RERF update RERF

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

Volume 5, Issue 3 | Hiroshima & Nagasaki | Autumn 1993

Collaboration with Chelyabinsk Scientists Underway

Exchanges of data and technical expertise are materializing as scientists from the Ural Research Center for Radiation Medicine (URCRM), Chelyabinsk, Russia, arrive at RERF for extended stays, following the signing of an RERF–URCRM agreement in May 1992 (see *RERF Update* 4[2]:1, 1992) and visits by RERF scientists to Russia in October 1992 (*RERF Update* 4[4]:1, 1993).

RERF and URCRM scientists have been exploring possible joint research in such areas as epidemiology/statistics, dosimetry, and medical follow-up of radiation-exposed populations. URCRM scientists are following up about 28,000 radiation-exposed persons from an area in the southern Ural Mountains that was contaminated when radioactive waste was accidently released into the Techa River at a plutonium reprocessing site (*RERF Update* 3[1]:1, 1991). RERF's work has focused on the Life Span Study cohort that in 1950 comprised 91,000 atomic-bomb survivors and suitable comparison subjects. In 1990, this population was estimated to be about 52,000.

In late August, two URCRM researchers began extended stays at the Hiroshima Laboratory.

During her 6-week stay, **Olga V Vjyushkova**, physician and epidemiologist, will familiarize herself with how the tumor registry, the Life Span Study, and other epidemiological studies are conducted at RERF. With RERF researchers, she will discuss methods for analyzing the Techa River data in collaboration with RERF's departments of Epidemiology, Statistics, and Epidemiologic Pathology.

Alexandra Vozilova of the URCRM Clinical Physiology Department will devote most of her three months at the RERF Cytogenetics Laboratory to mastering various cytogenetic techniques for efficiently scoring radiation-induced chromosome aberrations in the somatic cells of irradiated people. The techniques include conventional, G-banding, and fluorescence in-situ hybridization (FISH) methods. Vozilova has expressed particular interest in learning the FISH, or "chromosome painting," technique.

Forty blood specimens from both irradiated and unirradiated residents of the Chelyabinsk area were carried from Russia to Hiroshima by Vozilova to begin a joint RERF–URCRM study. Chromosome analysis of these samples is already underway.

Future interactions with other Chelyabinsk scientists will include discussions of issues related to clinical follow-up and dosimetry. ❑

Anniversaries of Atomic Bombings Marked by Thousands in Hiroshima and Nagasaki

About 45,000 persons in Hiroshima and close to 25,000 in Nagasaki gathered for formal memorial services on 6 and 9 August, respectively, to honor the Japanese, Koreans, and others who perished as a result of the atomic bombings in 1945. In both cities, at the times of detonation, the tolling of temple and church bells prompts a minute or two of silence among countless others who are unable to attend the official ceremonies.

This year, at RERF's laboratories, commemorative activities included lectures and films. At the Nagasaki Lab, Permanent Director **Yutaka Hasegawa**'s greeting was followed by a film titled "In the Minds of Men," a 30-minute documentary about the realities of modern, "high-tech" warfare. At the Hiroshima Lab, **Kazuo Neriishi**, chief of the Internal Medicine Division, spoke about his participation in the biennial medical consultations with atomic-bomb survivors living in North America. ❑

CHUGOKU SHIMBUN

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

In Hiroshima's Peace Park near the burial site of thousands of unidentified persons, prayers, flowers, and incense are offered in tribute on 6 August.

In This Issue

Perspectives

The 'Other' Role of the Radiation Effects Research Foundation

by Seymour Abrahamson, RERF Chief of Research & Update Editor in Chief

At the RERF Board of Directors meeting on 11 June, the following resolution was approved.

> Whereas the Radiation Effects Research Foundation (RERF) has been besieged in recent years by physicians and scientists from many parts of the world (eg, 336 visitors in 1992), all seeking advice on radiation effects programs and studies, the Board of Directors at RERF has resolved that the United Nations [UN] should be approached to identify and support at RERF the UN International Radiation Health Effects Advisory Institute. The World Health Organization [WHO], the International Atomic Energy Agency, the United Nations Scientific Committee on the Effects of Atomic Radiation, as well as the governments of Japan and the US, should be advised of this approach and be asked to support it.

This resolution is now being circulated, and we are pleased to report that WHO Executive Director **W Kreisel** has warmly endorsed it. (RERF has been a WHO Collaborating Center for Radiation Effects on Humans since 1979.) In the past year, more than 50 physicians of various specialities, epidemiologists, health physicists, and members of the Ministries of Health of the republics of Russia, Ukraine, Belarus, and Kazakhstan spent up to several weeks with staff of RERF's various research programs. The longer visits generally involved training in cytogenetics, radiobiology, data management, health monitoring, and epidemiologic analysis. As reported on page 1 of this issue, training programs are also underway for scientists from Chelyabinsk, the region extensively contaminated due to nuclear-weapons production. Financial support for most of these visitors generally comes from international, national, or private agencies, with the largest block from the private sector, ie, the Hiroshima International Council for Health Care of the Radiation-exposed.

The Japanese government also conducts health-related training for scientists from Asia, the Middle East, and South and Central America, including one-day briefings here at RERF by our scientific staff.

Various other agencies have also used our staff to help set up clinical and epidemiological programs in regions with radiation-exposed populations. RERF's status as an independent, authoritative foundation engenders great confidence in the assistance and evaluations of our scientists. We are trusted by people undergoing health surveillance much more than are teams from their own or other governments. **Shizuyo Kusumi**, RERF Department of Clinical Studies, will discuss one example of such a program in a future issue. Our relatively small professional staff and their associates fulfill a far larger role than foreseen by RERF's founders. Recently, such RERF training programs have been constrained by lack of laboratory space and by reduced budgets. Even so, we think our contributions to such training are an important part of our mandate "to contribute to the enhancement of the health of all mankind." ❑

News Briefs

✓ International Advisory Committee Participation

Department of Epidemiology Chief **Kiyohiko Mabuchi** attended the International Association of Cancer Registries annual meeting in Bratislava, Slovakia, 13–16 September. He is a member of the association's executive board.

Mabuchi also attended a meeting of Committee I of the International Commission on Radiological Protection in Bournemouth, UK, 20–24 September.

✓ Research Staff News

Hiroshima

Department of Radiobiology: Research scientist **Yoichiro Kusunoki** of the Laboratory of Immunology will spend two years at the Fred Hutchinson Cancer Research Center in Seattle, Washington. He will study the differentiation and maturation of the human hematopoietic stem cell and the lymphoid stem cell.

Nagasaki

Department of Clinical Studies: **Masazumi Akahoshi** was promoted to assistant department chief on 1 September. He is concurrently serving as acting chief of the Division of Medicine and acting chief of the Division of Radiology.

✓ US National Cancer Institute Scientist in Hiroshima

In early September, longtime ABCC/RERF associate **Gilbert Beebe** of the US National Cancer Institute (NCI) spent about a week at the Hiroshima Lab, continuing work on liver-cancer incidence among the atomic-bomb survivors. He is collaborating with RERF research scientist **M Tokunaga** and **Charles Land** of NCI's Radiation Epidemiology Branch.

✓ Reprint Requests Received from 42 Countries

During fiscal year 1992–93, RERF received 486 reprint requests from 42 countries. American researchers requested 32% of the total. Investigators from Germany followed with 10%, France 7%, Japan 5%, and Canada 4%.

