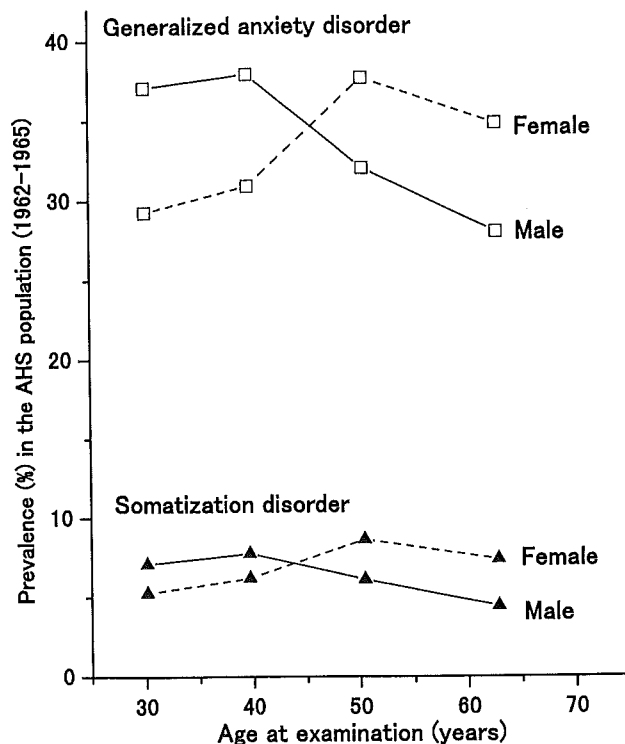
Information Related to Psychological Issues in the Adult Health Study

by Shizue Izumi, Chief, Statistical Analysis Laboratory, Department of Statistics

Two surveys including questions about psychological factors have been conducted in the AHS population. Dr. Michiko Yamada and I have used a self-administered medical questionnaire completed by 9,421 participants between 1962 and 1965 to examine the prevalence of generalized anxiety disorder (GAD) and somatization disorder. (See above article.) The figure plots the prevalence of GAD and somatization disorder by sex and age at examination. Overall prevalence is substantially higher for GAD than somatization disorder. For both disorders, prevalence increases with age for women but decreases for men.

The AHS master questionnaire administered between 1986 and 1993 includes six questions related to psychological factors, such as hours of daily sleep and frequency of use of medications such as tranquilizers. Currently, data on 4,305 participants in the Hiroshima Clinic are available for analysis. Information on Nagasaki participants has not yet been entered into the research data base.

A further AHS epidemiological survey was carried out between 1968 and 1970. Although it did not cover psychological factors directly, it did include information concerning family composition (father, mother, spouse, siblings, and children) and vital status of family members including family deaths resulting from the atomic bombings for 11,199 AHS participants (68% from Hiroshima). Other information on lifestyle and socioeconomic status was also obtained using this survey. These data will be used for future research regarding the psychological impact of the atomic bombs on survivors.



Psychological Sequelae, continued from previous page
ported in the questionnaire, Yamada *et al.* concluded that neuroticism was not necessarily related to physical disorders resulting from the bombings.⁹ They found that physical symptoms were greatest among those persons within 2,000 meters of the hypocenter, particularly among those with acute radiation symptoms.

Until now, no analysis has been conducted using a standardized method for establishing psychological diagnoses, such as the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV), which was published in 1994. Post-traumatic stress disorder (PTSD) is likely to have accompanied the aftermath of the bombings. Generalized anxiety disorder (GAD) and somatization disorder also must have increased among atomic-bomb survivors since these mental disorders are known to be comorbid among individuals with PTSD. The criteria to diagnose PTSD, GAD, and somatization disorder in DSM-IV are defined independently and include multiple different criteria (Criteria A-F for PTSD, A-F for GAD, and A-D for somatization disorder). Criteria C and D for PTSD, Criterion C for GAD, and Criterion B for somatization disorder are used for diagnosing symptoms of these mental disorders. The 1962-1965 self-administered questionnaire asked enough questions to determine Criterion C for GAD and Criterion B for somatization disorder, but no DSM-IV criteria for PTSD are addressed sufficiently in the questionnaire for diagnosis.

In a new research study, therefore, Ms. Shizue Izumi and I used Criterion C for GAD and Criterion B for somatization disorder as modified criteria to assess the psychological effects of exposure to the atomic bombings. The frequencies of GAD and somatization disorder were observed in 3,105 (33.0%) and 612 (6.5%), respectively, among the 9,421 AHS participants who completed the self-administered medical questionnaire. Izumi reports the prevalence of GAD and somatization disorder in the accompanying "Facts and Figures" feature (previous page). The relation of these disorders to GAD and somatization dis-

order with regard to age, sex, city, acute radiation symptoms, exposure status (in city or not in city), and ground distance will be the subject of future analysis.

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Lecture Series, continued from page 7

23 February 2000 **Margaret R. Karagas, Ph.D.**, associate professor, Department of Community and Family Medicine, Section of Biostatistics and Epidemiology, Dartmouth Medical School, Hanover, New Hampshire, USA: *A population-based study of nonmelanoma skin cancers in New Hampshire: Incidence trends, radiotherapy exposure, and genetic factors*

3 March 2000 **Masamoto Kanno, Ph.D.**, professor, Department of Immunology and Parasitology, Hiroshima University School of Medicine, Hiroshima, Japan: *Chromatin silencing and its function by polycomb group genes in the immune system and tumorigenesis (in Japanese)*

6 March 2000 **Kenji Wakai, M.D.**, lecturer, Department of Preventive Medicine, Nagoya University Graduate School of Medicine, Nagoya, Japan: *Seasonal allergic rhinoconjunctivitis and fatty acid intake*

10 March 2000, Hijiyama Hall **Nobuhiro Uchida, Ph.D.**, research scientist, Laboratory of Experimental Radiology, Aichi Cancer Center Radiation Institute, Nagoya, Japan: *Mismatch repair and microsatellite instability in esophageal cancer cell*

17 March 2000 **Duncan Thomas, Ph.D.**, professor, Department of Preventive Medicine, School of Medicine, University of Southern California, Los Angeles, California, USA: *Age at exposure and dose-rate effects for radiation-related cancer: Mechanistic models and measurement errors*

RERF Hiroshima Statistics Study Group Lecture Series, 1 October 1999 through 31 March 2000

1 October 1999, RERF Hiroshima auditorium **Kenichi Satoh, Ph.D.**, research associate at the Department of Environmetrics and Biometrics, Research Institute for Radiation Biology and Medicine, Hiroshima University, Hiroshima, Japan: *Modification of AIC-type criterion in multivariate linear regression with a future experiment*

29 October 1999, Hijiyama Hall **Masaaki Matsuura, Ph.D.**, associate professor, Department of Environmetrics and Biometrics, Research Institute for Radiation Biology and Medicine, Hiroshima University, Hiroshima, Japan: *Survival analysis for dynamic population and carcinogenesis modeling*

Basics of Radiation Explained to RERF Guests***Nearly 700 Visitors Attend Hiroshima and Nagasaki Open Houses******Nagasaki Open House***

On Japan's Labor Thanksgiving Day, Tuesday, November 23, 1999, RERF's Nagasaki laboratory opened its doors to the public for its third annual open house. Chairman Shigenobu Nagataki, Vice Chairman and Chief of Research Sheldon Wolff, Permanent Director Senjun Taira, and Secretariat Chief Kazumasa Kunitoshi attended from the Hiroshima laboratory. The product of the work of all staff members, the open house was coordinated by Dr. Masazumi Akahoshi, the chief of Clinical Studies in Nagasaki. Dr. Nagataki made opening remarks at 10:00 a.m., and the open house continued until 4:00 p.m.

Intended as an event to educate the public regarding the Foundation's work, the open house offered panels describing the direct damages from the atomic bombings of Hiroshima and Nagasaki and showing the history, study methods, and results of RERF's Life Span and Adult Health Studies. In response to the September nuclear accident in Tokaimura, a panel entitled "Basics of Radiation" explained the characteristics of alpha, beta, and gamma rays as well as neutrons. Additionally, guests were invited to prepare slides of their own cells, carrying out all the steps in staining and fixing the cells for examination under a microscope. They could also observe ultrasound images of their thyroid glands and have their blood pressure taken and body fat calculated. Computers were available to enable visitors to explore the Internet and sites concerned with the Tokaimura accident and other issues. RERF's new promotional video was shown to give an overview of the Foundation, and other videos on health issues, such as breast cancer and self examination, were shown throughout the day. A very basic demonstration using liquid nitrogen was given to familiarize visitors with the process involved in freezing and storing blood and tissue samples; balloons and flowers were fast-frozen in the liq-

uid. Throughout the facility, clinicians and researchers were on hand to answer questions and explain their daily activities.

Though the day was rainy, attendance still reached 233. Open house information was prepared to appeal to a wide audience, represented by the family groups in attendance, and hands-on activities enabled even the youngest attendees to comprehend some of the science that is basic to all research. At the same time, panels and diagrams of research findings provided objective reports on the health effects of radiation that could be analyzed in more detail with the assistance of staff members if necessary.

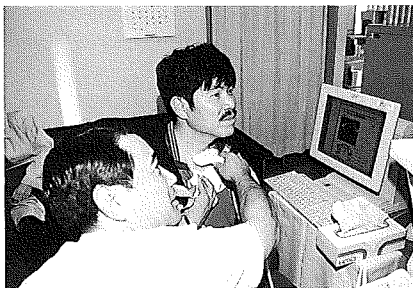
Hiroshima Open House

RERF's Hiroshima laboratory held its fifth annual open house on Saturday, November 27, from 10 a.m. until 4:30 p.m., welcoming some 466 visitors. In addition to the standard educational exhibits and demonstrations presented each year, including several new exhibits, Department of Genetics Chief Nori Nakamura spoke on "What is Radiation?" in a special afternoon lecture. RERF's new promotional video was also featured. As always, each of RERF's seven research and support departments, Clinical Studies, Epidemiology, Genetics, Radiobiology, Statistics, Information Technology, and Publications and Documentation displayed poster panels and offered demonstrations, and department members were available to explain their activities in detail.

The Department of Clinical Studies presented panels explaining the procedures for the Adult Health Study (AHS) examination; summarizing AHS findings on hyperparathyroidism, chronic liver disease, myoma uteri, cardiovascular disease, and thyroid diseases; illustrating radiation cataract; indicating mail survey and medication survey results; introducing bone mass measurements and



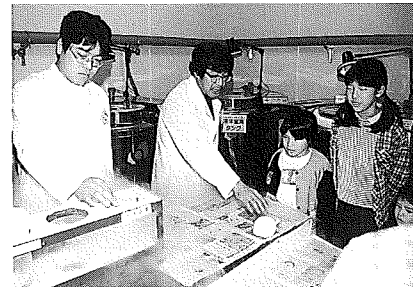
Welcome to RERF Above: Sayumi Yamakawa and Sayori Tomonaga, Nagasaki receptionists in Clinical Contacting, and Mamiko Araki, Tomoe Naito, and Ryoko Onitsuka, of the Registry Office, greet visitors with RERF brochures, questionnaires, and souvenirs. Below: Masumi Yamada, of General Affairs, explains to visitors the significance of photographs displayed in Hiroshima.



