Annual Report

1 April 1992–31 March 1993
Annual Report

1 April 1992–31 March 1993

 Radiation Effects Research Foundation

A Cooperative Japan–United States Research Organization
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Introduction

A Message from the Chairman

by Itsuzo Shigematsu, M.D.

In publishing the RERF annual report for Fiscal Year 92, I wish to express my deep appreciation to the atomic-bomb survivors and many other people for their cooperation in the research program of the Foundation.

To begin with, the report of the RERF Committee to Determine Future Resource Requirements for Research Activities was approved at the Board of Directors meeting this year, which has historical significance for RERF. The future resource requirements have carefully been reviewed since establishment of the in-house Review Committee in September 1981. Also, in response to the strong request Hiroshima City has been making for some years for the relocation of the Hiroshima Laboratory facilities, negotiations have been held between the authorities of the U.S. and Japan who are in charge of RERF. With promising prospects for relocation in sight, some suggestions on research projects and resource requirements were offered in the report recently approved, assuming relocation at or about the end of 1996. I hope that the officers and staff will act as one and proceed with all the energy they have for the cooperation of construction of the new facility and for carrying out steadily RERF’s future research direction.

As for international collaborative activities, RERF has, in addition to the on-site investigation of the late effects of the Chernobyl nuclear-power-plant accident, actively extended its cooperation in the acceptance and training of research scientists from the former Soviet Union. I believe that we should continue to offer our cooperation in this field provided that it does not interfere with the principal activities of RERF. Furthermore, importance should be attached to our relationship with the local communities, particularly in Hiroshima with the Hiroshima International Council for Health Care of the Radiation-exposed (HICARE) and in Nagasaki with the Nagasaki Association for Hibakushas’ Medical Care (NASHIM).

In the appointment of officers, the following changes have occurred. Dr. Mortimer L. Mendelsohn, scientific councilor, was elected to the vacant post of permanent director. Dr. Seymour Abrahamson and Dr. John B. Little were elected, respectively, as successors to Dr. James E. Trosko, chief of research, and Dr. Mendelsohn, scientific councilor. Mr. Tadashi Nakaoka, assistant chief of the Nagasaki Laboratory Secretariat, was appointed as successor to Mr. Yoshio
Okamoto, Operating Committee member (chief of administration of the Nagasaki Laboratory), who retired, having reached the mandatory retirement age. I wish to express my deepest appreciation to the retiring directors and the Operating Committee member for their contribution to the Foundation. The total number of officers and staff of the Foundation as of the end of FY92 was 431, of whom 62 were research scientists.

With enactment of the child-care leave law, the "Regulations concerning Child-care Leave" were developed at the Foundation and put into effect on 1 April 1992.

As for the settlement of accounts for this fiscal year, the income—mainly subsidies provided equally by the U.S. and Japanese governments—amounted to ¥4,914,003,334, and the expenditures ¥4,614,362,352. The balance of ¥299,640,982—a surplus in the budget for personnel costs—will be returned to the governments of the two countries.

In conclusion, I pray for the repose of the many atomic-bomb survivors who passed away during the year.
A Message from the Vice Chairman  
by J.W. Thiessen, M.D.

Last year I referred to a crescendo in RERF's research activities. This year confirms the trend: 29 reports were approved, compared with 25 last year, again with some landmark publications among them. The first comprehensive report on solid-tumor incidence, covering the period 1958 through 1987, was approved, followed a little later by one on leukemia incidence from 1950–1987. In this year, the systematic study of the factors confounding the radiation response in specific cancers was begun. A number of reports on breast cancer illustrate this issue, and others will follow in the coming years. Some studies provide updates of the old tentative 1965 dosimetry-based data using Dosimetry System 1986 (DS86), e.g., those on cataracts and stable chromosome aberrations. The reader is urged to scan the summaries of the technical publications in this report (see p. 35), which will provide an annual insight into RERF's research developments over a time span of 1 year that is hard to obtain otherwise.

In the last 5 years or so, it has become customary to have one workshop per year devoted to a particular issue of interest in the framework of RERF's research activities. This has become an especially efficient way to identify those areas in which improvement can and should be obtained. World authorities are invited to these "working meetings." This year's workshop was devoted to medical surveillance, i.e., the periodic examination of apparently healthy people to determine early signs of disease, especially radiation-induced disease. The recommendations of this workshop will give guidance to the Adult Health Study, which needs to address the special problems related to an aging and decreasing population, with an attendant decrease of relevant information on health and disease. Increasing the examination frequency, improving the periodic contacts with the study participants, and the addition of tests and examinations of particular importance in older individuals are being considered.

This vice chairman will be retiring soon after the beginning of the next fiscal year, to be succeeded by Mortimer Mendelsohn. My tenure here has lasted nearly 6 years, during which period I have seen continuous change to a leaner RERF, but—I hasten to add—also a more productive research program. In these years, I have become impressed with the enormity of the task remaining and with the little time
available for it. It will become extremely important to maintain the highest degree of participation of the A-bomb survivors, especially those who were very young at the time of the bombings, and who are beginning to enter a period in which aging and disease are beginning to make themselves felt. Given the degree of cooperation we have enjoyed in the past, I am sure that the future will allow us to finish our studies in an appropriate and efficient fashion. I hope that both governments will see fit to maintain their support of this unique research endeavor, so important to science and medicine worldwide.
Research Activities

Fiscal Year 1992 Progress Report

Departments of Statistics and Epidemiology

We have completed the Life Span Study (LSS) on cancer incidence, which will be described in four papers to be published as a special issue of the journal Radiation Research. Table 1 summarizes solid-cancer risk estimates by cancer site or organ system. What is not obvious from this table is that both liver and nonmelanoma skin cancer now demonstrate significant excess relative risk with radiation exposure. The risk of solid tumors is also about two times greater in females than males, and relative risk decreases with increasing age at the time of exposure. More specifically, as described below for breast cancer, the highest relative risks were seen among the youngest groups; older cohorts have a relatively constant relative risk.

A series of four reports on breast-cancer studies through 1985 was completed. Some of the important points are summarized as follows. The relative radiation risk is higher in the cohorts who were younger at the time of the bombings (ATB), i.e., the groups exposed in childhood and adolescence. Surprisingly, although the natural incidence of breast cancer among Japanese women is extremely low relative to Caucasian populations, the level and temporal pattern of the excess absolute risks were similar in both groups (Japanese and Caucasian). In a site-specific study of 807 breast cancers, nearly 40% occurred in women who were less than 20 years old ATB. For those cases manifest before the age of 35, the excess relative risk was seven times greater than in the groups age 35 or older ATB (14 vs 2). The authors postulate that the early-onset cases could represent cases in which the women had inherited a defective tumor-suppressor gene predisposing them to radiation-induced events. Since the Radiobiology Department has already begun molecular analyses of breast-tumor tissue, we can expect this model to be tested. A case-control study on breast cancer investigated the involvement of other risk factors. Age at first pregnancy was strongly and positively associated with risk, whereas the number of births and lactation periods were strongly and negatively associated with risk. Clearly this demonstrates that hormonal interactions play an important role. Further studies conducted in Nagasaki also have demonstrated that menopause onset was earlier in all birth cohorts by as much as 1 year for women exposed to high doses, and investigating a possible association between breast cancer and early onset of menopause is of great importance. Also we note that tamoxifen may become widely used as a prophylaxis, particularly for women at high risk of breast cancer, and we should be alert to its use in Japan.
### Table 1. Summary of risk estimates by cancer site or organ system

<table>
<thead>
<tr>
<th>Cancer site/organ system</th>
<th>Percent of total cases</th>
<th>ERR(_{1\text{sv}})</th>
<th>EAR per 10,000 PYS(_{v})</th>
<th>AR%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total solid tumors</td>
<td>100.0</td>
<td>0.63</td>
<td>29.7</td>
<td>11.6</td>
</tr>
<tr>
<td>Oral cavity and pharynx</td>
<td>1.5</td>
<td>0.29</td>
<td>0.23</td>
<td>9.1</td>
</tr>
<tr>
<td>Digestive system</td>
<td>55.7</td>
<td>0.38</td>
<td>10.4</td>
<td>7.8</td>
</tr>
<tr>
<td>Esophagus</td>
<td>2.1</td>
<td>0.28</td>
<td>0.30</td>
<td>6.5</td>
</tr>
<tr>
<td>Stomach</td>
<td>30.9</td>
<td>0.32</td>
<td>4.8</td>
<td>6.5</td>
</tr>
<tr>
<td>Colon</td>
<td>5.3</td>
<td>0.72</td>
<td>1.8</td>
<td>14.2</td>
</tr>
<tr>
<td>Rectum</td>
<td>4.1</td>
<td>0.21</td>
<td>0.43</td>
<td>4.4</td>
</tr>
<tr>
<td>Liver</td>
<td>6.8</td>
<td>0.49</td>
<td>1.6</td>
<td>10.9</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>3.4</td>
<td>0.12</td>
<td>0.18</td>
<td>2.2</td>
</tr>
<tr>
<td>Pancreas</td>
<td>2.8</td>
<td>0.18</td>
<td>0.24</td>
<td>3.5</td>
</tr>
<tr>
<td>Respiratory system</td>
<td>11.9</td>
<td>0.80</td>
<td>4.4</td>
<td>16.3</td>
</tr>
<tr>
<td>Trachea, bronchus, and lung</td>
<td>10.1</td>
<td>0.95</td>
<td>4.4</td>
<td>18.9</td>
</tr>
<tr>
<td>Nonmelanoma skin</td>
<td>2.0</td>
<td>1.0</td>
<td>0.84</td>
<td>24.1</td>
</tr>
<tr>
<td>Female breast</td>
<td>6.1</td>
<td>1.6</td>
<td>6.7</td>
<td>31.9</td>
</tr>
<tr>
<td>Uterus</td>
<td>8.4</td>
<td>–0.15</td>
<td>–1.1</td>
<td>–3.3</td>
</tr>
<tr>
<td>Ovary</td>
<td>1.5</td>
<td>0.99</td>
<td>1.1</td>
<td>17.7</td>
</tr>
<tr>
<td>Prostate</td>
<td>1.6</td>
<td>0.29</td>
<td>0.61</td>
<td>7.0</td>
</tr>
<tr>
<td>Urinary organs and kidney</td>
<td>3.8</td>
<td>1.2</td>
<td>2.1</td>
<td>22.3</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>2.4</td>
<td>1.0</td>
<td>1.2</td>
<td>16.3</td>
</tr>
</tbody>
</table>

Continued
Table 1. Continued

<table>
<thead>
<tr>
<th>Cancer site/organ system</th>
<th>Percent of total cases</th>
<th>ERR$_{1Sv}$</th>
<th>EAR per 10,000 PYSv</th>
<th>AR%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney, renal pelvis, and ureter</td>
<td>1.2</td>
<td>0.71 (0.11; 2.2)</td>
<td>0.29 (-0.50; 0.79)</td>
<td>15.2 (-2.6; 41.3)</td>
</tr>
<tr>
<td>Nervous system</td>
<td>1.5</td>
<td>0.26 (-0.23; 1.3)</td>
<td>0.19 (-0.17; 0.81)</td>
<td>5.7 (-5.3; 24.5)</td>
</tr>
<tr>
<td>Thyroid</td>
<td>2.6</td>
<td>1.2 (0.48; 2.1)</td>
<td>1.6 (0.76; 2.5)</td>
<td>25.9 (12.4; 40.7)</td>
</tr>
</tbody>
</table>

*254 solid cancers of other and ill-defined sites are included in the "Total solid tumors" category.

Notes: ERR = excess relative risk; EAR = excess absolute risk; AR = attributable risk.

For the leukemias, the pooled analyses of all subtypes showed a statistically significant nonlinear dose response that exhibits a complex dependence on sex and time since exposure. Analyses of specific subtypes showed statistically significant excess risks for acute lymphocytic leukemia, acute myelogenous leukemia, and chronic myelogenous leukemia. We found no evidence that the shape of the dose response differed by subtype but found significant differences between these leukemia subtypes with respect to the nature of the effects of sex and age at exposure on excess risk. No evidence was found for a radiation effect on adult T-cell leukemia incidence, which accounts for about 30% of all Nagasaki leukemia cases in the LSS. The LSS did not provide any useful information on chronic lymphocytic leukemia. The much-larger incidence studies (as compared to the mortality studies) provided no convincing evidence for a dose-related increase in either lymphoma or myeloma.

In our continuing studies on the in-utero-exposed cohort, reanalysis of earlier data on body size determined at maturity, using the Dosimetry System 1986 (DS86) doses demonstrated a dose-related reduction in all endpoints measured, with no evidence of a specific sensitivity for different gestational ages. These results parallel those also recently recalculated for body size and weight for the postnatal groups age 0–10 years.

A report by Tore Straume et al. (*Health Physics* 63:421–6, 1992), based on neutron-activation studies, described indirectly discrepancies in DS86 with respect to neutron dose. Their estimates suggested that neutron doses should be increased by a factor of 2 at 1 km and by a factor of 10 at 1.6 km. Members of the Statistics Department reanalyzed the cancer mortality data with the recommended correction factors and concluded that a decrease in excess relative risk, ranging between 3% and 22% for a relative biological effectiveness (RBE) of 1–20, would occur, primari-
ly because of the large population with low doses, for whom little absolute change in total dose equivalent would be manifest. To gain some perspective on the size of these changes, it is useful to note that allowing for random errors in individual dose estimates tends to increase risk estimates by 10% to 15%.

Over the past few months several RERF staff members from both departments have been considering several issues related to the presentation and use of cancer-risk estimates derived from the LSS data. Two of the primary factors motivating this review are (1) the need to reconsider the nature of the LSS mortality reports now that detailed information on cancer incidence is available for the LSS cohort and (2) the involvement of RERF's Statistics Department chief in the revision of a United Nations Scientific Committee on the Effects of Atomic Radiation report on epidemiological studies of radiation carcinogenesis.

Of particular concern are the inadequacies of the simple average risk estimates, e.g., the excess relative risk at 1 Sv or the average excess absolute risk per 10^4 person-year-sievert (PYSv), used to summarize radiation risks. These statistics are of limited use because they depend on the length of follow-up and because they involve an implicit weighting by age at exposure and sex that is dependent on the age-at-exposure and sex distributions of the LSS population. Among other things, concerns about the nature of the standard risk summaries have led us to consider uncertainties in lifetime risk estimates for the LSS data.

An important consideration in the use of the LSS data for risk estimation concerns the impact of projection beyond the end of the current follow-up. Table 2 presents solid-tumor lifetime risk estimates computed from current LSS mortality data (1950–1987) under various assumptions about methods for projecting risks beyond the end of the current follow-up period. Three projection methods were considered, all based on the same time-constant relative-risk model in which the excess relative risk is allowed to depend on sex and age at exposure. The first two columns of Table 2 contain estimates of the percentage of the population that will incur a radiation-induced excess death (RIED) and of the years of life lost per excess cases (LLC) assuming that risks will remain at their current level. The next four columns involve nonconstant risk projections, for which risks are allowed to decrease starting 45 years after exposure. The first of these models assumes that by the time a person reaches age 90 he/she will have excess relative risks identical to those of a person who was 50 at the time of exposure. The second model assumes that excess risk falls to zero by age 90. Comparing the numbers in this table indicated that for survivors who were older than about 30 ATB the method used for projecting risks has virtually no effect on the RIED or LLC. However, changing the assumptions regarding changes in risks in the remaining years of follow-up can change this measure of lifetime risk by an order of magnitude for the youngest survivors. This result highlights the importance of continued follow-up of the LSS.
Table 2. Lifetime excess solid-tumor risks following exposure to 1 Gy at various ages

<table>
<thead>
<tr>
<th>Age at exposure (y)</th>
<th>Excess lifetime risk (%)</th>
<th>LLC (y)</th>
<th>Excess lifetime risk (%)</th>
<th>LLC (y)</th>
<th>Excess lifetime risk (%)</th>
<th>LLC (y)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Constant relative risk&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Risk at exposure (age 50)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Zero&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>18.2</td>
<td>12.5</td>
<td>10.2</td>
<td>14.9</td>
<td>0.6</td>
<td>41.7</td>
</tr>
<tr>
<td>5</td>
<td>16.3</td>
<td>12.4</td>
<td>10.1</td>
<td>14.6</td>
<td>1.0</td>
<td>36.8</td>
</tr>
<tr>
<td>10</td>
<td>14.5</td>
<td>12.3</td>
<td>9.9</td>
<td>14.3</td>
<td>1.5</td>
<td>32.3</td>
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<tr>
<td>15</td>
<td>12.9</td>
<td>12.2</td>
<td>9.7</td>
<td>13.9</td>
<td>2.2</td>
<td>28.2</td>
</tr>
<tr>
<td>20</td>
<td>11.5</td>
<td>12.1</td>
<td>9.4</td>
<td>13.5</td>
<td>3.0</td>
<td>24.5</td>
</tr>
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<td>25</td>
<td>10.2</td>
<td>11.9</td>
<td>8.9</td>
<td>12.9</td>
<td>4.0</td>
<td>21.0</td>
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<td>30</td>
<td>9.0</td>
<td>11.7</td>
<td>8.4</td>
<td>12.3</td>
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<td>17.6</td>
</tr>
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<td>35</td>
<td>7.9</td>
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<td>40</td>
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<td>45</td>
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</tr>
<tr>
<td>55</td>
<td>4.7</td>
<td>9.7</td>
<td>4.7</td>
<td>9.7</td>
<td>4.7</td>
<td>9.7</td>
</tr>
<tr>
<td>60</td>
<td>4.0</td>
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<td>8.7</td>
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<td>8.7</td>
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<tr>
<td>65</td>
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<td>70</td>
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<td>2.6</td>
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<tr>
<td>75</td>
<td>1.9</td>
<td>4.4</td>
<td>1.9</td>
<td>4.4</td>
<td>1.9</td>
<td>4.4</td>
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</tbody>
</table>

Notes: Estimates of the risk of radiation-induced excess death (RIED) computed using sex and age-at-exposure specific relative risks estimated for the LSS cancer mortality data for the period from 1950 to 1987. Risks were applied to 1985 Japanese death rates. Since sex-specific estimates of the excess risk were virtually identical, the estimates in this table are averaged over sex. LLC = life lost per case.

<sup>a</sup>Risk was assumed constant for all time after exposure.

<sup>b</sup>Constant relative risk for the first 45 years after exposure; the risk then decreases geometrically. At attained age 90 the risk is equal to that for a person aged 50 at exposure.

<sup>c</sup>Constant risk for the first 45 years after exposure; the risk then decreases geometrically. At attained age 90 the risk is 0.

<sup>d</sup>Percent of population that would die due to a radiation-induced cancer (radiation-induced excess death).

<sup>e</sup>Average years of life lost per radiation-induced excess death. The average years of life lost per exposed person is equal to LLC × RIED + 100.
Since 1991 the members of these two departments have been associated with 92 journal publications.

**Department of Clinical Studies**

Research resulting from the clinical program that follows up the Adult Health Study (AHS) population continues to provide deeper insights into radiation-induced mechanisms of chronic disease.

Studies of cardiovascular diseases have revealed a dose-related increase, particularly among the high-dose, young-ATB individuals. The issue is whether the increase in the relative risk of diseases such as myocardial infarction (MI) is a direct effect of radiation or an indirect effect through interaction with other risk factors. Cox regression analysis indicated that systolic blood pressure, cholesterol level, and tobacco smoking, in addition to sex and age, had a significant effect on MI incidence but radiation had no such effect. These results suggest that radiation acts indirectly on coronary heart disease through its interaction with these other risk factors. Given that the AHS population primarily comprises those who were young ATB, one can expect to collect a wealth of informative data as this population reaches the ages when cardiovascular disease becomes the prevalent cause of death.

The temporal incidence of natural menopause has been continuously studied since 1958 among more than 1500 members of the Nagasaki Adult Health Study. The excess relative risk of early onset of natural menopause in relation to ovarian dose follows a purely quadratic response regardless of the cohort’s age. At a dose of 2 Gy, early onset of menopause, i.e., 1–2 years (median age) earlier, was seen. This study supports the hypothesis that the progress to certain physiological endpoints is accelerated by radiation exposure. Research projects are now being planned to monitor hormonal changes in premenopausal women. Since, as described earlier, hormonal changes and age at menopause are factors that affect the onset of breast cancer, the menopause studies may augment RERF’s epidemiological data on the radiosensitivity of breast and other hormonally responsive tissue.

Members of this department have co-authored 21 publications since 1991.

**Department of Radiobiology**

Specific-locus somatic mutations in T cells have clearly demonstrated a survival curve (showing about a 2-year half-life) similar to that of unstable chromosome aberrations. Thus, such mutations are not useful biodosimetric markers for the A-bomb survivors, unlike erythrocyte glycophorin-A (GPA) mutations and stable chromosome aberrations. However, the T-cell marker systems developed at RERF are indeed useful as a measure of recent radiation exposures, as was demonstrated using radiotherapy patients. Theoretical analyses developed at RERF appear to show that the precursor T-lymphocyte stem-cell population, which repopulates the naive T-cell population over a several-year interval, is relatively small (10^4 cells or less).
In such a small number of stem cells, appreciable numbers of radiation-induced mutations at a specific locus are not likely to be found since induced mutation rates are on the order of $10^{-5}$ or much less at the doses received by the AHS survivors. For these and other reasons, new assays are being developed using neutrophil cells that, like erythrocytes, are derived from hematopoietic stem cells. Because the neutrophils are nucleated, this system offers the advantage of revealing the molecular nature of induced mutations, which is not possible with red blood cells.

As for the GPA mutation assay, a new, less-expensive assay that allows detection simultaneously of four mutant phenotypes was developed using the FACScan. In addition, erythroid progenitor stem cells that express GPA in culture after 2 weeks can be isolated. Therefore, the study of stem-cell mutations of A-bomb survivors in culture appears possible, and this work is being actively pursued. To date, GPA mutation rates in more than 1000 survivors in both cities have been ascertained. Since the individuals in these cohorts overlap those also studied for chromosome aberrations and other clinical endpoints, it might be possible to determine how well such endpoints correlate and what conditions may have influenced the response of outlier individuals—more specifically whether, e.g., outliers represent unique radioresistant or radiosensitive individuals, dosimetry errors, or are simply the result of random sampling.

Considerable progress has been made toward cloning of the human gene that corrects the defect causing severe combined immunodeficiency (SCID) in the mouse; i.e., various transfection experiments using SCID mouse fibroblast cells have converted these highly radiosensitive cells to a radioresistant and bleomycin-resistant phenotype. Successful cloning of the normal and/or mutant SCID gene is expected to provide valuable information on the nature of radioresistance or radiosensitivity and the role of gene products. SCID mice, in addition to being extremely radiosensitive, have abnormal B- and T-cell functions, which are being studied. Cell-free systems are being established to analyze the function of SCID gene products in the rearrangement of the VDJ regions of the immunoglobulin genes.

In the area of molecular epidemiology, analysis of molecular changes of the p53 gene and other tumor-suppressor systems in breast, lung, and skin cancer using polymerase chain reaction (PCR) techniques is in progress. In in-vitro irradiation studies of normal cells, chromosome rearrangements at the RET and ABL oncogene sites were observed, simulating the natural occurrence of these malignant events. DNA sequence studies have shown that the rearrangements occur at the same two DNA sites as found in cancerous tissue and, in several cases, at sites within the gene that have not yet been described as being associated with in-vivo cancer.

During the 1991–93 period, the department has been responsible for more than 40 journal publications.
Department of Genetics

Laboratory of Cytogenetics

The main objective of the cytogenetic project at RERF is to investigate the relationship between the frequency of stable chromosome aberrations (mostly reciprocal translocations) and estimated radiation doses assigned to individual A-bomb survivors.

The results obtained to date confirmed the usefulness of the frequency of cells with stable chromosome aberrations, detected by conventional techniques, as a long-term indicator of the effect of radiation exposure. However, detection methods now in use are considered to be too time-consuming and laborious to detect induced chromosome aberrations for a large population (50 cells/day/examiner for the conventional staining method). This is especially true of the G-banding method (20 cells/day/examiner). Furthermore, identifying the subtle structural alterations of chromosomes is difficult even for experienced cytogeneticists, and such aberrations could easily be overlooked.

To overcome such technical difficulties, joint research was conducted by RERF and Lawrence Livermore National Laboratory to test the utility of the fluorescence in-situ hybridization (FISH, or “chromosome painting”) technique for rapidly and accurately detecting reciprocal translocations observed in the peripheral lymphocytes of A-bomb survivors.

Recent advances in RERF’s cytogenetic studies are summarized as follows:

1. Conventional cytogenetic analysis: an update

Daniel Stram et al. (RERF Technical Report 13-92; Radiat Res 136:29–36, 1993) statistically updated stable chromosome aberration data on 1703 AHS subjects by including data obtained between 1968 and 1985. Their major finding was an indisputable relationship between stable chromosome aberration frequencies and estimated radiation dose. They attempted to model this dose response as a quadratic function of dose, which appears to fit the data reasonably well over the dose range of 1–4 Sv, with a neutron RBE of 10. The dose-response shape, however, differs significantly by city on the basis of the quadratic component of the model. Data from Nagasaki showed much more of an upward curvature than is shown by the chromosome data in Hiroshima. The differences in the apparent dose-response shape between the two cities is not easily explained by differences in the neutron RBE.

Stram et al. have further observed that time-of-assay effects occurred despite efforts throughout the course of the examination to maintain consistent laboratory methods. Some of the difference can clearly be attributed to improvements gained through experience in both cell-culture technique and the techniques for scoring chromosome aberrations. In the early 1970s, a decision made to reduce the volume of material processed may also have improved the quality of chromosome slide preparations.
The data also suggest a complex, nonlinear interaction between radiation and age at exposure on the stable chromosome aberrations measured many years later. Evidence was found that radiation exposure was more effective in producing these aberrations at some lower ages at exposure, although interpretation of the pattern of this interaction is difficult.

Adjustment of the regression results for random dose errors of approximately 35% and 50% increases both the estimated dose response and the strength of its quadratic component, findings consistent with the discussion of Donald Pierce and Michael Vaths (RERF Commentary and Review Series 2-89). DS86 dose estimates contain systematic errors due to inaccuracies in current knowledge of survivor location and the yield of the bombs or in factors affecting radiation transport. The task of biologically assessing dose, using dosimeters such as stable chromosome aberrations, includes validating the existing physical dosimetry and using biological outcome as a surrogate for unavailable physical dosimetry. The aberration data for the A-bomb survivor cohort may be regarded as biologically verifying the plausibility of the DS86 system used in assigning doses to the survivors. New biological dosimetry data, such as measurements of somatic cell mutations (e.g., obtained via the GPA mutation assay), currently are being added to RERF's collection of biological evidence of radiation exposure of the A-bomb survivors. Thus, the A-bomb-survivor data are distinguished not only by a physical dosimetry but also by biological data related to radiation exposure.

To determine if differences in the biological effects can be attributed to differing neutron doses in the two cities, a study was begun to analyze the Poisson distribution in the number of breaks per cell among survivors having doses ranging between 0.5–2.0 Gy in both Hiroshima and Nagasaki. After adjustment for dose, the data did not suggest a city difference in the distributions of multiple events per cell, on the basis of the sample size studied.

A routine cytogenetic assay, involving conventional aberration analysis, was recently completed on 622 Hiroshima AHS subjects whose blood samples were collected between 1984 and 1986. This study included 424 proximally exposed survivors (0.005–4.0 Sv; neutron RBE of 10) and 198 distally exposed survivors (0 Sv). Excluded were (1) those who had been diagnosed as having malignant tumors before cytogenetic examination, (2) those who had ever received radiation treatment, and (3) those who were found to carry a clone of cells with stable chromosome aberrations.

Preliminary analysis showed the dose response to be linear among the Hiroshima survivors. This trend has been repeatedly demonstrated by Richard Spoto et al. (RERF Technical Report 7-90; Radiat Res 128:157–69, 1991) and Stram et al. (loc cit).
2. G-banding data

To determine the types and frequencies of radiation-induced chromosome damage, K. Ohtaki and E. Nakashima (RERF Technical Report 1-93; *Jpn J Hum Genet* 37: 245–62, 1992) carried out an extensive G-band analysis of somatic chromosomes of 63 Hiroshima A-bomb survivors (11 distally exposed, 52 proximally exposed), assuming that G-band analysis can detect all chromosome aberrations with full scoring efficiency. The results confirmed previous findings from conventional analysis that cells with stable chromosome aberrations predominated among the aberrant cells detected. The dose response seemed linear for stable chromosome-aberration frequencies.

3. FISH technique for detecting translocations in A-bomb survivors

To determine the power of the scoring efficiency for detecting translocations, both FISH and G-band analyses were performed on 36 Hiroshima survivors having estimated DS86 kerma ranging from 0–4 Gy (J. Lucas et al. (RERF Technical Report 16-92; *Int J Radiat Biol* 62:53–63, 1992)). FISH was applied to metaphase spreads using a mixture of composite DNA probes specific for chromosomes 1, 2, and 4, so that targeted chromosomes were stained yellow, whereas nontargeted chromosomes were stained red. The translocations could be recognized as being bicolor. Using both FISH and G-banding data plotted against DS86 bone-marrow dose (neutron RBE of 10), a dose-dependent increase in translocation frequency is seen. With a few exceptions, intraindividual agreement between the FISH and G-banding analyses was remarkable. The slope of a linear regression coefficient between FISH and G-banding data was 0.84 (*r* = 0.95, *p* < 0.001, *n* = 36). Consequently, the patterns in the dose response for translocation frequencies in the two determinations were similar.

The in-vivo study using the FISH technique showed that using whole-chromosome probes allows rapid and accurate screening for structural aberrations that have persisted for several years in lymphocytes of A-bomb survivors. The power of translocation scoring efficiency was about 500 metaphase/day/examiner for FISH compared to 20–30 metaphases/day/examiner for G-banding, and about 50 cells/day/examiner for conventional analysis.

Regarding whether the outliers seen in our dose-response studies represent individuals with markedly different radiosensitivities or represent dosimetry bias, one final point is quite important.

A small fraction of survivors had grossly discrepant translocation frequencies relative to the DS86 dose estimates. When the shielding factors for individuals were considered, the range of variation in translocation frequencies became narrower for those survivors exposed inside a Japanese-type house. However, the range of variation was wider for those who were either exposed in the open or who were outdoors but shielded by a Japanese-type building. Since the present results were
derived from only a few cases, further detailed study is needed, but the implications of the aberration with regard to dosimetry bias are obvious.

Laboratory of Biochemical Genetics

Extensive studies on the children of survivors of the atomic bombings thus far have shown no statistically significant increase in genetic effects compared with a control population. To genetically evaluate these children, technologies for screening mutations at the nucleotide level have been developed and permanent B-lymphocyte cell lines from families of A-bomb survivors and controls have been established. The Workshop on Human Germline Mutagenesis, held at RERF in 1991, recommended completing the sample collection and initiating a pilot study to compare various types of DNA as potential targets for the detection of DNA damage using molecular techniques. These three projects are described next.

1. Establishment of cell lines

The goal of this project is to establish cell lines from members of 1000 families, including 500 families in which one or both parents were exposed to the A-bombings and the combined parental dose is more than 0.01 Sv. The average combined parental dose for these families will be 0.5 Sv. The remaining 500 families are the controls. Each family comprises a mother, a father, and all available children, the minimum being the mother-father-child trio. Thus far, the average is 1.5 children per family. Cell lines are first allowed to proliferate to approximately $1 \times 10^9$ cells and are then preserved in liquid nitrogen. Aliquots of intact lymphocytes and granulocytes are also preserved in liquid nitrogen, as references in the event of unusual findings. To date, cell lines have been established from approximately 2900 individuals (812 trios). Two or three more years will be needed to complete the project.