The titles and summaries of published journal articles that are based on approved RERF manuscripts are listed on the last pages of *RERF Update*. RERF journal-article reprints are available on request by contacting the RERF Publication and Documentation Center, 5-2 Hijiyama Park, Minami-ku, Hiroshima, 732 Japan.

✓ In Memoriam: David G Cogan

David G Cogan, 85, a Harvard University ophthalmologist who participated in early Atomic Bomb Casualty Commission studies of delayed injury to the eyes of atomic-bomb (A-bomb) survivors, died of a heart attack on 9 September 1993 while traveling in Michigan. With **S Forrest Martin**, **Samuel J Kimura**, and **Hiroshi Ikui**, Cogan published in 1950 the results of the first ophthalmological survey of A-bomb survivors in which they reported 10 cases of radiation cataract among a group of more than 1200 persons who had been 1–2 kilometers from hypocenter at the time of the bombings. The first cases of lenticular opacities were first observed among the A-bomb survivors by Japanese ophthalmologists **Hirose Kinnosuke**, **Fujino Tadashi**, and Ikui during the summer of 1949. ❑

Issues

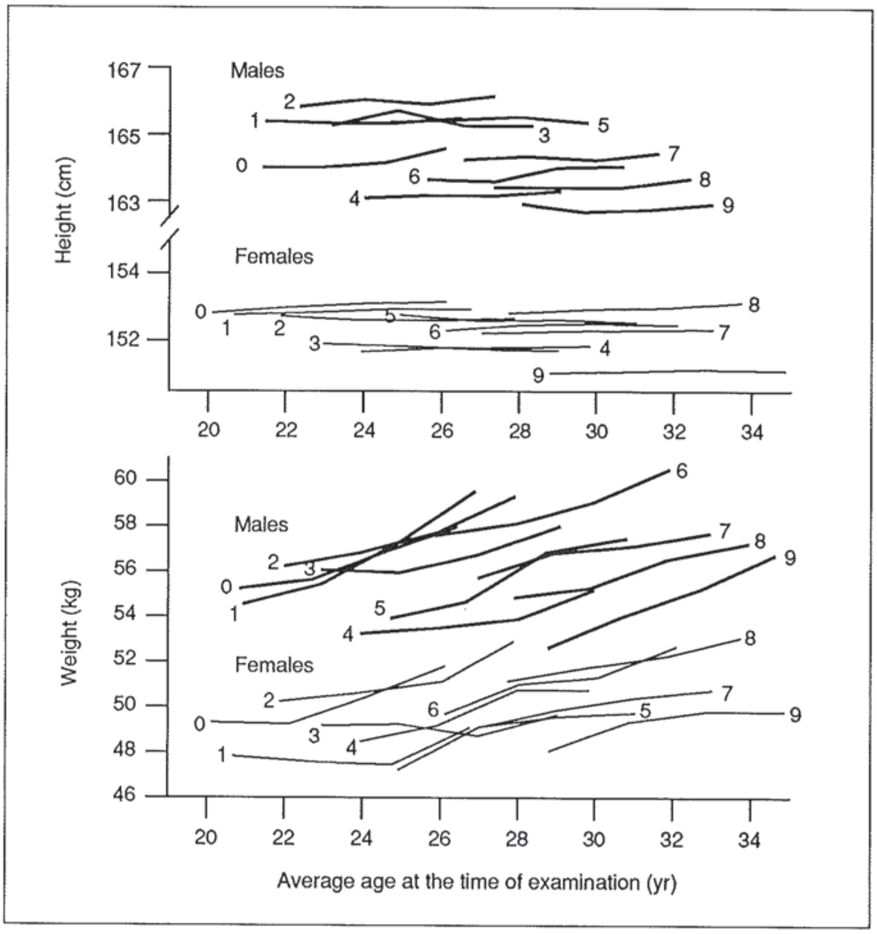
Growth and Development of Atomic-bomb Survivors Exposed during Childhood

Results of the author's analysis suggest an association between radiation exposure at ages under 10 years and subsequent altered patterns of growth.

by Masanori Otake, Department of Statistics, RERF

In 1958, clinical examinations of about 20,000 atomic-bomb (A-bomb) survivors began as part of the Atomic Bomb Casualty Commission's Adult Health Study (AHS). Still continuing today, the AHS examinations have biennially collected many physiological and biochemical measurements, including body size. A recent analysis of repeated measurements of stature recorded at various times among the prenatally exposed A-bomb survivors (M Otake et al, *Radiat Res* 134:94–101, 1993) has revealed a signficant growth retardation associated with radiation exposure among survivors exposed during the first and second trimesters of pregnancy.

In this study, we evaluated growth retardation in persons exposed when less than 10 years old. The analysis was based on repeated measurements of height and weight made during the fourth through seventh examination cycles (1964–1972). The observed mean heights and weights for ages 0–9 years at the time of the bombings (ATB) showed a definite trend when subjects for both cities were combined after categorization by sex and average age at the time of examination (ATE) (Figure 1). The observed mean values for height and weight, plotted in Figure 2 by city, sex, Dosimetry System 1986 (DS86) dose group, and examination-cycle year, differed slightly between Hiroshima and Nagasaki according to DS86 dose group. The mean heights by sex and average age ATE appeared to have remained unchanged for the 1964–72 period, and mean weights by sex and average age ATE increased with average age ATB.



FIGURES BY K KANEOKA & S FUNAMOTO

Figure 1. Mean values of height and weight by sex, age at examination, and age at exposure for examination cycles 4–7. Numbers located near the lines indicate the age (yr) of the subcohort at the time of the bombings.

Using statistical methodology known as growth-curve analysis, the relationships between height, weight, and age ATE were modeled. Since by 1964, most of the subjects had reached the adult stage of growth and development (ie, they were over 18 years old), growth could be analyzed without the complexities that arise in attempts to model the adolescent growth spurt, which differs greatly between men and women. We found that altered patterns of secondary growth seemed to depend upon exposure before the age of 3 years. When the subjects were categorized by examination cycle, correlation between height and weight was significant—ranging from 0.41 to 0.46. A multivariate approach using as covariates city, sex, DS86 dose group, and age ATB was considered more suitable than application of a cross-sectional technique by examination cycle.

A highly significant growth retardation associated with radiation exposure was observed when subjects were analyzed according to DS86 group and the analysis was restricted to the 567 individuals for whom at least four repeated measurements of height and weight had been recorded. The restriction to only those individuals with a complete set of height and weight measurements was made because our growth-curve model is not yet applicable to a series of multivariate measurements from which values are missing. An additional analysis, carried out to examine the effect of

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Growth and Development

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extending the analysis to include the 254 individuals with measurements from only three examination cycles, yielded an identically significant growth retardation. For the 254 persons, missing measurements were estimated from simple linear-regression models for height and weight fit to the three available values for each person. Among the several comparisons made by city, sex, DS86 dose, and age ATB, the most significant difference was between males and females. These were a 12.5-cm difference in height and about a 7-kg difference in weight.

Values for Hiroshima and Nagasaki differed significantly. On average, persons in Hiroshima were roughly 2.1 cm taller and 2.1 kg heavier than those in Nagasaki. The radiation-related growth retardation due to A-bomb radiation exposure was significant. Survivors with doses in excess of 2 Gy were on average 1.5 cm shorter and 1.5 kg lighter than survivors with DS86 dose estimates less than 0.01 Gy, after adjustment for city, sex, and age-ATB effect (Figure 3).