Departments of Clinical Studies Above: In Nagasaki, Isao Sakamoto, of the Division of Radiology in the Department of Clinical Studies, uses ultrasound equipment to examine the thyroid gland of a visitor. Below: Dr. Masayuki Hakoda, in Hiroshima's Department of Clinical Studies, explains display panels and answers questions for guests.



Epidemiology and Statistics Above: Hirotsuke Tasaki, of the Pathology Laboratory of Nagasaki's Department of Epidemiology, assists visitors in staining their own buccal mucosal cells for examination under the microscope. Below: Nobuaki Taira and Takahiro Suga, Division of Clinical Laboratories, put balloons and flowers in liquid nitrogen in the biological specimens storage room.



results; and describing the procedures for storing all X-ray films using optical disks. In addition to the panel presentations, the department offered demonstrations of a blood autoanalyzer with explanation of the biochemistry involved and invited visitors to examine blood and urine cells under the microscope and have their blood pressure, body fat, and bone mass measured.

A new computer demonstration in the epidemiology and statistics departments allowed visitors to click on any location on a map of Hiroshima to ascertain the rough estimate of radiation dose received by an individual at that geographical point. Three estimates were given: 1) for skin dose for a person in the open (unshielded) and 2) inside an average Japanese house and 3) for colon dose inside an average house. For comparison, an adjacent panel illustrated doses received by other means, such as x-rays in a doctor's office. Another panel explained the limitations of the demonstration, which included simplified calculations and general shielding parameters. Many visitors spent time clicking on different parts of the city map and asking questions.

The Department of Genetics offered panels explaining chromosomes and how they are affected by radiation as well as explanations of electron spin resonance, which is used to evaluate radiation exposure in the tooth enamel of survivors. Cytogenetics exhibits included computer and microscope displays of chromosomes after conventional, G-banding, 2-color FISH, and 24-color FISH staining.

The radiobiology department displayed posters describing the main features of their ongoing studies on the effects of radiation on the immune system and on the molecular basis of radiation-induced cancer. They also provided demonstrations of DNA analysis and lymphocyte flow cytometry and noted that visitors seemed to be particularly impressed when given the opportunity to observe cancer cells under the microscope. The liquid nitrogen tanks where lymphocytes are frozen for future studies were also on display, and researchers explained their use.

As in previous years, the Information Technology Department provided visitors with the opportunity to explore the Internet in a visit to the RERF computer classroom, and a map explained how RERF fits into the world-wide communication web.

In the Publication and Documentation Center, all past issues of *RERF Update* were on display as well as the most current issue of the *Japanese Newsletter*, and staff explained how research is published in various formats, including international journals and internal publications, such as the RERF Commentary and Review Series.

Each year since 1995, RERF's open houses have challenged staff to present their work to the public in new and different ways and according to the current situation and needs of the day. At the same time, RERF strives to adapt its presentations to the interests and concerns of the broad spectrum of individuals who attend by asking those who come to complete questionnaires evaluating their visits. This year, Dr. Nakamura developed the general lecture on radiation that was presented to some 80 people in response to the September nuclear plant accident in Tokaimura. Children attending the open house were encouraged to document their visits to each area for a pocket monster "passport stamp," their efforts rewarded with small prizes.

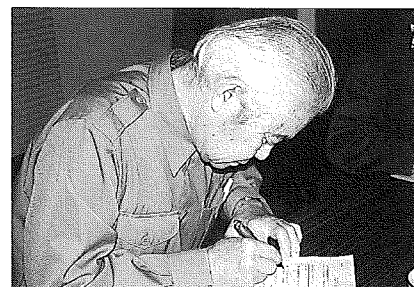
In addition to the benefits the open houses provide in educating the public, the open houses offer RERF staff members the opportunity to look at their work from the perspectives of those who will benefit from it and are curious about it and to assume the role of teacher in presenting their activities in a way comprehensible to a very broad audience. They also enable them to learn about the activities of their coworkers and to better understand for themselves all the jobs and research that make up the Foundation. The open houses are times of collegial activity that each year prove to be well worth the efforts involved to welcome the community and each other into our individual workaday worlds.



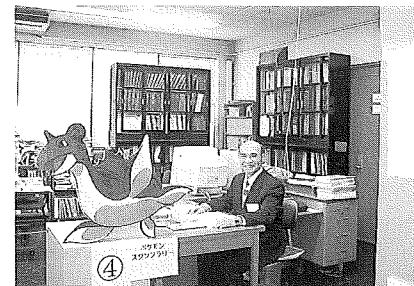
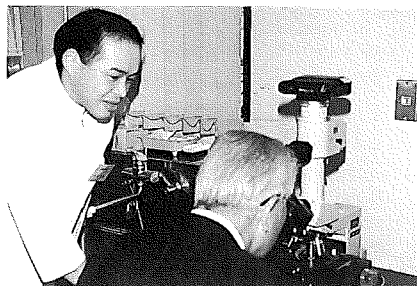
Radiobiology and Genetics Above: Hiroshima radiobiologists Tomonori Hayashi, Yoichiro Kusunoki, and Seishi Kyoizumi, and technicians, Mika Yamaoka and Yoshiko Kubo were available to explain their research. Below: A visitor makes a microscopic examination of cancer cells as Nagasaki staffer, Yoshiro Saito, offers assistance.



Information Technology Department and Publication and Documentation Center Above: Hiroko Shinohara, of the Clinical Contact Section, shows a Nagasaki visitor the web site explaining the new elderly care insurance system. Below: PDC staffers Fumie Maruyama and Naoko Ueda demonstrate the data management system for publications to guests at Hiroshima.



Before leaving, (above) RERF visitors to both labs were asked to fill out questionnaires describing their responses to their day's visit. Below: In Hiroshima, Megumi Mukai, of Property and Supply, manned the library checkpoint for young visitors collecting Pokemon stamps in their RERF passports. (Hiroshima photos by Margaret Irwin; Nagasaki photos, Hiroshi Fuchi and Masayoshi Yoshida)



A Visit to Nagasaki: Interviews with Drs. Akahoshi, Soda, Suyama, and Usa

Editor's Note: I went to Nagasaki to observe the November open house and took the opportunity to interview staff members there. What follows are my notes from those interviews as well as extra material provided by Dr. Akahoshi and a write-up of Dr. Soda adapted from an earlier Japanese Newsletter translation.—Rosie Vu, Managing Editor, RERF Update

**Dr. Masazumi Akahoshi**

A cardiologist by training, Nagasaki Clinical Studies Department Chief Masazumi Akahoshi joined RERF in April 1987. After graduating from the Nagasaki University School of Medicine, he joined their Third Department of Internal Medicine, which specialized in cardiovascular diseases.

He related that during his internship, his life-long career direction in research was initiated as he learned about congenital heart diseases, valvular diseases, arrhythmia, and hypertension by actually seeing patients and by measuring renin and aldosterone, which are vasopressor substances, as he worked on the hypertension study group. He then went to *Yoikuen*, a hospital specializing in the care of the aged in Tokyo, where he received training in geriatrics, particularly in cardiovascular and respiratory diseases. With the hypertension study group there, he measured bradykinin, a depressor substance. He returned to the Third Department of Internal Medicine at Nagasaki University, treating emergency patients in the Coronary Care Unit, then went to the United States, to the Hypertension Research Laboratory operated by Dr. Carretero at the Henry Ford Hospital in Detroit, Michigan. Upon his return to Japan, before joining RERF, he again went to Nagasaki University, where he studied how blood pressure and heart rate changed with changes in intracerebral electrolyte concentrations.

Dr. Akahoshi is studying the relation between obesity, blood pressure, and ischemic heart diseases (IHD). With regard to obesity, visceral fat accumulation is closely related as a risk factor for ischemic heart disease, hypercholesterolemia, diabetes, and hypertriglyceridemia, and Dr. Akahoshi has demonstrated that a fatty liver, an indicator for visceral obesity, is strongly associated with IHD risk factors among the Adult Health Study (AHS) population. He has also revealed that obesity delays the onset of menopause. Using longitudinal data from the AHS, Dr. Akahoshi is studying whether high body mass index (BMI) or an increase in BMI contributes to an increase in blood pressure or development of hypertension. In adolescents from 10 to 18, he has demonstrated that the velocity of weight increase is strongly associated with blood pressure. He has also associated BMI increase with hypertension in those in their 40s and 50s, whereas it is associated with hypertension in those in their 60s.

Dr. Akahoshi related that after making these associations, it is now necessary to elucidate the association between the fatty liver and radiation dose. Among A-bomb survivors, those with higher radiation doses have demonstrated higher levels of visceral fat. On a genetic level, Dr. Akahoshi hypothesizes that those people with the gene for obesity were better able to survive the harsh condi-

tions following the atomic bombings, including the malnutrition resulting from anemia and diarrhea, because their bodies were able to metabolize more slowly the same number of calories consumed by those without the fat gene. In effect, they were able to absorb more calories from the same amount of food consumed by others. As the survivors have aged and economic conditions have improved, obesity has become a problem for many. This phenomenon has been reported in native Americans, and Dr. Akahoshi feels that this reflects their ability to survive the harsh circumstances experienced migrating from Asia thousands of years ago. Obesity and diabetes are now primary health concerns among native Americans.

Explaining how research is conducted at RERF, Dr. Akahoshi wrote,

"When we study the relationship between radiation exposure and a certain disease, we make it a point to first study whether the characteristics of the disease (sex difference, relation with age, relation with risk factors, etc.) as it has been observed among other cohorts are also observed among the AHS population. We do not start analyzing the relation between the disease and radiation exposure until the result of the above study is accepted by a scientific journal. With these efforts we are trying to prove that the methods and criteria we use for diagnoses are appropriate and that the AHS population is not special."

Dr. Akahoshi's future study plans include further consideration of the obesity-related gene(s) in relation to BMI, IHD, and radiation dose to explain why IHD is frequently observed in A-bomb survivors.

Though he does not have much opportunity to pursue his cardiology interests, Dr. Akahoshi keeps up-to-date on the latest procedures by talking with colleagues, and he sees patients at private hospitals on the weekends.

**Dr. Midori Soda**

Editor's Note: The following article on Dr. Soda is adapted from the translation of an article written by her in the November 1999 issue of the Japanese Newsletter (25[6]). It is supplemented by information obtained by interview.