2. The pilot study

The workshop recommended a pilot study to compare various types of DNA as potential targets for the detection of germinal mutations. The workshop recommended examining 50 families from the exposed population and 50 from the control population, selected from the 1000 families for which permanent cell lines are being established.

In keeping with the recommendations, a pilot study was started in 1992. The "exposed" 50 families comprised 50 pairs of parents and 64 children, and the control families comprised 50 pairs of parents and 60 children. Among the 50 "exposed" families, both parents were exposed in only one family, and the mean gonad dose of the 51 parents was 1.8 Sv. Three experimental methods will be used to detect various types of DNA variants. They are 1) denaturing gradient gel electrophoresis of fragments amplified by polymerase chain reaction (PCR-DGGE), 2) Southern blot
analysis of the products of conventional agarose-gel electrophoresis, and 3) high-resolution electrophoresis of PCR-amplified microsatellites. For methods 1 and 2, we previously carried out feasibility studies, but the third method has just been introduced into our study.

(1) PCR-DGGE: This is currently the technique of choice for detecting “small” variations such as nucleotide substitutions and deletions and insertions of less than 50 nucleotides in genomic DNA. This approach achieves a sequence-specific separation of DNA molecules on a gel. To detect variations in mRNA, a modification of this technique involving reverse transcription (RT) was used in which amplified cDNA, that was reverse transcribed from mRNA is examined. Detectability of variations is, in theory, 100% in a fragment with an artificially attached GC-rich sequence (GC clamp). In the adaptation of this technique employed in our laboratory, a target sequence of approximately 2500 bp of genomic DNA or cDNA was amplified with GC clamps attached at both terminals, cleaved into 4 or 5 fragments of approximately 500 bp with restriction enzymes, and examined by DGGE in a single lane on one 24-lane gel. DNA molecules on the gels were made visible with ethidium bromide.

Genomic sequences of 7636 bp from the p53 gene, genomic sequences of 19,476 bp from the F9 gene encoding human factor IX, cDNA sequences of 3357 bp from the retinoblastoma (RB) gene, and cDNA sequences of 1668 bp from the phosphoglycerate kinase 1 (PGKI) gene of each individual from the 100 families have been examined. No mutations were detected in a total of 3563 kb examined for the 64 children of the “exposed” families and a total of 3095 kb for the 60 control children.

During the screening for mutations in the F9 genes, 18 types of hereditary variants were detected in the children and 4 types of variants were detected only in the parents. In the p53 genes seven types of hereditary variants were detected, and in cDNA of the RB genes one hereditary variant was detected. Those variants for which sequence analysis was completed showed nucleotide substitutions. Thus, this technique can detect small variations.

(2) Southern blotting: This technique is primarily for detecting large insertions/deletions/rearrangements (I/D/R) in unique sequences and changes in number of unit sequences in tandem-repetitive-sequences such as VNTRs or minisatellites, which comprise short-sequence units iterated in tandem to form arrays of about 0.1–20 kb. For the unique sequences, in principle, the I/D/R events can be recognized when bands of abnormal length are detected in at least two independent examinations employing different enzymes with different restriction sites. This procedure excludes the possibility that the abnormal bands are produced by gain or loss of cleavage sites for restriction enzymes due to nucleotide substitutions. For the minisatellites, however, the I/D/R events, resulted in changes in unit numbers, which can be recognized by the appearance of new bands in single examinations.
The children and their parents were examined for RB, p53, and PGK genes with their cDNAs as probes and the α-globin-gene complex with a genomic DNA fragment from the ζ-globin gene as a probe. No mutations were detected in the 64 children from the exposed population and the 60 control children after examinations of 18,392 kb and 16,836 kb, respectively, for these unique sequences.

These children were also examined for the repetitive loci with probes of Pc-1, Co15, M18, and λMS1. The children were examined for the λMS-1 locus on chromosome 1, and four mutations were detected in four children from the exposed families (total number examined 691 kb), whereas eight mutations were detected in seven control children (total number examined 648 kb). However, among the four children in the “exposed” families, only one child showed a mutant allele originating from the exposed father, and the three other children showed alleles originating from the non-exposed parent in the “exposed” families. Therefore, because only one child among 64 children from the “exposed” families has both parents exposed, 65 alleles were derived from the exposed parents and 183 alleles were from the non-exposed parents. The mutation rate per gamete was 1.5% in the exposed parents and 6.0% in the non-exposed parents, which is similar to the 5.2% observed in 40 large families from the Centre d'étude du polymorphisme humain panel composed of 344 offsprings (688 gametes) of Alec J. Jeffreys, who provided the λMS-1 probe. The overall mutation rate per gamete was 4.8%. Heterozygosity for the λMS-1 locus in 200 unrelated parents was 0.97. Although the mutation rate was high at this locus, parental exposure did not seem to affect the germline instability.

No mutations were detected in the remaining Pc-1, Co15, and M18 loci. Thus, among a total of 3300 kb for the repetitive sequences, except for the λMS-1 locus, no mutations were detected. Heterozygosities for the Co15, M18, and Pc-1 loci were 0.95, 0.77, and 0.70, respectively.

(3) PCR high-resolution electrophoresis for microsatellites: Screening of microsatellites for mutations was recommended by the workshop. Microsatellites consist of around 10–50 copies of motifs from 2–6 bp that can occur either in perfect tandem repetition, as imperfect repeats or together with another repeat type. They are highly polymorphic in copy number of motifs, randomly distributed in human DNAs, and occur frequently. In addition, the aberrant expansion of exonic trinucleotide repeats has recently been found to result in four genetic diseases and represents a new form of mammalian mutagenesis.

Sequences including the trinucleotide repeats are amplified and labeled with $^{32}$P using PCR, and electrophoresis of the products is carried out on a sequence gel. The repeat number in the products can be deduced from the lengths of bands. The CTG repeats in the myotonin kinase gene in the 124 children were examined, and no mutations were detected. Trinucleotide repeats in the FMR-1 gene and the AR gene are being examined.
3. Development of technologies

A technique has been developed that can clearly detect heterozygous carriers of a deletion or a duplication. Specific target sequences were amplified by PCR, and the products were quantitated by high-performance liquid chromatography. The method was applied to the detection of Duchenne-muscular-dystrophy carriers and hemophilia-B carriers. Heterozygous carriers of deletions and carriers of a duplication were clearly differentiated. The efficiency of this technique for mass screening was not determined.

Bands of abnormal length were screened to detect I/D/R events. However, to detect deletions that removed all single alleles, a quantitative analysis searching for a 50% decrease in band intensity is required, because such a mutation would usually be detected by the presence of only one normal allele. Quantitation of chemiluminescent bands on Southern filters for this purpose has just been started, using an image analyzer equipped with a highly sensitive photon camera. Preliminary results show that this technique will be feasible for our purpose.

Two-dimensional gel electrophoresis (2-DE) of DNA, called restriction landmark genomic scanning (RLGS), for screening of mutations has been introduced and improved. One-dimensional electrophoresis was carried out in a vertical agarose disk gel produced in a Teflon tube, and the two-dimensional electrophoresis was carried out in a vertical polyacrylamide slab gel. DNA samples were sequentially digested with two restriction enzymes before the one-dimensional electrophoresis. Between the two digestions, fragments from the first digestion were labeled with $^{32}$P. DNA fragments fractionated by size in the disk gel were digested with a third enzyme, and the resulting gel was overlaid on the two-dimensional gel. After several improvements, aliquots from a single DNA sample presented distribution patterns of spots that could be superimposed.

This method can detect not only base-pair substitutions in the restriction sites but also small I/D/R events. With accurate quantitation of the spots, i.e., detection of a 50% decrease or increase in the intensity of the spots, deletions or duplication occurring in heterozygotes will be detected. The most attractive aspects of this technique are 1) more than 1000 spots are separated, 2) no probes are necessary, and 3) abnormal sequences can be deduced from the sequences analyzed by cloning the spots on the gel. At present, efforts are being made to determine distribution of the spots accurately and to quantitate the intensity of the spots by employing an image analyzer purchased in January 1993.

Quantitation of bands on Southern filters and of spots on 2-DE gels will be introduced into the pilot study when the usefulness of these techniques for mutation screening is confirmed.

The absence of significant differences between the two groups studied in these pilot experiments was not unexpected. Given the assumptions regarding the spontaneous mutation rates of nucleotides, the genetic doubling dose, and the estimated
conjoint parental gonadal dose, we believe that two samples of approximately $10^{10}$ nucleotides must be examined to demonstrate a significant difference between the mutation rates of the two groups.

Members of the Department of Genetics co-authored 31 journal papers since 1991.

**Research Information Center**

In fall 1991, the move began from a mainframe-based computer system to a network of personal computers (PCs) and reduced-instruction-set-computing (RISC) workstations. The first aim of this effort is to improve capabilities and procedures for a) data processing and management, b) integration of data into research applications, c) electronic communication, and d) accessibility to software and information resources. The second aim is to reduce the overall cost of maintaining the new computing system. The combination of running new database software on a workstation and making the database accessible through a network should provide the type of performance and features that allow discontinuation of the inefficient processing and file operations currently conducted on the mainframe computer.

**Personal computers**

To improve the accessibility of computing resources to users, we continued to increase the number of PCs available for use, with a net increase of 23 computers in 1992, bringing the total number at RERF to 193. To test lower-cost alternatives for providing RISC workstation computing capabilities, a Sun Sparc2 clone workstation and a workstation X-terminal were installed within the Research Information Center (RIC).

To provide researchers and research assistants in the departments of Statistics and Epidemiology with access to the analysis and graphics software of their choice and to cut network connection costs in half, PCs in these departments were replaced with IBM-compatible PCs. This transition is nearly complete.

**Network activities**

A total of 26 PCs, 1 RISC workstation, 1 X-terminal, and the NEC ACOS mainframe computer were connected to the RERF network in 1992 (the total number of networked PCs and RISC workstations is 31 and 5, respectively). This effort focused on providing the Departments of Statistics and Epidemiology with computing resources that will eliminate their dependence on mainframe computing. Consequently, nearly all PCs in those areas were integrated into the network. In addition to using PC software to fill analysis needs, staff from these departments can now access workstations to a) use an interim database, b) gain access to additional hard-disk storage space, c) run statistical software (EPICURE, SAS, MATLAB), and d) send output to any laser printer on the network. The network will also enable staff
in these areas to participate in planning and testing activities for database development work pertaining to data from the Master File, Tumor Registry, Life Span Study, and Dosimetry System 1986.

Until all source data are transferred to the workstations, some staff need to access the mainframe computer to download data to PCs or workstations for analysis. The ability to connect to the mainframe computer from an IBM-compatible PC was therefore established. RERF is one of the few organizations where this is possible; previously, only NEC computers and terminals could provide this function. IBM connectivity to the mainframe during the transition to the workstation/PC network eliminates the need for any researcher using IBM PCs to maintain a second computer solely to access data on the mainframe.

To transfer routine data-entry and update activities for the Master File and Tumor Registry data from the mainframe computer to the network and workstations, the activities of both the Hiroshima and Nagasaki laboratories must be transferred off the mainframe simultaneously. This requires linkage of both cities to the RERF network. Accordingly, planning for the establishment of the link with Nagasaki (initially in the departments of Epidemiology and Biometrics and Epidemiologic Pathology) was begun. Linkage of the two cities to form an RERF enterprise-wide network will allow further improvement of communication between the two laboratories by lessening the difficulties posed by physical distance. The link will also improve access to computing resources for the Nagasaki Laboratory.

Electronic communication services

The interim system established to provide limited electronic-mail (e-mail) service at RERF was replaced in July 1992 with a full-featured system through cooperative efforts with staff at Hiroshima and Keio universities. The Japan Widely Integrated Distributed Environment (WIDE) network was extended to Hiroshima and a network operations center (NOC) was established at Hiroshima University. RERF installed a dedicated, high-speed communications line to connect to the NOC. The connection provides 24-hour operation of e-mail within Japan and to/from international sites. Transmission time is nearly instantaneous. Since installation of the new system, e-mail has been found to be the preferred method of communication with countries such as the republics of the former Soviet Union, where telephone-line noise renders communication by fax quite unreliable.

In October 1992, approval of international registration of RERF on the Internet network allowed high-speed file transfer and remote login to other computing facilities located within Japan and around the world. Through the Internet, RERF now has access not only to research scientists in the international community but also to a wide variety of resources, databases, and information services maintained at sites around the world.
E-mail is available in both Japanese and English on the workstations. However, only English-language e-mail is available on PCs at RERF, because appropriate Japanese-language PC e-mail software could not be found.

**Workstation activities**

Workstation software and services were made available for the first time to users in 1992.

Newly introduced software on the workstation in 1992 include SAS statistical software and S+ graphics software, both of which allow faster processing and larger analyses than were previously possible. *EPICURE* and *MATLAB*, both statistical software packages, were also installed.

The workstations were configured to provide specific functions on the network. Of the three Sun Microsystems workstations (Sparc2 model), one functions as the mail server, processing all e-mail and news within RERF and to/from points outside RERF. A second acts as the database server, which handles database development work and user access to the RERF database. A third workstation functions as an application server, handling execution and processing of all workstation statistical and graphics software. A fourth NEC workstation serves as the gateway through which the mainframe computer is accessed. A fifth workstation, a Sun Sparc2 clone, is used for systems administration work and handles multi-user execution of the *Crisp* text-editor software. The workstation X-terminal is used by RIC programmers for application development work.

Planning began for the transfer off the mainframe computer of RERF business administration activities, which include accounting, payroll, personnel, supply, and inventory. The hardware and software constituting the new system must be compatible with computers already being used in RERF departments so that information collection and reporting between departments and the Secretariat will be timely, efficient, and relevant to needs at both the Foundation-wide and departmental levels.

**System integrity**

The workstations provide improved system integrity compared to the mainframe computer in two important aspects. First, all workstations have been connected to uninterruptible power supply (UPS) units. These devices provide protection against short power outages and automatically conduct an orderly shutdown of the workstations and network in the event of a long power outage.

**System security**

Two software-security systems were installed on the network. The first, *CRACK*, checks for easily guessed user passwords. *CRACK* checks the passwords against an English dictionary file, to which the RIC has added a large Japanese language dictionary. *CRACK* also checks for passwords formed from other information related to
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each user account. Users with null passwords are also identified. The second system, COPS, is a collection of programs and shell scripts that attempt to address as many security problems as possible. Its goal is to prevent a breach in security by identifying situations (e.g., file access permissions that are too liberal) that could damage systems, corrupt files, or permit undesired access to certain resources or files. COPS is run weekly.

International collaboration programs

During this past year three RERF scientists visited the former Soviet Union to initiate joint research efforts with scientists from the Ural Research Center for Radiation Medicine, Chelyabinsk, Russia, and a joint research agreement was arranged. Four Russian scientists will visit RERF for periods of 6–12 weeks to work in cytogenetics, radiobiology, statistics, and epidemiology. (Travel funds will be provided by outside agencies.) The Chelyabinsk area and the Techa River were heavily contaminated with radioactivity from nuclear-weapons activities. Members of the nuclear work force as well as civilians at certain of the institutions in the area received high doses over protracted periods. If comparative studies on health effects are possible, considerable improvements in risk estimates may be achieved.
Future Research Directions for Fiscal Year 1993

In the Departments of Epidemiology and Statistics, work on Life Span Study (LSS) Report 12 is in progress. This report will be based on a population larger than in previous studies because an additional 10,500 persons have been assigned doses. Of special interest in this report will be the cancer risk of survivors who were young (>10 years old) at the time of the bombings (ATB), changes in the temporal pattern of cancer risk, and further information on noncancer mortality. In addition, a series of case-control studies is in progress to determine relationships between smoking and lung cancer and between hepatitis-B-virus infection and liver cancer. The tumor registries will continue to be a valuable source of information for cancer incidence studies and comparisons with cancer mortality data.

The role of genetic contribution to chronic disease will receive increasing attention in the LSS and AHS studies. A pilot study initiated in Nagasaki has determined that at least 1000, AHS participants have siblings in this study group and that more than 3500 individuals have at least one sibling in the AHS group. When parent-offspring relationships are considered, the number of interrelated individuals will double. For the LSS sample, the numbers will be considerably larger. Unraveling the gene--environment--dose--disease--aging relationships will be no simple matter, but such studies should expand our understanding of cancer-prone families and radiosensitivity, noncancer disease association, and clinical measurements obtained by means of the AHS over the past 36 years. This may help to elucidate the background differences observed between the cities for disease entities. As pointed out by the Scientific Council, no other body of patient information compares to that collected by RERF for studying genetic susceptibility to disease.

The Clinical Study Program will try to redesign health-surveillance aspects of the AHS program to improve the frequency of contacts with the oldest members of the cohort and to improve diagnostic procedures, as recommended by a recent workshop.

A pilot study will soon be started on the molecular nature of M-proteinemia, because the disease is believed to frequently progress to multiple myeloma and because methods of tracking the genetic steps are now available.

Further work on bone-mineral-density studies to eliminate artifacts in past techniques is being planned, if modern equipment can be purchased. Aging and dementia studies are now included in examinations in both Nagasaki and Hiroshima.

In the Department of Radiobiology, the immunology subgroup is continuing work on T-cell-receptor repertoire in relation to dose. Certain T-cell subtypes clearly are differentially affected by high dose as well as by age and sex. Just how these changes impact the health of the survivors, however, remains unclear at present.

As mentioned earlier, several approaches are being developed to try to understand the molecular changes involved in radiation-induced cancer. Collection of breast and thyroid tumor tissue from exposed and unexposed individuals is being actively
undertaken, with over 78 cases now available. Blood cells (lymphocytes) from more than 4500 individuals have already been preserved cryogenically, and about 600 B-cell lines have been transformed by Epstein-Barr virus. This work will continue.

Studies of skin-fibroblast immortality associated with specific chromosome arrangements will continue, using more-precise protocols and culture conditions to determine if reproducibility can be achieved.

The Laboratory of Cytogenetics will continue to expand the Hiroshima–Nagasaki chromosome-aberration analyses, using FISH techniques, with special emphasis on analyzing clonal events that have considerable bearing on the kinetics of T-cell production. Associations among age ATB and dose response, shielding, and other factors that might clarify apparent “sensitivity” differences observed among the A-bomb survivors will be studied.

A study has been initiated on the induction in vitro of fragile sites within chromosomes to determine if unique fragile-site distributions correlate with subsequent cancer susceptibility and with possible differences in radiosensitivity.

The Laboratory of Biochemical Genetics will continue expanding its family-trio cell lines and developing DNA technologies to increase its mutation-detecting capabilities.

If financial resources adequate to pursue our major ongoing studies described above are provided, RERF will continue to provide much relevant and substantial information pertaining to radiation risks and to both the direct and indirect health effects of radiation exposure.
Major Meetings and Conferences

The 20th meeting of the RERF Scientific Council

The 20th meeting of the RERF Scientific Council was held at the Nagasaki Koseinenkin Kaikan, 29–31 March 1993. Nine scientific councilors, six observers, and two supervisors attended the meeting.

Approximately 20 reports from the research departments on the status of ongoing studies were presented, the results of completed studies were reviewed, and recommendations were made. In particular, the recommendations of the Health Monitoring Workshop were approved at the meeting. (The agenda, list of participants, and minutes of the Scientific Council begin on page 129 of the Appendix.)

Health Monitoring Workshop

The Health Monitoring Workshop, held at RERF’s Hiroshima Laboratory, 25–27 January 1993, was attended by scientists from Japan and abroad. The workshop participants discussed the advisability of introducing a health-monitoring study to offset any loss of information during the intervals between the biennial AHS examinations, reconsidering the examination cycle to ensure sufficient numbers of study participants, and expanding the examination items.
At the workshop, Chief of Research Seymour Abrahamson, Clinical Studies Department Chief Kazunori Kodama, and Clinical Studies Department Assistant Chief Hideo Sasaki summarized the AHS and its problems. Committee members and guest speakers presented a wide range of topics, and a discussion ensued.

Consequently, it was recommended that 1) studies be prioritized; 2) the participation rate in biennial examinations be increased; 3) the examination interval be shortened; 4) examination items be reconsidered; and 5) the surveillance system for collecting morbidity and mortality data be improved. (The agenda, list of participants, and recommendations of the workshop begin on page 141 of the Appendix.)

**Ninth RERF-NIRS-RINMB Research Exchange Seminar**

The ninth research exchange seminar of the RERF, the National Institute of Radiological Science (NIRS) and the Research Institute for Nuclear Medicine and Biology (RINMB) was held at the RERF Hiroshima Laboratory on 18 June 1992. These exchange seminars have been held alternately at RERF and NIRS. This year three scientists from NIRS, one from RINMB, and two from RERF presented papers.

The following topics were presented at the seminar:
- "Solid cancer incidence in A-bomb survivors" by Kiyohiko Mabuchi, RERF Department of Epidemiology
- "The effect of radiation on human hematopoietic progenitor cells engrafted into severe combined immunodeficient mice" by Seishi Kyoizumi, RERF Radiobiology Department
- "Transgenerational carcinogenesis using hepatic tumors in mice" by Hiromitsu Watanabe, RINMB
- "Characterization and clonality of prelymphoma cells of B10 mice treated with fractionated X-irradiation" by Masahiro Muto, NIRS
- "Expression of the interleukin-1β gene induced by ionizing radiation in murine myeloid cells," by Hiroshi Ishihara, NIRS
- "Age-dependent doses to members of the public from intake of radionuclides," by Jiro Inaba, NIRS

**Fifth Japan Cardiovascular Disease Prevention Seminar**

The fifth Japan Cerebro-cardiovascular Disease Prevention Seminar was held 26–31 July 1992 at Hiroshima Koseinenkin Kaikan.

This seminar is held by the Japan Heart Foundation and the Japanese Association for Cerebro-cardiovascular Disease Control, which are promoting activities aimed at eliminating cerebro-cardiovascular diseases in Japan and training expert leaders. Four meetings have been held since 1988 in Akita, Yufuin, Saku, and Toya. This time the meeting was held in Hiroshima City, with RERF Chairman Itsuzo Shigematsu acting as honorary president and Clinical Studies Department Chief Kazunori Kodama
serving as representative organizer. Thirty-six doctors from institutions nationwide participated in the meeting. Lectures were given on various topics, ranging from an introduction to epidemiology to acquiring skills in the latest technology.
Scientific Lectures and Seminars

April 1992–March 1993

Jolyon H. Hendry, Radiobiology Department, Paterson Laboratories, Christie Hospital, Manchester, United Kingdom: Cellular repair after different LET irradiations. 15 April

Akihiro Shima, Department of Biology, Faculty of Science, University of Tokyo: Development of the Japanese medaka as a new model for studying environmental germ-cell mutagenesis. 1 May

David C. Spray, Albert Einstein College of Medicine, Yeshiva University, Bronx, New York: Molecular physiology of gap-junction channels. 15 May

Colin F. Arlett, Sussex University, Falmer Brighton, United Kingdom: Human cellular radiosensitivity. 15 May

Yoko Watamori, Department of Mathematics, Faculty of Science, Hiroshima University. 122nd Hiroshima Joint Statistics Seminar: Some asymptotic approaches to statistical inference of directional data. 29 May

Flemming Brandt Sørensen, University Institute of Pathology, Århus Kommunehospital, Århus, Denmark: Unbiased stereology used for objective histopathologic quantification in solid neoplasms: Technical aspects and prognostic value. 1 June

David J. Pawel, Department of Statistics, RERF. 123rd Hiroshima Joint Statistics Seminar: An overview of geostatistics. 26 June

Colin R. Muirhead, Epidemiology Group, United Kingdom National Radiological Protection Board: Mortality and occupational radiation exposure: First analysis of the UK National Registry for Radiation Workers. 8 July

Michael N. Gould, Department of Human Oncology, University of Madison, Wisconsin Medical School, Madison, Wisconsin: Oncogenes and suppressor genes in rat mammary carcinogenesis. 26 August
Charles E. Land, Radiation Epidemiology Branch, U.S. National Institutes of Health, National Cancer Institute, Bethesda, Maryland: An overview of recent findings on radiation-related breast cancer risk among A-bomb survivors. 16 September

Dong-Kyu Kim, Department of Biometrics, Research Institute for Nuclear Medicine and Biology, Hiroshima University. 124th Hiroshima Joint Statistics Seminar: Analysis of mortality to be applicable to causes with even few deaths. Birth-cohort-specific risk by prefecture derived from Poisson model considering age and period in the mortality of liver cancer and chronic liver disease and cirrhosis. 25 September

Richard T. Okinaka, Los Alamos National Laboratory, Los Alamos, New Mexico (visiting scientist at National Institute of Radiological Sciences, Chiba): A DGGE approach to detect mutational hotspots induced by x-rays in human cell cultures. 23 October

Donald A. Pierce, Department of Statistics, RERF. 125th Hiroshima Joint Statistics Seminar: Heterogeneity in Mantel-Henszel-type models. 30 October

Darwin R. Labarthe, Epidemiology Research Center, School of Public Health, University of Texas, Houston: Cardiovascular risk factors in children: A new design for new questions. 6 November

Angelo Capri, Department of Nuclear Medicine, University of Pisa School of Medicine, Pisa, Italy: Fine and large needle biopsy in thyroid nodule preoperative selection. 12 November

Norio Niikawa, Atomic Bomb Disease Institute, Nagasaki University School of Medicine: Chromosome microdissection-microcloning and its application to chromosome painting. 20 November

Lonnie Kapp, Laboratory of Radiobiology and Environmental Health, University of California, San Francisco: Cloning and characterization of a candidate gene for AT complementation group D. 25 November

Teruo Fujioka, Department of Mathematics, Faculty of Science, Hiroshima University. 126th Hiroshima Joint Statistics Seminar: Variance estimation in nonparametric regression model. 27 November

Robert J. Molinari, AT Biochem: Improved methods and materials for mutation detection. 11 December
Raymond R. Tice, Genetic Toxicology Division, Integrated Laboratory Systems, Research Triangle Park, North Carolina: The single-cell gel (SCG) assay: An electrophoretic technique for the detection of DNA damage in individual cells. 14 December

Marc T. Goodman, Department of Epidemiology, RERF. 127th Hiroshima Joint Statistics Seminar: The association of dietary cholesterol and fat with the risk of lung cancer. 18 December

Yasunori Fujikoshi, Department of Mathematics, Faculty of Science, Hiroshima University. 128th Hiroshima Joint Statistics Seminar: Growth-curve models with random-effects covariance structure for multivariate repeated data. 5 February

O.E. Barndorff-Nielsen and P. Blæsild, Department of Theoretical Statistics, Århus University, Århus, Denmark: 129th Hiroshima Joint Statistics Seminar: Orthogeodesic models and higher order independence. 12 March
Professional Staff Appointments

April 1992
Seigo Teraoka, who formerly worked at the Hiroshima Prefectural Hospital, was appointed, effective 1 April, as a research scientist with the Laboratory of Epidemiology, Department of Radiobiology, Hiroshima.

May 1992
David J. Pawel, was appointed, effective 14 May 1992, as a research scientist with the Department of Statistics, Hiroshima. He formerly worked for the Center for Veterinary Medicine, U.S. Food and Drug Administration.

June 1992
Jean-Valéry Coumans, medical student, University of Rochester, Rochester, NY, was accepted from 16 June to 13 August as a visiting research student assigned to the Laboratory of Biochemical Genetics, Department of Genetics, Hiroshima.

Jodi Kefer, medical student, University of Rochester, Rochester, NY, was accepted from 16 June to 13 August as a visiting research student assigned to the Department of Epidemiology, Hiroshima.

Mortimer L. Mendelsohn, formerly associate director for biomedical and environmental research, Lawrence Livermore National Laboratory, was appointed as an RERF permanent director as of 24 June.

Kazuyuki Takayama, visiting research fellow, Laboratory of Cell Biology, Department of Radiobiology, Nagasaki, completed training as of 30 June.

Shigeko Umeki, research scientist, Laboratory of Immunology, Department of Radiobiology, Hiroshima, terminated employment as of 30 June.

Michael A. Edington, research scientist, Editorial and Publications Section, Publication and Documentation Center, Hiroshima, terminated employment as of 30 June.

July 1992
Saeko Fujiwara, associate senior scientist, Division of Medicine, Department of Clinical Studies, Hiroshima, was promoted, effective 1 July, to senior scientist.
Junichi Asakawa, associate senior scientist, Laboratory of Biochemical Genetics, Department of Genetics, Hiroshima, was promoted, effective 1 July, to senior scientist.

Yuko Hirai, research scientist, Department of Radiobiology, Hiroshima, was promoted, effective 1 July, to associate senior scientist.

R.L. Carter, research scientist, Department of Statistics, Hiroshima, terminated employment as of 13 July.

August 1992
Seymour Abrahamson was appointed, effective 15 August, as an RERF permanent director.

Marc T. Goodman was appointed, effective 18 August, as a research scientist with the Department of Epidemiology. He is on leave from the University of Hawaii Cancer Research Center.

September 1992
Donald A. Pierce was appointed effective 5 September as a research scientist with the Department of Statistics, Hiroshima. He is on leave from Oregon State University where he is a statistics professor.

Gao Amin, visiting research scientist Department of Statistics, Hiroshima, completed his term of appointment as of 19 September.

November 1992
Suminori Akiba resigned from the post of assistant chief, Department of Epidemiology, Hiroshima, as of 30 November.

December 1992
Kiyohiko Mabuchi, chief, Department of Epidemiology, concurrently chief, Department of Epidemiologic Pathology, Hiroshima, was appointed, effective 1 December, concurrently chief, Laboratory of Pathology.

Yukiko Shimizu, senior scientist, Department of Epidemiology, Hiroshima, was concurrently assigned, effective 1 December, as chief, Tumor & Tissue Registry Office, Department of Epidemiologic Pathology.
Masaharu Nobuyoshi, graduate of Hiroshima University School of Medicine, was appointed, effective 16 December, research scientist with the Division of Medicine, Department of Clinical Studies, Hiroshima.

Jeanette Nakada, research scientist, Editorial & Publications Section, Publication & Documentation Center, Hiroshima, terminated employment as of 18 December.

January 1993
Yoshisada Shibata, chief, Department of Epidemiology & Biometrics, Nagasaki, was concurrently assigned, effective 1 January, as chief, Computer Management Office.

March 1993
Tomonori Hayashi, research scientist, Laboratory of Immunology, Department of Radiobiology, Hiroshima, terminated employment as of 1 March.

Robert R. Delongchamp, formerly with the Dow Corning Corporation, was appointed, effective 2 March, as a research scientist with the Department of Statistics, Hiroshima.

Hideo Sasaki resigned from the post of assistant chief, Department of Clinical Studies, Hiroshima, as of 31 March.

Yasuko Amasaki resigned from the post of chief, Division of Radiology, Department of Clinical Studies, Nagasaki, as of 31 March.
Initiated Research Projects

1 April 1992–31 March 1993

RP 3-92  Tumor suppressor gene alterations in lung tumors from Japanese mustard gas workers and atomic bomb survivors. Y Takeshima, T Seyama, WP Bennett, RA Metcalf, S Akiba, M Fujihara, Y Hayashi, S Yonehara, T Ito, T Mizuno, K Inai, M Yamakido, N Nakamura, M Akiyama, S Tokuoka, K Mabuchi, CE Land, CC Harris.