Although there seems to be a clear relationship between A-bomb radiation exposure and altered patterns of growth and development, it is difficult to evaluate the possible contributing effects of other factors, such as nutritional deprivation and disruption of normal family life in the years immediately following World War II. Reporting in 1966 on the results of a mail survey about cardiovascular disease (ABCC Technical Report 19-66), **H Kato** et al noted there was little difference by occupation or educational level among the exposed groups; however, the nonexposed differed from the exposed. In regard to housing conditions, the area per person did not differ significantly with exposure status in either Hiroshima or Nagasaki. The subjects of this survey were limited to the exposed population.

Since stature is primarily a result of genetic influences, the size of the parents would have been a useful covariate in evaluating a subject's expected adult height; however, parental height and weight were not available to us. In 1971, **J Belsky** et al noted that there was no significant height variation by dose for subjects

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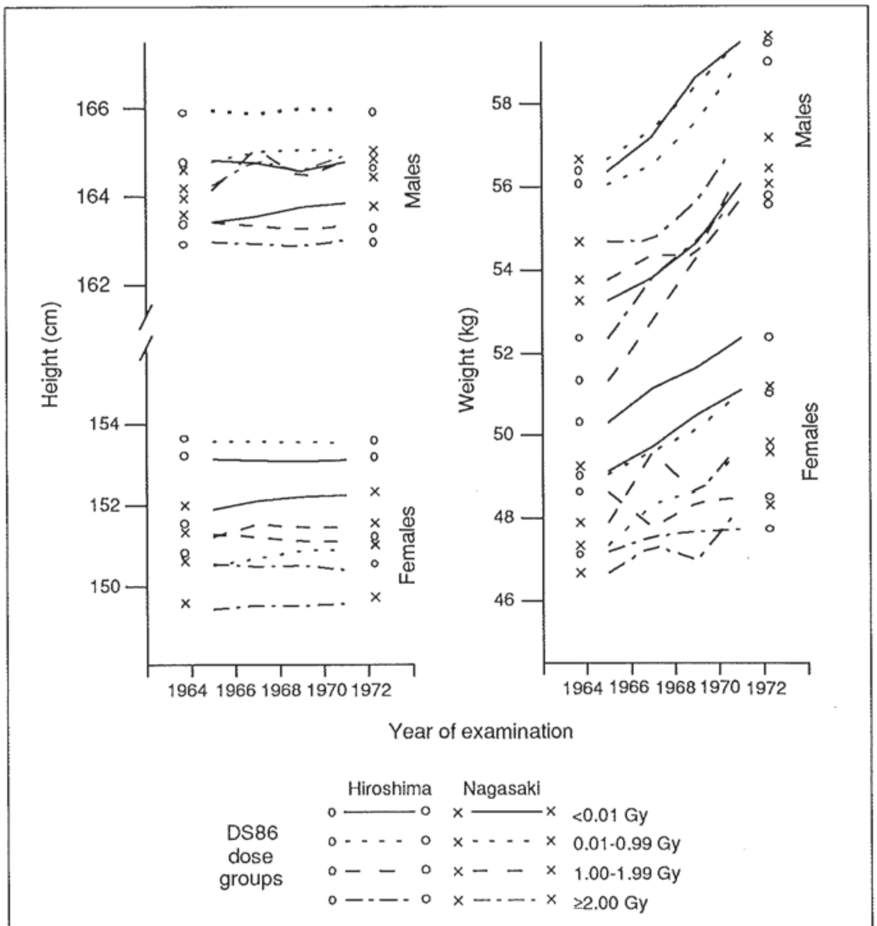

Figure 2. ***Observed mean values of height and weight of persons 0–9 years old at the time of the bombings. DS86 = Dosimetry System 1986.***

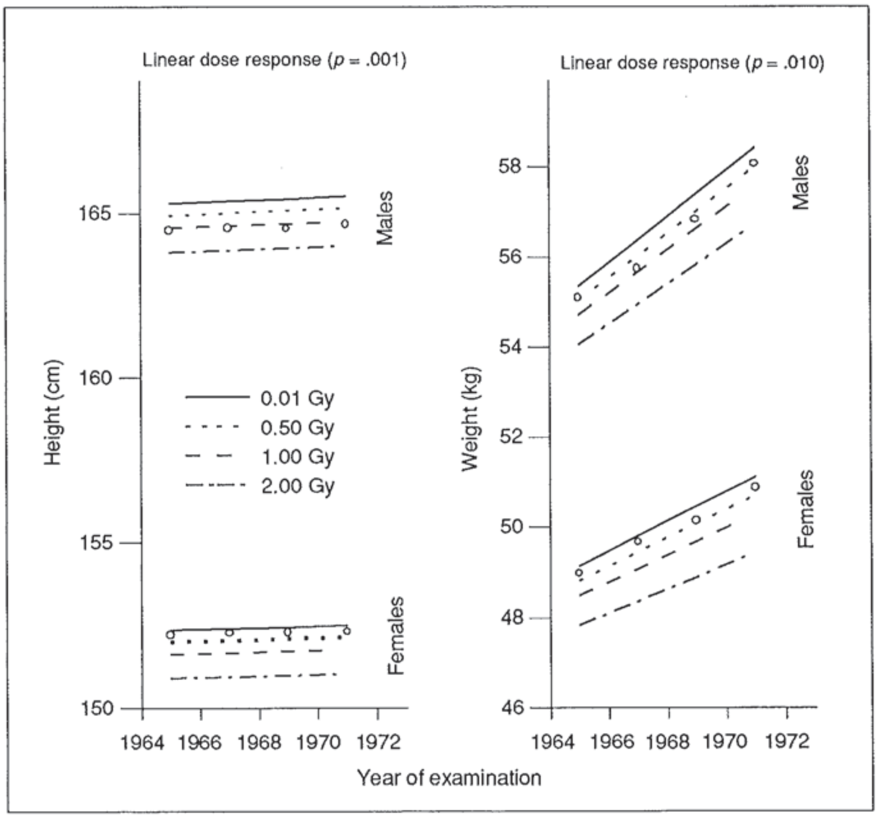

Figure 3. Observed and expected values for height and weight of subjects who were 0–9 years old at the time of the bombings. Observed total means of height and weight are plotted with circles.

Issues

Anthropometric Studies of Prenatally Exposed Atomic-bomb Survivors

Does the body size of survivors exposed in utero exhibit a dose response? If so, is it contingent upon gestational period at the time of the bombings?

by Eiji Nakashima, Department of Statistics, RERF

The ABCC-RERF In Utero Clinical Study Sample was established in 1959 and comprises 1608 subjects from Hiroshima and Nagasaki who were at various gestational stages at the time of the bombings (ATB). Five body measurements at age 18 years—standing height, body weight, sitting height, chest circumference, and intercristal diameter (the distance between the two iliac bones)—were recorded for 754 exposed subjects in this sample. Using the tentative 1965 dosimetry system (T65DR), **T Ishimaru** et al analyzed this data set with an emphasis on finding relative biological effectiveness (RERF Technical Report 19-84).

The objective of the present analysis is to answer two questions. Does body size exhibit a dose response? If there is a dose effect, does it depend on gestational period ATB?

Gestational age ATB was divided into four periods: 0–7 weeks, 8–15 weeks, 16–25 weeks, and 26–38 weeks. This categorization is based upon one used in a study of radiation-induced brain damage by **WJ Schull** and **M Otake** (RERF Technical Report 7-86).