Dr. Midori Soda, assistant chief of the RERF's Nagasaki laboratory's Department of Epidemiology, trained as a pediatrician at the Nagasaki University School of Medicine and practiced that specialty for two years before coming to the Radiation Effects Research Foundation in November 1979. Now, after more than 20 years, Dr. Soda is actively engaged working on the city's tumor and tissue registry, seeing patients, and looking into the effects of radiation on menopause. Dr. Soda's continued interest in pediatrics has developed into a particular interest in *in utero* studies as well, but political concerns limit the possibilities of such work.

While completing her pediatric residency, Dr. Soda

first became interested in chromosome study when she examined a patient with a minor deformity. She then moved on to the Atomic Disease Institute* of the medical school, where she was a member of a team of physicians who assisted with chromosomal analyses of leukemia and preleukemia (myelodysplastic syndromes). Her involvement with these analyses led to an invitation by another member of the team, Dr. Naoki Sadamori, to join a genetic counseling session. Dr. Shotaro Neriishi, who was RERF Nagasaki's assistant epidemiology chief at that time, had organized the monthly sessions with the approval of the local medical association and with the underlying intention of providing such assistance to the children of atomic-bomb survivors (F_1). At that time, RERF was engaged in an F_1 evaluation. In addition to the counseling sessions, Dr. Soda attended a monthly genetic seminar to learn how to counsel patients and their families.

Dr. Soda's acquaintance with Dr. Shotaro Neriishi through the genetic counseling work of the medical association led to his inviting her to join the RERF staff. When she arrived, she examined Adult Health Study participants, conducted chromosome evaluations, and reported daily on the laboratory's biological genetic study (BGS) examination results to junior and senior high school students who visited RERF.

Outside RERF, she helped with the chromosomal examinations of couples with histories of successive miscarriages referred by obstetrics and gynecology clinics in Nagasaki. From 1984 to 1987, Dr. Soda saw genetics department outpatients at Nagasaki University's pediatric outpatient office as assistant to Dr. Niikawa.

In July, 1986, Dr. Soda was assigned to the cancer registry, where she began in earnest to introduce and stabilize the new registry system that was being put into place. Today, her activities at RERF are focused on evaluating the effects of radiation on cancer incidence and mortality in survivors. She is particularly interested in the concentration of lymphoma, lung cancer, and liver cancer cases and the number of hepatitis C carriers in Nagasaki. Adult T-cell leukemia (ATL) is especially frequent in the Nagasaki population.

Dr. Soda has also been engaged in leading an investigation of about 2,000 AHS women in Nagasaki in an effort to determine if radiation accelerates the onset of menopause. The preliminary findings (not yet published) suggest that it can, and so, she and other RERF researchers are prospectively measuring hormones and obtaining detailed information about the reproductive cycle in several hundred Hiroshima and Nagasaki premenopausal AHS women to look more closely at whether the accelerated onset in some women relates to variation in radiation sensitivity.

Though Dr. Soda's career has taken a number of turns she never expected in her medical school days, which sometimes left her feeling "that it would not be possible to go back," Dr. Soda concludes that her "satisfaction at finally finding a fulfilling career was greater" than her sense of loss. She says that her work with the cancer registry has "broadened [her] world," enabling her to meet a broad range of people.

As she looks to the future, Dr. Soda will continue her cancer registry work, and she will continue to see members of the Adult Health Study cohort during their bien-

nial examinations.** In addition, Dr. Soda will be engaged in the health examinations of the children of the atomic-bomb survivors, the F_1 *** Unlike the F_1 study conducted in her early days at RERF, which involved chromosomal analysis in biological genetics study participants, the new study will only evaluate the health status of participants.

**The Atomic Disease Institute (ADI) of the Nagasaki University School of Medicine conducts studies on diseases that are common among A-bomb survivors and others. One department is involved in diagnosis and treatment of patients, and another does research. Blood diseases, such as leukemia and malignant lymphoma, are special ADI concerns.*

***The Adult Health Study population in Nagasaki now numbers less than 3,000.*

****An update on F_1 study progress appears on the back page of this issue of Update.*



Dr. Akihiko Suyama

The arrival of Dr. Akihiko Suyama as RERF Nagasaki's new epidemiology chief was reported in the last issue of *Update* (10[9]: 21). Dr. Suyama came to RERF from the Tottori University School of Medicine, from which he graduated and where he continued his career for 18 years in its departments of internal medicine and hygiene. His preliminary studies in medical engineering technology proved useful as a means to manage information on infectious diseases for use by local physicians. Such information, which must be reported to a national center each year, was not easily available back in the community after it was filed nationally. Dr. Suyama was instrumental in getting that information to local physicians, who need to know quickly about epidemics.

In his more recent work with the Tottori Prefecture's cancer registry, Dr. Suyama has spent one or two days a week in the mass screenings of individuals, teaching, and conducting research related to the cancer registry and cancer epidemiology as well as computer science and medical information technology. He became involved with the study of low-dose radiation effects in Misasa Spring, where radon warms the hot springs frequented by the local community as well as others. In a population of about 3,000 people, he examined the possibility that low levels of radon may actually be beneficial in preventing cancer. At the same time, radon exposure has been noted as a contributor to lung cancer in the general population. At the Misasa Spa, a study was made of actual lung cancer deaths in the population with controls being matched for age, sex, and city.

Dr. Toshiro Usa



Dr. Toshiro Usa joined RERF Nagasaki's clinical studies department November 1 as a research scientist in the Division of Medicine. Dr. Usa graduated from the Nagasaki University School of Medicine in 1988 and completed his postgraduate work there

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in 1995. He holds a medical practitioner's license and a Ph.D. in medical science.

Following his graduation from medical school, Dr. Usa stayed on at Nagasaki University in the First Department of Internal Medicine, which comprises divisions of endocrinology, metabolism, gastroenterology, collagen studies, and autoimmunology, among others. Dr. Usa served an internship at the National Nagasaki Central Hospital, was on the internal medicine staff at Nagasaki University Hospital, completed his internal medicine residency at the National Sanatorium Kawadana Hospital, and served as an internal medicine physician at Sasebo Central Hospital prior to entering his postdoctoral program. He spent almost three years in Boston as a research fellow in the Division of Endocrinology of the Department of Internal Medicine at Massachusetts General Hospital followed by physician staff assignments in the Departments of Internal Medicine at Takahashi Hospital, Showakai Hospital, and Nagasaki University Hospital before arriving at RERF.

Dr. Usa's postdoctoral research focused on the regulation of oncogenesis by growth factors in the cell. This consisted of *in vitro* studies to determine which growth factors contribute to the progression of oncogene development.

During his fellowship in the United States, Dr. Usa conducted parathyroid hormone receptor studies. Dr. Usa has been involved in thyroid studies for some time and will conduct RERF's thyroid follow-up study, which was described by Dr. Tan Tominaga in the last issue of *RERF Update* (10[2]: 11). That study will include ultrasound follow-up of 190 patients diagnosed with thyroid nodules in an earlier Nagasaki study. First steps have included the setting up of the ultrasound recording equipment. After the follow-up examinations, evaluations will be made of another 5,500 as yet unidentified AHS participants. Thyroid diseases of concern include Hashimoto's disease, carcinoma and adenoma of the thyroid, and autoimmune thyroiditis.



Mr. Yoshio Okamoto

In a recent interview, Mr. Yoshio Okamoto, former chief of General Affairs at Nagasaki, remembered his almost 37 years at ABCC-RERF and the time of the reorganization of the Commission into the Foundation. Some of his memories follow. He began his affiliation

Commission in June, 1956, interviewing survivors as a part of ABCC's shielding study. Mr. Okamoto collected information from the survivors regarding their shielding status so that the radiation doses they received might be estimated. Eight field workers (sometimes up to ten) surveyed 8,000 individuals who were within two kilometers of the bombing hypocenter in Nagasaki to determine their physical positions at the time of the bombing, preparing so-called shielding histories, which included narrative histories, acute symptoms, and other information. Their work took some 18 years and was the foundation of the 1965 Dosimetry System (T65D), the first system in which the calculated doses were used for the quantitative analysis of radiation health effects.

Questions regarding shielding fell into twelve categories, and the circumstances of the survivors varied a great

deal. More than 50% were in typical wooden houses. Many were farmers, whose houses were slightly different, with thatched roofs and other variations from urban dwellings. Dose estimations were particularly difficult for those in the vicinity of the ten concrete buildings of the Nagasaki University Medical College. Because of the locations and availability of survivors, interviews were conducted day and night.

Upon completion of the data collection, doses had to be calculated, and Chairman George Darling invited the health physics division chief at Oak Ridge Laboratories in the U. S., Dr. K. Z. Morgan, to provide training for ABCC staff. In response, each year for about five years, one Oak Ridge scientist came to Japan to assist with the use of shielding information for calculations. The chief of the project was Dr. John Auxier. In addition, Mr. Okamoto and Mr. Yamada, from the Hiroshima laboratory, were sent to Oak Ridge for 14 months during 1971 and 1972 to learn how to calculate doses for those inside concrete enclosures.

In 1976, a year after ABCC's reorganization into RERF, Mr. Okamoto became the chief of the investigation section within the Department of Epidemiology, and in 1980, he became involved in a dosimetry study begun to re-evaluate the T65D dose estimations. A collaborative effort of the Japanese and Americans, three joint meetings were held. Dr. Eizo Tajima chaired the Japanese committee. (See *Update* (10[1]: 26, Spring 1999, Dr. Tajima's obituary.) The main role of the Japanese side was to measure exposed materials, such as tiles, for gamma exposure, and rocks, iron, and other such materials for neutrons, and Mr. Okamoto, who had by then been transferred to the accounting section of General Affairs, engaged with other RERF staff in collecting these samples. For the reassessments, the shielding information that had been used for T65D calculations, supplemented by additional subsequent data, was entered into the computer, becoming the basis for the DS86 system adopted in 1986. DS86 re-evaluated all the factors (source term, air transport, gamma and neutron measurements, and shielding) from free-in-air kerma and shielded dose to organ dose.

Mr. Okamoto was promoted to section chief and then department head of General Affairs in Nagasaki, joining the Operating Committee in 1991, and retiring from RERF in 1992, after more than 36 years of service.

Mr. Okamoto reminisced fondly about his days out in the field. He enjoyed the contact with the survivors and the sense of satisfaction in doing what he could to help them and others who would benefit from ABCC's research. However, he reported that he was often unwelcome, and survivors often did not wish to speak with him. He sometimes felt great anguish, he said, but in the end, it was a rewarding calling. When he moved into the office and began to be an administrator caught up in filling out forms and shuffling papers, his sense of satisfaction waned.