This study, jointly conducted by the Radiation Effects Research Foundation (RERF), Hiroshima University, and the US National Cancer Institute, will attempt to characterize the molecular alterations in the p53 gene of lung tumors presumed to be induced by two distinctly different agents: ionizing radiation and mustard gas. This study is considered to be a pilot effort in our plans to develop future molecular-epidemiologic studies aimed at identifying the molecular origins of cancers and other conditions induced by radiation exposure. The p53 gene was selected for this study because of the recent literature suggesting an important role this tumor suppressor gene may play in carcinogenesis and specific molecular changes in lung tumors associated with different types of carcinogenic exposures. Archived lung-tumor tissues will be collected from RERF, Hiroshima University, and other pathology laboratories in Hiroshima for the following study subjects: 12 male lung cancer patients who were exposed to mustard gas while employed at the Tadanoumi army factory and the same number of lung cancer patients not exposed to mustard gas but matched with respect to year of birth, year of diagnosis, type of specimen (autopsy or surgical), cigarette smoking habits, and tumor cell type (small cell or nonsmall cell); and 15 non-smoking lung cancer patients exposed to 20.1 Gy of radiation and the same number of lung cancer patients matched for age at the time of the bombings, year of birth, and sex with exposures of < 0.01 Gy, both identified from among the Life Span Study Hiroshima subjects. Laboratory methods to determine molecular alterations of the gene will include immunohistochemical analysis and sequencing DNA amplified using the polymerase chain reaction.


Few reports have been published on the risk of tumors of the central nervous system due to radiation exposure. The proposed study will assess, under the RERF
guidelines for the conduct of site-specific cancer incidence studies, tumors of the central nervous system in the period 1950–87 among male and female members of the RERF extended Life Span Study cohort in Hiroshima and Nagasaki. The shape of the dose-response curve and the risk by city, age at the time of the bombings, time since exposure, and type of tumor will be examined.

Tumor cases will be ascertained mainly from autopsy records, surgical pathology records, and death certificates maintained at RERF, as well as from the tumor and tissue registries of Hiroshima and Nagasaki. Consideration will also be given to the detection and collection of cases from clinical records, as well as from autopsy and surgical pathology records maintained at major medical institutions in both cities.


A wide spectrum of radiation effects on the central nervous system has been well documented in clinical and epidemiologic studies, especially for individuals who were exposed prenatally or during childhood. Nonetheless, the hypothesis that exposure to ionizing radiation accelerates the aging process has been actively investigated for a number of years at the Atomic Bomb Casualty Commission–Radiation Effects Research Foundation (ABCC-RERF); however, the results have not been consistent. The effects of ionizing radiation on the mature central nervous system could possibly be manifested as an accelerated neurologic aging, but this has not, as yet, been well established.

The study proposed here will examine the association, if any, between exposure to the atomic bomb and the subsequent occurrence of impaired cognitive function and senile dementia. To ascertain persons with dementia, standardized screening instruments for cognitive function, history of cognitive deterioration, etc, will be used. In the clinical evaluation of patients with dementia, standardized neurological examinations will be performed, including computing tomography scan, magnetic resonance imaging, etc. We will also attempt to determine those factors, if any, that modify the association of these neurologic disorders with ionizing radiation.
RP 6-92 Establishment and operation of a system for collecting and storing leukemia cells. S Kusumi, M Nobuyoshi, K Kodama, K Mabuchi, M Akiyama, H Dohi, N Kamada, A Kuramoto

A system will be established for collecting and storing leukemia cells derived from bone marrow and peripheral blood from leukemia cases occurring among Life Span Study participants.


Ionizing radiation predominantly induces mutations associated with deletions. Therefore, if the increased risks of cancer development among the survivors are assumed to be the direct consequence of genetic changes due to radiation exposure, tumors in high-dose-exposed people would be expected to carry deletions of tumor-suppressor genes more frequently than would tumors in people in the non-exposed control group. In the present study, we propose to examine deletions of the tumor-suppressor gene p53 in breast cancers, the risk for which is known to be the highest among all solid tumors for atomic-bomb survivors.


Heritable chromosome fragile sites are rare and obey strict Mendelian rules of inheritance. Common fragile sites may be caused by environmental factors such as chemical agents, radiation, and/or viruses. Most heritable fragile sites and many common fragile sites have been shown to correspond to, or occur close to, nonrandom cancer-specific breakpoints. Individuals with such fragile sites may be at high risk for the development of malignancies.

Although several studies have been performed using the fragile-site assay, as yet no studies have been made on a possible relationship between radiation sensitivity and fragile-site expression. Furthermore, some important technical aspects of the fragile-site assay (such as reproducibility and sensitivity to in-vitro irradiation) are relatively unexplored. In this pilot study, we propose first to investigate the reproducibility (over time and following long-term sample storage in liquid nitrogen) and sensitivity of the assay in volunteers (preliminary phase). If intraindividual
variation is relatively small, we will then examine fragile sites in 150 atomic-bomb (A-bomb) survivors with differing radiosensitivities (actual-testing phase). Before the actual testing phase is initiated, however, the results obtained with volunteers' samples will be reviewed by the Chief of Research and qualified outside reviewer(s) chosen by the Chief of Research. The results of this review will be presented to the Research Protocol Committee for approval to continue with the actual-testing phase. Both rare and common fragile-site expressions in peripheral-blood lymphocytes will be analyzed by the proposed method.

Pending results of this study, we hope in the future to evaluate the fragile-site assay as a measure of susceptibility to radiation-induced cancer in a large sample of A-bomb survivors. Future studies would involve prospective follow-up of A-bomb survivors to identify incident cancers and to analyze fragile-site expressions in relation to cancer-specific chromosomal breakpoints and oncogene loci. Such analyses are expected to provide information useful for cellular/chromosomal epidemiological studies of human carcinogenesis. The present study will contribute information concerning the feasibility of such long-term studies.

**RP 9-92 Study of liver diseases in the Adult Health Study sample: relationship between radiation dose and infection by B and C hepatitis virus. S Kusumi, K Kodama, K Neriishi, H Nonaka, M Akahoshi, M Akiyama, K Mabuchi, JB Cologne, K Shimaoka.**

The relationship between liver diseases and atomic-bomb-radiation dose found in the previous studies at Atomic Bomb Casualty Commission/Radiation Effects Research Foundation (ABCC/RERF) can, at least partially, be explained by the increased prevalence of hepatitis-B virus (HBV) carriers in highly exposed survivors, although the mechanisms involved in the increased prevalence of the carriers are yet to be elucidated. With the availability of the serum assay of hepatitis-C virus (HCV), the role of its infection in the natural history of hepatitis and other liver disorders has recently become the focus of attention. It is suspected that the HCV infection may assume a major role in the development of liver diseases in Japanese. In the proposed study, HCV and HBV serum assays will be done for Adult Health Study (AHS) participants in both Hiroshima and Nagasaki 1) to determine the HCV infection rate as a function of atomic-bomb-radiation dose and 2) to identify HBV carriers and then to determine their HBV envelope (HBe) antigen levels. Also proposed in this protocol is the follow-up of HCV-antibody-positive subjects and HBV carriers to improve our understanding of the natural history of HCV- and HBV-related liver disorders in the atomic-bomb (A-bomb) survivors. The HBV data to be obtained will help clarify the association of radiation dose with the HBe antigen level, which is considered to be related to hepatitis-B activity, and will help
as well determine the seroconversion rate among the HBV carriers identified during this study or past RERF HBV studies. Data from this study will also enable us to analyze the risk of liver disorders associated with HCV and HBV infection among the A-bomb survivors.
This report presents, for the first time, comprehensive on the incidence of solid cancer data and risk estimates for A-bomb survivors in the extended Life Span Study (LSS-E85) cohort. Among 79,972 individuals, 8613 first primary solid cancers were diagnosed between 1958 and 1987. As part of the standard registration process of the Hiroshima and Nagasaki tumor registries, cancer cases occurring among members of the LSS-E85 cohort were identified using a computer linkage system supplemented by manual searches. Special efforts were made to ensure complete case ascertainment, data quality, and data consistency in the two cities. For all sites combined, 75% of the cancers were verified histologically, 6% were diagnosed by direct observation, 8% were based on a clinical diagnosis, and 12.6% were ascertained by death certificate only. A standard set of analyses was carried out for each of the organs and organ systems considered. Depending on the cancer site, Dosimetry System 1986 (DS86) organ or kerma doses were used for computing risk estimates. Analyses were based on a general excess relative-risk model (the background rate times one plus the excess relative risk). Analyses carried out for each site involved fitting the background model with no dose effect, a linear dose-response model with no effect-modifiers, a linear-quadratic dose-response model with no effect modifiers, and a series of linear dose-response models that included each of the covariates (sex, age at exposure, time since exposure, attained age and city) individually as effect modifiers. Because the tumor registries ascertain cancers in the registry catchment areas only, an adjustment was made for the effects of migration. In agreement with prior LSS findings, a statistically significant excess risk for all solid cancers was demonstrated [excess relative risk at 1 Sv (ERR\textsubscript{1 Sv}) = 0.63; excess absolute risk (EAR) per 10\textsuperscript{4} person-year-sievert (PYSv) = 29.7]. For cancers of the stomach (ERR\textsubscript{1 Sv} = 0.32), colon (ERR\textsubscript{1 Sv} = 0.72), lung (ERR\textsubscript{1 Sv} = 0.95), breast (ERR\textsubscript{1 Sv} = 1.59), ovary (ERR\textsubscript{1 Sv} = 0.99), urinary bladder (ERR\textsubscript{1 Sv} = 1.02) and thyroid (ERR\textsubscript{1 Sv} = 1.15) significant radiation associations were observed. There was some indication of an increase in tumors of the neural tissue (excluding the brain) among persons exposed to the bombs before age 20. For the first time, radiation has been associated with liver (ERR\textsubscript{1 Sv} = 0.49) and nonmelanoma skin (ERR\textsubscript{1 Sv} = 1.0) cancer incidence in the LSS cohort. The present analysis also strengthened earlier findings, based on a smaller number of cases, of an effect of A-
bomb radiation on salivary gland cancer. There was no significant radiation effect for cancers of the oral cavity and pharynx as a group, esophagus, rectum, gallbladder, pancreas, larynx, uterine cervix, uterine corpus, prostate, kidney and renal pelvis.

Analyses of solid tumors individually and in combination revealed no appreciable differences between Hiroshima and Nagasaki ($P > 0.5$). The combined solid tumor analysis demonstrated a two-fold greater relative risk for females than males and a trend for a decreasing relative risk with increasing age at exposure ($P < 0.001$). Females had a higher relative risk of cancers of the lung, total respiratory system, and urinary system than males. The excess relative risk decreased with increasing age at exposure for salivary gland cancer and for combined gastrointestinal, stomach, skin, breast, and thyroid cancers. For solid cancers combined, the excess cancer rate increased with increasing attained age and was proportional to the background incidence rate. Unadjusted for age at exposure, the excess relative risk for most sites tended to decrease with increasing attained age. For some cancers (colon, breast, central nervous system, and kidney) models that allowed the excess relative risk to vary with attained age fit at least as well as models that included age-at-exposure effects. For all solid tumors, excess cancers increased with time since exposure, based on an absolute excess risk model. Averaged over all ages at exposure the relative risk decreased with time since exposure. Examination of temporal patterns by age-at-exposure groups suggested that the excess relative risk decreased with time for the younger-age-at-exposure groups and remained virtually constant for the older cohorts. The LSS has served as one of the major sources of data used for cancer risk estimation. Previous studies focused primarily on the association between cancer mortality and radiation exposure. Although these mortality studies are extremely valuable, the accuracy of cancer diagnoses is limited, and death certificates do not provide adequate information on cancers with relatively high survival rates. Although incidence data also have their limitations (e.g., incomplete case ascertainment and partial reliance on death certificate diagnoses) they can provide more-complete data on cancers with lower mortalities, on histologic type, and on time from exposure to cancer onset. Thus, future analyses of atomic-bomb survivors should focus on both cancer mortality and incidence.

TR 6-92 Radiation-related small head sizes among prenatally exposed atomic bomb survivors. M Otake, WJ Schull.

The population prenatally exposed to the atomic bombings of Hiroshima and Nagasaki, referred to as the In Utero Clinical Sample, on whom Dosimetry System 1986 doses are available consists of 1566 individuals (1242 in Hiroshima and 324 in Nagasaki). Of these study subjects, 1473 had the circumference of their heads
measured at least once between ages 9 to 19. Among these 1473 individuals, 62 had small heads—the circumference of the head was two standard deviations or more below the observed specific age-at-measurement mean. Twenty-six of the 30 cases with severe mental retardation described elsewhere are included among these subjects. Of these 26 severely mentally retarded cases, 15 (58%) had small heads. Most (86%) of the individuals with small heads were exposed in the first or second trimester of pregnancy—55% in the former period and 31% in the latter.

Various dose-response relationships, with and without a threshold, have been fitted to the data grouped by the trimester or postovulatory age (weeks after ovulation) at which exposure occurred. A significant effect of radiation on the frequency of individuals with atypically small heads is observed only in the first and second trimesters and for the intervals postovulation of 0–7 weeks and 8–15 weeks. Although the risk of a small head at 0–7 weeks postovulation increases significantly with increasing dose, no increase in risk for severe mental retardation is noted in this period. No excess risk of a small head was seen in the third trimester or among individuals exposed at ≥16 weeks postovulation.

The estimated threshold, based either on a linear or a linear-quadratic dose-response relationship, is zero or thereabouts. This apparent absence of a threshold and the somewhat different periods of vulnerability suggest an embryological difference in the development of both a small head and mental retardation. Mean IQ (using the Koga test) and its standard deviation are 63.8 and 8.5, respectively, for the severely mentally retarded cases with small heads and 68.9 and 11.9 for the severely mentally retarded cases without small heads. These values are 96.4 and 19.8 for cases with small heads only. The mean IQ and standard deviation for the overall sample are 107.8 and 16.4, respectively. No significant difference exists between the first two IQ means identified above, but both are significantly less than the mean for individuals with small heads but without severe mental retardation. The mean IQ of individuals with small heads but without severe mental retardation does not differ significantly from the mean for the entire sample. The relationship of small head size to four other anthropometric measurements (standing height, body weight, sitting height, and chest circumference) is described.


In an attempt to determine the distribution of recombinase activity in the mouse thymus, spleen, and lymph nodes, we used the in situ hybridization method to examine the expression of the recombination activating genes RAG-1 and RAG-2. Expression of RAG-1 was found in most cortical thymocytes but not in the majority of medullary thymocytes. Although hybridization signals of RAG-2 were not as
intense as those of RAG-1, the localization of RAG-2 transcripts was similar to that of RAG-1. In the spleen, expression of RAG-1 was found only in limited cells near the splenic sinus, and the majority of the cells within the follicle were negative for RAG-1 transcript. In nude mice, RAG-1–expressing cells were detected in the same regions, which suggests that in situ hybridization signals of RAG-1 in the spleen are due to the cells of B-cell origin. In the lymph nodes, expression of RAG-1 was found only in the medullar region. Expression of RAG-2 transcript in the spleen and the lymph nodes, if any, was too faint to allow determination of the specific localization. These results suggest that most of the cortical thymocytes and some cells in the spleen are capable of rearranging T-cell receptor genes and immunoglobulin genes, respectively, but the possible involvement of the RAG-1 transcript in RAG-1–positive cells of the spleen and the lymph nodes in functions other than the rearrangement of genes could not be ruled out.

TR 8-92 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.

An in-vitro colony assay was employed for X-ray dose-survival studies of peripheral-blood lymphocytes from 117 Adult Health Study participants with Dosimetry System 1986 doses $<0.005$ Gy and from 84 participants with doses of $\geq 1.5$ Gy. The mean (coefficient of variation [CV]) $D_{10}$ values (the X-ray dose required to kill 90% of cells) for these two groups were 3.40 Gy (7.5%) and 3.34 Gy (7.8%), respectively. No statistically significant differences in their distributions were detected. In addition, neither sex nor age affected the in-vitro radiosensitivity of lymphocytes for either group or for all subjects combined. Therefore it was concluded that, as far as the $G_0$-lymphocyte colony assay is concerned, there is no evidence for preferential loss of individuals with higher cellular radiosensitivity among the high-dose atomic bomb survivors. However, it should be noted that the interindividual variations in cellular radiosensitivity were not large compared with the experimental variations. Consequently, the above-mentioned results should be considered due to the small heterogeneity of lymphocyte radiosensitivity among the survivors.

The risk of female breast cancer in association with radiation exposure is well established, on the basis of follow-up studies of the atomic-bomb survivors and other exposed populations. This association is especially strong for women exposed before age 20 yr and appears to be much weaker among women exposed after age 40 yr. In this study, breast-tissue autopsy samples from high-dose and low-dose individuals in the Radiation Effects Research Foundation Life Span Study sample were examined in detail to determine whether nonproliferative or proliferative breast lesions are associated with radiation exposure.

The results suggest that proliferative disease in general and atypical hyperplasia in particular are associated with radiation exposure and that the risk is strongest for subjects who were ages 40–49 yr at the time of the bombings. It is hypothesized that this finding may be related to the age dependence of radiation-induced breast cancer, in the sense that potential cancers reflecting early-stage changes induced at these ages by radiation exposure may receive too little hormonal promotion to progress to frank cancers.


If A-bomb survivors include a disproportionately large number of either radioreistant or radiosensitive persons, the surviving population would provide a biased estimate of the true risk of radiogenic cancer. To test this hypothesis, the in vitro X-ray sensitivities of peripheral blood lymphocytes obtained from 937 A-bomb survivors were measured with a cytokinesis-blocking micronucleus assay. Background frequencies (no irradiation in vitro) of micronuclei show a wide distribution. Frequencies in both males and females tend to increase with increasing donor age. Frequencies in females are significantly higher than in males. Donor age decreases the sensitivity of lymphocytes to in vitro X-ray exposure at a rate of about 0.001 micronuclei per cell per year per gray. There is no effect of donors' sex on in vitro radiation sensitivity. Atomic bomb radiation and cigarette smoking had no significant effect on background and X-ray–induced micronuclei frequencies. Thus, there is no difference in radiosensitivity of peripheral blood lymphocytes between proximally and distally exposed survivors.
TR 11-92 Radiation cataracts among Hiroshima atomic bomb survivors, 1949–64. WJ Schull, M Otake, S Funamoto.

This report reexamines the quantitative relationship of exposure to ionizing radiation to the occurrence of cataracts (posterior lenticular opacities) seen in the years 1949–64 among 2249 Hiroshima atomic bomb survivors with Dosimetry System 1986 (DS86) doses. Among several dose-response relationships with or without two thresholds, the best fit based on binomial odds-regression models is achieved with a linear-linear dose-response relationship that assumes different thresholds for the two types of radiation. The neutron and gamma-ray regression coefficients, 199 Gy (90% CI: 28–473 Gy) and 5.14 Gy (95% CI: 1.38–14.77 Gy), based on this model, are suggestively higher for the neutron dose and significantly higher for the gamma dose than previously reported. The estimates of the two thresholds are also significantly different from zero: 0.06 Gy with 95% lower and upper bounds of 0.03 and 0.10 Gy for the neutron dose and 1.08 Gy with 95% bounds of 0.51 and 1.45 Gy for the gamma-ray dose, respectively. The safety zone for radiation-induced cataracts is estimated to be a 1.75-Sv threshold with 95% lower and upper bounds of 1.31 and 2.21 Sv using DS86 eye-organ-dose equivalents, assuming a neutron relative biological effectiveness of 18, derived from the ratio of the two thresholds, that is, 1.08 Gy for gamma rays and 0.06 Gy for the neutrons.

TR 12-92 Thyroid diseases among atomic bomb survivors in Nagasaki. S Nagataki, Y Shibata, S Inoue, N Yokoyama, M Izumi, K Shimaoka.

To elucidate the current thyroid disease status for the Nagasaki Adult Health Study cohort, Radiation Effects Research Foundation, a survey study was conducted. Among cohort members of the Nagasaki Adult Health Study who received biennial health examinations from October 1984 to April 1987 (n = 2856), a total of 2587 subjects remained after exclusion of persons exposed in Hiroshima or in utero and those who were not in Nagasaki at the time of the bombing. Thyroid radiation dose by the dosimetry system established in 1986 was available for 1978 of the 2587 subjects. Thyroid diseases were diagnosed using uniform procedures including ultrasonic scanning. The relationship of the prevalence of each thyroid disease with thyroid radiation dose, sex, and age was analyzed using logistic models. A significant dose-response relationship was observed for solid nodules, which include cancer, adenoma, adenomatous goiter, and nodules without histological diagnosis, and for antibody-positive spontaneous hypothyroidism (autoimmune hypothyroidism) but not for other diseases. The prevalence of solid nodules showed a monotonic dose-response relationship, yet that of autoimmune hypothyroidism displayed a
A concave dose-response relationship reaching a maximum (±SE) level of 0.7±0.2 Sv. The present study confirmed the results of previous studies by showing a significant increase in solid nodules with dose to the thyroid and demonstrated for the first time a significant increase in autoimmune disease among atomic bomb survivors. A concave dose-response relationship indicates the necessity for further studies on the effects of relatively low doses of radiation on thyroid disease.


Analysis of data on stable chromosome aberrations collected between 1968 and 1985 by the Radiation Effects Research Foundation (RERF) on 1703 individuals exposed to A-bomb radiation in Hiroshima and Nagasaki, Japan, reveals different dose-response relationships in the two cities, as well as significant effects of both time of assay and age at exposure. In Hiroshima, the proportion of cells with aberrations increased by 0.080 per sievert at low doses, assuming a constant neutron radiation RBE of 10 relative to γ radiation, for assays performed during the latest period (1981–1985). In Nagasaki, the low dose increase was 0.0126 per sievert. There was evidence that radiation exposure was more effective for producing stable aberrations at some younger ages at exposure, although the interpretation of this interaction is difficult. Modeling neutron and γ-ray components of dose separately in a way which allows the neutron RBE to vary with dose yielded an estimated low-dose limiting value of RBE of 707 (95% confidence bound 200–∞), with a low-dose response of approximately 0.008 aberrations per sievert. This RBE is much higher than the published RBEs for induction of aberrations in vitro. The high estimated RBE and the differences in dose response by city both are suggestive of systematic dose estimation errors in which either neutrons were under-estimated in Hiroshima and/or γ rays were overestimated in Nagasaki.


Antibody titers to Epstein-Barr virus antigens were determined in the sera of 372 atomic bomb survivors to evaluate the effect of the previous radiation exposure on immune competence against the latent infection of the virus. The proportion of persons with high titers (≥1:40) of IgG antibodies to the early antigen was significantly elevated in the exposed survivors. Furthermore, the distribution of IgM titers against the viral capsid antigen was significantly affected by radiation dose with an
increased occurrence of titers of 1:5 and 1:10 in the exposed persons, although the dose effect was only marginally suggestive when persons with rheumatoid factor were eliminated from the analysis. These results suggest that reactivation of Epstein–Barr virus in the latent stage occurs more frequently in the survivors, even though this might not be affected by the radiation dose. Otherwise, there was neither an increased trend in the prevalence of high titers (≥1:640) of IgG antibodies to the viral capsid antigen among the exposed people nor a correlation between the radiation exposure and distributions of titers of IgA antibodies to the viral capsid antigen or antibodies to the anti-Epstein-Barr virus-associated nuclear antigen.


Colorectal cancer incidence in the LSS sample during 1950–80 was investigated. A total of 730 incidence cases of colorectal cancer were confirmed from a variety of sources. Sixty-two percent of the cancers were microscopically verified, and 12% were ascertained through death certificate only.

The risk of colon cancer increased significantly with intestinal dose, but no definite increase of risk was observed for rectal cancer. Relative risk at 1 Sv and excess risk per 10^4 person-year-sievert for colon cancer were 1.80 (90% confidence interval 1.37–2.36) and 0.36 (90% confidence interval 0.06–0.77), respectively. City and sex did not significantly modify the dose response of colon cancer, but the risk decreased with age at the time of the bombings. The relative risk of colon cancer does not vary substantially over time following exposure. A nonlinear dose response did not significantly improve the fit. Further, the anatomic location of the tumors indicate that the cecum and ascending, transverse and descending, and sigmoid colon seem equally sensitive to radiation. No difference in the distribution of tumor histological types was observed by radiation dose.

**TR 16-92** Rapid translocation frequency analysis in humans decades after exposure to ionizing radiation. JN Lucas, AA Awa, T Straume, M Poggensee, Y Kodama, M Nakano, K Ohtaki, HU Weier, D Pinkel, J Gray, G Littlefield.

This paper presents an analysis of the utility of fluorescence in situ hybridization (FISH) with whole-chromosome probes for measurement of the genomic frequency of translocations found in the peripheral blood of individuals exposed to ionizing radiation. First, we derive the equation: \[ F_p = 2.05 p(1-p) F_G \], relating the translocation frequency, \( F_p \), measured using FISH to the genomic translocation frequency, \( F_G \),
where \( f_p \) is the fraction of the genome covered by the composite probe. We demonstrate the validity of this equation by showing that: (a) the translocation detection efficiency predicted by the equation is consistent with experimental data as \( f_p \) is changed, (b) the translocation frequency dose-response curves measured \textit{in vitro} using FISH agree well with dicentric frequency dose-response curves measured \textit{in vitro} using conventional cytogenetic procedures, and (c) the genomic translocation frequencies estimated from FISH measurements for 20 Hiroshima A-bomb survivors and four workers exposed to ionizing radiation during the Y-12 criticality accident are approximately the same as the translocation frequencies measured using G-banding. We also show that translocation frequency dose response curves estimated using FISH are similar for Hiroshima A-bomb survivors and for first division lymphocytes irradiated \textit{in vitro}. We conclude with a discussion of the potential utility of translocation frequency analysis for assessment of the level of acute radiation exposure independent of the time between analysis and exposure.

\textbf{TR 17-92 A novel blocker-PCR method for detection of rare mutant alleles in the presence of an excess amount of normal DNA.} T Seyama, T Ito, T Hayashi, T Mizuno, N Nakamura, M Akiyama.

A novel polymerase chain reaction method was developed to preferentially amplify a segment of DNA containing a base substitution mutation. This technique uses a pair of dideoxynucleotide-labeled oligonucleotides (18 mers) of normal sequences as blockers located between the two primers. By virtue of a subtle difference in the melting temperature between the blocker-normal DNA and blocker-mutant DNA hybrids, the method allows preferential amplification of the mutant DNA. We used the human \textit{N-ras} gene as a model. Two different types of \textit{N-ras} mutations could be effectively amplified when they were present with an excess amount of normal DNA at a ratio of 1:10^3. Furthermore, the sensitivity was increased 10-fold by using single strand conformation polymorphism analysis for the amplified products, and mutant DNA was detected in the presence of a 10^4 times excess amount of normal DNA.

To examine the potential causes of increased levels of calcium in serum with increasing dose of atomic bomb radiation, which was obtained from the previous preliminary analysis, levels of parathyroid hormone (PTH) and calcitonin in serum were examined among 1459 subjects in Hiroshima and Nagasaki. A significant effect of radiation on levels of calcium, PTH and calcitonin in serum was found, even after patients with hyperparathyroidism were excluded. The level of calcium in serum increased with radiation dose; this can be explained partly by the increase in the level of PTH with radiation dose. However, the dose effect on calcium remained even after adjustment for PTH, calcitonin and confounding factors such as renal function, serum albumin level and medication. Parathyroid hormone increased initially by 6.8% per gray, but the dose response leveled off after about 1 Gy. The level of calcitonin increased with radiation dose, probably in part due to feedback mechanisms stimulated by the increase in calcium. However, after adjustment for the level of calcium, the increase in the level of calcitonin with dose was still found. Although the etiological mechanisms of the effect of radiation on serum levels of calcium, PTH and calcitonin are unclear, radiation exposure may affect secretion of PTH and calcitonin and regulation of calcium a long time after atomic bomb exposure.


Growth retardation due to atomic-bomb exposure has been evaluated for 455 individuals with nine repeated measurements of stature at age 10–18 yr using growth curve analysis and either two covariates, Dosimetry System 1986 (DS86) uterine absorbed dose and postovulatory age (weeks), or three covariates, DS86 uterine dose, DS86 uterine dose squared, and postovulatory age. Of the several comparisons made by city, sex, DS86 dose, and postovulatory age, the largest significant difference was between males and females. However, on the basis of a linear-quadratic (L-Q) dose-response, no significant difference was found between Hiroshima and Nagasaki males or females except for all trimesters (of pregnancy) combined and for males only exposed in the first trimester. A highly significant growth retardation due to DS86 uterine absorbed dose (in gray) was observed for all trimesters combined and for the first and second trimesters. In the first trimester, all parameter estimates based on a linear (L) or L-Q dose-response relationship were negative in relation to DS86 uterine absorbed dose. The parameter estimates in the second trimester were
negative for a constant term and positive for an L or L-Q term, but growth and
development (stature) evidently showed a declining trend dependent on DS86 uterine
dose. The positive estimate tends slightly to be close to a control level with an
increase of dose. A significant difference is determined by a multivariate test statistic
to examine whether a set of two or three parameter estimates including a constant
term related to an L or L-Q dose-response relationship is significantly different from
zero. The longitudinal repeated measurements of stature for individuals age 10–18
yr demonstrated radiation-related growth retardation. The dose effect in the third
trimester was not significant with either the L or the L-Q model.

The first outward sign of the beginning of the secondary development of boys
(the adolescent growth spurt) appears at age 14 yr on the average. Accordingly, a
growth analysis, based on an L dose-response relationship, was made for 704 and
838 children with four repeated measurements of stature from ages 10–13 and 15–18
yr, respectively. An analysis by prematurity and maturity was made by increasing
the number of individuals, which in turn increases the statistical power. The retarda-
tion effect is clearly evident at age 10–13 and continues unabated through age
15–18. Growth retardation in the group age 10–13 was highly significant for all
trimesters combined but suggestive only for the first trimester. However, the group
age 15–18 revealed a highly significant growth retardation for both the first and
second trimesters. The relationship between birth weights and repeated measure-
ments of stature in adolescence was discussed on the basis of the results obtained by
a growth curve analysis.

TR 20-92 Radiation-associated lung cancer: a comparison of the histology of
lung cancers in uranium miners and survivors of the atomic bombings of
Hiroshima and Nagasaki. CE Land, Y Shimosato, G Saccomanno, S Tokuoka, O
Auerbach, R Tateishi, SD Greenberg, S Nambu, D Carter, S Akiba, R Keehn, P
Madigan, TJ Mason, M Tokunaga.

A binational panel of Japanese and American pulmonary pathologists reviewed
tissue slides of lung cancer cases diagnosed among Japanese A-bomb survivors and
American uranium miners and classified the cases according to histological subtype.
Blind reviews were completed on slides from 92 uranium miners and 108 A-bomb
survivors, without knowledge of population, sex, age, smoking history, or level of
radiation exposure. Consensus diagnoses were obtained with respect to principal
subtype, including squamous-cell cancer, small-cell cancer, adenocarcinoma, and less
frequent subtypes. The results were analyzed in terms of population, radiation dose,
and smoking history. As expected, the proportion of squamous cell cancer was
positively related to smoking history in both populations. The relative frequencies of
small-cell cancer and adenocarcinoma were very different in the two populations, but
this difference was accounted for by differences in radiation dose or, more specifically, dose-based relative risk estimates based on published data. Radiation-induced cancers appeared more likely to be of the small-cell subtype, and less likely to be adenocarcinomas, in both populations. The data appeared to require no additional explanation in terms of radiation quality ($\alpha$ particles vs $\gamma$ rays), uniform or local irradiation, inhaled vs. external radiation source, or other population difference.