Three hundred thirty-six persons from the In Utero Clinical Study Sample whose mothers were not in city (NIC) ATB were excluded from the main part of the analysis. This decision was based in part on a comparison of the body measurements of this group and of the 409 cohort members assigned estimated doses of less than 1 mGy. The five body measurements tended to be greater for the NIC group. The observed differences were suggestive for standing height and not significant for the other four measurements. In contrast to other studies in which the NIC group and groups exposed to less than 1 mGy have been combined into a 0-Gy Dosimetry System 1986 (DS86) category, the NIC group was excluded in this analysis because the differences in body measurements might bias the statistical inference. At least two distinctions between the groups might account for the differences in body measurements. The NIC group might have benefited from better living conditions (eg, better nutrition) after the bombings, and the group exposed to less than 1 mGy might reflect low-dose effects.

Table. Amount of reduction in body-size measurements per 1 Gy of radiation exposure among a selected cohort of the In Utero Clinical Study Sample

Body measurement	Amount of reduction
Standing height	−2.65 cm ($p < .001$)
Weight	−2.46 kg ($p = .001$)
Sitting height	−0.92 cm ($p = .006$)
Chest circumference	−1.37 cm ($p = .010$)
Intercristal diameter	−0.32 cm ($p = .037$)

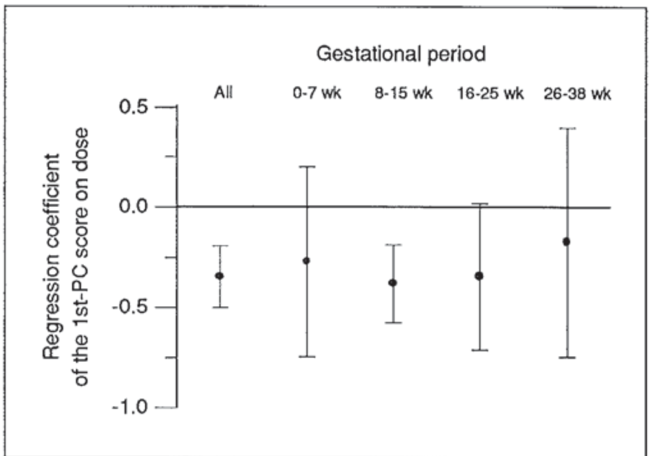

Figure 1. Parameter estimates of the dose response of the first-principal-component (1st-PC) score by gestational period (which accounts for 66% of total variation in body measurements). Ninety-percent confidence intervals are shown.

The results of linear-regression analyses of five body measurements on total uterus-absorbed dose for the 754 exposed subjects are shown in the Table. These regression coefficients are underestimated because of dosimetry error (D Pierce et al, RERF TR 2-89). The multivariate test statistic for the overall dose effect on five body measurements was significant ($p < .001$), but the dose effect did not appear to depend on gestational period ($p = .521$). These separate analyses of the five measurements were somewhat unsatisfactory because of the correlation among them, so a principal-component analysis (PCA) was carried out to overcome this problem.

When using a PCA, one develops a series of ordered, uncorrelated scores (eg, a linear combination of five standardized body measurements) from the original data. The scores are constructed so that the first accounts for the largest part of the variability, the second accounts for the largest fraction of remaining variability, and so on. In this case, the first three scores accounted for 95% of the total variation in the five body measurements.

Dose effects on the first principal component (PC) are shown in Figure 1. The first PC is a linear combination of the five standardized body-measurement variables with positive coefficients .47 (standing height), .50 (weight), .48 (sitting height), .42 (chest circumference), and .34 (intercristal diameter) and is roughly equal to the average of the five standardized measurements. Therefore, we can call this factor the overall body size. This score accounts for 66% of the total variation in body measurements. Using

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Feedback

Rogue Lymphocytes: New Evidence

James V Neel, University of Michigan Medical School, Ann Arbor, and Akio A Awa, Department of Genetics, RERF, write the following:

We have reviewed the article on the current state of knowledge of rogue lymphocytes in the general human population (*RERF Update* 5[1]:7–9, 1993). Since our article was written, new information on the characteristics of rogue cells has accumulated. For example, **M Nakano** et al, RERF Department of Genetics, have encountered a rogue lymphocyte, stained using fluorescence in-situ hybridization, using whole-chromosome probes from chromosomes 1, 2, and 4 in a distally exposed female survivor in Hiroshima. As anticipated, this metaphase shows complex rearrangements, including translocations, deletions, and insertions due to multiple breaks and rejoining.

Observed at RERF on 27 July 1993, this rogue cell might be the first of its kind to be stained using fluorescence in-situ hybridization— also known as "chromosome painting"—using whole-chromosome probes for chromosomes 1, 2, and 4. Chromosomal segments of different size produced from the breaking of targeted chromosomes (stained yellow) have been either translocated or inserted in various ways into nontargeted chromosomes (stained red).

Regarding a possible etiology for rogue cells, we have collaborated with **Eugene O Major**, chief of the Molecular Virology and Genetics Section, National Institute of Neurological Disorders and Stroke, Bethesda, Maryland, to conduct a viral assay on sera from rogue-cell carriers and their controls (non-rogue-cell cases) in the atomic-bomb-survivor F_1 study population. An exciting preliminary result emerged; the antibody titers to the human polyoma virus, or JC virus, are impressively higher in the sera of individuals with rogue cells (11 cases) than in the sera of controls (8 cases). Higher titer values were noted in two control cases. Although much remains to be done, we apparently may have encountered a virus responsible for the rogue-cell phenomenon. Further viral assays in collaboration with Major are underway. ❑

Anthropometric Studies

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linear regression of this score on total dose, the overall main effect of dose was significantly negative ($p < .001$). However, the difference in dose response by gestational period was not significant ($p = .938$).

Dose effects on the second-PC score are shown in Figure 2. The second-PC score is a linear combination of the five standardized body-measurement variables –.52 (standing height), .28 (weight), –.50 (sitting height), .54 (chest circumference), and .33 (intercristal diameter), is roughly a weighted average of breadth minus a weighted average of standing and sitting heights, and may be interpreted as a measure of stockiness. This score accounts for 15% of the total variation in body measurements. The overall main effect of dose was not significant for this component ($p = .791$). However, there was a suggestion of variation in dose response by gestational period ($p = .067$), and the dose effect was significantly positive at 0–7 weeks of gestation ($p = .022$).

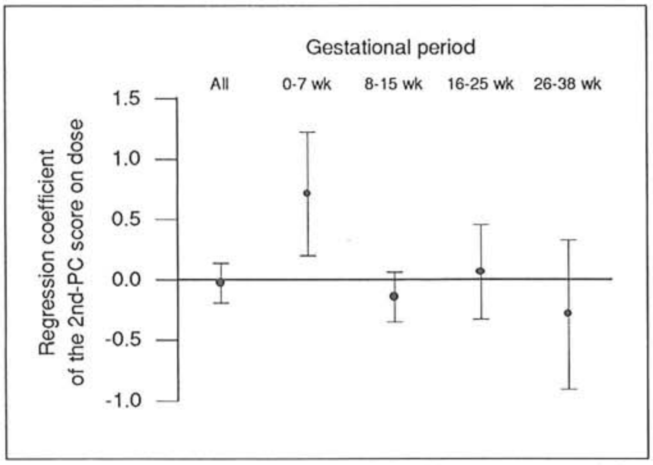

Figure 2. Parameter estimates of the dose response of the second-principal-component (2nd-PC) score by gestational period (which accounts for 15% of the total variation in body measurements). Ninety-percent confidence intervals are shown.