Mr. Okamoto remembers the period of transition from ABCC to RERF as a difficult time for employees, a time of great uncertainty about the future. In 1973, he recalls, many visitors from the Japanese government and the National Academy of Sciences came to ABCC and many meetings were held that foreshadowed the reorganization. It was a time of "dramatic change." One thing that stands out in his recollection is the decrease in staff that has taken place in 25 years, especially the last ten years, with the Nagasaki staff about halved, reduced from about 150 to about 70.

One Hundred Attend Millennial Chernobyl Symposium

Kazuo Neriishi, Chief, Division of Medicine, Department of Clinical Studies

(Editor's note: This article was adapted from an article that appeared in RERF's Japanese Newsletter. A description of the 1999 meeting and a brief history of the program appeared in RERF Update last spring [10(1): 6].)

On February 17 and 18, 2000, in their second joint meeting, international researchers in health studies related to the Chernobyl accident met in RERF's auditorium for the Japanese Ministry of Foreign Affairs' (MFA) symposium, this year entitled "Special Open Symposium 2000: Health Condition of Residents after the Chernobyl Nuclear Plant Accident." The symposium is held annually as part of MFA's researcher exchange program, which is intended to relieve the health effects generated by the Chernobyl nuclear plant accident. Until 1999, each participating institute held its exchange program on a small scale, but the new joint gatherings enable dissemination of more information to a wider number of members. The 100 participants included Mr. Akira Maejima, MFA assistant director, a representative of HICARE, researchers from the National Institute of Radiological Sciences (NIRS), Hiroshima University, Nagasaki University, and RERF, as well as guest speakers. Belarus's Ambassador to Japan Petr K. Krauchanka also joined the symposium.

Renowned researchers from both Japan and the former Soviet Union participated in the symposium, which started off the exchange program, and the primary areas of concentration related to dosimetry, thyroid diseases,

hematology, and health check-up methodology, and data processing. The participants from the former Soviet Union were Dr. Leonid A. Ilyin from Moscow's Russian Institute of Biophysics, Dr. Pavel V. Ramsaev from St. Petersburg, Dr. Anatoly F. Tsyb from Obninsk, Dr. I. I. Dedov from Moscow, Dr. Eugeny P. Demidchik and Dr. Larisa N. Astachova from Minsk, and Drs. Anatoly E. Romanenko, Nikolai D. Tronko, and Ilya A. Likhtarev from Kiev. Dr. Demidchik presented a histological study on thyroid diseases, which preceded his paper to be printed in *Nature*. Important scientific information available only in this study program was passed on to the Japanese researchers. Although many research programs relating to Chernobyl are being conducted on a three-country basis, by Japanese institutes, nongovernment organizations, and the Commonwealth of Independent States, our research program is the only one officially sponsored by the Japanese government.

As years go by, support for Chernobyl-related health effects studies from international organizations, including the World Health Organization, the European Union, and the International Atomic Energy Agency, and from Japan, has decreased as new projects have begun and continue, including those related to radiation exposure in the Mayak/Techa River region, Russia and Semipalatinsk, Kazakhstan. It is a common understanding among researchers, however, that continued Chernobyl studies are important and expected to continue in the future.

RERF Staff News

Administration

Dr. Clark W. Heath, Jr., associate chief of research, resigned effective 31 December 1999, after serving in that position for one year. Dr. Heath was a member of RERF's Scientific Council for eight years, from 1990 until 1997, and had served as vice president for epidemiology and surveillance research with the American Cancer Society from 1988 to 1998. During his year at RERF, Dr. Heath was actively involved in all aspects of the research program, participating in the genetics and immunology workshops in March, April's Scientific Council meeting, the Nagasaki board meeting in June, and the genetics peer review in November. He also served as editor-in-chief of *RERF Update* and spent considerable efforts in exploring the history of ABCC and RERF. In addition, he was instrumental in bringing to publication an RERF handbook that had been tabled a number of times prior to his arrival, and he contributed greatly to the editing of the English version of RERF's new promotional video. Dr. Heath returned to the U.S. and his home in Georgia to enjoy retirement with his wife, Janet,



Clark W. Heath, Jr.

and his basenji, Khari. Mrs. Heath with Mrs. Nagataki initiated what is hoped to be an annual event, the decoration of Christmas trees for RERF's lobby with a thousand paper cranes folded by RERF staff members. The live trees, planted afterward at Hijiyama Hall, remain as a legacy of the contributions both the Heaths made in their brief stay at RERF.

Hiroshima

Department of Clinical Studies

Dr. Gen Suzuki became RERF's new chief of clinical studies effective January 1. See a profile of Dr. Suzuki on page 4, following his story on the radiation accident in Thailand.

Dr. Masaharu Nobuyoshi resigned his position as a research scientist, seeing patients in the Division of Medicine of the Department of Clinical Studies, effective March 31, after serving RERF more than seven years. He left to join the staff of Hiroshima University's Research Institute for Nuclear Medicine and Biology.

From April 1995 until September 30 1999, Dr. Nobuyoshi held a concurrent appointment in the Immunology Laboratory of the Department of Radiobiology,

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Gen Suzuki

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where he created an animal model for studying human hematopoiesis by implanting human hematopoietic stem cells into severe combined immunodeficient (SCID) mice. By using this model, he demonstrated that human dendritic cell precursors can be maintained in SCID mice.

Departments of Epidemiology and Statistics

Dr. Catherine Sauvaget was appointed as a research scientist in the Department of Epidemiology effective 17 January 2000, coming to RERF after four years of postgraduate studies in the Department of Public Health of Tohoku University School of Medicine in Sendai, where she also served as an assistant professor. Dr. Sauvaget received her medical and postdoctoral degrees from the Department of Public Health of Rennes I University School of Medicine in France. Her Ph.D. dissertation was entitled "Health expectancies in three longitudinal studies of aging," and her medical dissertation, "Demographic and medical description of the patients from Saint-Avé Mental Hospital." In France, Dr. Sauvaget was a physician in the geronto-psychiatric ward at the Saint Avé Mental Hospital, and she was physician in charge of blood donation at the Vannes Blood Center. Dr. Sauvaget's research interests are the consequences of aging on the quality of life, the burden of chronic and nonfatal diseases on life expectancy, age-related diseases among atomic-bomb survivors, and noncancer diseases among A-bomb survivors.



Catherine Sauvaget

Dr. Kiyohiko Mabuchi resigned as epidemiology department chief effective 14 April 2000 to assume a position in the Radiation Epidemiology Branch of the National Cancer Institute of the U.S. National Institutes of Health in Rockville, Maryland. Dr. Mabuchi came to RERF as a research scientist in the then Department of Epidemiology and Statistics in September 1984 and served over the next five years first as chief of the Tumor and Tissue Registry Office and then department chief of Epidemiologic Pathology before his appointment as department chief of the Department of Epidemiology in July 1989.

Dr. Mabuchi received his M.D. from the Osaka University School of Medicine and his M.P.H. and D.P.H. from Johns Hopkins University School of Hygiene and Public Health in Baltimore. He was an assistant professor in the Department of Epidemiology and Preventive Medicine at the University of Maryland School of Medicine before his arrival at RERF. Prior to that, Dr. Mabuchi served as a research associate and section head of the Cancer Section of the Division of Epidemiology of the American Health Foundation in New York, and he was a visiting investigator and research fellow in the Division of Environmental Carcinogenesis at the Sloan-Kettering Institute for Cancer Research in New York.

From the time Dr. Mabuchi came to work for RERF, he contributed to the development and the strengthening of Hiroshima's Tumor Registry. He completed a comprehensive report on cancer incidence in the Life Span Study in 1994. He has also promoted collaborative research with many external organizations. Since 1993, he has served actively as a member of Committee I (Biological Effects)

of the International Commission on Radiological Protection (ICRP).

We are sorry to lose Dr. Mabuchi, but we trust that he will be involved in collaborative research with RERF, and we wish him continued success in his new ventures.

Dr. Yasuyuki Fujita, assistant department chief of Epidemiology resigned effective 31 March to become director of the Kaseda Health Center in Kagoshima Prefecture, his home prefecture. Dr. Fujita was employed as assistant department chief of the Department of Epidemiologic Pathology in April 1993 and became assistant department chief in 1995. He received his M.D. from Kumamoto University School of Medicine and his D.M.Sc. from the Kagoshima University School of Medicine. His postdoctoral work concentrated in industrial health and epidemiology. Before coming to RERF, he was senior lecturer at the Department of Public Health of Jichi Medical School in Tochigi Prefecture. We trust that Dr. Fujita will devote himself to the health and welfare of the people of Kaseda, making the most of his past experience.

Dr. Donald Pierce, research scientist in the Departments of Statistics and Epidemiology, retired effective 31 December 1999, after almost twelve years with RERF (served over an 18-year period). However, following the mandatory-age retirement, Dr. Pierce was re-employed in the same capacity effective 1 January.

Dr. Pierce was employed in September 1981 as a research scientist in the Department of Statistics and became chief of that department in July 1986. After returning to the U.S. in 1989, he came back to RERF's Department of Statistics in 1992 as a senior research scientist. In 1994, he was also given a concurrent appointment in the Department of Epidemiology. Through the years, Dr. Pierce has engaged in the statistical evaluation of research and studies conducted in all RERF departments, and he helped develop a statistical method to estimate random errors in radiation dose assessments. In recent years, he has been involved in academic exchanges in statistics and has provided counsel to young researchers, contributing to the introduction and promotion of statistics among Japanese researchers.

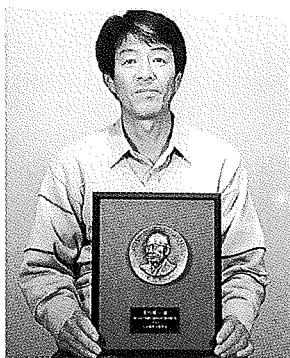
Dr. Pierce was a professor of statistics at Oregon State University for more than 25 years. In recognition of his varied and significant contributions to statistical science, he has been elected as a fellow of the American Statistical Association and member of the International Statistics Institute. For many years, he has served as an associate editor of *Biometrika*, one of the premier biostatistical journals. Because of his knowledge of radiation effects, Dr. Pierce has been invited to serve on various high-level review panels, including the National Academy of Sciences' committees on the health effects of radon and on electromagnetic fields and a recent ICRP task group on the effects of low-dose radiation exposures.

Dr. Pierce received his bachelor's and master's degrees in engineering and his doctorate in statistics from Oklahoma State University, and he completed a postdoctoral fellowship at Johns Hopkins University.