A binational panel of four Japanese and four American pathologists examined 208 pulmonary neoplasms, according to the World Health Organization (WHO) recommendations, second edition, for the histologic typing of lung tumors. The study design included independent evaluations by pathologists working alone, followed by group reviews. The individual evaluations, and their implications for reproducibility of the WHO recommendations, are reported. Consensus (agreement by six or more pathologists) with respect to major (ie, first digit) diagnosis was obtained for 76.4% of the cases. Consensus was obtained for 72.5% of the cases with any major diagnosis of small cell cancer; the comparable figures for adenocarcinoma and squamous cell carcinoma were 56% and 48%, respectively. American pathologists were twice as likely as Japanese pathologists to diagnose large-cell cancer, the only significant national difference. Consensus was far less frequent with the minor (ie, second digit) diagnosis categories. This study shows that lung cancers continue to be difficult to classify reproducibly.


In the course of feasibility studies to examine the efficiencies and practicalities of various techniques for screening for genetic variations, the human coagulation factor IX ($F9$) genes of 63 Japanese families were examined by PCR–denaturing gradient gel electrophoresis (PCR-DGGE). Four target sequences with lengths of 983–2891 bp from the $F9$ genes of 126 unrelated individuals from Hiroshima and their 100 children were amplified by PCR, digested with restriction enzymes to approximately 500-bp fragments, and examined by DGGE—a total of 6724 bp being examined per individual. GC-rich sequences (GC-clamps) of 40 bp were attached to
both ends of the target sequences, as far as was feasible. Eleven types of new nucleotide substitutions were detected in the population, none of which produced RFLPs or caused hemophilia B. By examining two target sequences in a single lane, approximately 8000 bp in a diploid individual could be examined. This approach is very effective for the detection of variations in DNA and is applicable to large-scale population studies.

**TR 22-92** Accurate and rapid detection of heterozygous carriers of a deletion by combined polymerase chain reaction and high-performance liquid chromatography. J Asakawa, C Satoh, Y Yamasaki, S Chen.

We have developed a technique to detect accurately heterozygous carriers of a deletion. Specific target sequences were amplified using the polymerase chain reaction (PCR), and the products were subsequently analyzed by high-performance liquid chromatography. Examples from four loci demonstrated that 24–27 cycles of amplification for a single-copy DNA, based on 50-ng genomic DNA, results in excellent quantitation that readily permits the detection of heterozygous carriers of a deletion. We have demonstrated that triplex PCR (three targets in a single PCR) entails no loss of precision: We have also demonstrated that this method could accurately differentiate the heterozygous carriers of a deletion from normals in four family studies, three for Duchenne muscular dystrophy patients and one for a hemophilia B patient.

**TR 23-92** Immune responses to Epstein–Barr virus in atomic bomb survivors: study of precursor frequency of cytotoxic lymphocytes and titer levels of anti-Epstein–Barr virus-related antibodies. Y Kusunoki, S Kyoizumi, Y Fukuda, H Huang, M Saito, K Ozaki, Y Hirai, M Akiyama.

Precursor frequencies of cytotoxic lymphocytes to autologus Epstein–Barr virus-transformed B cells and serum titers of anti-Epstein–Barr virus-related antibodies were measured in 68 atomic bomb survivors to clarify the immune mechanism controlling Epstein–Barr virus infection. The precursor frequency was negatively correlated with the titer of anti-early antigen IgG, which is probably produced at the stage of viral reactivation. A positive correlation between the precursor frequency and titer of anti-Epstein–Barr virus-associated nuclear antigen antibody was also observed, indicating that the precursor frequency reflects the degree of in vivo destruction by T cells of the virus-infected cells. These results suggest that T-cell memory specific to Epstein–Barr virus keeps the virus under control and that the precursor frequency assay is useful for the evaluation of immune responses to Epstein–Barr virus.
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virus. However, no significant effect of atomic bomb radiation on the precursor frequency was observed in the present study, probably due to the limited number of participants.


This paper presents an analysis of data on the incidence of leukemia, lymphoma, and myeloma in the Life Span Study cohort of atomic bomb survivors during the period from late 1950 through the end of 1987 (93,696 survivors accounting for 2,778,000 person-years). These analyses add 9 additional years of follow-up for leukemia and 12 for myeloma to that in the last comprehensive reports on these diseases. This is the first analysis of the lymphoma incidence data in the cohort. Using both the Leukemia Registry and the Hiroshima and Nagasaki tumor registries, a total of 290 leukemia, 229 lymphoma, and 73 myeloma cases were identified. The primary analyses were restricted to first primary tumors diagnosed among residents of the cities or surrounding areas with Dosimetry System 1986 dose estimates between 0 and 4 Gy kerma (231 leukemias, 208 lymphomas, and 62 myelomas). Analyses focused on time-dependent models for the excess absolute risk. Separate analyses were carried out for acute lymphocytic leukemia (ALL), acute myelogenous leukemia (AML), chronic myelocytic leukemia (CML), and adult T-cell leukemia (ATL). There were few cases of chronic lymphocytic leukemia in this population. There was strong evidence of radiation-induced risks for all subtypes except ATL, and there were significant subtype differences with respect to the effects of age at exposure and sex and in the temporal pattern of risk. The AML dose-response function was nonlinear, whereas there was no evidence against linearity for the other subtypes. When averaged over the follow-up period, the excess absolute risk (EAR) estimates (in cases per 10^4 PY Sv) for the leukemia subtypes were 0.6, 1.1, and 0.9 for ALL, AML, and CML, respectively. The corresponding estimated average relative risks at 1 Sv are 9.1, 3.3, and 6.2, respectively. There was some evidence of an increased risk of lymphoma in males (EAR = 0.6 cases per 10^4 PY Sv) but no evidence of any excess in females. There was no evidence of an excess risk for multiple myeloma in our standard analyses.

This report describes the G-band analysis of somatic chromosomes in lymphocytes from 63 atomic-bomb survivors in Hiroshima to determine the type and frequency of radiation-induced chromosome aberrations.

Summary findings are as follows:

1. The cells with stable-type chromosome aberrations (Cs cells) predominated among the aberrant cells and showed a dose-dependent increase. All stable chromosome aberrations were classified into 9 types: reciprocal translocations (t), translocations of complex type (t-cx), insertions (ins), complex exchanges (e-cx), peri- and paracentric inversions (inv-peri, inv-para), terminal and interstitial deletions (del-ter, del-int), and unidentified rearrangements. Aberration frequencies increased with increasing dose for all aberration categories. Among the chromosome aberrations classified, reciprocal translocations predominated in all dose ranges. The frequencies of complex aberrations were low at the low-dose level but increased sharply as dose increased.

2. The linear model was fitted to test the dose-response relationship for Cs-cell frequencies. With a constant neutron relative biological effectiveness of 10, an estimated linear slope of 15.2%/Sv was obtained for Dosimetry System 1986 bone-marrow dose with an intercept of 2.9% at dose 0. The present observation confirmed a wide variability of Cs-cell frequencies among individual survivors in every dose category.

3. Statistical analysis of data on 3370 break sites showed good correlations between relative DNA content and the distribution of chromosome breaks involved in translocations, although the involvement of chromosome 1 is significantly higher, for as-yet-unknown reasons.

*RERF Technical Reports (TR) had been printed and published at RERF until the end of 1992. However, beginning in 1993 the TRs were replaced by research results published in scientific journals. Consequently, RERF Reports will be used in lieu of TRs for archival purposes and for limited distribution. RERF Report numbers will be assigned to journal reprints to be purchased from journal publishers. These reprints will be bound into an RERF Report cover with a Japanese summary, and, if necessary, data not published in the scientific journal will be included. For some reports, Japanese versions will be produced by RERF.
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Women with breast cancer (n = 196) and without the disease (n = 566), selected from the Life Span Study sample of A-bomb survivors and nonexposed residents of Hiroshima and Nagasaki, Japan, and matched on age at the time of the bombings, city, and estimated radiation dose, were interviewed about reproductive and medical history. A primary purpose of the study was to identify strong breast cancer risk factors that could be further investigated for possible interactions with radiation dose. As expected, age at first full-term pregnancy was strongly and positively related to risk. Inverse associations were observed with number of births and total, cumulative period of breast feeding, even after adjustment for age at first full-term pregnancy. Histories of treatment for dysmenorrhea and for uterine or ovarian surgery were positively and significantly associated with risk at ages 55 or older, a finding that requires additional study. Other factors related to risk at older ages were the Quetelet index (weight [kg]/height [cm]^2) at age 50, history of thyroid disease, and hypertension. Neither age at menarche nor age at menopause was associated significantly with risk. Subjects appeared to be poorly informed about history of breast cancer or other cancer in themselves or in their close relatives; this finding suggests that innovative strategies may be required when studying familial cancer patterns in Japanese populations.

RERF Report No. 3-93  Clonal fibroblastic cell lines established from a heavily exposed atomic bomb survivor. T Honda, N Sadamori, M Itoh, O Kusumi. (Published in Mutat. Res. 291:125–33, 1993.)

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.

Three breast cancer risk factors were evaluated in terms of their interactions with radiation dose in a case-control interview study of Japanese A-bomb survivors. Cases and controls were matched on age at the time of the bombings and radiation dose, and dose-related risk was estimated from cohort rather than case-control data. Each factor—age at first full-term pregnancy, number of deliveries, and cumulative lactation period summed over births—conformed reasonably well to a multiplicative interaction model with radiation dose (the additive interaction model, in which the absolute excess risk associated with a factor is assumed to be independent of radiation dose, was rejected). An important implication of the finding is that early age at first full-term pregnancy, multiple births, and lengthy cumulative lactation are all protective against radiation-related, as well as baseline, breast cancer. Analyses by age at exposure to radiation suggest that, among women exposed to radiation in childhood or adolescence, a first full-term pregnancy at an early age following exposure may be protective against radiation-related risk.
Commentary and Review Series Abstracts

1 April 1992–31 March 1993


We describe an application of the generalized estimating equation (GEE) method (Liang K-Y, Zeger SL: Longitudinal data analysis using generalized linear models. Biometrika 73:13–22, 1986) for regression analyses of correlated Poisson data. As an alternative to the use of an arbitrarily chosen working correlation matrix, we demonstrate the use of GEE with a reasonable model for the true covariance structure among repeated observations within individuals. We show that, under such a split-plot design with large clusters, the asymptotic relative efficiency of GEE with simple (independence or exchangeable) working correlation matrices is rather low. We also illustrate the use of GEE with an empirically estimated model for overdispersion in a large study of radiation sensitivity where cluster size is small and a simple working correlation structure is sufficient. We conclude by summarizing issues and needs for further work concerning efficiency of the GEE parameter estimates in practice.

CR 3-92  Rogue lymphocytes among Ukrainians not exposed to radioactive fallout from the Chernobyl accident: possible role of this phenomenon in oncogenesis, teratogenesis, and mutagenesis. JV Neel, AA Awa, Y Kodama, M Nakano, K Mabuchi.

Cultured lymphocytes exhibiting extreme cytogenetic damage (rogue cells) were observed in preparations from 8 of 24 individuals sampled in Krasilovka, a Ukrainian village receiving little or no increased radiation following the Chernobyl disaster, but were not observed in an additional 24 persons from two Russian towns in the more-contaminated area. This observation corroborates the worldwide occurrence of these cells. The present data plus a review of the literature establish that rogue cells appear in brief bursts simultaneously in certain individuals in discrete populations. It is suggested that the pattern is consistent with the action of a viral trigger that acts directly or indirectly, the latter possibly through the activation of latent chromosomal retroposons. If this phenomenon occurs in other tissues, it may have important implications for oncogenesis, teratogenesis, mutagenesis, and evolution.

The temporal distribution of exposure-related cancers is relevant to the study of carcinogenic mechanisms. Statistical methods for extracting pertinent information from time-to-tumor data, however, are not well developed. Separation of incidence from "latency" and the contamination of background cases are two problems. In this paper, we present methods for estimating both the conditional distribution given exposure-related cancers observed during the study period and the unconditional distribution. The methods adjust for confounding influences of background cases and the relationship between time to tumor and incidence. Two alternative methods are proposed. The first is based on a structured, theoretically derived model and produces direct inferences concerning the distribution of interest but often requires more-specialized software. The second relies on conventional modeling of incidence and is implemented through readily available, easily used computer software. Inferences concerning the effects of radiation dose and other covariates, however, are not always obtainable directly. We present three examples to illustrate the use of these two methods and suggest criteria for choosing between them. The first approach was used, with a log-logistic specification of the distribution of interest, to analyze times to bone sarcoma among a group of German patients injected with $^{224}$Ra. Similarly, a log-logistic specification was used in the analysis of time to chronic myelogenous leukemias among male atomic-bomb survivors. We used the alternative approach, involving conventional modeling, to estimate the conditional distribution of exposure-related acute myelogenous leukemias among male atomic-bomb survivors, given occurrence between 1 October 1950 and 31 December 1985. All analyses were performed using Poisson regression methods for analyzing grouped survival data.


A workshop to evaluate the status of the emerging DNA-oriented techniques for the study of mutation was held at the RERF Hiroshima Laboratory, 12–14 November 1991.

Following are the recommendations of the workshop.

1. The workshop recognized that the traits used as indicators of genetic damage in the previous studies on the genetic effects of A-bomb radiation all ultimately trace back to variation at the DNA level, some more directly than others, and expressed
the opinion that it would be useful to attempt to estimate the amount of $F_1$ DNA that had in effect already been screened for mutational damage.

2. The workshop, in view of the recent molecular characterization of many of the genes responsible for “sentinel phenotypes” and the resulting possibility of specifying the total amount of DNA being screened by a consideration of these phenotypes, raised the possibility of further medical examinations of the $F_1$, with particular reference to the occurrence of “sentinel phenotypes.” The sentinel phenotypes should include microdeletion syndromes and an assessment of mental retardation. Given the increased knowledge of genetic diseases, particularly polygenic/multifactor diseases, further medical evaluations of the $F_1$ cohort (or review of health records) should be considered.

3. The workshop agreed that it would be appropriate to initiate at this time a major pilot study employing the DNA methodologies discussed by C. Satoh, including denaturing-gradient-gel electrophoresis and Southern-blot analysis to look for insertions/deletions/rearrangements and possibly high-resolution electrophoresis for microsatellite loci. The precise efficiencies achieved with the various techniques discussed will need to be evaluated after several years of experience.

4. With respect to the choice of loci for this pilot study, basically two alternatives were recognized: to study a relatively few loci in the entire material or to study in a subsample of the material more loci (perhaps 10–15); the latter would be selected to be representative of various components of the genome. Genes mentioned in the course of the discussion include the loci encoding for the HLA, immunoglobulin, FMR-1, factors VIII and IX, globin genes, several VNTRs, and microsatellite loci. The p53 gene might be a valuable gene to study for comparing the accumulated data on the somatic-mutation analysis of this important human tumor-suppressor gene with any germinal-mutation-spectrum data. It was suggested that the appropriate selection of loci be studied in approximately 50 of the family constellations available for the exposed population and another 50 from the controls.

A minority of the panel expressed the view that it might be desirable to base the initial studies on genes sensitive to radiation mutagenesis, with the thought that if these showed no damage, the study would not be carried further. However, it was agreed that current knowledge did not permit the selection of such genes.

5. The workshop recognized the large body of data on population variation that would result from this study and the complexity of the resulting data base. It therefore recommended that work be initiated on the design of an appropriate data base, which, in view of the desirability of data exchange, should be compatible with the data bases of various national genome projects.

6. In view of the magnitude of the program, and the desirability of collaborative arrangements that would supplement the efforts of RERF staff, guidelines for such collaboration should be developed. Three initial issues with respect to the guidelines were the following: a) Because of local sensitivities in the cities of Hiroshima and
Nagasaki, collaborative projects should, if possible, be carried out at RERF. To send such samples abroad for analysis might be construed as a breach of the agreement under which the samples were obtained. b) Collaborative projects initiated by outside investigators should be fully funded by these investigators. c) Any collaborative projects directed at a particular gene should require the study of the full material pertaining to that gene; ie, investigators should not be encouraged to study a subsample of what is available for a particular sequence in a way that might satisfy the investigators' needs but not those of RERF.

7. Through this discussion the workshop participants recognized that there was a dearth of data on the mutagenic effects of radiation at the molecular level to guide the proposed studies, and participants encouraged the collection of such data under whatever auspices seemed most appropriate.

8. An effort was suggested, if feasible, to collect surgical and autopsy samples from the members of the study cohort for possible future studies, as well as to complete the project to establish lymphoblastoid cell lines.


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.
Journal Publications

1 April 1992–31 March 1993


Abe M, Takayama K: Analysis of V(D)J recombination by transient assay system. Taisha [Metabolism] 29S:115–24, 1992


Ban S, Cologne JB: X-ray induction of micronuclei in human lymphocyte subpopulations differentiated by immunoperoxidase staining. *Hiroshima Igaku* [J


Honda T, Morikawa A, Sadamori N, Okajima S: Chromosome study of inhabitants in the Nishiyama district, Nagasaki (the fourth report). In: FY-1991 Report of


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Oral Presentations

1 April 1992–31 March 1993

Radiation and Society: A Pedagogical Symposium, 5–10 April 1992, San Francisco, California, USA
- Studies of children in utero during atomic bomb detonations
  Yoshimoto Y, Soda M, Schull WJ, Mabuchi K

11th International Conference on Calcium-regulating Hormones, 24–29 April 1992, Florence, Italy
- Effect of radiation exposure on calcium metabolism

US–Japan Joint Symposium on Cardiovascular Research, 29 April–1 May 1992, Kauai, Hawaii, USA
- Changes in risk factor profiles in adults
  Kodama K

International Conference on the Prevention of Atherosclerosis and Hypertension in Youth, 21–23 May 1992, Orlando, Florida, USA
- Neuromuscular coordination in adolescents and development of hypertension in adults
  Kasagi F, Sasaki H, Kodama K, Akahoshi M, Labarthe DR
- Correlation of blood pressure levels between childhood and adulthood
  Sasaki H, Kasagi F, Kodama K, Akahoshi M

International Open Symposium on Cardiac Arrhythmias, 24 May 1992, Hiroshima
- Arrhythmia in atomic bomb survivors
  Kodama K

33rd Late A-bomb Effects Research Meeting, 7 June 1992, Nagasaki
- Cytogenetic study on the A-bomb exposed human population—A conspectus of cytogenetic findings at ABCC-RERF
  Awa AA
- Association between prevalence of isolated systolic hypertension and dose in the Adult Health Study population
  Kasagi F, Kodama K, Yamada M, Sasaki H, Akahoshi M
Annual Report 92–93

- Humoral immunity in anti-HTLV-1 antibody-positive A-bomb survivors
- Correlation between A-bomb irradiation, tobacco smoking, alcohol consumption, and socioeconomic status
  Akiba S, Kimura M
- Cancer and somatic mutation among the radiation-exposed
  Akiyama M, Umeki S, Kusunoki Y, Kyoizumi S, Mori T, Ishikawa Y, Tatsumi K
- Gene mutation in children of A-bomb survivors—studies at the protein level
  Satoh C
- Epidemiological studies of the F<sub>1</sub> children of A-bomb survivors
  Yoshimoto Y
- Effects of A-bomb radiation on the human immune response. (10) Results of a study on immune response to the EB virus
  Kusunoki Y, Kyoizumi S, Ozaki K, Saito M, Cologne JB, Akiyama M
- Frequency of somatic mutations at the erythrocyte glycoporphin A locus among A-bomb survivors in Nagasaki
  Kyoizumi S, Umeki S, Kusunoki Y, Tanabe K, Nakamura N, Akiyama M
- Frequency of HPRT-deficient mutant cells in peripheral blood lymphocytes of A-bomb survivors
  Hirai Y, Abe N, Kusunoki Y, Akiyama M
- CML-specific BCR-ABL fusion genes are inducible by X-irradiation in vitro
  Ito T, Seyama T, Mizuno T, Hayashi T, Tsuyama N, Dohi K, Nakamura N, Akiyama M

Workshop of the Japanese Society of Hygiene and the Japan Epidemiological Association, 11 June 1992, Osaka
- Establishment and evaluation of mutation assay in human peripheral blood lymphocytes
  Akiyama M

6th Biennial Meeting of the International Society for Free Radical Research, 16–20 June 1992, Trino, Italy
- Oxidative stress in atomic bomb survivors
  Neriishi K

68
International Association of Cancer Registries Annual Meeting, 28–30 June 1992, Ottawa, Canada
- Use of Hiroshima and Nagasaki tumor registries for cancer incidence studies in A-bomb survivors

The International Conference on Low Dose Irradiation and Biological Defense Mechanisms, 12–16 July 1992, Kyoto
- Use of fluorescence in situ hybridization (FISH) technique for detecting radiation-induced translocations in atomic bomb survivors
- Study on the titers of anti-EB virus antibodies in the sera of atomic bomb survivors
  Kusunoki Y, Kyoizumi S, Ozaki K, Cologne JB, Akiyama M
- Flow-cytometric measurements of somatic cell mutations in Thorotrast patients
  Akiyama M, Umeki S, Kusunoki Y, Nakamura N, Sasaki MS, Mori T, Ishikawa Y, Cologne JB
- Dose-response analysis among atomic-bomb survivors exposed to low-level radiation
  Shimizu Y, Kato H, Schull WJ, Mabuchi K,
- The shape of the cancer incidence dose-response curve for the A-bomb survivors
  Væth M, Preston DL, Mabuchi K

Fukui Workshop on Health Risks: Perspectives and Research, 17–19 July 1992, Fukui
- Role of somatic mutations for risk evaluation of various high risk cancer groups
  Akiyama M, Umeki S, Kyoizumi S, Kusunoki Y, Nakamura N, Tatsumi K, Ohama K, Yamakido M

7th International Conference of the International Society of Differentiation, 19–23 July 1992, Helsinki, Finland
- Unique association of p53 mutations with undifferentiated but not with differentiated carcinomas of the thyroid gland
  Ito T, Seyama T, Mizuno T, Tsuyama N, Hayashi T, Hayashi Y, Dohi K, Nakamura N, Akiyama M
60th General Meeting of the Japan Statistical Society, 21–24 July 1992, Ishinomaki
- A longitudinal study of growth and development of stature
  Otake M, Fujikoshi Y, Schull WJ, Izumi S

- Quantitation of gene dosage: accurate and rapid detection of heterozygous carriers of a deletion by combined PCR and HPLC
  Asakawa J, Satoh C, Kodaira M, Hiyama K
- The study of genetic instability of tandem-repetitive-elements in human germ cells
  Kodaira M, Kaneko J, Satoh C

10th General Meeting of the Japanese Society of Bone Metabolism, 23–25 July 1992, Tokyo
- Changes in calcium-regulating hormones among A-bomb survivors

17th Meeting of the Chugoku District Radiation Research Study Group, 24 July 1992, Higashi Hiroshima
- Evaluation of lymphocyte kinetics in vivo using chromosome aberration data
  Nakamura N, Awa AA, Umeki S, Akiyama M
- Somatic mutation frequencies among radiation-exposed people affected by the Chernobyl accident
  Kusunoki Y, Hayashi T, Kyoizumi S, Seyama T, Nakamura N, Kodama Y, Sasaki H, Dohi K, Akiyama M

2nd International Conference on Theories of Carcinogenesis, 15–21 August 1992, Oslo, Norway
- Are p53 mutations associated with tumor progression?
  Seyama T, Ito T, Mizuno T, Tsuyama N, Hayashi T, Hayashi Y, Nakamura N, Akiyama M
- BCR-ABL fusion genes are inducible by X-irradiation in vitro
  Mizuno T, Ito T, Seyama T, Hayashi T, Nakamura N, Akiyama M

14th International Congress of the Transplantation Society, 16–21 August 1992, Paris, France
- HLA class II DNA typing using the PCR-SSCP method for screening of transplant donors
  Hayashi T, Kusunoki Y, Hirai Y, Nakamura N, Dohi K, Akiyama M
- Hematopoietic malignancies among A-bomb survivors
  Kusumi S, Nonaka H, Dohy H, Tomonaga M, Kamada N, Kuramoto A

8th International Congress of Immunology, 23–28 August 1992, Budapest, Hungary
- DNA analysis of somatic recombinants at the HLA locus
  Akiyama M, Hayashi T, Kusunoki Y, Hirai Y

11th International Congress on Photobiology, 7–12 September 1992, Kyoto
- Evaluation of radiation damage to human hematopoietic progenitor cells engrafted in SCID mice
  Kyoizumi S, Akiyama M, McCune JM, Namikawa R

20th Meeting of the Japan Society for Clinical Immunology, 10–12 September 1992, Saitama
- Analysis of somatic recombination sites of a cancer-prone hereditary disease, Bloom’s syndrome by HLA DNA typing
  Hayashi T, Kusunoki Y, Hirai Y, Nakamura N, Akiyama M
- Analysis of somatic cell mutation at the HLA-A locus of patients with Bloom’s syndrome, a highly cancer-prone disease
  Kusunoki Y, Hirai Y, Hayashi T, Nakamura N, Akiyama M

19th Meeting of the Radiation Risk Evaluation Committee, 16–17 September 1992, Tokyo
- Measurement of biological dose using somatic cell mutations and identification of high risk groups
  Akiyama M

Symposium on “Recent Advances in Two-dimensional Electrophoresis,” 18 September 1992, Tsukuba
- Two-dimensional gel electrophoresis with immobilized pH gradients in capillary tubes in the first dimension
  Asakawa J

Meeting of the American Association for Cancer Research, 23–26 September 1992, Naples, Florida, USA
- Biological dosimetry applicable to cancer epidemiology
  Mendelsohn ML
International Conference on the Sociopsychological Consequences Caused by the Chernobyl Nuclear Power Plant Accident, 28–30 September 1992, Kiev, Ukraine
- Psychological consequences produced by radiation exposure
  Kusumi S, Yamada M, Wong FL, Kodama K, Nakamura S

51st Annual Meeting of the Japanese Cancer Association, 29 September–1 October 1992, Osaka
- Analyses of somatic cell mutations induced in uterine cervical cancer patients receiving radiotherapy
  Hirai Y, Ohama K, Akiyama M
- Analysis of p53 genes in Li-Fraumeni syndrome patients
  Mizuno T, Yuasa H, Ito T, Seyama T, Nakamura N, Tokunaga M, Akiyama M
- cDNA cloning of a highly expressing gene in various human cancer cell lines and cancer tissues
- Evaluation and measurement of somatic mutation among people who have high risk of cancer development
- Analysis of somatic recombination sites at the HLA locus of a cancer-prone hereditary disease, Bloom’s syndrome
  Hayashi T, Kusunoki Y, Hirai Y, Seyama T, Ito T, Nakamura N, Akiyama M
- Application of TCR mutant frequency analysis to evaluation of cancer risks
- Unique association of p53 mutations with undifferentiated but not with papillary adenocarcinoma of the thyroid gland
  Ito T, Seyama T, Mizuno T, Tsuyama N, Hayashi T, Hayashi Y, Dohi K, Nakamura N, Akiyama M
- BCR-ABL fusion genes are inducible by X-irradiation in vitro
  Seyama T, Ito T, Mizuno T, Hayashi T, Tsuyama N, Dohi K, Nakamura N, Akiyama M
14th Annual Meeting of the American Society for Bone and Mineral Research, 30 September–4 October 1992, Minneapolis, Minnesota, USA
- Parathyroid hormone, calcitonin, and osteocalcin levels among Japanese—a population-based study

1st China–Japan Conference on Medical Genetics, 8–10 October 1992, Beijing, China
- Radiation-induced translocations in peripheral lymphocytes of Hiroshima atomic bomb survivors measured using FISH, G-banding, and conventional analyses

39th General Meeting of the Japan Society of Clinical Pathology, 14–16 October 1992, Nagasaki
- Review of bone ALP measurement with Hitachi 7050
  Kobayashi Y, Kitagawa T, Kusumi S, Fujiwara S, Kodama K

  Kabuto M, Akiba S, Neriishi K
- Tracking phenomenon of body mass index
  Kasagi F, Sasaki H, Yamada M, Kodama K, Akahoshi M, Shimaoka K
- Correlation between skin elastance and subsequent deaths
  Kubo Y, Kasagi F, Sasaki H, Fujita S, Kodama K
- Report on the status of medication among RERF Adult Health Study participants (Report 1)
  Masunari N, Fujiwara S, Yamada M, Okibayashi I, Minami K, Kodama K

Mini-symposium on Cancer Progression and Metastasis, 23 October 1992, Hiroshima
- Genetic alteration in thyroid tumor progression: association with p53 gene mutation
  Akiyama M, Ito T, Seyama T, Hayashi Y, Dohi K
35th Annual Meeting of the Japan Radiation Research Society, 28–30 October 1992, Otsu

- Radiation-related ophthalmologic changes and aging among Hiroshima and Nagasaki A-bomb survivors: A statistical reanalysis
  Otake M, Finch SC, Choshi K, Takaku I, Mishima H, Takase T
- Frequency of translocations and dicentrics induced by X-irradiation in vitro as determined by the FISH method
- Chromosome aberrations originating from a single stem cell in peripheral blood lymphocytes of an A-bomb survivor
  Kodama Y, Kusunoki Y, Hirai Y, Akiyama M, Awa AA
- Translocation frequencies in A-bomb survivors by fluorescence in situ hybridization (FISH) technique. I. Comparison with G-banding and conventional analyses
  Awa AA, Kodama Y, Nakano M, Ohtaki K, Lucas JN, Gray JW
- Spontaneous frequency of chromosomal fragile site expressions: A pilot test for an A-bomb survivors feasibility study
  Ban S, Cologne JB, Nerishi K, Akiba S
- Incidence of myocardial infarction among A-bomb survivors
  Kodama K, Shimizu Y, Sasaki H, Shimaoka K
- G-banding analysis of radiation-induced chromosome damage in lymphocytes of Hiroshima A-bomb survivors
  Ohtaki K, Nakashima E, Awa AA
- Dose-response among atomic-bomb survivors exposed to low-level radiation
  Shimizu Y, Kato H, Schull WJ, Mabuchi K
- Analysis of somatic mutation frequency among those exposed to radiation from the Chernobyl nuclear power plant accident
- Frequency of HPRT-deficient mutant cells in peripheral lymphocytes of about 250 A-bomb survivors
  Hirai Y, Abe N, Kyoizumi S, Kusunoki Y, Akiyama M
- Detection of BCR-ABL genes in peripheral blood from gynecological cancer patients who have undergone radiotherapy
  Mizuno T, Ito T, Seyama T, Iwamoto KS, Kodama T, Ohama K, Nakamura N, Akiyama M
- Immune responses to anti-EB virus in A-bomb survivors. I. Study on humoral immune responses
  Kusunoki Y, Kyoizumi S, Ozaki K, Cologne JB, Akiyama M
A study on somatic mutations in A-bomb survivors—erythrocyte GPA gene mutation in A-bomb survivors in Hiroshima and Nagasaki
Akiyama M, Umeki S, Kusunoki Y, Kyoizumi S, Mizuno T, Nakamura N, Akahoshi M, Kodama K

Human lymphocyte kinetics in vivo deduced from chromosome aberration data
Nakamura N, Umeki S, Akiyama M, Awa AA

A trial in human radiobiology using SCID-hu mouse—effects of X-ray on human bone marrow
Kyoizumi S, Akiyama M, McCure JM, Namikawa R

Lymphocyte chromosome aberrations and TCR gene mutations in radiotherapy patients
Iwamoto KS, Hirai Y, Umeki S, Kusunoki Y, Kyoizumi S, Kodama T, Ohama K, Nakamura N, Akiyama M

Immune response to EB virus in atomic bomb survivors. II. Cellular immunity study
Hayashi T, Kusunoki Y, Kyoizumi S, Ozaki K, Saito M, Akiyama M