Body-size results (ie, those based on the first-PC score) provide clear evidence of a radiation effect, but little convincing support for the hypothesis that this effect varies with gestational period. However, when the results of the second-PC score are considered, there does seem to be an effect of gestational period on body shape or stockiness. ❑

Looking Back

The Dawn of Radiation Effects Research

The author recalls not only the* Fukuryu Maru (Lucky Dragon) *radiation-contamination incident, but also the social, political, and scientific consequences of it.

by Eizo Tajima, Nuclear Safety Research Association, Tokyo

Editor's note: In the previous two issues of RERF Update, *Merril Eisenbud, former US Atomic Energy Commission employee and Atomic Bomb Casualty Commission (ABCC) contract administrator, told of his and ABCC's involvement in follow-up of the contamination of a Japanese fishing vessel by the* BRAVO *nuclear test. In this issue, Eizo Tajima, who has long been involved in joint US–Japanese atomic-bomb dosimetry reassessments, provides a Japanese perspective on the same incident.*

PHOTO COURTESY OF EIZO TAJIMA

The Japan–US Radiation Conference was held on 15 November 1954 in Ueno, Tokyo. Participants included, seated at the left side of the table from the front: Yasuo Miyake, Takeo Ito, Sakae Shimizu, Kenjiro Kimura, Fumio Yamasaki, the author, Masanori Nakaidzumi (Atomic Bomb Casualty Commission associate director, 1956–64), Kouki Kakehi, Koichi Murachi, Masahisa Maeno, and Tatsuji Hamada. Sitting on the right side of the table from the front: WR Boss, WD Claus, M Salisbury, Yoshio Fujioka, PB Pearson, M Eisenbud, J Harley (partially obscured), SB Hendricks, Kakuma Nagasawa, and Shingo Mitsui. Other committee members not shown were Yakichi Noguchi, Yoshio Hiyama, and Daigoro Moriwaki.

It was on 16 March 1954 that I learned of the Bikini incident from the Yomiuri evening newspaper, while having an early dinner in Yokohama. In banner headlines, the news was reported nationwide: "Japanese fishermen encounter atomic-bomb test at Bikini, 23 afflicted with atomic disease, one diagnosed in serious condition at Tokyo University." Ironically, on 5 March—seven days earlier, the Japanese House of Representatives had approved a budget of ¥250 million for an atomic-energy development program.

The Bikini incident

The *Fukuryu Maru*, a small fishing boat of less than 100 tons with a crew of 23 men, was long-lining for tuna 80 miles east of Bikini atoll in the South Pacific, when at about 3 AM, on 1 March, the fishermen were surprised by a flash and a rumbling sound like that of distant thunder. They said that later something like chalk powder fell all over the deck thickly enough to show footprints. Sensing danger, the fishermen left the spot in haste. Thinking the white substance to be something valuable, because they had never had such an experience before, some crew members scooped it up, put it into small bottles with their bare hands, and kept it bedside in their small cabins. Shortly before their return to Yaizu port on 15 March, some experienced inflammation of parts of their skin, some started to feel sick, and some vomited. As soon as they returned to port, they were seen by a Yaizu doctor and put in an isolation ward at once. At that time, atomic disease was strongly suspected, and two serious cases were sent to the Tokyo University Hospital. It was concluded that the fishermen had encountered an atomic-bomb test near Bikini atoll and were suffering from a radiation-related disease.

The tuna scare

The *Fukuryu Maru*'s load of tuna was transported to the Tsukiji fish market [in Tokyo] and was found to be heavily contaminated with radioactive substances. The tuna was buried under instruction of the Fisheries Agency, Ministry of Agriculture, Forestry, and Fisheries. From that day, almost all the tuna caught in the South Pacific was more or less radioactively contaminated, and it was buried regardless the extent of contamination. So, the kitchens of Tokyoites were suddenly involved in the incident. A radiation uproar occurred all over Japan, causing great confusion. Five ports—Yaizu, Miura, Shiogama, Hachinohe, and Tsukiji—were designated as tuna unloading ports by the Fisheries Agency to allow examination of not only tuna, but also fishermen and fishing boats.

In those days, there were only a handful of people in

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Japan with the expertise to measure radioactivity. No university had yet established a department of nuclear engineering; therefore, nuclear research was being conducted by people from only a few universities having nuclear physics professorships and by the Yamasaki Laboratory of the Scientific Research Institute in Tokyo. They developed measuring instruments, because they were not available commercially. The government agencies had to enlist the help of these people to measure radiation and to interpret the results. I went to the fish markets in Misaki, Tsukiji, and Shiogama before dawn with officials of the Fisheries Agency to conduct radioactivity tests. If the fish were found to be contaminated, they were discarded under instruction of the agency. Even when the tuna was not contaminated, its price plunged only because it had been caught in the South Pacific. Radioactivity tests of fishing boats and tuna were detested by fishermen. The day's auction price fell drastically just because of our appearance in white lab coats at the fish market. We therefore lodged near the port the day before fishing boats came back to the port and went to the fish market at midnight without wearing white coats so that the brokers would not notice us. The fishermen were put in an unbearable situation because, upon returning to their long-awaited home port after absences of up to a year, the fish they had caught either had to be discarded or sold off at dirt-cheap prices at best. The situation was harsh enough to provoke anti-American sentiment. Along with the nuclear-test opposition that had been spreading among the citizens, a strong anti-American sentiment flared up.

Visit of the US representative

It was around the beginning of April that I was requested by the Foreign Ministry to accompany **Merril Eisenbud**, who was scheduled to come to Japan to inspect the *Fukuryu Maru*. It was his second visit since the incident. Besides myself, **Fumio Yamasaki, Kouki Kakehi**, and two officials of the Foreign Ministry were to accompany him. Although I had mixed feelings, I complied with the request because I had experience living in the United States for one year just after the war and had a friendly feeling toward Americans. Our group flew to Yaizu in a small American plane. The *Fukuryu Maru* was moored at a pier and roped off at a considerable distance (probably 200 meters) to keep people away. At the rope, we were surprised to see the survey Geiger-Müller (GM) counter that we had brought reacting violently. Upon boarding the vessel, we found that glass-ball floats and fishing nets were scattered about in a very small cabin. We were all impressed by the boldness of the fishermen to venture as far as the South Pacific in such a tiny boat. The survey-meter needle was already indicating at the top of its scale. Sensing danger, we did not go any further inside the vessel, and we left in haste. **Eisenbud, Kakehi**, and the officials of the Foreign Ministry went to the hospital to inquire after the health of the fishermen. An account of the above, plus the fact that a nonphysician [Eisenbud] had consulted with the patients, was reported in detail in the next morning's newspaper, which stirred up anti-American sentiment again.

Fallout in Japan from the H-bomb test

On 6 March, it was reported that the background radiation level had risen in the area around Irako Peninsula [a coastal area south of Nagoya], but it was discounted as impossible. I held a research post in the Yamasaki Laboratory, in addition to being a professor at St Paul's University. So I often paid a visit to the laboratory. On the evening of 16 May, **Fumio Yamasaki** and I were taking a walk around the premises of the institute with a GM counter. We accidentally pointed the GM counter at the new leaves of a shrub, and it started to sound loudly. This led us to check various places on the premises, and everywhere the radiation level was considerably higher than the background level. The level was inordinately high where rain puddles had formed and in vessels for catching rainwater. We sensed at once that this was the effect of an H-bomb test and that the elevated radiation level at Irako Peninsula was also the effect of an H-bomb test. This meant that there was radioactive fallout everywhere in Japan. This was a serious matter. The last thing we had expected to happen became real. We informed **Sakuichiro Hanzawa**, chief of the *Asahi Newspaper*'s Scientific Department, and the news was given front-page prominence in the newspaper the following morning.