Department of Genetics

Dr. Jun-ichi Asakawa received the 38th Kodama Award at the 50th general meeting of the Japanese Electrophoresis Society held in Ube, Yamaguchi Prefecture,

17 and 18 November 1999. The award is named after one of the founders of the society, Dr. Keizo Kodama, a former dean of Tokyo University School of Medicine, who is pictured on the award plaque (See photo). Dr. Asakawa, a senior research scientist in the Department of Genetics, was recognized for his achievements in the development and application of procedures for separating proteins and DNA by two-dimensional electrophoresis.



Dr. Jun-ichi Asakawa

Department of Radiobiology

Dr. Keisuke S. Iwamoto, senior scientist in the cell biology laboratory, resigned effective 12 November 1999 to return to the U.S. to join the cancer oncology laboratory of the Department of Radiation Oncology at the University of California, Los Angeles as an assistant professor. Dr. Iwamoto came to RERF from UCLA's Laboratory of Biomedical and Environmental Sciences in the spring of 1992 to study the molecular mechanism of radiation carcinogenesis as it relates to tumor suppressor genes. In his more than seven and a half years with the Foundation, Dr. Iwamoto's major work comprised the molecular analysis of mutations in *p53* and other cancer-associated genes of liver cancers from A-bomb survivors and Thorotrast recipients. He found the dose-dependent increase of *p53* gene mutations in liver cancers of A-bomb survivors (Iwamoto KS, Mizuno T, Tokuoka S, Mabuchi K, Seyama T. Frequency of *p53* mutations in hepatocellular carcinomas from atomic bomb survivors. *Journal of the National Cancer Institute* 1998 [August 5]; 90[15]:1167-1168.) and the involvement of *p53* gene mutations in liver cancer development in Thorotrast recipients (Iwamoto KS, Mizuno T, Kurata A, Masuzawa M, Mori T, Seyama T. Multiple, unique, and common *p53* mutations in a Thorotrast recipient with four primary cancers. *Human Pathology* 1998 [April]; 29[4]:412-416; and Iwamoto KS, Fujii S, Kurata A, Suzuki M, Hayashi T, Ohtsuki Y, Okada Y, Narita M, Takahashi M, Hosobe S, Doishita K, Manabe T, Hata S, Murakami I, Hata S, Itoyama S, Akatsuka S, Ohara N, Iwasaki K, Akabane H, Fujihara M, Seyama T, Mori T. *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).

In addition to his skills as a researcher, RERF has benefited from Kei's cartooning skills and his keen sense of humor. In several recent issues of the *Japanese Newsletter*, his cartoons have been featured, and he has agreed to offer occasional artistic contributions in the future.

Dr. Terumi Mizuno resigned her appointment as a research scientist in the Laboratory of Cell Biology effective 31 January after almost nine years in the Department of Radiobiology. Dr. Mizuno received her undergraduate and graduate degrees in pharmacology from Kanazawa University, and she completed a postgraduate course in natural sciences there. Dr. Mizuno holds a pharmacist's license. During her time in the department, Dr. Mizuno's

work involved demonstrating that X-irradiation could cause preferential induction of the RET/PTC rearrangement both in cultured human cells and in human thyroid cells transplanted into SCID-hu mice (Mizuno T, Iwamoto KS, Kyoizumi S, Nagamura H, Shinohara T, Koyama K, Seyama T, Hamatani K. Preferential induction of RET/PTC1 rearrangement by X-ray irradiation. *Oncogene* 2000; 19: 438-443.), demonstrating that decades-old archival tissue blocks could be used in attempting to determine the causes of cancer in people who had been exposed to irradiation (Iwamoto KS, Mizuno T, Ito T, Akiyama M, Takeichi N, Mabuchi K, Seyama T. Feasibility of using decades-old archival tissues in molecular oncology/epidemiology. *American Journal of Pathology* 1996; 149: 399-406; Mizuno T, Nagamura H, Iwamoto KS, Ito T, Fukuhara T, Tokunaga M, Tokuoka S, Mabuchi K, Seyama T. RNA from decades-old archival tissue blocks for retrospective studies. *Diagnostic Molecular Pathology* 1998; 4: :202-208.); she also recently prepared papers describing demonstrations that the "patched" gene might play an important role in radiation-related basal cell carcinoma, and that the exposed hepatocellular carcinoma (HCC) atomic-bomb survivors were more frequently infected with hepatitis C virus than were non-exposed HCC controls.

The resignations of both Dr. Iwamoto and Dr. Mizuno, two young and productive scientists, at more or less the same time are greatly regretted not only by the department but by their many other friends at RERF. All of their former colleagues in Radiobiology hope that they have made good starts in their new careers and that they are once again involved in productive and satisfying work.

Information Technology

Michael K. Morimoto, research scientist, resigned effective 21 October 1999. He accepted a position in Tokyo with the Nokia Company. In his two years at RERF, Michael assisted American staff and others with computer-related problems and developed an interactive web page for Hiroshima's Department of Epidemiology, which is currently available on RERF's internal home page and which will be available in the future on the external page.

Publication and Documentation Center

Mrs. Reiko Sasaki, PDC's administrative assistant department chief since January 1999, was concurrently assigned as section chief of the center's Editorial and Publications Section, effective 1 January 2000.

Nagasaki

Editor's Note: See story on Nagasaki researchers, Drs. Akahoshi, Soda, Suyama, and Usa, on pages 12-14.

Dr. Masazumi Akahoshi, chief of the Department of Clinical Studies, was concurrently assigned as acting chief of the Division of Clinical Laboratories, effective 1 November 1999.

Dr. Tan Tominaga resigned as chief of the Division of Clinical Laboratories of the Department of Clinical Studies, effective 1 November 1999.

Dr. Toshiro Usa was employed as a research scientist in the Division of Medicine of the Department of Clinical Studies, effective 1 November 1999.

*Six-Month Progress Report***Establishing an RERF Archive: Concerns in Getting Started***by Margaret A. Irwin, Information Specialist, Publication and Documentation Center*

In undertaking the establishment of an archive, the Radiation Effects Research Foundation has demonstrated a strong institutional commitment to the preservation of the history of the Foundation, its predecessor, the Atomic Bomb Casualty Commission, and the work of its individual members. It is a monumental task, but at the same

time, it is an exciting opportunity to put into place procedures for identifying records of historical significance and unique to the institution, to preserve them, and to increase their availability. At present, ABCC-RERF has an outstanding living institutional memory that can offer a comprehensive view of the attitudes, goals, and activities of the Commission from the late 1940s through its evolution into RERF. For the archive to be successful, there must be a corporate culture that encourages creativity, respects diversity and values risk-taking, communication, commitment, and loyalty. The final plan for the archive is farseeing and firmly rooted in day-to-day reality; maintaining an archive is an ongoing task.

Necessitated by the most cataclysmic event of the century, the breadth, scope and duration of the work of ABCC-RERF has given the organization an unparalleled position in the history of science and of medicine. Primary and secondary resources document the history and foster the mission of the RERF research program, expand the knowledge of investigators in the field of radiation research, and assist in the care of survivors. Preservation of and access to these resources can only contribute to the global understanding of ABCC-RERF's valuable work. The ABCC-RERF Collections have enduring value; they are of current and historical interest and therefore should be protected against deterioration and damage so that they can be used as long as possible. The collection at RERF has intrinsic value. From my initial evaluation, the artifactual, associational, and symbolic values are tremendous.

I have devoted the past six months to planning and evaluation and consulting with former and senior ABCC-RERF staff members. Some documents of high priority have been identified, reviewed, and transferred, and I have conducted preliminary physical evaluation and appraisal of these documents. Materials are fragile and in danger of being lost forever. Significant deterioration has occurred due to several inter-related causes: the inherent chemical instability of the materials, unsuitable environmental conditions, and inapt storage and handling practices. Storage in space unprotected from temperature and humidity fluctuations results in the disintegration of both paper documents and photographic images. Computer-created records are endangered by the instability of computer tapes and discs. I have started identifying and referring items for preservation treatment and carrying out some rudimentary conservation measures. I have also struggled to ascertain the most reliable, efficient, intuitive, and sustainable bilingual hardware and software for electronic access, scanning, and digitization, communicating with in-house experts and soliciting recommendations from leading international experts.

According to early staffers, preliminary efforts to establish an institutional archive involved committee identification of materials to be surveyed and accessioned. After locating and indexing the designated materials, an inventory roster was created in print and computerized form. Some documents were rehoused and stored in various locations throughout the Foundation. It is unclear whether the print or electronic versions of the lists were ever used for retrieval. No reference or bibliographical support is apparent for the archival records that were inventoried. The rosters have been moved to my office, and I am exploring the idea of converting the material to another data base. Archival documents and photographs that were under the management of the library were also transferred to the archive office and have been reviewed, analyzed, and deaccessioned [redistributed].

The documents and photographs I have examined and tested show signs of acidity, brittle paper, and infestation of mold, insects, and other contaminants. Uncontrolled lighting has caused some photochemical damage. Ozone is also a great concern because of the damage that it can do to the collection, including corrosion in metal discoloration, fading or color changes in pigments, cracking of rubber, and fading and color changes in textile dyes. Due to the fragility of the documents, photographs, and inadequate storage conditions, we must move quickly to identify the remaining archival materials and house them in appropriate surroundings. Paramount is the identification of a dedicated space for archive storage; appropriate environmental control is the foundation on which all preservation and conservation activities rest. It is therefore extremely important that every repository holding documentary resources of enduring value integrate preservation into its entire range of operations.

An archival research facility needs a solid collection policy that defines the scope of the current collections and indicates areas in which future collections must be developed. The collection policy is based on the institutional mission statement, which enunciates the goals the collection is to achieve. Some basic considerations for determining archival materials are the age, uniqueness, informational content, historical significance, format, volume, and condition of materials.

Other activities in which I have been involved these past six months are providing reference and bibliographical support, attending an afternoon session of a conference on digital archives in Japan, writing articles, and taking digital photographs of the RERF Hiroshima open house. A few of the photos were mounted on the RERF web page, and several appear in this issue of *RERF Update*. (See pages 10 and 11.) I have discussed in detail my ABCC Collections work at the Houston Academy of Medicine-Texas Medical Center Library with RERF staff and demonstrated features of the Web page I created for the Collections, which is now linked to the RERF home page.

Presently, I will compile a list of recommendations to effectively control documents in all formats, developing selection criteria, policies, and processing procedures for records determined to be archival. I also look forward to

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locating more materials in Hiroshima and Nagasaki. The proper storage and protection of these materials is vital to halt the insidious threats of acidic paper and nitrate-based film stock, pests, water and light damage. We can not provide public access to records for as long as needed unless we can preserve them for as long as needed. Once the planning and designing phase is complete, implementation and maintenance of the archive's automated management and descriptive systems begins. The production of finding aids, repository level guides, and other descriptive access tools will establish links that will expedite research and information communication, hopefully ending duplicated efforts and creating a seamless system for managing the documents and providing electronic access.