Application of the TCR mutant frequency assay for biological estimation of exposure doses

Dietary habits among the A-bomb survivors and assessments of the late effects of A-bomb radiation
Yoshimoto Y, Yamada M, Hayabuchi H, Akiba S, Mabuchi K

35th Annual Meeting of the Japan Radiation Research Society, Japan Late Effects Group Research Meeting, 30 October 1992, Otsu
Somatic mutations in human increased with aging and induced by radiation
Akiyama M

37th Meeting of the Japan Human Genetics Society, 29–31 October 1992, Tsukuba
Deletions and insertions detected among Japanese in the α-globin gene cluster and the retinoblastoma gene
Kodaira M, Kaneko J, Miura A, Satoh C

Verification of a proposed phylogeny for the principal alleles of human phosphoglucomutase (PGM1) by DNA sequencing
Takahashi N, Kimura Y, Kaneko J, Omine H, Satoh C
Detection of DMD carriers with deletions or duplications: application of quantitation of gene dosage using combined PCR and HPLC

35th Meeting of the Thyroid Division of the Japan Endocrine Society, 4–6 November 1992, Omiya
Factors for establishing normal value of thyroid volume

33rd General Meeting of the Japan Lung Cancer Society, 5–6 November 1992, Nagoya
Study on mutagenesis of T-cell receptor genes by chemotherapeutic agents
Umeki S, Yamakido M, Dohi K, Kuraoka T, Kyoizumi S, Akiyama M

Analysis of cancer risk based on longitudinal information on smoking habits
Akiba S

Nagoya International Symposium on Aging and Health, 13–14 November 1992, Nagoya
Longitudinal study on aging of A-bomb survivors
Sasaki H

22nd Annual Meeting of the Japanese Society for Immunology, 25–27 November 1992, Nagoya
Mapping of a human gene complementing the SCID (severe combined immunodeficient) mutation in the mouse
Itoh M, Hamatani K, Abe M
Analysis of relationship between transcription and V(D)J recombination
Abe M, Takayama K, Shiku H
Analysis of in vivo differentiation of human blood cells using genetic markers. I. Analysis using chromosomal aberrations as markers
Kusunoki Y, Hirai Y, Kyoizumi S, Akiyama M
Analysis of in vivo differentiation of human blood cells using genetic markers. II. T cell differentiation from a HPRT mutant stem cell
Hirai Y, Kusunoki Y, Akiyama M
Analysis of somatic recombinants at the HLA locus
Hayashi T, Kusunoki Y, Seyama T, Ito T, Hirai Y, Akiyama M
Effects of hematopoietic factors and radiation on human bone marrow transplanted into SCID mice
Kyoizumi S, Akiyama M, McCune JM, Kaneshima H, Murray L, Namikawa R

Conference on the Decline in Stroke Mortality, 30 November–1 December 1992, Bethesda, Maryland
- Stroke trends in Japan
  Kodama K

24th National Institute of Radiological Sciences Symposium, 3–4 December 1992, Chiba
- Gene rearrangement and radiation carcinogenesis—BCR/ABL and RET genes
  Ito T, Seyama T, Dohi K, Nakamura N, Akiyama M
- The SCID-hu mouse and its application to human radiobiology—effects of radiation on human bone marrow
  Kyoizumi S, Akiyama M, McCune JM, Namikawa R
- p53 in differentiation of thyroid cancer
  Seyama T, Ito T, Hayashi Y, Dohi K, Akiyama M

15th Annual Meeting of the Molecular Biology Society of Japan, 7–10 December 1992, Kyoto
- Identification of a human chromosome complementing the mutant gene of the SCID (severe combined immunodeficient) mouse
  Itoh M, Hamatani K, Abe M
- Detection of variations in DNA by denaturing gradient gel electrophoresis
  Takahashi N

16th International Biometric Conference, 7–11 December 1992, Hamilton, New Zealand
- Applying the growth curve model to repeated measurements of stature of prenatally exposed survivors
  Otake M, Fujikoshi Y, Schull WJ, Izumi S

3rd General Meeting of the Japan Epidemiological Association, 21–22 January 1993, Utsunomiya
- Physical activity and mortality
  Shimizu Y, Kodama K, Sasaki H
- Use of blood chemistry for the study of an intractable disease—Parkinson’s disease
  Neriishi K, Akiba S, Kodama K
■ Cerebrovascular dementia in the AHS population
   Sasaki H, Shimizu Y, Kodama K
■ Evaluation of estimated physiological age—results of prognosis follow-up
   Fujita S, Kasagi F, Sasaki H, Kodama K, Shimizu Y

6th International Conference on Environmental Mutagens, 21–26 February 1993, Melbourne, Australia
■ Somatic mutation studies for the monitoring of radiation exposures including those of A-bomb survivors
   Akiyama M, Kyoizumi S, Umeki S, Kusunoki Y, Hirai Y, Nakamura N
■ A pilot study for the detection of mutations in the children of atomic bomb survivors
   Satoh C, Takahashi N, Kodaira M, Asakawa J, Hiyama K

6th International Conference on Environmental Mutagens, Satellite Symposium, 1–4 March 1993, Barossa Valley, Australia
■ Analysis of human in vivo somatic mutations by flow cytometry
   Akiyama M, Umeki S, Kusunoki Y, Kyoizumi S, Nakamura N

Radiation Biology Center International Workshop: Origin of Mutation and Risk of Cancer, 2–3 March 1993, Kyoto
■ X-irradiation induces BCR-ABL fusion gene transcripts in cultured cells in vitro
   Nakamura N, Ito T, Seyama T, Mizuno T, Iwamoto KS, Hayashi T, Akiyama M
■ The study of genetic instabilities of tandem-repetitive-elements in germ cells of atomic bomb survivors
   Kodaira M, Satoh C

30th Nagasaki Prefectural General Public Health Research Meeting, 5 March 1993, Nagasaki
■ Use of a pedometer for promotion of health at work
   Ide M, Yamashita Y, Ohishi K

57th Annual Scientific Meeting of the Japanese Circulation Society, 25–27 March 1993, Chiba
■ Effects of physical development on blood pressure change in adolescence
   Akahoshi M, Soda M, Shimaoka K, Nakashima E, Carter RL, Seto S, Yano K
Spine fracture prevalence is similar among Caucasians and Japanese-Americans but greater among native Japanese women

Predictors of bone mass differ between native Japanese and Japanese-Americans and between birth cohorts
Report from the Secretariat

The 26th meeting of the Board of Directors

The 26th meeting of the Board of Directors was held for 3 days, 24–26 June, at the Nagasaki Koseinenkin Hall in Nagasaki City and at the Huis Ten Bosch in Sasebo City.

Present personnel status, summary of the recommendations of the Human Germline Mutagenesis Workshop, and status of international collaborative activities were reported. Also, it was reported that new research areas such as molecular epidemiology and molecular biology will be emphasized and that relocation of the Hiroshima facilities is targeted for 5 years later. (The minutes of the Board Meeting are in the Appendix, starting on page 117.)

Change of directors

The Board of Directors of the Radiation Effects Research Foundation elected Mortimer L. Mendelsohn (an RERF scientific councilor and formerly associate director for biomedical and environmental research, Lawrence Livermore National Laboratory) as an RERF permanent director to fill a vacant position. Seymour Abrahamson (a professor of zoology at the University of Wisconsin) was elected as successor to Chief of Research James E. Trosko, who will resign on 14 August. John B. Little (professor of radiobiology at Harvard University) was elected to replace Dr. Mendelsohn, as an RERF scientific councilor.

Tadashi Nakaoka was appointed as successor to Yoshio Okamoto, Operating Committee member (business administrator, Nagasaki Laboratory), who will retire on 30 June.

Personnel

RERF employees totaled 431 as of 31 March 1993, a decrease of 3 compared to a year ago. Because of the policy of gradually reducing budgeted positions, employment of new general employees is being kept to a minimum.

Salary revision

A Fiscal Year 1992 (FY92) salary increase of 2.87% (¥9072) was enacted for national government employees as recommended by the National Personnel Authority. The salaries of RERF's general employees were increased by 2.65% (¥8780), on the basis of the action taken for national government employees. The salaries of directors and professional employees were revised, taking into consideration a balance with general-staff salaries. The salary increase was effective retroactive to 1 April 1992.
Organization of RERF
Organization of the laboratories

Hiroshima

- Department of Clinical Studies
- Department of Genetics
- Department of Radiobiology
- Department of Epidemiology
- Department of Statistics
- Department of Epidemiologic Pathology
- Research Information Center
- Publication & Documentation Center

Nagasaki

- Department of Clinical Studies
- Department of Radiobiology
- Department of Epidemiology & Biometrics
- Department of Epidemiologic Pathology

Radioisotope Facility

Division of Medicine
Division of Radiology
Division of Clinical Laboratories
Nursing Section
Clinical Administration Section
Clinical Contacting Section
Laboratory of Cytogenetics
Laboratory of Biochemical Genetics
Laboratory of Cell Biology
Laboratory of Immunology
Master File Section
Coding Section
Field Investigation Section
Laboratory of Pathology
Tumor & Tissue Registry Office
Information Systems Laboratory
Computer Section
Administration & Support Section
Editorial & Publications Section
Library & Archives
Library Office
Archives Office
Radioisotope Facility
Organization of the Secretariat

Hiroshima

- General Affairs Section
  - Director's Office
  - General Affairs Unit
  - Archives & Document Unit
- External Affairs Section
  - Administrative Unit
  - International Relations Unit
  - Public Relations Unit
- Personnel Section
  - Personnel Unit
  - Payroll Unit
- Accounting Section
  - Accounting Unit
  - Receipts & Disbursement Unit
- Supply and Property Section
  - Supply Unit
  - Physical Plant Unit
- Operations Section
  - Operations Unit
  - Welfare Unit
  - Food Service Unit

Nagasaki

- General Affairs Section
  - Public Relations Office
  - General Affairs Unit
  - Employees Unit
- Accounting Section
  - Accounting Unit
  - Supply Unit
Establishment of RERF regulations
Following the enforcement of the Law Concerning Child Care Leave, the Regulations Concerning Child Care Leave, etc., were established and effected as of 1 April 1992.

Personnel as of 31 March 1993

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<th>Full-time personnel</th>
<th>Hiroshima</th>
<th>Nagasaki</th>
<th>Total</th>
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<td>Directors</td>
<td>6 (3)</td>
<td>6 (3)</td>
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<td>Professionals*</td>
<td>49 (15)</td>
<td>13 (1)</td>
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<td>General</td>
<td>260 (2)</td>
<td>103</td>
<td>363 (2)</td>
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<tr>
<td>Total</td>
<td>315 (20)</td>
<td>116 (1)</td>
<td>431 (21)</td>
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* Numbers in parentheses are personnel recruited in the U.S.

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<tr>
<th>Department/division</th>
<th>Consultants</th>
<th>Panel members</th>
<th>Part-time professionals</th>
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<td>Total</td>
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<td>Clinical Studies</td>
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<tr>
<td>Total</td>
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* Two members of the Secretariat staff are the industrial health physicians (part-time).

Note: H = Hiroshima. N = Nagasaki.
## Personnel composition

**As of 31 March 1993**

<table>
<thead>
<tr>
<th>Department or section</th>
<th>Directors</th>
<th>Research scientists</th>
<th>A Administrative</th>
<th>B Manual &amp; gen. tech.</th>
<th>C Medical &amp; technical (I)</th>
<th>D Medical &amp; technical (II)</th>
<th>Total</th>
<th>Visiting scientists</th>
<th>Temporary employees*</th>
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<tr>
<td><strong>Hiroshima</strong></td>
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<td>Epidemiologic Pathology</td>
<td></td>
<td></td>
<td></td>
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<td>Publication &amp; Docum. Ctr</td>
<td>2</td>
<td>31</td>
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<td>33</td>
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<tr>
<td>Radioisotope Facility</td>
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<td></td>
<td></td>
<td></td>
<td>2</td>
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<tr>
<td>Senior consulting scientists</td>
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</tr>
<tr>
<td>Secretariat</td>
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<td>15</td>
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<td><strong>Total</strong></td>
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<td>49</td>
<td>176</td>
<td>22</td>
<td>48</td>
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<td><strong>Nagasaki</strong></td>
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<td>Associate chief of research</td>
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<tr>
<td>Clinical Studies</td>
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<td>22</td>
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<tr>
<td>Radiobiology</td>
<td>4</td>
<td>1</td>
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<td>7</td>
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<td></td>
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<tr>
<td>Epidemiologic Biometrics</td>
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<tr>
<td>Epidemiologic Pathology</td>
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<td>3</td>
<td>3</td>
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<tr>
<td>Radioisotope Facility</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>1</td>
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<td></td>
</tr>
<tr>
<td>Senior consulting scientists</td>
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<td></td>
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<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secretariat</td>
<td></td>
<td></td>
<td>19</td>
<td>4</td>
<td></td>
<td></td>
<td>23</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>13</td>
<td>67</td>
<td>6</td>
<td>22</td>
<td>8</td>
<td>116</td>
<td>431</td>
<td>2</td>
<td>9</td>
</tr>
</tbody>
</table>

*Supported by entrusted funds

Note: Among the 243 administrative and clerical staff, 173 are in research support units and 70 are in the Secretariat.
Mandatory retirement

The following employees (six in Hiroshima and 11 in Nagasaki) reached the mandatory retirement age in FY92.

**Hiroshima Laboratory**

June: Kenji Yorichika and Masatoshi Kawakami
December: Noboru Kosaka, Yasukuni Okadoi, Kiyoharu Aoki, and Keiko Yamada

**Nagasaki Laboratory**

June: Yoshio Okamoto, Teibi Ikeyama, Keiko Masuda, and Kiyoko Yamashita
December: Hiroyuki Miyaji, Hitoshi Tokai, Toshiharu Matsuo, Akiko Fukagawa, Yasuko Kanematsu, Reijiro Sakamoto, and Kazutoshi Machida

Long Service Award ceremonies

Long Service Award ceremonies were held on 14 April in Hiroshima and on 30 April in Nagasaki to express appreciation to employees (16 in Hiroshima and 7 in Nagasaki) for their many years of devoted service.

**Hiroshima Laboratory**

- **Thirty-year award recipients**: Kiyoko Yamayoshi, Kazumi Tanabe, Toshiharu Ueno, Kunie Atsuta, Iwao Osaki, and Morito Dote
- **Twenty-year award recipient**: Yayoko Hirofuji
- **Ten-year award recipients**: Yoshitaka Sakamoto, Setsuko Konishi, Hiroko Moriwaki, Fusako Hasegawa, Hiromi Tagawa, Jill L. Ohara, Hideo Sasaki, Nobuaki Harachi, and Hideaki Murata

**Nagasaki Laboratory**

- **Thirty-year award recipients**: Yoko Sakuma, Kuniyo Yamaguchi, and Makiko Hamamatsu
- **Ten-year award recipients**: Shoko Tani, Tomoko Yamaguchi, Nami Sakata, and Shinichiro Ichimaru
Fiscal and property report

The RERF budget and settlement of accounts for FY92 are presented here. A list of major equipment items purchased during the fiscal year is included.

Budget and settlement of accounts

The subsidy income that is the main source of regular income is equally provided by the governments of Japan and the United States based on the principle of equal support.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>¥3,761,014,000</td>
<td>¥4,059,500,000</td>
<td>¥4,318,030,000</td>
</tr>
<tr>
<td>Personnel expenses</td>
<td></td>
<td>(99.7%)</td>
<td>(107.9%)</td>
<td>(106.4%)</td>
</tr>
<tr>
<td>Operational expenses</td>
<td></td>
<td>772,648,000</td>
<td>824,834,000</td>
<td>855,612,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(102.7%)</td>
<td>(106.8%)</td>
<td>(103.7%)</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>4,533,662,000</td>
<td>4,884,334,000</td>
<td>5,173,642,000</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(100.2%)</td>
<td>(107.7%)</td>
<td>(105.9%)</td>
</tr>
</tbody>
</table>

The total RERF budget for operations was ¥5,173,642,000, an increase of ¥289,308,000 (+5.9%) over the previous year. The major increases were a ¥258,530,000 (+6.4%) increase in personnel expenses and a ¥30,778,000 (+3.7%) increase in operational expenses.

In the settlement of accounts for FY92, there was a surplus of ¥299,640,982 in personnel funds and ¥298,358,991 of the surplus was returned to the Japanese government and ¥1,281,991 to the U.S. government.
### Equipment

Major items of equipment costing ¥1 million or more purchased during FY1992 are listed below:

**Hiroshima**

<table>
<thead>
<tr>
<th>Equipment</th>
<th>Cost</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sceptre Computer System #486/33 IBM</td>
<td>¥1,228,799</td>
<td>Computer Section</td>
</tr>
<tr>
<td>Freezer Ultra #ULT-1386-7 REVCO</td>
<td>1,699,500</td>
<td>Lab. of Pathology</td>
</tr>
<tr>
<td>Freezer Ultra #ULT-1786-7 REVCO</td>
<td>2,018,800</td>
<td>Div. of Clinical Laboratories</td>
</tr>
<tr>
<td>Pulsed-field Gel Electrophoresis PHARMACIA</td>
<td>2,486,420</td>
<td>Lab. of Cell Biology</td>
</tr>
<tr>
<td>Electroporation Apparatus #165–2087 BIORAD</td>
<td>1,078,410</td>
<td>Lab. of Cell Biology</td>
</tr>
<tr>
<td>Fraction Collector #FRC-10A SHIMAZU</td>
<td>2,441,100</td>
<td>Lab. of Immunology</td>
</tr>
<tr>
<td>Tank Liquid Nitrogen #DR-430-LM DAIYA</td>
<td>4,014,940</td>
<td>Lab. of Immunology</td>
</tr>
<tr>
<td>Automatic Cell Deposition BECTON DICKINSON</td>
<td>2,729,500</td>
<td>Lab. of Immunology</td>
</tr>
<tr>
<td>Freebook Binding Machine #BQ-51 HORIZON</td>
<td>1,124,760</td>
<td>Editorial &amp; Publication Section</td>
</tr>
<tr>
<td>Microscope Fluorescence #X2F-EFD2 System NIKON</td>
<td>3,288,790</td>
<td>Lab. of Cytogenetics</td>
</tr>
<tr>
<td>Copying Machine Color 635 XEROX</td>
<td>2,533,800</td>
<td>Editorial &amp; Publication Section</td>
</tr>
</tbody>
</table>

**Nagasaki**

<table>
<thead>
<tr>
<th>Equipment</th>
<th>Cost</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean Bench #VSF-1300-RA NIHON-IKA</td>
<td>1,151,540</td>
<td>Lab. of Cell Biology</td>
</tr>
<tr>
<td>Meter Pulse Wave Velocity #PWV-200 FUKUDA-DENSHI</td>
<td>1,230,850</td>
<td>Div. of Medicine</td>
</tr>
<tr>
<td>Incubator CO2 #BL320 ASTEC</td>
<td>2,029,100</td>
<td>Lab. of Cell Biology</td>
</tr>
<tr>
<td>Chamber Draft #DE-212K DALTON</td>
<td>1,044,420</td>
<td>Lab. of Cell Biology</td>
</tr>
<tr>
<td>Two-dimensional Electrophorator #TEP-1 &amp; TEP-C1 SHIMAZU</td>
<td>4,037,600</td>
<td>Lab. of Cell Biology</td>
</tr>
</tbody>
</table>
Statement of income and expenditure, regular account
1 April 1992–31 March 1993

<table>
<thead>
<tr>
<th>Category</th>
<th>Budget</th>
<th>Settlement</th>
<th>Balance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a</td>
<td>b</td>
<td>a–b</td>
</tr>
<tr>
<td><strong>Income (yen)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subsidy income</td>
<td>¥(5,141,752,000)</td>
<td>¥(4,844,675,000)</td>
<td>¥(297,077,000)</td>
</tr>
<tr>
<td>GOJ treasury</td>
<td>2,570,876,000</td>
<td>2,570,876,000</td>
<td>0</td>
</tr>
<tr>
<td>GUS treasury</td>
<td>2,570,876,000</td>
<td>2,273,799,000</td>
<td>297,077,000</td>
</tr>
<tr>
<td>Independent income</td>
<td>(31,890,000)</td>
<td>(68,730,704)</td>
<td>(Δ 36,840,704)</td>
</tr>
<tr>
<td>Medical exams (ABSMTL)</td>
<td>31,890,000</td>
<td>28,622,941</td>
<td>3,267,059</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>0</td>
<td>40,107,763</td>
<td>Δ 40,107,763</td>
</tr>
<tr>
<td>Brought forward from special acct.</td>
<td>(0)</td>
<td>(597,630)</td>
<td>(Δ 597,630)</td>
</tr>
<tr>
<td>Dining room acct.</td>
<td>0</td>
<td>597,630</td>
<td>Δ 597,630</td>
</tr>
<tr>
<td><strong>Total income (A)</strong></td>
<td>5,173,642,000</td>
<td>4,914,003,334</td>
<td>259,638,666</td>
</tr>
<tr>
<td><strong>Expenditures</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personnel expenses</td>
<td>(4,318,030,000)</td>
<td>(3,742,938,018)</td>
<td>(575,091,982)</td>
</tr>
<tr>
<td>Operational expenses</td>
<td>(855,612,000)</td>
<td>(871,424,334)</td>
<td>(Δ 15,812,334)</td>
</tr>
<tr>
<td>Fees &amp; gratuities</td>
<td>33,956,000</td>
<td>38,929,141</td>
<td>Δ 4,973,141</td>
</tr>
<tr>
<td>Travel, directors &amp; staff</td>
<td>31,097,000</td>
<td>29,135,390</td>
<td>1,961,610</td>
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<tr>
<td>Travel, committee</td>
<td>15,051,000</td>
<td>6,991,087</td>
<td>8,059,913</td>
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<tr>
<td>Travel, relocation</td>
<td>28,330,000</td>
<td>25,645,531</td>
<td>2,684,469</td>
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<tr>
<td>Travel, overseas</td>
<td>12,160,000</td>
<td>14,557,629</td>
<td>Δ 2,397,629</td>
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<tr>
<td>Office &amp; lab. expenses</td>
<td>657,618,000</td>
<td>676,144,068</td>
<td>Δ 18,526,068</td>
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<tr>
<td>Rent, land &amp; buildings</td>
<td>50,000,000</td>
<td>50,103,599</td>
<td>Δ 103,599</td>
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<tr>
<td>Maintenance &amp; repair</td>
<td>26,500,000</td>
<td>29,084,139</td>
<td>Δ 2,584,139</td>
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<td>Taxes</td>
<td>900,000</td>
<td>833,750</td>
<td>66,250</td>
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<tr>
<td><strong>Total expenditures (B)</strong></td>
<td>5,173,642,000</td>
<td>4,614,362,352</td>
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<tr>
<td><strong>Balance (A) – (B)</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>(FY92 personnel expenses surplus)</td>
<td></td>
<td></td>
<td>299,640,982</td>
</tr>
</tbody>
</table>

Note: ABSMTL: Atomic Bomb Survivors' Medical Treatment Law
Δ Indicates income or expenditures in excess of budget
## Settlement of accounts, summary sheet

**1 April 1992 – 31 March 1993**

<table>
<thead>
<tr>
<th>Category</th>
<th>Total</th>
<th>Regular account</th>
<th>Cancer case - LSS SP. A/C</th>
<th>Radiation risk assessment SP. A/C</th>
<th>Shigematsu colla. study SP. A/C</th>
<th>Termination trust fund SP. A/C</th>
<th>NAS housing SP. A/C</th>
<th>HH dining room SP. A/C</th>
<th>Nagasaki Pref. Cancer Registry SP. A/C</th>
<th>Cancer research resources SP. A/C</th>
<th>A-bomb memorial SP. A/C</th>
<th>Aging &amp; Dementia Study SP. A/C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Income</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subsidy</td>
<td>4,844,675,000</td>
<td>4,844,675,000</td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operational income (interest, etc.)</td>
<td>132,232,453</td>
<td>68,730,704</td>
<td>29,627</td>
<td>5,581</td>
<td>57,662,456</td>
<td>1,027,753</td>
<td>4,776,332</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transferred from special account</td>
<td>597,630</td>
<td>597,630</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Entrustment fund</td>
<td>127,486,247</td>
<td>48,821,025</td>
<td>3,502,000</td>
<td>19,000,000</td>
<td></td>
<td>3,309,976</td>
<td></td>
<td></td>
<td>7,500,000</td>
<td>5,000,000</td>
<td>36,204,000</td>
<td>4,149,246</td>
</tr>
<tr>
<td>Carried over from previous year</td>
<td>1,173,739,298</td>
<td>254,891</td>
<td></td>
<td></td>
<td></td>
<td>1,172,476,535</td>
<td>1,007,872</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>Total income</strong></td>
<td>6,278,730,628</td>
<td>4,914,003,334</td>
<td>49,105,543</td>
<td>3,502,000</td>
<td>19,005,581</td>
<td>5,345,601</td>
<td>4,776,332</td>
<td>7,500,000</td>
<td>5,000,000</td>
<td>36,204,000</td>
<td>4,149,246</td>
<td></td>
</tr>
<tr>
<td><strong>Expenditures</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Personal expenses</td>
<td>3,962,382,624</td>
<td>3,742,938,018</td>
<td>19,631,081</td>
<td>0</td>
<td>186,581,066</td>
<td>3,376,300</td>
<td>0</td>
<td>9,856,159</td>
<td>0</td>
<td>26,347,841</td>
<td>4,149,246</td>
<td></td>
</tr>
<tr>
<td>Operational expenses</td>
<td>972,032,518</td>
<td>871,424,334</td>
<td>29,894,579</td>
<td>3,502,000</td>
<td>19,005,581</td>
<td>4,406,535</td>
<td>4,178,702</td>
<td>4,123,700</td>
<td>5,000,000</td>
<td>36,204,000</td>
<td>4,149,246</td>
<td></td>
</tr>
<tr>
<td>Transferred to regular account</td>
<td>597,630</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>597,630</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total expenses</strong></td>
<td>4,935,012,772</td>
<td>4,614,362,352</td>
<td>49,525,660</td>
<td>3,502,000</td>
<td>19,005,581</td>
<td>4,406,535</td>
<td>4,776,332</td>
<td>7,500,000</td>
<td>5,000,000</td>
<td>36,204,000</td>
<td>4,149,246</td>
<td></td>
</tr>
<tr>
<td><strong>Balance, income less expenses</strong></td>
<td>1,343,717,856</td>
<td>299,640,982</td>
<td>6420,117</td>
<td>0</td>
<td>0</td>
<td>1,043,557,925</td>
<td>939,066</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Note: SP. A/C = special account; LSS = Life Span Study; NAS = National Academy of Sciences; HH = Hijiyama Hall; Colla. = collaborative; all amounts are in yen.
### Regular account balance sheet as of 31 March 1993

<table>
<thead>
<tr>
<th>Category</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assets</strong></td>
<td></td>
</tr>
<tr>
<td>Current assets:</td>
<td></td>
</tr>
<tr>
<td>Cash, deposits</td>
<td>¥335,731,883</td>
</tr>
<tr>
<td>Accounts receivable</td>
<td>4,830,477</td>
</tr>
<tr>
<td>Interfund receivable</td>
<td>8,357,198</td>
</tr>
<tr>
<td>Deposit</td>
<td>949,940</td>
</tr>
<tr>
<td>Total current assets</td>
<td>349,869,498</td>
</tr>
<tr>
<td>Fixed assets:</td>
<td></td>
</tr>
<tr>
<td>Buildings</td>
<td>266,750,241</td>
</tr>
<tr>
<td>Equipment</td>
<td>412,523,564</td>
</tr>
<tr>
<td>Total fixed assets</td>
<td>679,273,805</td>
</tr>
<tr>
<td><strong>Total assets:</strong></td>
<td>1,029,143,303</td>
</tr>
<tr>
<td><strong>Liabilities</strong></td>
<td></td>
</tr>
<tr>
<td>Current liabilities:</td>
<td></td>
</tr>
<tr>
<td>Accounts payable</td>
<td>26,540,775</td>
</tr>
<tr>
<td>Salary deductions on hand</td>
<td>23,687,741</td>
</tr>
<tr>
<td>Balance of subsidy (personnel fund to be returned)</td>
<td>299,640,982</td>
</tr>
<tr>
<td>Total current liabilities</td>
<td>349,869,498</td>
</tr>
<tr>
<td><strong>Total liabilities:</strong></td>
<td>349,869,498</td>
</tr>
<tr>
<td>Property funds:</td>
<td></td>
</tr>
<tr>
<td>Basic property (buildings)</td>
<td>266,750,241</td>
</tr>
<tr>
<td>Operating property (equipment)</td>
<td>412,523,564</td>
</tr>
<tr>
<td>Total current liabilities</td>
<td>679,273,805</td>
</tr>
<tr>
<td><strong>Total liabilities and property funds:</strong></td>
<td>1,029,143,303</td>
</tr>
</tbody>
</table>
International Collaborative Activities

I. Participation in international collaborative activities by RERF staff members

Note: This listing does not include participation in international scientific meetings. For a list of papers delivered at national and international meetings, see p.67.

- Chernobyl-related collaborative activities
  The Sasakawa Foundation Chernobyl Project
  Yoshisada Shibata, chief, Department of Epidemiology and Biometrics, Nagasaki Laboratory, attended a meeting on data processing related to medical cooperation after the Chernobyl nuclear power plant accident (Moscow, April 1992).

  Shizuyo Kusumi, chief, Division of Clinical Laboratories, and Yoshisada Shibata, chief, Department of Epidemiology and Biometrics, Nagasaki Laboratory, participated in a symposium to evaluate the achievements of the first year of the Chernobyl medical cooperation program and visited various facilities (Russia, Belarus, May 1992).

  RERF Chairman Itsuzo Shigematsu participated in the Commonwealth of Independent States (CIS) Sasakawa project (Moscow, Mogilev, Minsk, Republic of Russia; May 1992).

  Yoshisada Shibata, chief, Department of Epidemiology and Biometrics, Nagasaki Laboratory, provided technical guidance on data management and computing (republics of Russia, Belarus, Ukraine; September 1992, January 1993).

Radiation Effects Association
Kiyohiko Mabuchi, chief, Department of Epidemiology, participated in follow up of the Chernobyl accident (Russia, Belarus, August 1992).

Ministry of Foreign Affairs
Under a cooperative research plan, between Japan and the former USSR, Suminori Akiba, assistant chief, Department of Epidemiology, and Fumiyoshi Kasagi, research scientist, Department of Statistics, visited the Ministry of Health of the former Soviet Union and other research institutes (Moscow, Minsk, Kiev; October 1992).

Hiroshima International Council for Health Care of the Radiation-exposed
Shizuyo Kusumi, chief, Division of Clinical Laboratories, attended an international conference on the sociological and psychological effects of the Chernobyl nuclear accident and visited various facilities later (Kiev, Moscow; September 1992).
• **Chelyabinsk-related cooperation**  
**RERF-sponsored project**  
Akio Awa, chief, Department of Genetics; Dale Preston, chief, Department of Statistics; and Hideo Sasaki, assistant chief, Department of Clinical Studies, participated in a meeting to plan collaborative research, on the basis of an agreement between RERF and the Ural Research Center for Radiation Medicine (Chelyabinsk, Russia; October 1992).

**U.S. Department of Energy-sponsored project**  
RERF Vice Chairman J.W. Thiessen participated in an international workshop on the Chelyabinsk nuclear accidents and their consequences, cosponsored by the U.S. Departments of Energy and Defense (George Mason University, Fairfax, Virginia, June 1992).