Spread of the radiation panic

All Japan was seized with alarm. Researchers at universities in various locations detected significant amounts of radioactivity in rain and air using improvised counters. All Japan was thrown into a radiation panic, because only the radiation levels in counts per minute without any interpretation of their meaning were reported in newspapers. Every day, many reports of the radioactivity of collected rain samples were sent to the newspapers from various places, as if in a competition to report the highest levels.

On 23 September, **Aikichi Kuboyama**, a *Fukuryu Maru* crew member, died, and fear of radiation reached its peak. Rumors spread that one would become bald if one did not wear a hat on a rainy day, and hats reportedly were much in demand. The US showed no sign of stopping A- and H-bomb tests, and, in fact, intended to increase the frequency of tests, which aroused resentment among the people of Japan. Neither the Japanese government nor the scientists could take any effective countermeasure. The ministries of Health and Welfare, of Education, and of Agriculture, Forestry, and Fisheries and the Japan Science Council each organized a committee to consider counterplans. At meeting after meeting, the same faces showed up because only a few people were versed in this matter. In particular, **Fumio Yamasaki, Yoshio Hiyama, Yasuo Miyake**, and I attended every meeting, greeting each other with, "I see we meet again."

Japan–US Radiation Conference

The Japan Science Council established an ad-hoc committee to investigate radiation effects in May 1954 with the immediate objective of fulfilling the scientists' responsibilities in dealing with the social confusion caused by the Bikini incident. Efforts were made to improve communication, coordination, and exchange of information among researchers, and future research policy was discussed. The Bikini incident brought together experts from various fields, including those who had had nothing to do with radiation before the incident occurred. Therefore, it was very worthwhile that such specialists gathered and discussed pertinent matters together.

In Tokyo, fish was no longer being sold, and patronage at sushi bars drastically dropped off. One university professor who had boasted, "Radiation is nothing to be afraid of. I have a stomachful of *sushi*," became the talk of the town. By and by, some scientists started to express concern about how long such a radiation panic would last. On 15 November 1954, a five-day meeting called the Japan–US Radiation Conference, proposed by the US, was held at the Japan Science Council headquarters in Tokyo. It was a meeting of 22 participants—seven from the US, including **Paul B Pearson** as leader, and 15 persons representing Japan, including **Kenjiro Kimura** as leader. Front-line Japanese scientists, who were busily engaged day and night in work relating to the incident, attended the meeting. Eisenbud and I participated, too. Items on the agenda were radiation measurement, permitted dose, decontamination, food contamination, and the use of isotopes. In principle, the meeting was for exchanging scientific opinions, but it was in reality a meeting to have the US team teach the Japanese team. The aim of the meeting was, so to speak, to train Japanese opinion leaders. The outcome of each day's meeting was reported at a daily press conference.

After this meeting, the reporting on radioactive rain and contaminated tuna by the news media became far more scientific, and the social unrest soon started to fade away. The Fisheries Agency discontinued examination of tuna and fishing boats before the end of the year.

The progression of events showed that the role of scientists was very great indeed—regardless of whether the outcome was good or bad. The major cause of the initial confusion was the inability of scientists, including myself, to provide appropriate suggestions and recommendations. Not only scientists but also government agencies were in confusion about the unexpected situation. Nevertheless, resolution of the situation owed much to the scientists. For me, my deep involvement in this incident had a decisive influence on my later life.

Ultimate consequences of the incident

Scientific papers written by Japanese scientists about the Bikini-atoll incident were compiled in *Research on the Effects and Influences of the Nuclear Bomb Test Explosion*, published by the Japan Society for the Promotion of Science (1956). Three papers of mine are among them. One showed the existence of and the approximate speed of a belt of ocean current running east to west north of the equator. This was the result of an analysis of the relationship between the contamination of 426 fishing boats and their courses of navigation. Another showed, from analyzing the results of serial measurements of artificial radioactivity in air, that it took only about 10 days for the radioactivity generated by a nuclear test in Nevada to reach Japan via the Atlantic Ocean. Furthermore, it was confirmed that radioactivity detected in the air in Tokyo would travel around the globe and reappear in Tokyo within about 12 days.

The Bikini incident had a great impact on the scientific world. After this incident, studies of radiation effects were actively conducted in Japan. The government appropriated large amounts of money for studies in this field, in particular, which led to expansion of the research facilities of universities and research institutes and appointment of more researchers. The National Institute of Radiological Sciences was established on 1 July 1957 in response to the recommendation of the Japan Science Council and the wish of the Ministry of Health and Welfare. And, it was around this time (5 December 1958) that the historic Symposium on Radiation Effects on Man in the Nuclear Age was held Tokyo. The Japan Radiation Research Society was established on 2 July 1959.

The Cold War between the US and the USSR continued to be very intense after the Bikini incident, and the frequency and scale of A- and H-bomb tests escalated. The combined yield of the atmospheric explosions conducted by the two countries was approximately 50 megatons (Mt) TNT for 1954, 110 Mt for the three consecutive years following 1956, inclusive, and 350 Mt for 1961 and 1962 combined. Japan somehow came through the ordeal of the Bikini incident, but a wave of fear spread from Japan to the European countries. Since books on the A-bomb disaster in English were nonexistent in those days, Europeans reportedly read versions of the *Report on the Hiroshima and Nagasaki A-bomb Disaster* (compiled in Japanese by the Japan Society for the Promotion of Science, 768 pages, 1953) that had been translated into their own languages. The society is said to have been delighted to quickly get rid of their large stock of the report.

Establishment of UNSCEAR

To address such a global situation, the United Nations (UN) decided to establish the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) at its 10th general assembly in 1955. This can perhaps be considered the international version of the earlier Japan–US Radiation Conference. Although Japan was not a member of the UN at that time, Japan was one of UNSCEAR's 15 member countries from the beginning because it had had much experience in this field. The first meeting of the committee was held for a week beginning on 14 March 1956 at the headquarters of the UN. I was appointed a secretary of UNSCEAR, in accord with the resolution made at that meeting. Other scientists who joined the Secretariat were **RK Appleyard** from the UK and **AP Jammet** from France. **D Beninson** from Argentina and **Obukof** from the USSR joined in the following year.

I served with the UNSCEAR Secretariat for one year and three months, during which time among other things I defined genetically significant dose and developed a formula ready for calculation. Then, I requested that each UN member nation calculate its own dose and submit it to UNSCEAR with the measured value of radioactive fallout. I deduced an experimental formula to show the relationship between strontium-90 in milk obtained from the Perry dairy farm in New York State and the amount of the isotope deposited on the farm. This formula played an important role in projections made in the first report of UNSCEAR. In this work, I was greatly assisted by Merril Eisenbud.

At about that time every country in the world with a few exceptions started studying in earnest radiation effects on humans as well as on the environment. Thus, domestically and internationally, the Bikini incident had great impact socially, economically, and scientifically. In the future, it might be impossible to talk about the history of radiation research without mentioning this incident. ❑

Facts & Figures

Collection of Chromosome-aberration Data at RERF

by David Pawel, Department of Statistics, RERF

To determine the effect of factors such as age, sex, and radiation dose on the proportion of cells exhibiting chromosome aberrations in the atomic-bomb survivors has been a goal of the ABCC/RERF cytogenetics program since its inception in 1968. To date, chromosome aberrations in circulating lymphocytes have been measured using conventional methods on 4312 blood samples from 2552 Adult Health Study (AHS) participants who have Dosimetry System 1986 (DS86) estimated doses and from whom at least 30 cells have been obtained. These data continue to be used to evaluate physical dosimetry systems, such as DS86, and to attempt to establish ways in which chromosome-aberration detection could be used as a surrogate for physical dosimetry.