Particular Considerations

The massive problem of deterioration and loss of the collections they contain threaten archives. For most archives and libraries, professional conservation treatment as a way to rectify the problem is and always will be prohibitively expensive. However, adequate preventative care for collections, including proper storage, handling, and security, is not an unrealistic goal. Preservation focuses on preventing deterioration of the collection as a whole and taking measures to correct physical or chemical deterioration that has occurred. Remedial preservation is labor intensive and often requires highly trained professionals to carry it out. Consequently, it is expensive and is often limited to portions of a total collection. Any planning process must be structured to produce a program that will incorporate both categories of activity.

Early photocopies were inherently unstable, and reformatting materials to a different medium, e.g., microfilm, is sometimes necessary—stable, cost-effective technology can reproduce originals with little resultant loss of image quality. While copying may damage the original negative or slide and some resolution will be lost, a copy provides some insurance against permanent loss of an image. It is then important to segregate the deteriorating originals from stable copies made on acid-free paper, storing positives and negatives separately. Researchers should use the surrogates. Digital imaging is not preservation; however much is gained by digitizing, permanence and authenticity are not among the gains. Nevertheless, technological innovations will continuously provide challenges in our work and opportunities to improve it, and we must have the capacity to adapt continuously to change. We have at our disposal a variety of options for disseminating information.

The uniqueness of the RERF archive can nourish research in a wide variety of disciplines. RERF archival material is of scholarly importance and holds rich research opportunities. A collaborative effort is needed to reach interested scholars and institutions. I would like to communicate with all the departments in RERF and other research institutions about the archive and to work with the library staff to understand one another's holdings and to share ideas about collaborative referencing. Some of the ideas I have for accomplishing this include a digital virtual open house, brochures, exhibits (on and off campus), online exhibits, articles, and creation of an archive Web page. In the future, we may consider applying for grants. The possibilities are endless for such a unique collection.

A Letter to the Editor***Archival Collections Related to the Bombings and Their Aftermath***

Dear Editor:

I've started reading the impressive Volume 10, Number 2 issue [Autumn 1999] and have an incidental comment concerning the unsigned article on establishing a data base on the atomic bombing, etc. ["Hiroshima and Nagasaki Peace Praying Hall Construction Scheduled," p. 3]. The documentary sources listed seem to me rather limited, but perhaps the listing is meant to be limited to sources that can be incorporated into the data base. I should think, however, that any such effort as establishing a data base on the bombing and its aftermath would at least reference other collections, among which are those of the NAS [National Academy of Sciences¹] and the MFUA [Medical Follow-Up Agency²], the collection espoused by [Dr. William J.] Schull in Houston, and possibly the AFIP [Armed Forces Institute of Pathology³], in Washington. Also, it was not clear to me that the list included the beneficiary of the shipment of material from the AFIP to Hiroshima two or more years ago. Schull would be a good one to advise you as he has been writing more than anyone else.

Sincerely,

Gilbert W. Beebe, Ph.D.

Department of Health and Human Services
National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

Dear Dr. Beebe:

Thank you for your kind words regarding the last issue of *RERF Update*. As noted at the end of the article mentioned, information regarding the collection of materials for the data base construction was skimmed from previous RERF annual reports. Further detail was not provided in those sources.

Dr. Schull reports and Dr. Shoji Tokuoka confirms that, as you have noted, AFIP materials, including items from photographs of victims and buildings to tissue samples, were returned to Hiroshima some time ago, going to Hiroshima University's Research Institute for Nuclear Medicine and Biology in 1973 and later to RERF. Dr. Schull notes that Dr. George Darling's papers are housed at Yale, Stafford Warren's are at UCLA, and materials collected by the Occupation may be found in the MacArthur Memorial Foundation's Jean MacArthur Research Center in Norfolk Virginia and the Prange Collection at the University of Maryland as well as other locations.

Margaret Irwin, who is now in Hiroshima archiving ABCC-RERF materials and who has worked with Dr. Schull as special collections librarian and coordinator of the ABCC Collections at the Texas Medical Center Library in Houston (*See previous page.*), reports the following partial listing of additional collections:

- The Houston Academy of Medicine-Texas Medical Center (HAM-TMC) Library's John P. McGovern Historical Collections and Research Center houses the largest single collection of ABCC-RERF manuscripts.

See Archive Letter on back page

Scientific Publications, 1 October 1999 to 31 March 2000

Following are listings of the 26 manuscripts reported published by RERF staff members for the second half of the 1999-2000 fiscal year. Publications are arranged in reverse order by research protocol (RP) number by study program.

A separate section follows for Chernobyl-related collaborative research, and 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.

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 22.):

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 14-78 and 11-69**

Key TJ (Imperial Cancer Research Fund [ICRF], UK), Sharp GB (EH), Appleby PN (ICRF), Beral V (ICRF), Goodman MT (Cancer Research Center of Hawaii), Soda M (EN), Mabuchi K (EH). *Soya foods and breast cancer risk: A prospective study in Hiroshima and Nagasaki, Japan*. British Journal of Cancer 1999 (December); 81(7): 1248-1256.

RP 1-75

Chomentowski M (University of Munich [UM], Germany), Kellerer AM (UM, GSF-National Research Center for Environment and Health, Neuherburg, Germany), Pierce DA (S). *Radiation dose dependences in the atomic bomb survivor cancer mortality data: A model-free visualization*. Radiation Research 2000 (March); 153(3): 289-294.

Pierce DA (S), Mendelsohn ML (Lawrence Livermore National Laboratory, Livermore, California, USA). *A model for radiation-related cancer suggested by atomic bomb survivor data*. Radiation Research 1999 (December); 152(6): 642-654. (RERF Report 11-99)

Adult Health Study**RP 2-75**

Kurisu T (CH), Yamada M (CH), Fujiwara S (CH), Kodama K (CH). *The contribution of senility to death in the Adult Health Study*. Kosei no Shihyo (Health Welfare Statistics) 1999 (November); 46(13): 10-15. (Japanese)

Immunology**RP 1-93**

Kusunoki Y (R), Kyoizumi S (R), Yamaoka M (R), Kasagi F (S), Kodama K (CH), Seyama T (R). *Decreased proportion of CD4 T cells in the blood of atomic bomb survivors with myocardial infarction*. Radiation Research 1999 (November); 152(5): 539-543. (RERF Report 2-99) (J)

Special Clinical Studies**RP 3-91 and 3-89**

Fujiwara S (CH). *Epidemiology of osteoporosis*. Sanka to Fujinka (Obstetrics

and Gynecology) 1999 (December); 66(12): 1728-1734. (Japanese)

Fujiwara S (CH). *Osteoporosis. The points of medical interview, considering risk factors*. Current Therapy 2000 (February); 18(2): 217-221. (Japanese)

Fujiwara S (CH). *Risk factors for osteoporosis*. The Bone 2000 (February); 14(1): 47-51. (Japanese)

Fujiwara S (CH). *The relationship between secular trends in the incidence of vertebral fractures and changes in Japanese life style*. Seikei Saigai Geka (Orthopaedic Surgery and Traumatology) 1999; 42(10): 1007-1013. (Japanese)

Nakamura T (University of Occupational and Environmental Health, Kitakyushu), Fujiwara S (CH). *Vertebral and hip fractures in Japan*. Bulletin of the World Health Organization 1999; 77(5): 430-431.

RP 6-85

Neriishi K (CH), Ezaki H (CH), Arihiro K (Hiroshima University School of Medicine [HUSM]), Okamoto H (HUSM). *Thyroid lymphoma of mucosa-associated lymphoid tissue with monoclonal gammopathy occurring in an atomic bomb survivor: Report of a case*. Surgery Today 2000 (January 25); 30(2): 202-206. (RERF Report 8-96)

RP 4-85

Yano K (Honolulu Heart Program, Kuakini Medical Center [HHP/KMC]; John A. Burns School of Medicine, University of Hawaii at Manoa [JABSM/UHM]), Kodama K (CH), Shimizu Y (EH), Chyou P (HHP/KMC; Marshfield Medical Research Foundation, Marshfield, Wisconsin, USA), Sharp DS (National Heart, Lung, and Blood Institute, Bethesda, Maryland, USA), Tracy RP (University of Vermont), Rodriguez BL (HHP/KMC; JABSM/UHM), Curb JD (HHP/KMC; JABSM/UHM), Kusumi S (CH). *Plasma fibrinogen and its correlates in elderly Japanese men living in Japan and Hawaii*. Journal of Clinical Epidemiology 1999 (December); 52(12): 1201-1206. (RERF Report 7-97)

Cell Biology Studies**RP 7-93**

Mizuno T (R), Iwamoto KS (R),

Kyoizumi S (R), Nagamura H (R), Shinohara T (R), Koyama K (R), Seyama T (R), Hamatani K (R). *Preferential induction of RET/PTC1 rearrangement by X-ray irradiation*. *Oncogene* 2000 (January); 19(3): 438-443. (RERF Report 17-99)

Cytogenetics

RP 8-93

Kodama Y (G), Ohtaki K (G), Awa AA (G), Nakano M (G), Itoh M (G), Nakamura N (G). *The F value for chromosome aberrations in atomic bomb survivors does not provide evidence for a primary contribution of neutrons to the dose in Hiroshima*. *Radiation Research* 1999 (November); 152(5): 558-562. (RERF Report 1-98)

Tumor and Tissue Registries

RP 18-61

Arisawa K (EN; Nagasaki University School of Medicine [NUSM]), Soda M (EN), Endo S (NUSM), Kurokawa K (NUSM), Katamine S (NUSM), Shimokawa I (NUSM), Koba T (NUSM), Takahashi T (NUSM), Saito H (NUSM), Doi H (Department of Health and Welfare, Nagasaki Prefecture), Shirahama S (Kamigoto Hospital, Nagasaki). *Evaluation of adult T-cell leukemia/lymphoma incidence and its impact on non-Hodgkin lymphoma incidence in southwestern Japan*. *International Journal of Cancer* 2000 (February 1); 85(3): 319-324.

Soda H (NUSH), Oka M (NUSH), Tomita H (Nagasaki Prefectural Medical Health Center), Nagashima S (NUSH), Soda M (EN), Kohno S (NUSH). *Length and lead time biases in radiologic screening for lung cancer*. *Respiration* 1999 (November); 66(6): 511-517.