• **Other international cooperation activities**  
**World Health Organization-sponsored meeting**  
Nori Nakamura, assistant chief, Department of Radiobiology, attended a coordination meeting of the World Health Organization’s Collaborating Centers in Radiation Emergency Medical Preparedness and Assistance (Ulm, Germany, November 1992).

**Marshall Islands project**  
Katsutaro Shimaoka, associate chief of research, Nagasaki Laboratory, participated in a meeting of the Rongelap Resettlement Project (Cambridge, U.K., August 1992).

**II. Visitors from overseas for briefing and training (337 persons)**  
*Note: Sponsors are sometimes listed in parentheses after the visiting group’s name.*

**Visitors related to Chernobyl (42 persons)**  
(All the following were sponsored by the Hiroshima International Council for Health Care of the Radiation-exposed [HICARE]).

• **Junod group**  
Three doctors from Kiev, the Republic of Ukraine, visited RERF for briefing on 13 April.

• **Japan Red Cross and Asahi Shimbun Cultural Operations**  
Two doctors from the Republic of Ukraine and two doctors from Gomel State, the Republic of Belarus, visited RERF for briefings, 20–24 July and 19–20 November, respectively.

• **Sendai Municipal Hospital**  
Two doctors from Minsk City, the Republic of Belarus, visited RERF for briefing on 7 October.
• Sasakawa Foundation
Seven people each from the ministries of health of Russia, the Republic of Belarus, and the Republic of Ukraine visited RERF on 16 October.
Two data-processing specialists from the Republic of Ukraine visited RERF for training from 16 February to 1 March 1993.

• YMCA International Community Center
Three doctors from Minsk City, the Republic of Belarus, visited RERF for briefing on 2 November.

• Radiation Effects Association
Five epidemiologist from the Republic of Russia visited RERF on 1 December.

• Ministry of Foreign Affairs
Four data-processing specialists from the republics of Russia and Belarus visited RERF for training, 10–26 February 1993.
Four doctors (leukemia specialists) from the republics of Russia and Belarus and 6 dosimetry specialists from the Republic of Russia, the Republic of Belarus, and the Republic of Ukraine visited RERF for briefings on 23 February and 25 February, respectively.

• International Physicians for the Prevention of Nuclear War (IPPNW)
Two doctors from the Republic of Russia visited RERF for briefings from 20 April to 21 May.

Visitors related to Semipalatinsk (3 persons, HICARE)
• IPPNW
One doctor from the Republic of Kazak visited RERF for training from 20 April to 21 May.

Other visitors related to HICARE (41 persons)
• Japan Atomic Industrial Forum
Four leukemia-studies specialists from British Nuclear Fuels Plc., visited RERF on 18 June.

• Medical Association of Los Angeles County
Two doctors from the Medical Association of Los Angeles County visited RERF for training, one 12–24 August and the other 19–24 August.

• Japan Newspaper Association
Eight members of the former Soviet Journalists League visited RERF on 16 October.

• Japan Atomic Energy Research Institute and International Atomic Energy Agency
Seventeen Asian-Pacific participants in a training course on radioisotopes and molecular techniques in the biological sciences visited RERF for briefing on 9 and 10 February 1993.
• **International Atomic Energy Agency**
  Three research scientists from the Polish Institute of Nuclear Chemistry and Technology visited RERF on 12 June.

• **Hawaii Medical Association**
  One doctor from Kuakini Medical Center visited RERF for training from 22–30 October.

• **Brazilian visitors**
  One visitor from the University of Rio de Janeiro was briefed on 6 October.
  One doctor from the Japan–Brazil Fraternal Hospital of the Nipo-Brasileira de São Paulo visited RERF for briefing from 7–10 December.

• **Other visitors**
  Four people from the atomic agencies of the governments of Russia and Belarus visited RERF on 22 January 1993.

**Visitors related to the Japan International Cooperation Agency (JICA)**
(54 persons)

• **Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association**
  Eleven persons in training to become leaders of tuberculosis prevention programs in southeast Asian nations visited RERF for briefing on 2 June.

• **Nuclear Safety Research Association**
  Eight attendees of a nuclear-medicine course from Asian nations visited RERF for briefing on 28 September.

• **Japan Analysis Center**
  Five participants in a course about environmental radioactivity from South Korea, Malaysia, Thailand, Brazil, and Vietnam visited RERF for briefing on 16 October.

• **JICA**
  Twenty South Korean trainees participating in a course about the environment visited RERF for briefing on 19 October.

• **National Cancer Center**
  Ten cancer-prevention trainees from Latin American and Asian nations visited RERF for briefing on 12 November.

**Other visitors** (197 persons)

• **International Physicians for the Prevention of Nuclear War (IPPNW)**
  Two doctors and 17 medical students from the South Korean branch of IPPNW visited RERF on 5 January 1993.

• **Japan Newspaper Association**
  Eight journalists from the former Soviet Union visited RERF on 26 October.

• **Miscellaneous visitors**
  One hundred and seventy researchers, doctors, and others visited RERF for tours of the facilities.
RERF New Facility Committee

I. Establishment of the New Facility Committee

After approval in Fiscal Year 1992 (FY92) of the budget necessary to formulate the basic plan for relocation of the Hiroshima Laboratory and approval of the report titled, “Research Program and Resource Requirements of the Radiation Effects Research Foundation for the Period Ending 1996,” submitted by the Committee to Determine Future Resource Requirements for RERF Research Activities at the 26th Board Meeting held in June 1992, the RERF New Facility Committee was established as of 1 July 1992 to review matters concerning the new Hiroshima facility. The basic review policy envisioned formulation of the basic plan for the new facility in FY92, preparation of the basic design and the working design in Fiscal Year 1993 (FY93), construction of the building in Fiscal Year 1994 (FY94) and Fiscal Year 1995 (FY95), and relocation at the end of the same year.

II. Summary of deliberation at the Committee meetings

To date, the Committee has met five times. Several U.S. and Japanese firms that wanted to submit basic plans for the new facility gave presentations during the first three meetings.

At the fourth meeting, many details were compared, such as company histories, technical standards, personnel composition, financial credit, relationship between the firms that would work jointly, production cost for the basic plan, and production period. The Committee assessed whether these firms were worthy of being entrusted with planning RERF’s new facility. The U.S. company, Cesar Pelli & Associates, Inc., and Yamashita Sekkei, Inc., Japan, were selected. While formulating their plans, these firms queried each department for their views.

At the fifth meeting, the chosen architectural firms explained their basic plan for RERF’s new facility, and the plan was approved after partial revision.

Following is a brief outline of the five committee meetings:

2 September 1992  Presentation by GPR Planners Collaboration, Inc., U.S.A.
2 December 1992  After comparing the presentations, the project was awarded to Cesar Pelli & Associates, Inc., and Yamashita Sekkei, Inc.
1 April 1993  The basic plan for the new facility was approved after partial revision.
III. Summary of the basic plan for RERF’s new facility

The basic plan was prepared after analyzing the site condition and establishing design conditions.

Characteristics of the basic plan
1. A facility that is “environment-friendly” and integrates well with its surroundings will be created.
2. The present facility is blessed with good surroundings, as will the new facility.
3. Above-ground parking will be minimized. As much parking as is possible will be underground.
4. The south side of the building will have stair-like terraces with plants to create open green space.
5. The terraces will be connected with stairs to allow traffic between departments.

Outline of plan
(1) Building
Address: Senda-machi 3 chome, Naka-ku, Hiroshima City, Hiroshima Prefecture
Site area: 7000.18 m²
Area, district: residential zone, semi-fire zone
Number of floors: 1 basement floor, 5 floors aboveground, and penthouse
Structure: steel-reinforced concrete structure
Building area: 2752 m²
Total floor space: 12,000 m²
Mandatory parking space: space for 27 vehicles

(2) Floor space and allocation to each department

<table>
<thead>
<tr>
<th>Floor</th>
<th>Floor space (m²)</th>
<th>Allocation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penthouse</td>
<td>286</td>
<td>Machine room</td>
</tr>
<tr>
<td>5</td>
<td>1,471</td>
<td>Directors’ offices, Secretariat (except Supply &amp; Property Section), Central Archives Office</td>
</tr>
<tr>
<td>4</td>
<td>1,776</td>
<td>Publication and Documentation Center, conference room, Research Information Center</td>
</tr>
<tr>
<td>3</td>
<td>2,081</td>
<td>Library, Epidemiology, Epidemiologic Pathology, Statistics, visiting research fellows’ rooms</td>
</tr>
<tr>
<td>2</td>
<td>2,386</td>
<td>Radiobiology, Genetics</td>
</tr>
</tbody>
</table>

Continued
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<table>
<thead>
<tr>
<th>Floor</th>
<th>Floor space (m²)</th>
<th>Allocation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2,752</td>
<td>Clinical Studies, Auditorium, Food Service, Secretariat (Supply &amp; Property Section), etc.</td>
</tr>
<tr>
<td>Basement 1</td>
<td>1,248</td>
<td>Radioisotope facilities, animal room, machine room, storage, parking space, etc.</td>
</tr>
<tr>
<td>Total</td>
<td>12,000</td>
<td></td>
</tr>
</tbody>
</table>

**Member of RERF New Facility Committee**

Committee chairman: Itsuzo Shigematsu, RERF chairman
Committee vice chairman: J.W. Thiessen, RERF vice chairman

**Committee members:**
Charles W. Edington, director, Board on Radiation Effects Research, Commission on Life Sciences, National Research Council, U.S. National Academy of Sciences
Yutaka Hasegawa, RERF permanent director
Tomoyuki Kono, RERF permanent director
Mortimer L. Mendelsohn, RERF permanent director
Seymour Abrahamson, RERF permanent director

**Executive secretary**

Takahiko Saeki, chief, Supply & Property Section, RERF Secretariat

**Members of the Working Subcommittee**

Chairman: Yasuhiko Hirano, Operations Administrator, RERF Secretariat

**Subcommittee members:**

Richard D. Sperry, business administrator, RERF Secretariat
Shizuo Inoue, assistant chief, RERF Secretariat
Michael E. Rappaport, RERF honorary advisor

**Subcommittee executive secretary**

Takahiko Saeki, chief, Supply & Property Section, RERF Secretariat
Development of an A-bomb-related materials database

As reported at the Board Meeting last year (June 1992), since Fiscal Year 1991 (FY91) RERF has been trying to develop an atomic-bomb-related materials database, under a special contract with the Japanese Ministry of Health and Welfare.

The work is actually being directed and coordinated by the Committee on Atomic-bomb (A-bomb) Materials and Information Network (chairman: Professor Emeritus Yasuo Yoshizawa, Tokyo University), which was established by RERF.

In Fiscal Year 1992 (FY92), the committee conducted the following work:

1. Pilot database development

The planned full-scale database will eventually provide the following services:

- Reference services. Information about the location of A-bomb-related materials, such as what institutions maintain them.
- Linkage with databases maintained at other institutions and organizations.
- Multimedia access to information, eg, pictures, moving images, and sound.

In FY92, a pilot database using personal computers was developed.

2. Implementing various investigations before complication of the database

- Determining which institutions and organizations in Japan possess A-bomb-related documentation and materials.

A survey was conducted in cooperation with the Ministry of Health and Welfare and prefectural offices handling relief measures for A-bomb survivors and identified 689 institutions and organizations.

- Determining pre-existing databases at major institutions and organizations possessing A-bomb-related documentation and materials

In Hiroshima and Nagasaki, 27 institutions and organizations were surveyed. Twenty of them (74%) already had databases of their own documentation and materials, and 4 of them (15%) had definite plans to create databases.

- Ascertaining the existence of materials related to A-bomb-survivor medical care located in national hospitals and sanatoria

Eight out of fourteen national hospitals (which had been army or navy hospitals during World War II) and sanatoria in and around Hiroshima and Nagasaki maintained some pertinent materials.

- Review of A-bomb-related documentation among General Headquarters (GHQ) materials kept in the National Diet Library

The National Diet Library owns a large number of microfiches of the GHQ documentation that were obtained from the U.S. National Archives in Washington, D.C. Review of these microfiches revealed that 300 contained A-bomb-related information. Photocopies were obtained.

- Determining existence of A-bomb-related materials in the U.S.
In six institutions in the U.S., including the Library of Congress and the University of Maryland Library, useful information and materials were obtained.

3. Other related work of the committee
To protect the confidentiality of personal data in the proposed database, a regulation was drafted to ensure proper handling of such data.

Visitors to RERF

A total of 1,200 trainees, medical-related persons, and visitors from abroad who were accepted through international exchange organizations, as well as government officials, medical-related persons, and members of citizen’s groups from inside Japan visited RERF.

Crown Prince Naruhito

On 15 July, when Crown Prince Naruhito came to Hiroshima to attend the 28th National Convention for Promoting Blood-donation Activities, he also visited the Hiroshima Laboratory. He observed the blood-donation activities of RERF employees in the auditorium and inspected the research facilities. His father, Emperor Akihito, had visited ABCC twice when he was Crown Prince.

At left, the Crown Prince watches a demonstration of a flow cytometer operated by research scientist Seishi Kyoizumi (seated) and explained by Radiobiology Department Chief Mitsushi Akiyama. Also observing the demonstration are, from left, RERF Vice Chairman J.W. Thiessen and RERF Chairman Itsuzu Shigematsu.
**U.S. Ambassador to Japan**

The U.S. Ambassador to Japan, Michael H. Armacost, who came to Hiroshima to attend a lecture organized by the Hiroshima Branch Office of the American–Japan Society, Inc., and other events, toured the Hiroshima Laboratory on 7 September. Chairman Itsuzo Shigematsu and Vice Chairman J.W. Thiessen briefed him on the activities of RERF.

**Honorary Secretary-general of the International Atomic Energy Agency**

Sigvard Eklung, honorary secretary-general of the International Atomic Energy Agency, visited the Hiroshima Laboratory on 26 October and met with Chairman Itsuzo Shigematsu and RERF staff.

Before he visited RERF, Eklung had inspected the Japan Atomic Energy Research Institute and the Japan Atomic Industrial Forum and had called on members of the Foreign Affairs Ministry and the Science and Technology Agency.

A partial, chronological listing of visitors to RERF follows:

**April 1992**

**Hiroshima Laboratory**

- **Hiroshi Nakajima**, director-general, World Health Organization, Geneva, Switzerland
- **Masanobu Kamata**, assistant chief, and **Kazuyuki Nakamura**, Industrial Technology Section, Department of Commercial and Industrial Labor, Hiroshima Prefectural Government, Hiroshima
- **Yoshiyuki Matsumoto**, assistant chief, Planning Division, Health Service Bureau, Ministry of Health and Welfare, Tokyo
- Three doctors, Republic of Ukraine: **Uyriy G. Antipkin**, chief, Department for Observation of the Chernobyl Children; **Alexander A. Yakovlev**, chief, Radiology Laboratory, Kiev Institute of Pediatrics, Obstetrics, and Gynecology; **Igor V. Komisarenko**, head, Surgical Department of Research Institute of Endocrinology and Metabolism
- Three doctors from the former USSR (20 April to 21 May): **Alexander V. Akleyev**, director, Chelyabinsk Branch, Institute of Biophysics, Russian Ministry of Health, Republic of Russia; **Nurlan K. Shaimardanov**, head, Laboratory of Epidemiology and Infectious Diseases, Republic of Kazakhstan; **Tamara V. Filippova**, assistant professor, Department of Medical Genetics, Moscow Medical Academy, Republic of Russia

**Nagasaki Laboratory**

- **Jitsuo Yasuda**, chief, A-bomb Survivors Measures Section, Department of Environmental Health, Nagasaki Prefectural Office
May

**Hiroshima Laboratory**
Thirty visitors, Institute of Medical Radiology Technologists, Self-Defence Forces Central Hospital, Tokyo

**Nagasaki Laboratory**
Mutsuharu Hayashida, secretary general, Nagasaki Atomic Bomb Casualty Council

June

**Hiroshima Laboratory**
Flemming Brandt Sørensen, research scientist, City Hospital affiliated with the Institute of Pathology, Århus University, Århus, Denmark

Ikuko Togawa, assistant chief, Planning Division, Health Service Bureau, Ministry of Health and Welfare, Tokyo

Tetsuya Mizogami, physician, Department of Clinical Epidemiology, University of Occupational and Environmental Health, School of Medicine, Fukuoka

Yumiko Yamaguchi, internal physician, Research Institute for Nuclear Medicine and Biology, Hiroshima University, Hiroshima

Sixteen visitors, Japan International Cooperation Agency “1992 Group Training Course in Tuberculosis Control for Administrative Medical Officers,” Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association: A. K. M. Rahimuddin Bhuiyan, junior consultant, Tuberculosis Control, Tuberculosis Complex, Faridpur, Bangladesh; Ferreira M. Jaime, medical coordinator, TB Control Program, Health Secretary of Santa Catarina, Brazil; Abd El Megid Mansour Ali, director, Osium Chest Dispensary, Ministry of Health, Egypt; Luis Enrique Jaime Portal, epidemiologist advisor, San Juan de Dios Hospital, Ministry of Health, El Salvador; L. Suryanarayana, senior medical officer, National Tuberculosis Institute, India; Ur Rehman Fazal, assistant director-general, Ministry of Health, Pakistan; Francisco Romero, chief, National Chain of Laboratories of Tuberculosis, Paraguay; Angeles M. Hernandez, medical coordinator, Ministry of Health, Philippines; Abdullah Mohamed, regional tuberculosis/leprosy medical officer, Tanga District, Tanzania; Kungswarn Samai, director, 6th Zonal TB Center, Thailand; Abdul A. H. Aziz, director, National Tuberculosis Control Program, Hadramout Governorate Branch, Yemen; Takashi Yoshiyama, medical doctor, Department of International Cooperation, Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, and four accompanying persons, Tokyo

Yuika Harada, internist, Division of Internal Medicine, Research Institute for Nuclear Medicine and Biology, Hiroshima University, Hiroshima
Michael W. Guinan, physicist, Lawrence Livermore National Laboratory, Livermore, California

Three trainees, International Atomic Energy Agency, Poland: Andrzej G. Chmielewski, deputy director, Research and Development, Institute of Nuclear Chemistry and Technology; Edward Iller, chief, Radiation Research Laboratory, Institute of Nuclear Chemistry and Technology; Zbigniew A. Zimek, head, Department of Radiation Chemistry and Technology, Institute of Nuclear Chemistry and Technology.

Four leukemia specialists, United Kingdom: Roger J. Berry, director, Department of Health and Safety, British Nuclear Fuels Plc.; John H. Gittus, director-general, British Nuclear Forum; Klaus Trott, head, Department of Radiation Biology, Medical College, St. Bartholomew’s Hospital; G. A. Harte, principal engineer, Health and Safety Department, Nuclear Electric Plc.

Nagasaki

Ikuo Togawa, assistant director, Planning Division, Health Service Bureau, Ministry of Health and Welfare, Tokyo

July

Hiroshima Laboratory

Jun Hamada, assistant director, and Michimura Kawano, Guidance and Survey Unit unit supervisor, Planning Division, Health Service Bureau, Ministry of Health and Welfare, Tokyo

Hitoshi Iki, chief, Research Division, A-bomb Survivors Relief Department, Bureau of Public Health, Hiroshima City

Crown Prince Naruhito and his entourage, Tokyo

Twenty visitors, Hiroshima Legal Affairs Bureau, and Family Registry Units of respective Ward Offices in Hiroshima City

Forty trainee physicians, The 5th Seminar on Prevention of Cardiovascular Diseases in Japan

Two trainees, The First Japan Red Cross Relief Activities for Chernobyl Nuclear Power Plant Accident Victims in 1992: Ekaterina Mihailovna Bruslova, senior scientist, and Irina Anatolievna Kryachok, research scientist, Institute of Clinical Radiation, Ukraine Science Center, Academy of Science, Ministry of Health, Republic of Ukraine

Nagasaki Laboratory

Tadashi Omura, chief, Medical Care Unit, A-bomb Survivors Measures Section, Department of Environmental Health, Nagasaki Prefectural Office, Nagasaki
Jun Hamada, assistant director, and Yoichi Sakoda, General Affairs Unit chief, Planning Division, Health Service Bureau, Ministry of Health and Welfare, Tokyo
Masanori Kawakami, chief, General Affairs Unit, Investigation Section, Department of Atomic Bomb Casualty, Nagasaki City Office, Nagasaki
Yoshitaka Orihata, Nagano Prefectural Cancer Detection Emergency Care Center, Nagano
Kesaaki Ito, Moriyoshi Muramatsu, Health and Disease Prevention Division, Nagano Prefectural Office, Nagano

August
Hiroshima Laboratory
Twenty-four visitors, Hiroshima Council Against A- and H-bombs, Hiroshima
Eiji Madokoro and Yoshinori Hiromoto, Relief Division, A-bomb Survivors Relief Department, Bureau of Public Health, Hiroshima City
Andrey G. Rosliakov, president, Khabarovsk National Medical College, and 12 visitors, Republic of Russia
Young C. Lin, professor of Reproductive Endocrinology, Department of Veterinary Physiology and Pharmacology, College of Veterinary Medicine, The Ohio State University, Columbus, Ohio
Yasuko Rikihisa, professor of Veterinary Pathobiology, College of Veterinary Medicine, The Ohio State University, Columbus, Ohio
Izumi Kurihara, section manager, Technology Research Department, Nuclear Safety Research Association, Tokyo
Nicholas D. James, lecturer in Oncology, Ludwig Institute for Cancer Research, St. Mary’s Hospital Medical School, London, United Kingdom
Dean Takao Yamaguchi, physician, Geriatric Research, Education and Clinical Center, West Los Angeles Veterans Affairs Medical Center, Los Angeles, California
David K. Fukuda, resident physician-surgeon, Family Practice Residency Program, Riverside General Hospital, Loma Linda University Medical Center, Loma Linda, California

Nagasaki Laboratory
Yasushi Hishiwaki, Department of Nuclear Safety, International Atomic Energy Agency, Vienna, Austria

September
Hiroshima Laboratory
Steven Rosenstein, president, GPR Planners Collaborative Inc., White Plains, New York

Yoshio Ito, director emeritus, Sanraku Hospital, Tokyo

Michael H. Armacost, ambassador, U.S. Embassy in Japan, Tokyo; Frank W. Stanley, secretary of Envoy Extraordinary and Minister Plenipotentiary, U.S. Embassy, Tokyo; David A. Pabst, consul-general, and his wife Sally, American Consulate General Osaka–Kobe, Osaka; Kensuke Ueda, consultant, and Robert S. Luke, consul, American Consulate General Osaka–Kobe, Osaka; Warren Soiffer, director, and Yasuo Satake, public relations officer, and three other persons, Osaka American Center, Osaka

Shigeru Sumitani, director, and Akitsugu Yamamoto, Special Measures Unit chief, Planning Division, Health Service Bureau, Ministry of Health and Welfare, Tokyo

Kazunori Kuwano, physician, and Hisao Ikeda, lecturer, The Third Section of Internal Medicine, School of Medicine, Kurume University, Fukuoka

Hiroshi Ikeda, assistant manager, Planning Section, Japan Atomic Energy Relations Organization, Tokyo

A. K. Shukla, associate professor, Department of Nuclear Medicine, Institute of Medical Sciences, Sanjay Gandhi Post-graduate School, India

Twelve trainees, “Nuclear Medicine Study Meeting,” Nuclear Safety Research Association, and Japan International Cooperation Agency, and four accompanying persons: Hong Yin, doctor of radiodiagnosis, Radiological Department, Xijing Hospital, China; Fikry El-Sayed Amin, medical officer, Medical Radiation Division, Nuclear Materials Authority, Egypt; Sarsono Suryometaram, staff member, Center of Standardization and Radiation Safety, Indonesia; Chang Woon Choi, physician, Department of Nuclear Medicine, Seoul National University Hospital, Republic of Korea; Mat Riff Bin Jusoh, physician, Nuclear Medicine Unit, General Hospital of Malaysia; Aamer Aziz, medical officer, Nuclear Oncology & Radiotherapy Institute, Pakistan; Osama Sameer Al Hajery, registrar, Radiology Department, Security Forces Hospital, Saudi Arabia; Karatpet Wangvithayakun, nuclear medicine physician, Faculty of Medicine, Srinakharinwirot University, Thailand

Nagasaki Laboratory

Olaf Malm, associate professor, Laboratory of Radioisotopes, Institute of Biophysics, Federal University of Rio de Janeiro, Brazil

October

Hiroshima Laboratory

Keichu Teranishi, president, American Society of Hiroshima–Nagasaki A-bomb Survivors, Walnut, California
Kaz Suyeishi, board of directors, American Society of Hiroshima–Nagasaki
A-bomb Survivors, Los Angeles, California
Kim Cheol-Su, researcher, Radiochemical Analysis Division, Radiation and
Environment Department, Republic of Korea
Masataka Nishiyama, chief, Research and Training Office, Japan Chemical
Analysis Center, Chiba
Toshiharu Miura, chief, Department of Surgery, and Junichiro Abe, chief,
Department of Pediatrics, Sendai City Hospital, Sendai
Helen Petrovitch, co-principal investigator, and Paul Bugden, epidemiolo-
gist, Kuakini Medical Center, Honolulu, Hawaii

Thirteen visitors, trainees, Exchange Program on Atomic Energy Studies:
Muslehuddin Sarker, Bangladesh Atomic Energy Commission; Thamzil
Las, engineer, Reactor Engineering Department, Indonesia Atomic Energy
Agency; Gannaga Satittada, Monkit Institute of Technology, Thailand;
Monoach Chimtin, Sombuun Jerachanchai, and Siriratana
Biramontri, Office of Atomic Energy for Peace, Thailand; William
Prasuad, Department of Physics, Indonesian Nuclear Energy Agency;
Darmawan Daruwis, Indonesian Nuclear Energy Agency; Bing Han,
Research Institution of Nuclear Techniques, Chinghua University,
People’s Republic of China; Shiwei Ni and Wei Li, Chinese Institute of
Radiation Protection, People’s Republic of China; and two accompanying
persons

Five trainees, course on “Environmental Radiation Analysis,” Japan Interna-
tional Cooperation Agency, and two accompanying persons, Japan Chemical
Analysis Center: Siyoung Jan, researcher, Korea Institute of Nuclear
Safety, Republic of Korea: Sukiman Sarmani, lecturer, Department of
Nuclear Science, University Kebangsaan Malaysia; Siriluck Lumjactas,
engineer for Radiation Measurement, Office of Atomic Energy for Peace,
Thailand; Sigma Goncalves, engineer, Brazil Environmental Sanitation
Company; Vu Ngoc Anh, member, Vietnam National Atomic Energy
Commission; Masataka Nishiyama, chief, Research and Training Office,
Japan Chemical Analysis Center, Chiba; Chiharu Sato, coordinator,
JICA, Tokyo

Twenty trainees, “Extra Study Course of Korean Environmental Territorial
Integrity,” Republic of Korea, and two accompanying persons, Japan
International Cooperation Agency
Eiji Ono, physician, Department of Surgery, School of Medicine, Hiroshima
University
Sigvard Eklund, honorary secretary-general, International Atomic Energy
Agency, Vienna, Austria
Mio Kimuro, chief, Planning Division, Japan Atomic Industrial Forum, Inc., Tokyo
Shuichi Tani, director-general, Health Service Bureau; and Mitsuo Yoshida, unit chief, Administration Unit, Office of Secretariat, Ministry of Health and Welfare, Tokyo
Hirozo Ueda, director, Bureau of Public Health, Hiroshima City
Toshinori Matsumura, chief, Investigation Section, A-bomb Survivors Relief Department, Hiroshima City
Olaf Malm, assistant professor, Laboratory of Radioisotope, Institute of Biophysics, Federal University of Rio De Janeiro, Brazil
Two physicians, Republic of Belarus: Natalia Martoplyas, chief, Neonatal Department, Maternity Home, and Irina Lebedeva, chief, Department of Neonatal Infection, The 7th City Clinical Hospital
Eleven visitors, former Soviet Ministry of Health (sponsored by the Sasakawa Foundation): Nikolai N. Vaganov, vice-minister, Russian Ministry of Health, Republic of Russia; Boris B. Spassky, senior officer for Radiology, Department of Vocational Diseases, Russian Ministry of Health, Republic of Russia; Nikolai A. Krysenko, vice-minister, Belorussian Ministry of Health, Republic of Belarus; Tadeush A. Krupnik, director, Mogilev Center, Republic of Belarus; Olga Aleksandrovna Bobyleva, chief, Department of Prevention of Residential Exposure from the Chernobyl Accident, Ukrainian Ministry of Health, Republic of Ukraine; Alexander Andreevich Vplkov, senior officer, International Administrative Section, Ukrainian Ministry of Health, Republic of Ukraine; Elena I. Bomko, senior officer, Department of Countermeasures for Aftermath of the Chernobyl Accident, Ukrainian Ministry of Health, Republic of Ukraine; Ilya V. Poshin, interpreter, Moscow Office, Sasakawa Foundation, Moscow, Republic of Russia; Suminori Nishizaki, director, Sasakawa Foundation, Tokyo; Hiroko Maki, chief, Countermeasures for the Chernobyl Accident, Sasakawa Foundation, Tokyo; Kenichi Nakagawa, interpreter, Sasakawa Foundation, Tokyo
George Suzuki, physician, Internal Medicine, Kuakini Medical Center, Hawaii Medical Association, Honolulu, Hawaii
Eight journalists, former USSR: Viktor Pavlovich Yukechev, editor, The Novosibirsk Newspaper, Novosibirsk, Republic of Russia; Vyacheslav Valentinoovich Subbotin, editor, The Volnoye Slovo, Ivanovo, Republic of Russia; Pavel Nikolaevich Gusev, editor-in-chief, Moskovskiy Komsoomolec, Republic of Russia; Ludmila Vasilievna Scherbina, first secretary, and Alla Alexandrovna Yaroshinskaya, The Moscow Union of Journalists, Moscow, Republic of Russia; Grigory Grigorievich Dyldayev, editor, The Asia, Republic of Kazakhstan; Yakov Yakovlevich
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Zaiko, editor, and Vitaly Grigorievich Melnichuk, economics observer, The Farmer-Svobodny Krestianin, Republic of Ukraine

Nagasaki Laboratory

Hiroshi Fuji, Roswell Park Cancer Institute, Buffalo, New York
Hiroshi Okada, chief, Internal Medicine, Kyoto National Hospital, Kyoto (former research scientist in the ABCC Clinical Studies Department)
Ricardo Kawaoka Miyake, Japan–Brazil Fraternal Hospital, Sao Paulo, Brazil
Yoshitaka Inoue, Hiroshima International Council for Health Care of the Radiation-exposed, Hiroshima Prefectural Office
Tadashi Omura, A-bomb Survivors Measures Section, Nagasaki Prefectural Office

November

Hiroshima Laboratory

Jun Mitsui, president of Tokyo Branch Office, Cesar Pelli & Associates, Inc., Tokyo
James E. Krause, associate professor of molecular neurobiology, Washington University, St. Louis, Missouri
Yasuo Takeda, researcher, Biology Laboratory, School of Medicine, Keio University, Tokyo
Hans D. Röher, professor of surgery, Heinrich-Heine Universität, Düsseldorf, Germany
Toshio Hiraoka and Hideki Okamoto, surgeons, Department of Surgery, School of Medicine, Hiroshima University
Charles M. Valadez, auditor, Price Waterhouse, Washington, D.C.