The RERF cytogenetics program has collected more than one sample from some participants to detect either attained-age-related trends in chromosome aberrations or changes in the effectiveness of chromosome-aberration counting methods. From 1968–69 and 1981–87, data collection concentrated on obtaining blood samples from as many participants as possible, whereas most of the repeated samplings of participants occurred from 1970–1980.

Table 1 shows the number of usable blood samples collected by period and the number of AHS participants by the period in which the first blood sample was taken for chromosome-aberration analysis. (Usable blood samples contain at least 30 cells, but usually 100 cells, in which stable and unstable aberrations were counted.) Age at the time of the bombings and the sex of Hiroshima and Nagasaki participants are shown in Table 2. The numbers of participants by DS86 estimated bone-marrow dose are shown in Table 3.

RERF's ongoing chromosome-aberration work will include using fluorescence in-situ hybridization, also known as "chromosome painting," on about 500 blood samples from Hiroshima and on 300 blood samples from Nagasaki to augment current RERF chromosome-aberration data.

For the results of a recent detailed analysis of RERF chromosome-aberration data, see **DO Stram** and **R Sposto** (*RERF Update* 5[1]:5–6, 1993). ❑

Table 1. Number of usable blood samples and by period first-time participants in the chromosome-aberration program

	Hiroshima		Nagasaki	
Period	Blood samples	New participants	Blood samples	New participants
1968–69	645	645	362	362
1970–71	329	130	354	186
1972–73	326	68	211	60
1974–80	463	10	472	1
1981–87	1031	971	119	119
Total	2794	1824	1518	728

Table 2. Number of chromosome-aberration-program participants by age at the time of the bombings (ATB), sex, and city

Age-ATB categories (yr)	Hiroshima participants		Nagasaki participants	
	Men	Women	Men	Women
0–4	50	58	25	12
5–9	28	59	19	30
10–19	293	307	99	140
20–29	108	284	35	110
30–39	180	256	85	96
≥40	85	116	31	46
Total	744	1080	294	434

Table 3. Number of chromosome-aberration-program participants by DS86 bone-marrow dose estimates and city

DS86 dose categories (Gy)	Hiroshima participants	Nagasaki participants	Total participants
0–0.005	627	341	968
0.005–0.1	200	35	235
0.1–0.5	228	92	320
0.5–1	296	110	406
1–2	282	123	405
2–3	125	15	140
3–4	33	6	39

Growth and Development

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aged 20–49 years ATB, an age range that includes the generation of the parents of the children who were 0–9 years old ATB (ABCC Technical Report 9-71).

Using the growth-curve model to examine the effects of socioeconomic factors, we evaluated as covariates occupation, education, household ownership, and eating habits (classified as Japanese, western, and Chinese cooking styles) that were available from the AHS epidemiological questionnaire for 1963–68. When compared with multivariate repeated measurements of height and weight, no significant difference among such concomitant variables was observed, but growth retardation associated with radiation exposure was manifest. Based on the growth-curve model, nutrition and socioeconomic status appeared to have a greater influence on the background estimates of parameters than either dose or age ATB. We have, therefore, assumed that concomitant factors, such as nutrition and socioeconomic status, affected equally all individuals studied, regardless of radiation exposure. It also seems reasonable to assume that genetic factors (ie, parental characteristics) affected members of a randomly selected population equally. ❑

Recent Scientific Publications

Editor's note: The 1992 report listed below will be distributed as soon as it is printed. Wording of the title and summary may be slightly altered before printing.

Approved Commentary and Review

Agreement between death-certificate and autopsy diagnoses among atomic-bomb survivors. Elaine Ron, Randolph L Carter, Seymour Jablon, Kiyohiko Mabuchi. **RERF CR 6-92.**

Using the Atomic Bomb Casualty Commission/Radiation Effects Research Foundation series of over 5000 autopsies, we examined death-certificate accuracy for several disease categories and assessed the effect of potential modifying factors on this accuracy. For 12 cause-of-death categories, the overall percent agreement between death-certificate and autopsy diagnoses was only 52.5%. Although neoplasms had the highest detection rate (on the death certificate) in the study, still almost 25% of cancers diagnosed at autopsy were missed on the death certificate. Only for neoplasms and external causes of death were confirmation and detection rates above 70%. Confirmation rates were between 50% and 70% for infectious and parasitic diseases and heart and other vascular diseases. Detection rates reached a similar level for infectious and parasitic, cerebrovascular, and digestive diseases. Specificity rates were above 90% for all but the cerebrovascular disease category.

Overall agreement decreased with increasing age of the decedents and was lower for deaths occurring outside of hospital vs those occurring in a hospital. There was some suggestion that agreement rates were higher for more-recent deaths but no indication that radiation dose, sex, city of residence, or inclusion in a biennial clinical-examination program influenced agreement. Because the inaccuracy of death-certificate diagnoses can have major implications for many aspects of health research and planning, it is important to be aware that death-certificate accuracy is low and can vary widely depending on the patient's age at death and the place of death.

Editor's note: As announced in the summer issue of RERF Update, *the RERF Technical Report Series, begun in 1959, will be terminated after the processing of 1992 manuscripts is complete. Beginning with this issue, summaries of journal articles based on approved RERF manuscripts will accompany the complete journal citation. Other selected summaries of interest will also be published occasionally.*

Publications in the Open Literature

Clonal fibroblastic cell lines established from a heavily exposed atomic-bomb survivor. T Honda, N Sadamori, M Itoh, O Kusumi. *Mutat Res* 291:125–33, 1993 (based on RERF Manuscript 3-93).

Two clonal fibroblastic cell lines with simple chromosome aberrations—one with del(3)(p24) and the other with t(1;16)(q21;q11.2)—were established from a high-dose (5.14 Gy) female atomic-bomb survivor by serial culture of skin fibroblasts. These two types of clonal cells showed a more extended life span than did the cells with 44 other types of chromosome aberrations and normal cells. In addition to these results, a prominent clonal population was observed in the peripheral-blood cells in this subject. It is assumed that these clonal populations arose in vivo as a result of radiation exposure to the atomic bomb.

Detection of partial deletion and partial duplication of dystrophin gene in Japanese patients with Duchenne or Becker's muscular dystrophy. K Hiyama, M Kodaira, C Satoh, T Karakawa, H Kameo, M Yamakido. *Jpn J Hum Genet* 38:169–76, 1993 (based on RERF Manuscript 8-93).

The dystrophin gene was analyzed in 59 Japanese patients with Duchenne muscular dystrophy (DMD) from 48 unrelated families, including 11 pairs of siblings, and three patients with Becker's muscular dystrophy (BMD) from two unrelated families, including one pair of siblings. The relationship between the type of gene abnormality and clinical symptoms was examined. Twenty-seven of fifty (54.0%) unrelated DMD or BMD patients were found to have partial deletions, and five (10%) appeared to have partial duplications in the dystrophin gene. Nine DMD patients, including three pairs of siblings, showed mental retardation, the existence of which was coincident in each pair of siblings, but deletion of an identical exon was not always related to mental retardation in unrelated patients.

A positive correlation between the precursor frequency of cytotoxic lymphocytes to autologous Epstein–Barr-virus-transformed B cells and antibody titer level against Epstein–Barr-virus-associated nuclear antigen in healthy seropositive individuals. Y Kusunoki, H Huang, Y Fukuda, K Ozaki, M Saito, Y Hirai, M Akiyama. *Microbiol Immunol* 37:461–9, 1993 (based on RERF Manuscript 12-93).