Atomic-Bomb Dosimetry Studies

RP 1-92

Romanyukha AA (Institute of Metal Physics [IMP], Russian Academy of Sciences [RAS]), Ignatiev EA (IMP/RAS), Vasilenko EK (Mayak Production Association, Russia [MPA]), Drozhko EG (MPA), Wieser A (GSF-National Research Center for Environment and Health [GSF-NRCEH], Institute for Radiation Protection [IRP], Neuherberg, Germany), Jacob P (GSF-NRCEH/IRP), Keriim-Markus IB (Institute of Biophysics, Ministry of Health [IB/MH], Russia), Kleschenko ED (IB/MH), Nakamura N (R), Miyazawa C (Ohu University School of Dentistry). *EPR dose reconstruction for Russian nuclear workers*. *Health Physics* 2000 (January); 78(1): 15-20. (RERF Report 4-99)

Chernobyl-Related Research

Yamashita S (Atomic Disease Institute [ADI], Nagasaki University School of Medicine [NUSM]), Shibata Y (EN), Hoshi M (Research Institute for Radiation Biology and Medicine [RIRBM], Hiroshima University [HU]), Fujimura K (RIRBM/HU), et al. *Results of medical examinations of children exposed to radiation from the Chernobyl nuclear power plant accident—the Chernobyl Sasakawa Health and Medical Cooperation Project 1991-1996 (II)*. *Hoshasen Kagaku (Radiological Sciences)* 1999 (October); 42(11): 338-348. (Japanese)

Yamashita S (Atomic Disease Institute [ADI], Nagasaki University School of Medicine [NUSM]), Shibata Y (EN),

Hoshi M (Research Institute for Radiation Biology and Medicine [RIRBM], Hiroshima University [HU]), Fujimura K (RIRBM/HU), et al. *Results of medical examinations of children exposed to radiation from the Chernobyl nuclear power plant accident—the Chernobyl Sasakawa Health and Medical Cooperation Project 1991-1996 (III)*. *Hoshasen Kagaku (Radiological Sciences)* 1999 (November); 42(12): 381-386. (Japanese)

Collaborative/Institutional/Directors' Publications

Barlow WE, Ichikawa L, Rosner D, Izumi S (S). *Analysis of case-cohort designs*. *Journal of Clinical Epidemiology* 1999 (December); 52(12): 1165-1172.

Hoffmann GR (College of the Holy Cross, Worcester, Massachusetts, USA), MacPhee DG (R). *Editorial: Reflections of Zhores Medvedev*. *Mutation Research* 2000 (January); 462(1): 1-2.

Nagataki S (D). *Health effects of radiation*. *Gen-ankyo Dayori (Tidings of the Nuclear Safety Research Association)* 2000 (February); No. 174: 1-2. (Japanese)

Nagataki S (D), Neriishi K (CH). *Issues involved in long-term follow-up of persons after radiation exposure*. Haraguchi Y, Tomoyasu Y, Kojima M, eds. *Nuclear or Radiation Disaster: A Simulation Model and a Scenario for Disaster Drills and a Manual-2000*. Tokyo: The Clinical Research Institute, National Hospital Tokyo Disaster Medical Center; 1999 (December), pp 74-77. (Japanese)

Ogawa T (R; Hiroshima Prefectural Hospital), Hayashi T (R), Kyoizumi S (R), Ito T (HUSM), Trosko JE (Michigan State University), Yorioka N (HUSM). *Up-regulation of gap junctional intercellular communication by hexamethylene bisacetamide in cultured human peritoneal mesothelial cells*. *Laboratory Investigation* 1999 (December); 79(12): 1511-1520.

RERF. *RERF directors, supervisors, and scientific councilors (as of August 1999)*. *Hiroshima Igaku (Journal of the Hiroshima Medical Association)* 1999 (October); 52(10): 932. (Japanese)

RERF. *RERF bibliography of publications, 1998*. *Hiroshima Igaku (Journal of the Hiroshima Medical Association)* 2000 (February); 53(2): 131-135. (Japanese)

Trosko JE (Michigan State University [MSU]), Chang CC (MSU), Wilson MR (MSU), Upham B (MSU), Hayashi T (R), Wade M (MSU). *Gap junctions and the regulation of cellular functions of stem cells during development and differentiation*. *Methods* 2000 (February); 20(2): 245-264.

Publications Using RERF Data

Editor's Note: The following two publications are authored by researchers outside RERF and include information obtained from RERF atomic-bomb-survivor data sets.

Lee S (Faculty of Environmental Science and Technology, Okayama University [FEST, OU]), Otake M (FEST, OU), Schull WJ (University of Texas, Health Science Center). *Changes in the pattern of growth in stature related to prenatal exposure to ionizing radiation*. *International*
See **Publications**, page 2

22 Meeting Participation

RERF Research Presented at Meetings, 1 October 1999 to 31 March 2000

RERF researchers reported attending three international meetings at which they made three presentations and 16 meetings in Japan at which they made 24 presentations between 1 October and 31 March. A chronological list of meetings attended is followed by a list of presentations by study and protocol number (unless otherwise indicated). Department codes used for affiliations are the same as those used for publications. (See page 20.)

Meetings Attended

International Meetings

European Molecular Biological Organization Workshop: Stem Cells, Growth Factor, and Cancer, 7-10 October 1999, Torino, **Italy**

Bridging Radiation Policy and Science, 1-5 December 1999, Virginia, **USA**

Forty-first Annual Meeting of the American Society of Hematology, 3-7 December 1999, New Orleans, **USA**

Meetings in Japan

Fifty-eighth Annual Meeting of the Japanese Society of Public Health, 20-22 October 1999, Beppu, **Japan**

First Annual Meeting of the Japan Osteoporosis Society, 27-30 October 1999, Kurashiki, **Japan**

Third Japan-France Workshop on Radiobiology, Imaging, and Environmental Sciences, 10-12 November 1999, Chiba, **Japan**

Sixth Meeting for Osteoporosis and Fracture, 13 November 1999, Matsumoto, Nagano, **Japan**

Forty-second Annual Meeting of the Japan Thyroid Association, 16-18 November 1999, Nagoya, **Japan**

Fiftieth Annual Meeting of the Japanese Electrophoresis Society, Satellite Symposium, 17 November 1999, Ube, Yamaguchi, **Japan**

Fiftieth Annual Meeting of the Japanese Electrophoresis Society, 18-19 November 1999, Ube, Yamaguchi, **Japan**

Forty-fourth Meeting of the Japan Society of Human Genetics, 17-19 November 1999, Sendai, **Japan**

Twenty-ninth Annual Meeting of the Japanese Society for Immunology, 1-3 December 1999, Kyoto, **Japan**

Twenty-second Annual Meeting of the Molecular Biology Society of Japan, 7-10 December 1999, Fukuoka, **Japan**

Twenty-second Annual Meeting of the Japanese Society of Hematopoietic Cell Transplantation, 16-17 December 1999, Hiroshima, **Japan**

Tenth General Meeting of the Japan Epidemiological Association, 27-28 January 2000, Yonago, **Japan**

Eleventh Meeting of Vitamin E Research, 28-29 January 2000, Kurashiki, Okayama, **Japan**

Thirty-third Annual Meeting of the Japanese Society of Gout and Nucleic Acid Metabolism, 3-4 February 2000, Kyoto, **Japan**

Thirty-first Special Seminar Concerning the Safety of Nuclear Power Plants, 16-18 February 2000, Tokyo, **Japan**

Eighth Meeting of Metabolic Bone Diseases, 11 March 2000, Tokyo, **Japan**

Oral Presentations at Meetings

Adult Health Study

RP 2-75 Masunari N (CH), Yamada M (CH), Fujiwara S (CH), Matsuoka K (CH). *Contribution and limitation of drug information to reliability of diagnoses of Parkinsonism and Hyperuricemia/Gout*. Fifty-eighth Annual Meeting of the Japanese Society of Public Health, 20-22 October 1999, Beppu, **Japan**

Neriishi K (CH), Nakashima E (S). *Relationship between radiation dose and smoking in inflammation markers in A-bomb survivors*. Eleventh Meeting of Vitamin E Research, 28-29 January 2000, Kurashiki, Okayama, **Japan**

Hakoda M (CH), Kasagi F (S), Yamada M (CH), Masunari N (CH), Fujiwara S (CH), Kodama K (Health Sciences, Hiroshima University School of Medicine). *The significance of serum uric acid value as a risk factor for cardiovascular disease*. Thirty-third Annual Meeting of the Japanese Society of Gout and Nucleic Acid Metabolism, 3-4 February 2000, Kyoto, **Japan**

Immunology Studies

RP 1-93 Hayashi T (R), Kusunoki Y (R), Seyama T (Yasuda Women's University), Kyoizumi S (R). *Role of caspase and active oxygen in radiation-induced apoptosis*. Twenty-ninth Annual Meeting of the Japanese Society for Immunology, 1-3 December 1999, Kyoto, **Japan**

Kyoizumi S (R), Kusunoki Y (R), Hayashi T (R), Hakoda M (CH), Seyama T (Yasuda Women's University). *Decrease of CD4 T-cell ratio in the peripheral blood of A-bomb survivors with a history of myocardial infarction*. Twenty-ninth Annual Meeting of the Japanese Society for Immunology, 1-3 December 1999, Kyoto, **Japan**

RP 11-89 Kusunoki Y (R), Kyoizumi S (R), Honma M (National Institute of Health Science), Hayashi T (R), Seyama T (Yasuda Women's University). *NK-mediated elimination of mutant lymphocytes that have lost expression of MHC class I molecules*. Twenty-ninth Annual Meeting of the Japanese Society for Immunology, 1-3 December 1999, Kyoto, **Japan**

RP 3-87 Kusunoki Y (R). *Roles of T cell subsets in bone marrow transplantation-Rejection prevention, GVHD, and immune reconstitution*. Twenty-second Annual Meeting of the Japanese Society of Hematopoietic Cell Transplantation, 16-17 December 1999, Hiroshima, **Japan**

Special Clinical Studies

RPs 3-91 and 3-89 Fujiwara S (CH). *Osteoporosis and fractures-An approach from epidemiological studies*. Sixth Meeting for Osteoporosis and Fracture, 13 November 1999, Matsumoto, Nagano, **Japan**

Fujiwara S (CH). *International comparison on osteoporosis-related fractures*. Eighth Meeting of Metabolic Bone Diseases, 11 March 2000, Tokyo, **Japan**

RP 3-89 Fujiwara S (CH), Kasagi F (S), Masunari N (CH), Morihara Y (CH). *Quality of life for the elderly and for osteoporosis patients*. First Annual Meeting of the Japan Osteoporosis Society, 27-30 October 1999, Kurashiki, **Japan**

Fujiwara S (CH), Masunari N (CH), Kasagi F (S), Naito K (Department of Oral Radiology, Hiroshima University School of Dentistry), Kodama K (Institute of Health Sciences, Hiroshima University School of Medicine). *Prediction of spinal fracture by bone mineral density*. Tenth General Meeting of the Japan Epidemiological Association, 27-28 January 2000, Yonago, **Japan**