Ten trainees and three accompanying persons, Japan International Cooperation Agency “Group Training Course of Clinical Oncology II ’92,” organized by the National Cancer Center Research Institute: Fernando B. G. Fluxa, gastroenterology, University of Chile; Guicheng Zhang, physician-in-charge, Xinxiang General Hospital, People’s Republic of China; Maria Helena Restrepo, resident in Oncology, National Cancer Institute, Colombia; Rajesh Kumar Grover, assistant professor, Department of Radiotherapy, Maulana Azad Medical College, Ministry of Health and Welfare, India; Carlos F. G. Carracedo, staff oncologist, Medical Department, National Hospital of Neoplastic Disease, Peru; Jose L. R. Medina del Carpio, assistant surgeon, Department of Surgery, National Hospital E. Rebagliati, Peru; Hongliang Lim, senior resident, Department of Medicine, National University Hospital, Singapore; Boonyaritipong Anchalee,
physician, Hematologic Medicine Department, Vajira Hospital, Thailand; Maleemonkul Sumonmal, instructor, Department of Obstetrics and Gynecology, Faculty of Medicine, Chiangmai University, Thailand; Emine G. Nilufer, clinical research fellow, Medical Faculty, Hacettepe University, Turkey

Ministry of International Trade and Industry, Tokyo: Kosuke Imashimizu, planning officer, Section on Nuclear Power, Resources and Energy Agency; Kayoko Sanada, senior officer, Planning and Research Division, Director's Secretariat, Resources and Energy Agency

Takeo Ikeda, assistant chief, Section of Resources, Department of Resources, Chugoku Bureau of International Trading and Industry, Hiroshima

The Chugoku Electric Power Co., Inc., Hiroshima: Yukio Furubayashi, assistant manager, Administration Section, Nuclear Power Department; Bintaro Izumi, manager, Public Relations Department

Three physicians, Republic of Belarus: Igor E. Solovei, director, and Elena Tolstaia, assistant director, Samariani Medical Center; Valentin Murashko, chief doctor, Belorussian Sanatorium

Two trainees, Republic of Belarus: The Second Japan Red Cross Relief Activities for Chernobyl Nuclear Power Plant Accident Victims in 1992: Youri Marianovitch Ivashkevitch, surgical endocrinologist, Tumor Prevention Clinic of Minsk City; Petr Vladimirovitch Gornostai, surgical endocrinologist, Health and Welfare Bureau, Gomel State Executive Committee

**Nagasaki Laboratory**

Angelo Carpi, professor, Department of Nuclear Medicine, University of Pisa, Italy

**December**

**Hiroshima Laboratory**

Tadashi Kawamura, lecturer, Laboratory of Radiation Medicine, School of Medicine, Ehime University, Ehime

Five epidemiologists from the Russian Academy of Medical Sciences related to the Chernobyl nuclear power plant accident, Republic of Russia: Anatoly F. Tsyb, director, Medical Radiological Research Center; Victor K. Ivanov, head, Department of Applied Mathematics, Medical Radiological Research Center; Vladimir Parshin, leading scientist, Medical Radiological Research Center; Valery Stepanenko, head, Laboratory of Dosimetry, Medical Radiological Research Center; Vyacheslav V. Pavlov, head, Division of Hematological Diseases, Medical Radiological Research Center
Ricardo Kawaoka Miyake, surgeon, Japan–Brazil Fraternal Hospital, Sao Paulo, Brazil

Nagasaki Laboratory
Trainees, Japan International Cooperation Agency: Michiko Tokashiki, senior scientist, Okinawa Prefectural Institute of Health and Environment, Okinawa; Miyako Oshiro and Naoko Inoh, training supervisors, Okinawa International Center; Rabilul Hossain, Bangladesh; Li Hui Juan, China; Sameh Zaki Nashed, Egypt; Salazar C. Maritza Elena, Nicaragua; Sirichai Phantana, Thailand; Claudia Toma, Argentina

January 1993

Hiroshima Laboratory
Three members, Korean Physicians for the Prevention of Nuclear War, and one interpreter: Chukul Lee, president, and Myunghwa Lee, executive vice-president, Korean Branch, International Physicians for the Prevention of Nuclear War, Republic of Korea; Myungken Lee, director, Kanghwa Hospital, Republic of Korea
Twenty-five members of the Korean Physicians for the Prevention of Nuclear War, Republic of Korea, and students from Hiroshima University
Kioko Kawai, assistant professor, 2nd Pathology Laboratory, Nagasaki University School of Medicine, Nagasaki
Enji Tsubakihara, assistant chief, National Property Examination Division, Financial Bureau, Ministry of Finance, Tokyo
Hideaki Matsutami, chief, and Sho Kubota, assistant chief, First Section of Direct Control of Property, Local Administration Department, Chugoku Local Finance Bureau
Akitsugu Yamamoto, chief, Medical Treatment Unit, Planning Division, Health Service Bureau, Ministry of Health and Welfare, Tokyo
Akira Miura, Medical Law Unit, Planning Division, Health Service Bureau, Ministry of Health and Welfare, Tokyo
T. M. Artemova, director, Consultative Center of Academy of National Economy, Russian Government, Republic of Russia
B. A. Marchenko, chief, Department of Update Technology, Belorussian Cabinet Council, Republic of Belarus
N. A. Streljtsvos, vice-chairman, Belorussian Scientific Industries Association, Republic of Belarus
G. A. Sharovarov, head, Institute of Radioecology, Belorussian Academy of Science, Republic of Belarus
February

Hiroshima Laboratory

Nobuo Onodera, president, Saitama Prefectural Medical Junior College, Saitama

Makoto Sawada, chief, General Affairs Section, Saitama Prefectural Medical Junior College, Saitama

Norimichi Hayakawa, director, Ningyo Toge Works, Power Reactor and Nuclear Fuel Development Corporation, Okayama

Victor I. Tsetlin, head, Laboratory of Neuropeptide Receptors, Shemyakin Institute of Bioorganic Chemistry, Russian Academy of Sciences, Republic of Russia

Shigeyuki Takada, unit chief, Payment Unit, General Affairs Section, Japan National Institute of Health, Ministry of Health and Welfare, Tokyo

Toshiko Oosaka, staff, General Affairs Section, Japan National Institute of Health, Ministry of Health and Welfare, Tokyo

Members of the Tajima Committee: Eizo Tajima, chairman, Nuclear Safety Research Association, Tokyo; Yoshiyuki Matsumoto, assistant director, Planning Division, Health Service Bureau, Ministry of Health and Welfare, Tokyo; Tatsuji Hamada, board member, Japan Radioisotope Association, Tokyo; Toshiso Kosako, assistant professor, Nuclear Power Research Center, Tokyo University

Seventeen trainees, International Training Program, “Utility of Radioisotope and Molecular Biochemical Technology in Bioscience,” Japan Atomic Energy Research Institute and IAEA, and three staff members: Reza Md. Shahjahan, Institute of Food and Radiation Biology, Atomic Energy Research Commission, Bangladesh; Huiping Li, Radiation Medicine Section, Research Center of Occupational Medicine, The Third Hospital Beijing Medical University, People’s Republic of China; Jinchang Wu, Radiation Medicine Section, Second Affiliated Hospital, Suzhou Medical College, People’s Republic of China; Ajay Kumar, Radiation Medicine Center, Bhabha Atomic Research Center, India; Atsushi Tanaka, Biotechnology Laboratory, Takasaki Radiation Chemistry Research Establishment, Japan Atomic Energy Research Institute, Gunma; Mohd Zaidan-bin Kandar, Nuclear Energy Unit, Ministry of Science, Technology and Environment, Malaysia; Rohani Md. Yasin, Division of Bacteriology, Institute for Medical Research, Malaysia; Mu Ya Than, Nuclear Medicine Research Division, Radioisotopes and Biological Techniques, Department of Medical Research, Myanmar; Shahnaz Murtaza, Research and Biochemistry Division, Institute of Radiotherapy & Nuclear Medicine, Peshawar University, Pakistan; Rubina Tabassum, National Institute for Biotechnology & Genetic Engineering, Pakistan; Vladimir Paredes-
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Bermudez, Natural Science Research Institute, University of the Philippines System, Philippines; Patricia Andrea C. Vinoya-Carrillo, Biomedical Research Group, Atomic Research Division, Philippine Nuclear Research Institute, Philippines; S. W. Gunasekara, Department of Biochemistry, Faculty of Medicine, University of Peradeniya, Sri Lanka; A. Ileperuma, Department of Biochemistry, General Hospital, Sri Lanka; Korbkit Cherdchu, Department of Radioisotopes, Faculty of Tropical Medicine, Mahidol University, Thailand; Panasda Isarangkul Na Ayuthaya, Immunology Section, Health Science Research Institute, Thailand; Thi Phi Phi Phan, Department of Immuno-Physiopathological Research, Hanoi Medical School, Vietnam

Four data-processing researchers related to the Chernobyl nuclear power plant accident, Commonwealth of Independent States (CIS): Oleg Viktorovich Rozhkov, head, Department of Applied Mathematics, Obninsk Medical Center of Radiology, Russian Academy of Medical Sciences, Republic of Russia; Elena Raulievna Maslova, mathematician, Moscow Center of Hematology, Republic of Russia; Valentin A. Stejko, chief, Department of Medical Care for Chernobyl Accident Effects, Ministry of Health, Republic of Belarus; Alexei E. Okeanov, director, Byelorussian Center of Medical Technologies and Information, Republic of Belarus

Two data-processing researchers related to the Chernobyl nuclear power plant accident, CIS: Vladimir Shulzhenko, director, Ukrainian Center of Information Technologies and Chernobyl Register, Ukrainian Ministry of Health, Republic of Ukraine; Andrey Bomko, programming technician, Ukrainian Center of Information Technologies and Register, Ukrainian Ministry of Health, Republic of Ukraine

Four researchers related to the Chernobyl nuclear power plant accident, Leukemia Team, CIS: Marina Alexandrovna Danilova, physician, Obninsk Medical Center of Radiology, Russian Academy of Medical Sciences, Republic of Russia; Galina Ivanovna Miljutina, physician, Hospital No. 1, Briansk, Republic of Russia; Tatjana I. Kozorezova, head, and Svetlena K. Morozova, assistant, Course of Pediatric Hematology and Transfusion, Institute of Improvement of Doctors, Pediatric Hematology Center, Republic of Belarus

Five researchers related to the Chernobyl nuclear power plant accident, Dosimetry Team, CIS: Nikolai Vorisovich Ryvkint, scientist, Bryansk Medical Service Center, Republic of Russia; Vladimir Anatoliyvich Serezhkenkov, senior research fellow, Institute of Chemical Physics, Russian Academy of Sciences, Republic of Russia; Alexandre V. Ulanovski, research associate, Radiation Medicine Research Institute, Minsk, Repub-
lic of Belarus; Valeri E. Shevtchouk, senior scientist, Radiation Hygiene Department, Scientific Research Institute for Radiation Medicine (Gomel Branch), Republic of Belarus; Toshiyuki Nakajima, director, Division of Radioecology, National Institute of Radiological Sciences, Ibaragi

**Nagasaki Laboratory**

Junichi Hitomi and Tomoaki Yasuda, Radiation Protection Division, Nuclear Safety Bureau, Science & Technology Agency, Tokyo

Tatsuya Ito, director, Nagasaki International Culture Hall, and other two persons

Data-processing specialists related to the Chernobyl nuclear power plant accident, CIS: Oleg Viktorovich Rozhkov, mathematician, Medical Radiological Research Center, Russian Academy of Medical Sciences, Republic of Russia; Elena Raulievna Maslova, mathematician, Hematology Research Center, Republic of Russia; Valentin A Stejko, chief, Department of Medical Effects of the Chernobyl Accident, Ministry of Health, Republic of Belarus; Alexei E. Okeanov, director, Belorussian Research Center for Medical Technologies, Information and Management of Health Services, Republic of Belarus

Data-processing specialists related to the Chernobyl nuclear power plant accident, CIS: Vladimir Shulzhenko, director, Ukrainian Center of Information Technologies and Chernobyl Register, Republic of Ukraine; Andrey Bomko, programmer, Ukrainian Center of Information Technologies and Chernobyl Register, Republic of Ukraine

**March**

**Hiroshima Laboratory**

Andrea Tannapfel, research scientist, Department of Pathology, University of Hannover, Germany, and two other persons

Kaoru Morita, assistant director, Morita Dental Office, Hiroshima

S. D. Bouffler, researcher, Department of Medicine for Biochemical Effects, National Radiological Protection Board, United Kingdom

Akira Endo, assistant director, Health Planning Division, Health Policy Bureau, Ministry of Health and Welfare, Tokyo

Hirozo Ueda, director-general, Public Health Bureau, Hiroshima City

Yuji Kanda, Social Division, Social Working Bureau, Hiroshima City

Masakazu Murakami, chief, Planning Section, National Institute of Radiological Sciences, Chiba

Satoru Yoshinaga, officer, Prime Minister’s Office, National Institute of Radiological Sciences, Chiba

Two data-processing specialists related to the Chernobyl nuclear power plant accident, CIS: Vladimir Shulzhenko, director, Ukrainian Center of Infor-
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information Technologies and Chernobyl Register, Ukrainian Ministry of Health, Republic of Ukraine; Andrey Bomko, programming technician, Ukrainian Center of Information Technologies and Register, Ukrainian Ministry of Health, Republic of Ukraine

Alexander Sekerbaev, vice-director, and Rafail I. Rosenson, chief research worker, Kazakh Scientific-Research Institute of Radiology and Ecology, Republic of Kazakhstan
Appendix
The 26th Board of Directors Meeting

24–26 June 1992
Koseinenkin Hall, Nagasaki City, and Huis Ten Bosch, Sasebo City

Agenda

I. Minutes of the 25th meeting of the Board of Directors (16–21 June 1991, Irvine, California)

II. Items for information
   1. Present personnel status
   2. Fiscal Year 1991 (FY91) salary revision, etc.
   3. Labor union’s Fiscal Year 1992 (FY92) demands for improvement of working conditions, etc.
   4. Others
      (1) Recommendations of the Human Germline Mutagenesis Workshop
      (2) Dosimetry reassessment
      (3) International cooperation
      (4) Ministry of Health and Welfare–entrusted project: Committee on A-bomb Materials and Information Network

III. Items for deliberation and action
   1. Recommendations of the 19th Scientific Council
   2. FY91 research activities report
   3. FY92 research plans and Fiscal Year 1993 (FY93) research directions
   4. RERF Future Planning Committee report
   5. FY91 settlement of accounts
   6. FY92 working budget plan
   7. Outline of the FY93 budget request
   8. Revision of the rules and regulations
   9. Election of directors and scientific councilors

IV. Scheduling of the next Board meeting

Participants

Full-time officers
   Itsuzo Shigematsu, chairman
   J.W. Thiessen, vicechairman
   James E. Trosko, permanent director and chief of research
   Mortimer L. Mendelsohn, permanent director
   Yutaka Hasegawa, permanent director
Appendix

Tomoyuki Kono, permanent director and chief of the Secretariat

Visiting directors
Teruhiko Saburi, chairman, Japan Foundation for Aging and Health
Kazuaki Arichi, executive director, Japan Institute of International Affairs
Tsutomu Sugahara, professor emeritus, Kyoto University
Warren K. Sinclair, former president, National Council on Radiation Protection and Measurements
Joseph E. Rall, deputy director for intramural research, National Institutes of Health
Seymour Jablon, expert, Radiation Epidemiology Branch, Division of Cancer Etiology, U.S. National Cancer Institute

Supervisor
David Williams, chief financial officer, U.S. National Academy of Sciences (NAS)

Scientific councilor
Toshiyuki Kumatori, chairman, Radiation Effects Association

Observers
Shigeru Sumitani, director, Planning Division, Health Service Bureau, Ministry of Health and Welfare
Akitsugu Yamamoto, chief, Medical Care Activities Unit, Planning Division, Health Service Bureau, Ministry of Health and Welfare
Charles W. Edington, director, Board on Radiation Effects Research, Commission on Life Sciences, National Research Council, NAS
Catherine S. Berkley, administrative associate, Board on Radiation Effects Research, Commission on Life Sciences, National Research Council, NAS

RERF Operating Committee
Katsutaro Shimaoka, associate chief of research
Akio Awa, chief, Department of Genetics
Yasukiyo Hirano, operations administrator
Richard D. Sperry, business administrator
Yoshio Okamoto, chief of administration, Nagasaki Secretariat
Summary of the minutes of the meeting

The 26th meeting of the Board of Directors of the Radiation Effects Research Foundation (RERF) was held 24–26 June 1992 at the Nagasaki Koseinenkin Hall and Huis Ten Bosch in Sasebo.

Due to the vacant position resulting from the resignation of Permanent Director William J. Schull, 11 of the 12 Board members were present. This satisfied the quorum required under Article 21 of the Act of Endowment. David Williams, supervisor, was also present. The RERF Scientific Council was represented by one of its co-chairmen, Toshiyuki Kumatori. The observers in attendance included representatives from the Japanese Ministry of Health and Welfare and the U.S. Department of Energy (DOE) representative from the U.S. Embassy, as well as representatives of the National Academy of Sciences.

RERF Chairman Itsuo Shigematsu presided over the meeting as provided for in Article 20 of the Act of Endowment. He, with the consent of the Board members, appointed permanent directors James E. Trosko and Tomoyuki Kono as signatories to the minutes of this meeting.

Before proceeding to the agenda, Dr. Shigematsu proposed the appointment of Mortimer L. Mendelssohn as permanent director. The proposal was approved. This increased the number of Board members present to 12.

The agenda which had been distributed to the Board members before the meeting was adopted.

I. Minutes of the 25th meeting of the Board of Directors (presented by Itsuo Shigematsu)

There were no special comments, and Dr. Shigematsu asked all Board members to forward their comments later, if they had any.

II. Items for information

1. Present personnel status (presented by Tomoyuki Kono)

The personnel strength as of 1 April 1992 was five directors—one less than the full number due to the resignation of Dr. Schull, 64 professional employees, and 368 general employees—437 in total. Since RERF was established, the total number of employees has decreased from 588 to 437. In contrast to the sizable decrease of 176 general employees, professional employees increased by 24, reflecting RERF’s strong interest in strengthening the research staff.

A large number of mandatory retirements has recently occurred, because of massive hiring in the early days of ABCC. Retirees are more numerous every 3 years because of interim measures to decrease the mandatory retirement age. The filling of vacancies resulting from retirement is an important issue. Careful review is underway, taking into account possible relocation of the laboratory in Hiroshima.
The average age of general employees decreases every year and is now 44 years and 9 months. Among the general employees the percentage of males to females is 41.3 to 58.7, with the percentage of females increasing yearly. The percentage of males to females the year before last was 47.0 to 53.0.

2. FY91 salary revision (presented by Tomoyuki Kono)

(1) Salaries for FY91 were revised as of 1 April 1991 by using as a guide the recommendations of the National Personnel Authority concerning revising the salaries of national government employees. The base pay was revised on average by 3.13% for professional employees and by 3.55% for general employees. Additional revisions included changes in the dependents allowance, an increase in the transportation allowance, an increase in the seasonal allowances by 0.1 month's pay, establishment of special-duty allowance for employees in supervisory positions, inclusion of the special-adjustment allowance in base pay for nurses, and rate revisions for extra pay in which the yearly working hours previously used will be replaced by actual working hours. Also, a special pay-step system was established, modeled after the grade-increase system for national government employees. On 1 April 1992, RERF implemented procedures similar to the FY91 recommendations made by the National Personnel Authority, in cases of promotion to a higher grade other than the starting grade. The rate of termination allowance was revised for employees with 20 or more years of service who are terminated due to death.

(2) Salaries of the directors were revised taking into consideration the balance between their salaries and the salaries of employees. Also, the salaries of senior consulting scientists were revised.

(3) Matrimonial leave, leave following child birth, and summer leave were established as special types of leave in accord with leave granted to national government employees.

(4) In association with the Law Concerning Child Care Leave and the Law Concerning Child Care Leave for National Government Employees, effected on 1 April 1992, provisions that were not in agreement with these laws were revised, as well as other provisions which required revision, and they were effected on 1 April 1992.

(5) With the advent of an aging society, the Care Leave System proposed by the Labor Ministry was established and effected on 1 April 1992.

3. Labor union’s FY92 demands for improvement of working conditions, etc. (presented by Tomoyuki Kono)

The RERF Labor Union has 248 members (enrollment rate: 94%) and is affiliated with the All Japan Prefectural and Municipal Workers’ Union. The labor union in FY92 requested that RERF’s clinical department be reorganized
into an “international center for people exposed to radiation” and that RERF’s system of equal funding by the U.S. and Japan be changed. The other priority demands of the union were (1) a salary increase and improvement of working conditions, (2) employment of replacements for vacancies, (3) complete availability of annual leave, and (4) establishment of a welfare pension fund.

Labor-management relations are satisfactory because collective bargaining on these demands is conducted with the union.

4. Others

(1) Recommendations of the Human Germline Mutagenesis Workshop
(presented by James E. Trosko)

At this workshop, specialists in the field from around the world (including Japan) were invited to give their advice on new techniques, to evaluate the present findings, and to outline the future direction of the studies.

The genetic effects of the atomic bombings are a great concern of the survivors, and their long-term study is important. James V. Neel of the University of Michigan has been involved in the program since its initiation. Among several endpoints used as potential indicators of hereditary changes, sex ratio was studied by Neel, and he attempted to find biochemical changes in proteins of the offspring of exposed parents. No change was observed. Chiyoko Satoh, assistant department chief of the Department of Genetics, described the techniques currently being employed and sought the opinions of the experts at the workshop. Three new techniques, which have been introduced at RERF and are being improved, were discussed. All participants pointed out the rapid progress of techniques in this field. Because new techniques are being developed rapidly, the tone of the recommendations was, on the whole, conservative.

It was further recommended that RERF collaborate with other human-genome projects in various countries. It is desirable to develop a cooperative system to supplement and support RERF studies. Also, continuous efforts to collect materials and to manage data were proposed.

(2) Dosimetry reassessment (presented by J.W. Thiessen and Warren K. Sinclair)

Discussions on dosimetry reassessment are continuing in Japan and the U.S. The recent reorganization of the U.S. committee reflects the strong American commitment to address the basic issues related to atomic-bomb dosimetry.

Discrepancies continue between measured and theoretical values of neutron radiation in Hiroshima. Although the discrepancies are slight within 1000 m of hypocenter, differences up to 10-fold appear at 1400–1500 m.
With respect to radiation-risk factors, Seymour Jablon explained the possible consequences of changing the proportion of neutron and gamma radiation.

Conceivable causes are possible systematic errors in the computation of 1) neutrons released from the Hiroshima bomb and 2) neutrons transmitted through air. These problems are greatly diminished in the Nagasaki dosimetry because of the relative sparsity of neutrons.

Independent corroboration of the dosimetry has been enhanced recently by highly sensitive methods of identifying neutron-induced isotopes in metal, roof tiles, concrete, glass, etc. However, as time passes, it is increasingly difficult to find and measure materials and to verify location at the time of the bombings.

RERF is not directly involved in the dosimetry reassessment, but plays a major role in making available suitable materials for dosimetry measurements.

(3) International cooperation (presented by Itsuzo Shigematsu)

RERF international activities increased briskly in recent years. RERF has budgeted for these activities in this and in the upcoming fiscal years, taking care that such work does not hinder the Foundation's original research program.

RERF has concluded an agreement on research cooperation with the Ural Research Center of Radiation Medicine (URCRM) in Chelyabinsk, Russia. Chelyabinsk is the site of major radiation contamination, and the URCRM has followed the problem for the last 20 years. The general agreement to cooperate will be followed soon by specific research protocols.

Dosimetry is central to any such study. Therefore, the agreement between RERF and the URCRM was concluded with the consent of the Nuclear Safety Research Association (Eizo Tajima, chairman) and the Japan Atomic Industrial Forum (Kazuhisa Mori).

Similar to the Hiroshima International Council for Health Care of the Radiation-exposed (HICARE), the Nagasaki Association for Hibakusha Medical Care was established in April 1992. Training coordination and funding will be provided through this association.

(4) Ministry of Health and Welfare-sponsored project: Committee on A-bomb Materials and Information Network (presented by Yutaka Hasegawa)

Funded by special contract with the MHW beginning in FY91, RERF established the Committee on A-bomb Materials and Information Network to study how to collect, preserve, and present atomic-bomb-related archival materials and information.
The 50th anniversary of the atomic bombings will be marked in 1995, and atomic-bomb survivor organizations have been demanding that the Japanese Government pay condolence money for each radiation-exposed person who has died. The Japanese Government has proposed some sort of memorial project and has asked RERF to establish a committee to study the issue.

Last year the committee sent a group, including RERF permanent directors J.W. Thiessen and Yutaka Hasegawa, to the U.S. to visit several data resources and to discuss cooperative efforts. The project will include medical-research and other materials.

III. Items for deliberation and action

1. Recommendations of the 19th Scientific Council (presented by Toshiyuki Kumatori)

The Scientific Council has found the research program of RERF to be active and supports its continuation. Further, the Council points out the necessity of interdepartmental cooperation and joint studies with outside investigators. A flexible-time system was adopted in this year’s meeting, but it is preferred in the future to have RERF scientists judge who and what should be on the agenda. Dr. Kumatori explained the highlights of the recommendations which included the following: 1) cardiovascular diseases and nonradiation risk factors, 2) biochemical genetics, 3) cytogenetics, 4) radiobiology, 5) biological dosimetry, 6) cancer incidence studies, 7) molecular oncological epidemiology, 8) studies on SCID mice, 9) information systems, and 10) collection and preservation of human pathology material.

The Board approved the recommendations of the Scientific Council, and Dr. Shigematsu expressed his appreciation to the councilors for their efforts.

The next meeting of the Scientific Council will be held in Nagasaki, 29–31 March 1993 (with a backup date of 22–24 March).

2. FY91 research activities report (presented by James E. Trosko)

Chief of Research Trosko reviewed the past year’s major accomplishments in each of the main projects.

Seven new research protocols were approved, 18 technical reports were produced, scores of abstracts were presented at various international and national meetings, and scores of papers have been published in the open scientific literature.

One new direction to uniquely meet RERF’s mission is initiation of a new field of research, “molecular oncological epidemiology.” Moreover, an important workshop was held on the future direction for human germline mutagenesis studies at RERF.
Further, RERF has promoted international cooperation in radiation-research studies, which requires the time and labor of RERF researchers, but extends the Foundation’s research potential.

Since Akira Shishido, supervisor in charge of the research audit, was absent, David Williams presented an audit report on his behalf, and the FY91 research activities report was approved.

3. FY92 research plans and FY93 research directions (presented by James E. Trosko)

Departmental research plans for the next 5 years have been outlined in the Future Planning Committee Report [see next entry in these minutes]. It is important to stay abreast of new findings and new, rapidly evolving techniques.

Interdisciplinary studies and joint studies among various departments and with outside investigators should be further promoted.

A new research protocol on the potential effects of radiation on the incidence of dementia among the atomic-bomb survivors was discussed.

The research plans for FY92 and research directions for FY93 were approved.

4. RERF Future Planning Committee Report (presented by J.W. Thiessen)

Fully recognizing its ongoing commitment and obligation to the atomic-bomb survivors and to the citizens of Hiroshima and Nagasaki, RERF established the Future Planning Committee to determine the resources needed in terms of space, personnel, and equipment to carry out RERF’s mission during the next 5 years.


Assuming that funding beyond the present level would be modest, the committee pointed out that greater efficiency in support services and continuing computerization of databases and analyses will permit sufficient growth of the research program to respond to the diversity of future studies.

To avoid pursuing research judged to be outside RERF’s primary mission, the committee recommended that only research that can best be performed at RERF should be supported.

As presently stated, the goals of RERF’s research program are to determine the late somatic and genetic effects produced in atomic-bomb survivors and their children from exposure to ionizing radiation and to study the modifying
factors that affect the consequences of such exposure. Within this framework, recent developments in molecular biology and cytogenetics leading to a new research area called "molecular epidemiologic oncology" are expected to play an important role in RERF’s future research program.

Since the last meeting of the Board of Directors, new-facility discussions between the Japanese and U.S. governments have been ongoing. However, at this Board meeting, it was explained that the Future Planning Committee Report is not a proposal for the new facility, but is a proposal about the research program.

After the report's approval, a committee consisting of an executive staff and experts from Japan and the U.S. will be organized promptly. The committee’s first assignment will be the creation of a preliminary design for the new facility.

Because of the relative newness of the Nagasaki Laboratory, planning for Nagasaki has been limited to minor reallocation of resources.

Some participants expressed their uncertainty about whether the report was addressing the research program after relocation to a new facility or the research program for the next 5 years, and whether the report considered problems anticipated beyond 5 years in the future. Board members decided these issues would be discussed further at executive meetings.

The Future Planning Committee Report was approved.

5. FY91 settlement of accounts (presented by Tomoyuki Kono)

The statement of income and expenditures for the regular account and nine special accounts, the balance sheet, and the inventory of assets for FY91 were presented.

The total income for the year after settlement of accounts was ¥4,554,734,267. This included the binational subsidy income of ¥4,467,159,000, the operational income of ¥87,060,072, and also an income of ¥515,195 transferred from a special account. Total expenditures were ¥4,163,290,712, which consisted of ¥3,304,603,445 for personnel costs and ¥858,687,267 for operational costs. The difference between income and expenditure of ¥391,443,555 will be returned to the U.S. government (¥3,182,278) and Japanese government (¥388,261,277).

One of the special accounts, the A-bomb Memorial Special Account, was newly established in FY91 with a research entrustment fund from the MHW.

Presently, the termination trust fund for former Atomic Bomb Casualty Commission (ABCC) employees totals ¥1,100,000,000 (with interest included), but it will be expended by the year 2007. Thus, there is concern that there will be no capital for employee welfare loans, that are now funded by diverting a portion of the termination trust fund.
David Williams presented his supervisor's report and indicated that the status of the accounts of the Foundation is satisfactory. As done in previous years, it was mentioned that no provisions exist in the Foundation's finances to cover the unfunded portion of the retirement-allowance liability and that the unfunded portion has increased by ¥228,000,000 over the previous year. The settlement of accounts report for FY91 was approved.

6. FY92 working budget (presented by Tomoyuki Kono)

A FY92 working budget of ¥4,562,900,000 has been developed. The personnel costs total ¥3,707,288,000, and operational costs are ¥838,570,000. This calculation was based upon an estimated salary increase of 5.3%. Also, since there are more than 30 retirees including mandatory-age retirements, ¥408,978,000 has been budgeted for termination allowances. Operational costs have been budgeted on the basis of the settlement of accounts for the previous year and requests from each department.

Expenses for foreign-staff home leave are included in the relocation travel costs. Costs for the international collaborative program and costs for reviewing the basic plans for relocation have been newly budgeted, and no budget has been appropriated for relocation planning.

The FY92 working budget was approved.

7. Outline of the FY93 budget request (presented by Tomoyuki Kono)

The FY93 budget request, developed by adding to the FY92 budget increases caused by rises in costs and requests for new items, is ¥4,967,279,000. Personnel costs (¥3,912,422,000) were calculated on the basis of a decrease of four in budgeted slots and an estimated increase of 5.3% for wage-scale revisions and anniversary salary increases combined. About ¥36,559,000 has been included as an insurance premium for the welfare fund.

The operating cost is ¥887,760,000, and the new items include an emergency power generator for the Nagasaki Laboratory, school and tuition costs (ie, for the foreign staff), increased land rental fee for the Hiroshima Laboratory, and an increase for research equipment. Several Board members supported the increased budget for research equipment. As for relocation-related costs, ¥167,097,000 has been budgeted for basic design of the proposed new facilities.

Considering the importance of relocation, Chairman Shigematsu asked Shigeru Sumitani, MHW, to report on the negotiations between the two governments.