A limiting dilution analysis was established to determine the precursor frequency (PF) of cytotoxic lymphocytes against autologous B cells transformed with the Epstein–Barr virus (EBV). This method was found to detect mainly self-restricted T-cell activity and little non-self-restricted cytotoxicity. The mean PF in 21 healthy EBV-seropositive persons was 1.4×10^{-3} for peripheral blood mononuclear cells, whereas 4 samples of mononuclear cells obtained from umbilical cord blood had PFs below 0.007×10^{-3}. A positive correlation was observed between the PF and serum antibody titers against EBV-associated nuclear antigen among the seropositive persons.

In-vitro irradiation is able to cause *RET* oncogene rearrangement. T Ito, T Seyama, KS Iwamoto, T Hayashi, T Mizuno, N Tsuyama, K Dohi, N Nakamura, M Akiyama. *Cancer Res* 53:2940–3, 1993 (based on RERF Manuscript 14-93).

Elevated risk of thyroid cancers among the atomic-bomb survivors as compared to the nonexposed population suggests that some genetic events related to thyroid cancer must be caused by ionizing radiation. Accordingly, inducibility of *RET* oncogene rearrangements, ie, the generation of the *RET*-PTC oncogene, specific for thyroid cancer, was investigated among human undifferentiated thyroid carcinoma cells (8505C), which do not have *RET* oncogene rearrangement after 0, 10, 50, and 100 Gy of in-vitro X-irradiation, by means of reverse transcription polymerase chain reaction. After testing 10^8 cells at each dose point, 3 independent samples obtained with 50 Gy of X-irradiation and 6 independent samples obtained with 100 Gy of X-irradiation showed a rearranged *RET* oncogene amplified band. No rearranged transcripts were obtained from cells irradiated with 0 or 10 Gy. All of the transcripts were sequenced and found to contain the D10S170 and *RET* sequence. Interestingly, two types of rearrangements were included in these transcripts: one is specific for thyroid cancer and the other, which contains a 150-base-pair insert, is atypical, not usually seen in vivo. This insert was found to be the exon of D10S170. Furthermore, in fibrosarcoma cells (HT1080), X-irradiation also induced *RET* oncogene rearrangements, which included the same two types of rearrangements observed in the X-irradiated thyroid cells (8505C). These results support the hypothesis that some radiation-induced thyroid cancers, including those among

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Recent Scientific Publications

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atomic-bomb survivors, might have developed when a growth advantage was obtained through a specific form of *RET* oncogene rearrangement induced by radiation exposure.

Genetic alterations in thyroid tumor progression: association with p53 gene mutations. T Ito, T Seyama, T Mizuno, N Tsuyama, Y Hayashi, K Dohi, N Nakamura, M Akiyama. *Jpn J Cancer Res* 84:526–31, 1993 (based on RERF Technical Report 3-92).

Report of a workshop on the application of molecular genetics to the study of mutation in the children of atomic-bomb survivors. JV Neel, C Satoh, RM Myers. *Mutat Res* 291:1–20, 1993 (based on RERF Commentary and Review 5-92).

Joint analysis of site-specific cancer risks for the atomic-bomb survivors. DA Pierce, DL Preston. *Radiat Res* 134:134–42, 1993 (based on RERF Technical Report 17-91).

Radiosensitivity of atomic-bomb survivors as determined with a micronucleus assay. S Ban, JB Cologne, S Fujita, AA Awa. *Radiat Res* 134:170–8, 1993 (based on RERF Technical Report 10-92).

Dose survival of G_0 lymphocytes irradiated in vitro: a test for a possible population bias in the cohort of atomic-bomb survivors exposed to high doses. N Nakamura, R Sposto, M Akiyama. *Radiat Res* 134:316–22, 1993 (based on RERF Technical Report 8-92).

Human chromosome 8 (p12→q22) complements radiosensitivity in the severe combined immune deficiency (SCID) mouse. M Itoh, K Hamatani, K Komatsu, R Araki, K Takayama, M Abe. *Radiat Res* 134:364–8, 1993 (based on RERF Manuscript 24-93).

Cytogenetic and molecular changes in leukemia among atomic-bomb survivors. N Kamada, K Tanaka, N Oguma, K Mabuchi. *J Radiat Res* (Tokyo) 32(S2):257–65, 1991.

The International Chernobyl Project. Technical Report. Assessment of Radiological Consequences and Evaluation of Protective Measures. IAEA International Advisory Committee (I Shigematsu, chairman). Vienna, IAEA, 1991. 640 pp

Approved Research Protocols

Repertoire of T-cell antigen receptors and activity of hematopoietic progenitor cells in peripheral blood of atomic-bomb survivors. Seishi Kyoizumi, Yoichiro Kusunoki, Seigo Teraoka, Yuko Hirai, Tomonori Hayashi, Mitoshi Akiyama, Shoichiro Fujita. **RERF RP 1-93.**

As part of its study of the late effects of atomic-bomb (A-bomb) radiation, the Department of Radiobiology has investigated immunology (RP 3-87), T-cell mutations (RP 4-87), and stem-cell mutations (RP 7-89). In this proposed study, a follow-up to these three earlier research protocols, the functions of T cells and hematopoietic progenitor cells in the peripheral blood of 1280 A-bomb survivors will be analyzed in more detail to elucidate further the late effects of A-bomb radiation on the hematolymphoid system. The repertoire of T-cell-receptor (TCR) variable-region (V) genes of mature T cells in peripheral blood will be studied by flow cytometry using antibodies against the products of TCR V genes and by T-cell responsiveness to superantigen staphylococcal enterotoxins. Peripheral-blood progenitor cells will also be measured using flow cytometry and the hematopoietic colony assay. These studies will address the late effects of radiation on the generation of T-cell diversity and the production of hematopoietic cells.

Development of assay for somatic mutation at the locus of the neutrophil Fcγ receptor III gene and preliminary study on atomic-bomb survivors. Yoichiro Kusunoki, Seishi Kyoizumi, Yuko Hirai, Shoichiro Fujita, Mitoshi Akiyama. **RERF RP 2-93.**

Mutant cells at the lymphocyte hypoxanthine-guanine-phosphoribosyl-transferase locus, T-cell-receptor loci, human-leukocyte-antigen loci, and erythrocyte glycophorin-A (GPA) locus have been analyzed to detect human somatic mutations. Here, we propose development of a novel assay to detect mutations at the neutrophil Fcγ-receptor-III (FcγRIII) locus and a preliminary study to determine whether the assay can be applied to biological dosimetry of atomic-bomb (A-bomb) survivors. Codominant alleles NA1 and NA2 exist at the neutrophil FcγRIII locus, and the assay is based on detection of mutant neutrophils lacking expression of NA1 or NA2 antigens, using flow cytometry, among cells from NA1/2 heterozygotes. Because about 50% of the Japanese population is NA1/2 heterozygous, mutant frequency will be measured among half of the A-bomb survivors. In the proposed study, detection of mutant cells will first be attempted using cells from several NA1/2 heterozygous volunteers to establish measurement conditions. Second, a preliminary investigation of somatic-mutation frequency will be conducted for about 60 NA1/2 heterozygous A-bomb survivors. Subsequently, for the subjects whose GPA mutation frequency has already been measured, the relationship between GPA and FcγRIII mutation frequencies will be established. If a dose-dependent increase of FcγRIII mutation frequency is observed, DNA analysis will also be attempted using separated FcγRIII mutant cells. The feasibility of a full-scale study will be evaluated on the basis of the results from these experiments. ❑

RERF **update** RERF

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

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