Biochemical Genetics Studies

RP 1-97 Takahashi N (G), Murakami H (G), Kasagi F (S), Yamada M (CH), Kodama K (CH), Nishishita T (Department of Biochemistry, Vanderbilt University School of Medicine [VUSM], USA), Inagami T (RERF Consultant and Department of Biochemistry, VUSM). *Association of a polymorphism at 5'-region of angiotensin II type 1 receptor with hypertension*. Forty-fourth Meeting of the Japan Society of Human Genetics, 17-19 November 1999, Sendai, **Japan**

RP 7-85 Kodaira M (G), Asakawa J (G), Ishikawa N (Ito Hospital), Ito K (Ito Hospital), Nagataki S (D). *Analysis of tissue-specific gene expression in human papillary thyroid carcinomas by two-dimensional differential display*. Forty-second Annual Meeting of the Japan Thyroid Association, 16-18 November 1999, Nagoya, **Japan**

Asakawa J (G), Kodaira M (G), Ishikawa N (Ito Hospital), Ito K (Ito Hospital), Nagataki S (D). *Analysis of gene expression in thyroid carcinomas by two-dimensional differential display*. Fiftieth Annual Meeting of the Japanese Electrophoresis Society, Satellite Symposium, 17 November 1999, Ube, Yamaguchi, **Japan**

Asakawa J (G). *Search of alterations in proteins and genomic DNAs by using two-dimensional electrophoresis*. Fiftieth Annual Meeting of the Japanese Electrophoresis Society, 18-19 November 1999, Ube, Yamaguchi, **Japan**

Asakawa J (G), Kodaira M (G), Katayama H (ITD), Funamoto S (S), Tomita S (S), Ito M (G), Preston DL (S), Nakamura N (G). *Spontaneous and X-ray induced germ cell mutations in mice detected by computer-assisted two-dimensional DNA gel analysis*. Fiftieth Annual Meeting of the Japanese Electrophoresis Society, 18-19 November 1999, Ube, Yamaguchi, **Japan**

Takahashi N (G), Tsuyama N (R), Sasaki K (G), Kyoizumi S (R), Ichihara T (Nisshinbo, Inc). *Application of DNA microarray system to comparative genomic hybridization*. Twenty-second Annual Meeting of the Molecular Biology Society of Japan, 7-10 December 1999, Fukuoka, **Japan**

Cell Biology Studies

RP 7-93 Hamatani K (R), Mizuno T (R), Ishikawa N (Ito Hospital), Ito K (Ito Hospital), Nagataki S (D). *Genetic analysis of thyroid papillary cancers by subtraction method based on polymerase chain reaction (PCR)*. Forty-second

Annual Meeting of the Japan Thyroid Association, 16-18 November 1999, Nagoya, **Japan**

Mizuno T (R), Asakawa J (G), Kodaira M (G), Hirai Y (R), Ishikawa N (Ito Hospital), Ito K (Ito Hospital), Nagataki S (D). *Analysis of genes abnormally expressed in human papillary thyroid carcinomas by two-dimensional differential display*. Forty-second Annual Meeting of the Japan Thyroid Association, 16-18 November 1999, Nagoya, **Japan**

RP 7-92 Ban S (R), Hirai Y (R), Shinohara T (R), Moritaku Y (R), MacPhee DG (R). *Radiation sensitivity of BRCA1- and BRCA2-defective cultured human cancer cells*. Third Japan-France Workshop on Radiobiology, Imaging and Environmental Sciences, 10-12 November 1999, Chiba, **Japan**

RP 18-81 Kyoizumi S (R), Koyama K (R), Hayashi T (R), Morishita Y (R), Tsuyama N (R), Seyama T (Yasuda Women's University). *Uncoupling of DNA synthesis and mitosis in human intestinal crypt stem cells following radiation exposure*. European Molecular Biological Organization Workshop: Stem Cells, Growth Factor, and Cancer, 7-10 October 1999, Torino, **Italy**

Nobuyoshi M (CH, R), Kusunoki Y (R), Seyama T (Yasuda Women's University), Kodama K (Hiroshima University School of Medicine), Fujiwara S (CH), Kimura A (Research Institute of Radiation Biology and Medicine, Hiroshima University), Kyoizumi S (R). *Human dendritic cell precursors in NOD/SCID mice transplanted with human cord blood mononuclear cells*. Forty-first Annual Meeting of the American Society of Hematology, 3-7 December 1999, New Orleans, **USA**

No RP

Nagataki S (D). *Quantitative analysis of radiation effects: A paradigm for studying health effects of environmental disorders*. Third Japan-France Workshop on Radiobiology, Imaging, and Environmental Sciences, 10-12 November 1999, Chiba, **Japan**

Hakoda M (CH), Kamatani N (Institute of Rheumatology, Tokyo Women's Medical College). *Fc binding activity encoded by every IgG4 molecule*. Twenty-ninth Annual Meeting of the Japanese Society for Immunology, 1-3 December 1999, Kyoto, **Japan**

Nagataki S (D). *Studies at the Radiation Effects Research Foundation*. Bridging Radiation Policy and Science, 1-5 December 1999, Virginia, **USA**

Kasagi F (S), Kodama K (Hiroshima University), Okayama A (Iwate Medical University), Ueshima H (Shiga Medical University). *Estimation of the effects of population and high-risk strategies on the nationwide downward shift in blood pressure level in Japan*. Tenth General Meeting of the Japan Epidemiological Association, 27-28 January 2000, Yonago, **Japan**

Nagataki S (D). *Health effects of radiation-atomic bombs, nuclear power plant accidents, and Tokaimura*. Thirty-first Special Seminar Concerning the Safety of Nuclear Power Plants, 16-18 February 2000, Tokyo, **Japan**

F₁ Health Study Update**Scientific and Ethical Advisory Committees Meet**by **Senjun Taira, Permanent Director**

As a result of meetings between RERF and the All-Japan Second-Generation A-bomb Victims Liaison Council (*Niseikyo*), scientific and ethics committees have been established to discuss the various issues surrounding the proposed F₁ study, and each of the committees has held a first meeting. The scientific committee met on 13 December 1999, and the ethics committee met on 24 January 2000. Both meetings were held in RERF Hiroshima's auditorium.

From the 88,000 individuals RERF has identified as children of exposed and unexposed parents in both Hiroshima and Nagasaki, 15,000 to 18,000 will be selected to participate in the mail survey. From them, about 10,000 persons will be selected for health examination. Questions asked relate to lifestyle practices, including items related to eating, smoking, and drinking habits as well as general health issues. Preliminary health examinations are scheduled to begin in 2001, and full-scale examinations will follow in 2002.

The twelve members of the scientific committee are chaired by Dr. Tadao Shimao, who is president of the Japan Anti-Tuberculosis Association in Tokyo. Members are researchers from Fukuoka, Hiroshima, Nagasaki, Osaka, Saitama, and Shiga Prefectures and the United States. In the December meeting, they considered items to be covered in a preliminary survey of 300 people, 200 persons in Hiroshima and 100 in Nagasaki; that survey is now expected to be sent in the spring. Based on those results, the question method is to be evaluated before the larger survey, which is planned for as early as September.

The ethical committee comprises five members, including a philosophy professor, a neuropsychiatry professor, a law professor, and an attorney in addition to the chairperson, Hiraku Takebe, who is a professor with the Atomic Energy Research Institute of Kinki University in Osaka. The five are responsible for assuring that ethical issues are thoroughly considered as the study is conducted. Privacy is an issue of particular concern to the second-generation survivors, and this first meeting involved itself with the manner in which the study's mail survey, which will be used to determine who will be examined, is carried out and the questions that will be included.

The two committees are scheduled to hold their next meetings in early summer.

Archive Letter, continued from page 19

- The Hoover Institute Library and Archive at Stanford University has an extensive East Asian collection and includes the SCAP collection, which includes the papers of General Crawford F. Sams, Chief of Public Health and Welfare, who reviewed the work of ABCC.
- Duke University is home to the collection of Warner Wells.
- James Yamazaki's materials may be found at UCLA and the HAM-TMC Library
- The Department of Energy has its own archive; other materials may be found at the University of Arizona and Johns Hopkins University
- Still other information can be obtained through the U.S. Army Medical Department Museum at Fort Sam Houston in San Antonio, Texas.

Ms. Irwin points out as well that though a collection is housed at a particular location, the materials in it may not be processed and substantial work might be required to make use of it.

Dr. Beebe, your letter is very much appreciated, and we hope that this inquiry perhaps leads to the identification of further collections elsewhere.

Many thanks,

Clark W. Heath, Jr., editor, *RERF Update*

¹The National Academy of Sciences/National Research Council has its own store of materials in Washington, D.C.

²The MFUP functions primarily to conduct medical follow-up of veterans of World War II and after.

³The AFIP is the organization to which the Joint Commission sent most, if not all, of its specimens and materials collected during its study of the early effects of exposure to the Hiroshima and Nagasaki bombings. Some related materials may be found at AFIP's National Museum of Health and Medicine.

25 Years and Nearly 3000 Research Publications

The Radiation Effects Research Foundation marked the beginning of its 25th year on April 1, 2000. In those 25 years, researchers produced nearly 3000 publications, including 530 research protocols, 832 technical reports (TR; in-house series produced until 1992), 135 *RERF Reports* (which replaced the TR series in 1993), and 25 *Commentary and Review* articles.

See **25-Year Publications**, page 5

This newsletter is published by the Radiation Effects Research Foundation (formerly the Atomic Bomb Casualty Commission), established in April 1975 as a private, nonprofit Japanese foundation. It is supported equally by the government of Japan through its Ministry of Health and Welfare and that of the United States through the National Academy of Sciences under contract with the Department of Energy.

RERF conducts research and studies—for peaceful purposes—on the medical effects of radiation on humans with a view toward contributing to the maintenance of the health and welfare of atomic-bomb survivors and to the enhancement of the health of all mankind.

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Contributions to Update receive editorial review only and do not receive scientific peer review. Consequently, the opinions expressed herein are those of the authors only and do not reflect RERF policies or positions.

Units of radiation and radioactivity are given as found in the source material.

Editorial Staff

Editor-in-Chief: Clark W. Heath, Jr.
 Managing Editor: Rosalyn Vu
 Editorial Consultants: Margaret Irwin, William J. Schull, Shoji Tokuwaka
 Production Assistants: Hiroshi Haba, Kozue Kaneoka, Fumie Maruyama, Nagi Saito, Kaori Shitanii
 Proofreader: Fumie Maruyama
 Photographer: Kiyoko Yamayoshi
 Printer: Sanko, Inc.

Mailing Address

RERF Update
 5-2 Hijiya Park
 Minami-ku, Hiroshima-shi
 732-0815 Japan

Facsimile

81-82-261-3197 or 81-82-263-7279

Internet Address

General inquiries and reprint requests:
 pub-info@rerf.or.jp

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