Mr. Sumitani stated that plans should be developed for constructing the proposed new facilities based on the Future Planning Report [approved on that same day during the meeting], using the relocation planning budget included in
the FY92 budget. A request for the relocation basic-design costs, included in
the RERF FY93 budget, will be submitted to the MHW Accounting Section.
Thereafter, a request will be made to the Ministry of Finance. The design work
is tentatively planned for completion next year, and construction in the follow-
ing 2 years. Mr. Sumitani expressed his hope that the U.S. and Japanese sides
will proceed in close contact with each other despite the difficult negotiations
both sides would have with the financial authorities.

The proposed budget request for FY93 was approved.

8. Revision of the rules and regulations (presented by Tomoyuki Kono)

The following proposals for establishing and revising the rules and regula-
tions were approved.

(1) Revision of the rules of employment
   a. Matrimonial leave (5 days), leave following child birth (2 days), and
      summer leave (3 days) were added as special types of leave.
   b. The prescription concerning the Regulations for Child Care Leave,
      etc., was included.

(2) Revision of wage regulations
   Following the revision of the Law Concerning the Wage for National
   Government Employees, the salaries of RERF directors and employees was
   revised.

(3) Establishing regulations concerning child care leave, etc.
   Following the enforcement of the Law Concerning Child Care Leave, the
   Regulations Concerning Child Care Leave, etc., were established, whereby
   employees who must take care of a child less than 1 year old may take
   leave for child care.

(4) Establishing regulations concerning care leave
   Provisions were made by which employees can take protracted leave for
   a maximum of 12 months, in units of a month, within a period of 2 years
   to look after their elderly parents, etc.

9. Election of directors and scientific councilors (presented by Itsuzo
   Shigematsu)

(1) Election of directors
   M.L. Mendelsohn was elected as a permanent director at the beginning
   of this Board meeting as successor to W.J. Schull. His term of appointment
   will be until 30 June 1993. S. Abrahamson was elected as successor to J.E.
   Trosko, chief of research. His term of appointment will be until 31 January
   1996.
(2) Election of scientific councilor

J.B. Little, professor of radiobiology, Harvard University, was elected as successor to M.L. Mendelsohn, who has been elected as an RERF permanent director. His term of appointment will be until 30 June 1993.

(3) Appointment of Operating Committee member

Since Nagasaki Laboratory Chief of Administration Yoshio Okamoto is scheduled to retire, Assistant Chief of the Secretariat Tadashi Nakaoka, who will be appointed as chief of administration, was appointed to the Operating Committee.

The term of appointment of directors and scientific councilors begins on 1 July, except for the two directors who assume the positions established when the number of directors was increased in July 1982, according to the views of the Ministry of Justice. Opinions were raised that a review should be made to standardize the appointment date.

IV. Scheduling of the next Board meeting

It was agreed that the next Board meeting would be held in Hiroshima, 9–11 June 1993.

Upon completing the discussion of all items on the agenda, Chairman Shigematsu and Vice Chairman Thiessen expressed their appreciation.
The 20th RERF Scientific Council Meeting

29–31 March 1993
Koseinenkin Kakan, Nagasaki, Japan

Agenda
Day 1
Executive session .................................................. Ei Matsunaga
Arno Motulsky

Greetings by RERF chairman ............................... Itsuzo Shigematsu
Report by the chief of research ......................... Seymour Abrahamson

Department of Clinical Studies
Objectives of the Adult Health Study (AHS) ............ Kazunori Kodama
Population demographics projections .................. Fumiyoshi Kasagi
Incidence of stroke in the AHS population ............ Kazunori Kodama
Bone-mineral density and calcium-regulating
hormones of atomic-bomb survivors ................. Saeko Fujiwara
Association of serum cholesterol and cancer
mortality/morbidity .............................................. Hideo Sasaki
Menopause study in Nagasaki ............................... Midori Soda

Department of Radiobiology
Department overview ........................................... Mitoshi Akiyama
Review and future plan of the glycoporphin A (GPA)
mutation study ....................................................... Seishi Kyoizumi
Cloning and characterization of the severe
combined immunodeficient (SCID) gene .......... Masumi Abe
Skin-cell transformation: possible association
with specific chromosome aberrations .............. Takeo Honda
In-vivo kinetics of T cells ...................................... Nori Nakamura

Department of Genetics
Department overview ............................................. Akio Awa
Fluorescence in-situ hybridization (FISH) and
G-banding comparative cytogenetics ................. Misako Nakano
Update on cytogenetic mutation rates .................. Akio Awa
Appendix

Research Information Center
Computing and network development activities ................. Jill Ohara
Current status of workstation database systems ............... Robert Allen

Day 2
Department of Epidemiology
Department overview .............................................. Kiyohiko Mabuchi
Family studies using the Life Span Study (LSS) cohort ... Marc T Goodman
Preliminary report on the 1991 mail survey .................. Yoshiisada Shibata
Thyroid-cancer risk factors: a case-control study .......... Yasuhiko Yoshimoto
Uses of the LSS mail-survey data ............................. Marc T Goodman
LSS Report 12 preview ......................................... Yukiko Shimizu

Department of Statistics
Summary of activities ............................................. Dale Preston
Cancer-incidence data and the LSS mortality data .......... Dale Preston
Interpretation and generalization of LSS risk estimates .... Donald Pierce
Comments: The impact of neutron radiation on cancer
  mortality in the LSS ........................................ Michael Vaeth
Anthropometric studies of in-utero survivors
  at age 18 .................................................... Eiji Nakashima
Growth and development after childhood radiation
  exposure ..................................................... Masanori Otake

Department of Genetics: Biochemical genetics
General overview .................................................. Chiyoko Satoh
DNA deletion-insertion-rearrangement mutations ............ Mieko Kodaira
Two-dimensional electrophoresis of DNA ...................... Jun-ichi Asakawa

Scientific councilors meet with individual research groups for informal
discussion.

Day 3
Executive session (closed)
Preparation of recommendations
Council recommendations ......................................... Arno Motulsky
Ei Matsunaga
Closing remarks by RERF vice chairman ...................... J. W. Thiessen

RERF Chairman Shigematsu and co-chairmen meet with members of the press.
Participants
Scientific councilors
Kunio Aoki, president, Aichi Cancer Center, Nagoya
Eisei Ishikawa, professor emeritus, Jikeikai University School of Medicine, Tokyo
Toshiyuki Kumatori, chairman, Radiation Effects Association, Tokyo
Ei Matsunaga, professor emeritus, National Institute of Genetics, Mishima
Shigefumi Okada, professor emeritus, University of Tokyo
Arno G. Motulsky, professor of medicine and genetics, School of Medicine, University of Washington
Clark W. Heath Jr., vice president for epidemiology and statistics, American Cancer Society
Leonard A. Herzenberg, professor of genetics, Stanford University School of Medicine
John B. Little, James Stevens Simmons professor of radiobiology, Harvard University School of Public Health

Observers
Shigeru Sumitani, director, Planning Division, Health Service Bureau, Ministry of Health and Welfare
Tsutomu Sugahara, professor emeritus, Kyoto University
Harry J. Pettengill, Deputy Assistant Secretary for Health, U.S. Department of Energy
Charles W. Edington, director, Board on Radiation Effects Research, Commission on Life Sciences, National Research Council
Alvin G. Lazen, acting executive director, Commission on Life Sciences, National Research Council
Ruey S. Lin, professor and chairman, Institute of Public Health College of Medicine, National Taiwan University

RERF supervisors
Akira Shishido, former director, Japanese National Institute of Health
David Williams, chief financial officer, National Academy of Sciences

RERF directors
Itsuzo Shigematsu, chairman
J.W. Thiessen, vice chairman
Seymour Abrahamson, permanent director and chief of research
Yutaka Hasegawa, permanent director
Mortimer L. Mendelsohn, permanent director
Tomoyuki Kono, permanent director and chief of Secretariat
Comments and Recommendations

The Council would like to thank the local staff and management for the excellent planning and support provided during this meeting. The presentations were carefully prepared and clearly presented. We appreciated the balanced presentations and thus felt that we obtained a good status report and an excellent appreciation of last year’s progress. We like being able to meet less formally with the various research groups for half of an afternoon.

In the future, we would greatly appreciate receiving all handouts, including the hard copies of slides when we arrive in Hiroshima or Nagasaki. It would also be helpful if all investigators scheduled to present reports were listed in the program together with their respective affiliations. If a photograph of each speaker were provided, it would allow us to associate faces with names.

The written reports should emphasize the critical problems the RERF researchers would like us to judge and at the same time should provide sufficient, but not overwhelming, background information.

We applaud the Research Information Center for trying to make personal computers available to most researchers. We strongly urge that arrangements be made for RERF’s business operation to stop using the mainframe computer. In these times of financial stringency, this step will save significant funds for the research operations.

Clinical Studies

Adult Health Study

Analyses of data from the Adult Health Study (AHS) grow steadily more important as the cohorts age and as illness frequencies increase. The Council is therefore pleased with the emphasis given this year to assessing the future course of the AHS. The study’s current and projected demographics show that about 35% of AHS participants are now dead, that the average age of survivors is now about 63 years, and that nonparticipation frequencies have risen to 15% and may well increase further, especially among subjects in the higher radiation-dose categories and partly as a result of illnesses interfering with usual clinic contacts. It is therefore timely that a workshop was held in January 1993 to consider how best to adjust AHS procedures to encourage subject participation and to record needed clinical data. The workshop made practical recommendations regarding AHS research priorities, methods for enhancing and increasing populations contacts, adjustments to the clinical examination, and approaches for increased surveillance of illness outcomes. The Council in particular endorses the workshop recommendation to decrease the interval between clinical examinations to 1 year. The importance of capturing data on health events in older cohort members strongly justifies such increased frequency, at least for persons over age 70. Greater use of mail and phone contacts, and even home visits, between clinic appointments should also be actively considered.
Data were presented regarding several important continuing investigations using AHS data. In three of these studies, health outcomes or clinical measurements seem related to radiation dose (stroke incidence, serum cholesterol levels, and age at menopause). In each instance, the Council would urge further analyses to consider the possible influences of nonradiation risk factors in shaping the observed associations. Variables related to socioeconomic status (e.g., occupation and education) might be linked to such associations. If such variables, as recorded in AHS or LSS records, were also related to radiation-dose categories, they deserve to be incorporated into the process of radiation-risk estimation.

Data were also presented regarding measurements of bone-mineral density in relation to atomic-bomb (A-bomb) radiation dose. Technical uncertainties in densitometry, however, make conclusions difficult. Such investigations deserve to continue because prior RERF work regarding parathyroid activity and calcium metabolism suggests the possibility of a real radiation effect.

**Epidemiology**

**Life Span Study mortality/morbidity studies**

A remarkable array of epidemiologic studies are in progress, including the developing area of molecular epidemiology. Of particular long-range importance is the 1991–92 Life Span Study (LSS) questionnaire survey which is now complete and is entering its analytic phases. The execution of the survey has been exceptionally thorough, and the response frequencies, after two reminder contacts, have been most encouraging. The Council looks forward to future analyses of survey results regarding LSS lifestyle patterns, both in relation to patterns as seen in the past surveys and eventually as cofactors in assessing future LSS mortality/morbidity estimates of A-bomb radiation risk.

Since national Japanese mortality statistics show substantial differences in various cancer and noncancer death rates in different occupational classes, it is to be expected that such social-class differences may also operate in Hiroshima and Nagasaki among irradiated populations, according to their particular location at the time of the bombings (ATB). It may be necessary for comparison of radiation effects to have another nonexposed control area matched with the social and occupational background of the heavily exposed groups.

**Case-control study of thyroid cancer**

The results of an excellent case-control study were presented with respect to thyroid cancers identified through the Hiroshima and Nagasaki tumor registries. In addition to suggesting that about 10% of such cases are related to A-bomb radiation exposure, the study identified several other nonradiation risk factors, including some indication of increased familial cancer occurrence. Such case-control analyses, using tumor-registry bases, may be a valuable analytic approach for future studies.
of other cancer sites, especially if they can suggest clues regarding the potential interaction of radiation with other risk factors. Studies on multiple primary cases will be of interest.

Mortality report (LSS)

The latest LSS mortality report (LSS Report 12) will cover cohort mortality from 1950 through 1990, with emphasis on cancer-mortality trends. It will also feature special analyses of cancer mortality in persons who were under age 10 years ATB and of the temporal patterns of cancer mortality in various age groups and with respect to noncancer mortality as first explored in LSS Report 11. The council considers that the regular publication of these comprehensive mortality reports is of central importance for RERF. It therefore applauds the emphasis being given to LSS Report 12 and encourages the expansion of radiation-risk estimations to include all variables that may materially influence those risk determinations. When excess risk levels are modest and when they concern causes of death or morbidity (cancer or noncancer) for which nonradiation lifestyle risk factors play a prominent role, it will be important over time to develop means for incorporating such LSS risk data into the models by which radiation effects are assessed.

Workshop on epidemiology/statistics

The Council was impressed by the large number of complex epidemiologic and biostatistical problems raised in different studies. In considering future topics for workshops, the directors should strongly consider holding an epidemiology and biostatistics workshop dealing with a variety of methodologic and substantive issues raised by ongoing studies. We feel that input by experienced epidemiologists and biostatisticians would be useful for ongoing studies at RERF.

Visiting Fellows in Epidemiology

To promote and strengthen epidemiological studies, it may be desirable to introduce a short-term Visiting Research Fellow system, because few young doctors are interested in epidemiology in Japan. RERF is one of the best places for training in epidemiology.

Statistical Problems

Work in the Statistics Department continues to be of the highest quality and to play central roles in collaborative support for all other RERF departments. Particular recent emphasis has been given to analysis of LSS cancer-incidence information. Such data were presented especially with respect to hematopoietic cancers and to cancer incidence/mortality comparisons. The greater frequency of chronic myelogenous leukemia in Hiroshima, the prominence of HTLV-I infection and nonradiation-
related T-cell leukemias in Nagasaki, and the uncertainty of myeloma risk in relation to radiation continue to be of special interest.

The current statistical process for calculating relative and absolute cancer-risk estimates related to radiation dose in the LSS cohort was the subject of major discussion. The failure thus far of such measurements to consider effect-related variables such as age at the time of the bombings may limit their informativeness. *The Council would encourage continued revision of the risk-estimation process so pertinent variables that might modify cancer risk or affect the expression of site-specific radiation-risk estimates are properly included and expressed.* Present uncertainty with respect to neutron radiation levels in A-bomb radiation estimates further complicates this overall risk-determination process. Although at present it seems unclear how neutron levels, in fact, affect exposure estimates, the Council hopes that over the next year such questions can be more satisfactorily resolved.

**Body growth and development**

On a less theoretical level, interesting analyses were presented regarding parameters of body growth and development in relation to radiation dose, both in the in-utero cohort and among persons under the age of 10 years ATB. Such analyses have received considerable attention in the past, and they continue to be of great importance as having a potential relationship with increasing dose. *The Council encourages continued analyses in this important area of possible radiation effect, but would suggest that the analyses consider socioeconomic differences that might have existed ATB and might have had some impact on these observed patterns of growth and development, independent of radiation exposure.*

**Genetics**

**Possible gene-environment interaction in radiation carcinogenesis**

The recent observation that about half of all surviving LSS subjects have a sibling relationship to other LSS subjects stirred great interest within the Council. It is likely, in view of recent biologic developments in cancer research, that certain individuals may be more susceptible to radiation-induced carcinogenesis. Since so many A-bomb survivors come from family groups, the proposed study of familial aggregation of radiation-induced cancer has a high priority. Cancer-concordant sibs could also be used for developing appropriate molecular-epidemiologic studies. Current estimates of cancer induced by radiation may represent an average value consisting of higher sensitivity for the genetically susceptible and greater resistance for the remainder. The demonstration of such a phenomenon would be a major advance. No other body of patient material exists to test this hypothesis in a large population. Other possible gene-environmental interactions following radiation effects also should be explored. Every effort should be made to carry out the appropriate searches to learn about family relationships among individuals who had
cancer and whose radiation dose is known. The Council feels that appropriate use of koseki records will make it possible to carry out such a study without endangering confidentiality and privacy. We realize that considerable expense and professional time would be required to assemble the necessary koseki information for such studies, especially if the entire LSS cohort, living and dead, were to be covered. It will be important to involve an experienced population geneticist in such a study. The Council strongly urges that RERF vigorously explore the possibilities for productive research in this intriguing area.

Genetic differences between the Hiroshima and Nagasaki populations

Most of the differences in radiation effects between Hiroshima and Nagasaki have been ascribed to differences in the physical nature of the radiation delivered by the different atomic bombs exploded in the two cities. However, we know of biologic differences unrelated to the atomic bombings, such as the complete absence of HTLV-I-related leukemia in Hiroshima and the lower frequency of chronic myelogenous leukemia in Nagasaki. To fully evaluate the city differences, we urge that careful population genetics studies of the two cities be continued using a variety of genetic markers including mitochondrial DNA. Such a study should be evaluated together with archaeologic and historic data. It is conceivable that some of the differences in radiation sensitivity could be explained by underlying genetic differences between the two cities.

DNA studies for mutation detection

Chiyoko Satoh’s research group continues to make steady progress in establishing the family-based repository, and the project might take 2 or 3 more years to complete, we are encouraged by continued progress in DNA technology. Although large-scale screening for DNA mutations is not yet feasible, several methodologic developments at RERF give hope that DNA screening may become a reality in the not-so-distant future. Three different methods are used: 1) polymerase-chain-reaction-denaturing gradient gel electrophoresis (PCR-DGGE) for unique genes; 2) Southern blotting for unique genes and minisatellites; and 3) PCR–high resolution electrophoresis for minisatellites and trinucleotide repeats. Fifty families from the exposed population and 50 from the control population have been examined at various loci using the three methods, and the results show that the methods are feasible for the group’s purpose. Furthermore, the group is now developing two new technologies: 1) quantitation of chemoluminescent bands on Southern filters using an image analyzer equipped with a highly sensitive photon camera, and 2) two-dimensional (2-D) gel electrophoresis of DNA, called restriction landmark genomic scanning (RLGS). We are encouraged by the reproducibility of 2-D DNA electrophoresis, and we encourage future pilot studies. The new methodology for nonradioactive labelling and detecting of DNA looks promising in early studies and ultimate-
ly may make mutation detection possible with a not-too-large number of probes in several hundred exposed and control individuals. Since reproducibility and efficiency are the key factors in choosing the best technology for detecting mutation at the DNA level, we strongly urge Dr. Satoh and her colleagues to continue with their pilot studies and to improve the efficacy of the techniques, preferably those involving automation.

Examining rearrangement in specific minisatellite or variable-number-of-tandem-repeats (VNTR) loci should continue in parallel with studying alteration in random DNA fragments, as can be done using the 2-D electrophoresis technique. These techniques are complementary: minisatellites are likely to be more unstable genetically and thus susceptible to rearrangement by radiation, and the 2-D technique allows the screening of a very large number of DNA sites. The investigators should not be deterred by finding a high mutant fraction at one VNTR locus; the frequency of spontaneous mutation of most minisatellites is quite low (around $10^{-5}$).

As in the past, we urge the DNA researchers to maintain close contact with both national and international investigators who are at the forefront of advanced DNA technology.

**Fluorescence in-situ hybridization**

Akio Awa’s research group has established (in collaboration with the Lawrence Livermore National Laboratory) the utility of the fluorescence in-situ hybridization (FISH) technique for rapidly and accurately detecting reciprocal translocations persisting in the peripheral lymphocytes of A-bomb survivors. They showed not only a high intra-individual agreement between FISH and G-banding analysis, but also, in an in-vitro irradiation experiment, nearly equal frequencies of induced translocations and dicentrics—a finding that was theoretically expected and that in turn confirmed the reliability of their technique. They also demonstrated that among those survivors whose translocation frequencies were grossly discrepant relative to the Dosimetry System 1986 (DS86) dose estimates, the range of variation in translocation frequencies became narrower if the survivors were exposed inside a Japanese house, whereas it was greater if they were exposed outside either directly or shielded by a Japanese building. This finding implies the rather homogeneous nature of Japanese wooden houses in terms of shielding effect.

We strongly urge Dr. Awa and his colleagues to continue using FISH to make detailed comparisons in dose-response curves between Hiroshima and Nagasaki, to evaluate the neutron relative biological effectiveness, and to verify the reliability of shielding information for individual survivors using the DS86 system. We also hope they establish a better correlation of FISH translocation data with other biological endpoints, such as somatic mutation data and acute radiation symptoms.

A new, interesting study entitled “The fragile site expression assay in peripheral blood lymphocytes” has been proposed by Sadayuki Ban et al. to evaluate the utility
of this assay for studies of radiation sensitivity and cancer susceptibility. Because Masaaki Hori at the National Institute of Radiological Sciences has had abundant experience in this field, we suggest that Dr. Ban seek advice from him.

**Radiobiology**

**Biologic radiodosimetry**

Mitoshi Akiyama, Nori Nakamura, Masumi Abe, Seishi Kyoizumi, Yoichiro Kusunoki and their collaborators in both Nagasaki and Hiroshima presented interesting data on their development of new molecular and cellular models for long-term biological radiodosimetry. They also found some potential dosimetry models that might be useful as long-term dosimeters using sophisticated flow-cytometric data.

Of the methods for somatic-mutation measurement in humans, the glycophorin assay continues to show dose-ATB-related mutations in erythrocytes. Since these cells have no RNA or DNA, these “mutations” cannot be directly confirmed. Thus, another somatic-mutation method using neutrophils has been proposed: mutant variants can be sorted by FACS and their RNA or DNA analyzed directly for the expected genetic change that could confirm these variants as true mutants. We **strongly support this study**.

Seishi Kyoizumi et al. presented data on two promising assays under development as potential dosimeters. Both assays use sophisticated flow cytometric/FACS methods followed by colony formation in vitro or RNA confirmation of mutations. These can now be used on aliquots of blood drawn for other purposes in the AHS studies. Again **we encourage development of these sophisticated methods as potential long-term dosimeters of radiation exposure.**

**Tumor-suppressor gene (p53) in thyroid carcinoma**

Toshio Seyama presented an interesting analysis of p53 in thyroid carcinoma. **Such a molecular epidemiological approach should be continued and expanded further by formulating crisp hypotheses and developing sound and pragmatic strategies to select and analyze samples from cases and controls.**

**Isolation of the severe combined immunodeficient (SCID) gene**

Masumi Abe continues to work on isolation of the SCID gene from humans. Somatic-cell hybrids between SCID mouse murine cells and human cells localized the SCID human homologue on human chromosome 8 (M. Itoh et al., *Radiat Res* 134:364–8, 1993). He has transfected either a genomic human DNA or a cDNA expression library into SCID murine cells and has isolated several putative radiation-resistant cell clones. The cDNA-transfected cells contain human sequences. This DNA sequence information should allow the isolation of specific human cDNA in an expression vector for transfection into SCID murine cells to determine if the radiation-resistant phenotype can be transfected with high frequency. If successful,
isolating the human homologue of the SCID gene will be considered a major achievement, and a biochemist will be required to advance this project.

**In-vitro recombination assay using purified proteins**

Putative RAG1 and RAG2 proteins have been produced in bacteria and SF9 insect cells. Polyclonal and monoclonal antibodies to RAG1 and RAG2 are being characterized. Masumi Abe recognizes the high-risk/high-reward nature of these two projects. He plans to test cross hybridization of the cDNA and genomic transfec tant clones soon. The results will determine which direction to pursue.

**Skin-cell transformations**

This project, which was started 4 years ago, will determine whether diploid skin-fibroblast cell strains derived from A-bomb survivors are susceptible to spontaneous neoplastic transformation. Morphologic transformation occurs rarely in normal human fibroblasts, and the occurrence of spontaneous immortalization of such cells has not been documented.

Takeo Honda has succeeded in establishing three different clonal fibroblast cell populations using long-term serial culture from two A-bomb survivors. One of the three clonal populations, t(1q−; 16q+), derived from a high-dose survivor, was spontaneously transformed. Another clonal population bearing a chromosome 3p deletion may be in the early stages of transformation.

We find this work of potentially great interest and suggest pursuing this research along the lines suggested by Scientific Councilor John B. Little (see the following section).

**Specific recommendations by J.B. Little regarding the study of skin-cell transformations**

Fibroblast strains were established in culture and maintained in confluence in large flasks for 2–3 years. During this time, they were subcultivated at periodic intervals. Signs of senescence appeared, but monoclonal populations characterized by marker chromosomes have emerged from cell strains derived from two heavily irradiated survivors. No such changes have thus far been observed in strains derived from two normal controls.

One monoclonal population bearing a chromosome 1;16 translocation that arose from a cell strain derived from a 76-year-old female (in 1989) has become morphologically transformed. This survivor received 5.14 Sv ATB and subsequently developed a breast cancer (1991). The transformed cells show a number of karyotypic changes in addition to altered morphology and growth characteristics. However, they have not as yet been shown to be immortal or tumorigenic in nude mice. Another clonal population bearing a chromosome 3p deletion may be in the early stages of transformation.
This is an interesting project with the potential for providing significant results. It has required a great deal of patience and perseverance, as well as a careful culture technique. These RERF investigators should consider several factors related both to this specific and to future experiments. The genetic identity of this t(1;16) clone must be established to prove that it is not a tumor-cell contaminant. This has apparently been done by DNA fingerprinting in relation to the original fibroblasts, but if possible, fingerprinting should also be carried out in comparison with normal tissue from the same patient (e.g., blood). If genetic identity is confirmed, then the possibility of a germline mutation in the p53 tumor-suppressor gene should be explored. Infection with SV-40 should be excluded by immunocytochemistry. Samples of these cells should be cryopreserved at regular intervals to allow for further studies at later times, particularly if the clonal strain becomes senescent. The cells should be maintained in rapid exponential growth with regular passaging (ideally at least weekly at 1:4 dilution) to determine if or when immortalization occurs. This should be evident by the Scientific Council meeting next year when an additional 75–100 population doublings should have occurred. If the cells do not immortalize, Dr. Honda might consider exposing them to radiation or another mutagen/carcinogen to determine whether they are more susceptible to induced immortalization.

These investigators should be sure to codify a protocol to be followed in all future experiments in which subcultivation is carried out at standard intervals and the number of mean population doublings the cells undergo is precisely determined. They should consider increasing the number of exposed survivors in the study, perhaps focusing on those individuals who have developed skin cancer. In this way, their assay might be used as a method for detecting a predisposition to radiation-induced skin cancer. Determining the p53 status of morphologically transformed or immortalized cell lines would also be of interest.

Overall, the future prospects for this project should become much more evident during the coming year.
Health Monitoring Workshop

RERF Hiroshima Laboratory
25–27 January 1993

Agenda

Day 1
Morning, Session 1: Introduction and Overview
Session co-chairmen: J. David Curb and Hiroshi Yanagawa
Welcoming remarks by the RERF chairman ............... Itsuzo Shigematsu
Introduction of participants .................................. J. David Curb and Hiroshi Yanagawa
Summary of relevant RERF data and research materials ...................... Seymour Abrahamson
Overview of the Adult Health Study (AHS) ................. Kazunori Kodama

Morning, Session 2: Morbidity/mortality Surveillance
Session co-chairmen: J. David Curb and Hirotugu Ueshima
Surveillance and disease registry in epidemiological studies ....................... Hiroshi Yanagawa
Hospital surveillance in Honolulu Heart Program ............. J. David Curb

Afternoon, Session 2: Morbidity/mortality Surveillance
Session co-chairmen: J. David Curb and Hirotugu Ueshima
A study of the occurrence of cardiovascular disease and subsequent physical inability using the cardiovascular-disease registration data from the western part of Shiga Prefecture, Japan .......... Hirotugu Ueshima
Community-surveillance program of cardiovascular disease in Suita, Japan .............. Shunroku Baba
Long-term surveillance of cardiovascular disease:
Lessons from New Zealand ......................... Robert Beaglehole
Hospital surveillance of hip fracture in Japan ................ Tsutomu Hashimoto
Discussion/summary of the day’s sessions ................. Session chairmen

Day 2
Morning, Session 3: Introduction and Overview
Session co-chairmen: J. David Curb and Hiroshi Yanagawa
AHS medical examination procedures ....................... Hideo Sasaki
Morning, Session 4: Medical Examination Program
Session co-chairmen: J. David Curb and Hiroshi Yanagawa
Appropriate examination frequencies for an aging population .................................................. Robert B. Wallace
Surveying older persons; responding to modern scientific questions about aging ......................... Robert B. Wallace
Markers for detection of subclinical diseases; related to cardiovascular disorders .......................... J. David Curb

Afternoon, Session 4: Medical Examination Program
Session co-chairmen: Gary D. Friedman and Shigeru Hisamichi
Osteoporosis screening procedures in a population survey ......................................................... Tsutomu Hashimoto
Using pharmaco-epidemiological techniques in the survey of older persons ................................ Robert B. Wallace
Case-control evaluation of screening for cancer of the large bowel and prostate ............................ Gary D. Friedman
Mass-screening programs for cancer and their evaluation in Japan ............................................. Shigeru Hisamichi
Discussion/summary of the day's sessions .................................................................................. Session chairmen
Tour of RERF clinical facility (1 hour)

Day 3
Morning, Session 5: General Discussion and Preparation of Recommendations
Session co-chairmen: J. David Curb and Hiroshi Yanagawa
Preparation of recommendations (closed session)
Presentation of workshop recommendations ............................................................................... Session chairmen
Closing remarks by RERF vice chairman ................................................................................. J.W. Thiessen

Participants
Panel Members
Co-chairmen
J. David Curb, professor, Department of Medicine, University of Hawai at Manoa, Honolulu, Hawai
Hiroshi Yanagawa, professor and chairman, Department of Public Health, Jichi Medical School, Tochigi-ken, Japan

Members
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Gary D. Friedman, director, The Permanente Medical Group, Inc., Division of Research, Oakland, California
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Hirotugu Ueshima, professor and chairman, Department of Health Science, Shiga University of Medical Science, Ohtsu, Japan
Robert B. Wallace, professor and head, Department of Preventive Medicine & Environmental Health, University of Iowa College of Medicine, Iowa City, Iowa

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Robert Beaglehole, professor and head, Department of Community Health, School of Medicine, University of Auckland, Auckland, New Zealand

**Observers**
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* RERF science councilor
**RERF visiting director
RERF directors

Itsuzo Shigematsu, chairman
J.W. Thiessen, vice chairman
Seymour Abrahamson, permanent director and chief of research
Mortimer L. Mendelsohn, permanent director
Yutaka Hasegawa, permanent director
Tomoyuki Kono, permanent director and chief of the Secretariat

Recommendations of the Health Monitoring Workshop

I. Introduction

The Adult Health Study (AHS) is a cohort of 20,000 subjects established in 1958, and data have been accumulated on this cohort for over 30 years, mainly from the biennial health examinations. The major objective of the AHS is to elucidate the health effects of atomic-bomb (A-bomb) radiation, and, to date, wide-ranging research achievements concerning various diseases have resulted from epidemiological studies, aging studies, somatic-cell studies, and cell-biology and cytogentic studies.

These accumulated data are expected to contribute greatly to clarifying not only radiation health effects but also risk factors of circulatory diseases, cancer, diabetes, and aging. So, a policy for effectively using these data must be considered.

As the AHS cohort has aged, 40% of the subjects have already died and the participation rate of the elderly has been decreasing. Therefore, future data collection may be insufficient, and we recommend the following means by which the AHS cohort can be more effectively studied in the future.

II. Key issues

1. Selection of priority research topics

Concerted efforts have been made to study cancer and leukemia as target diseases, and excess risks have been observed in relation to A-bomb radiation exposure. Benign tumors, stroke, coronary heart disease, diabetes, and age-related diseases will be given high priority as additional target diseases for research. In particular, the possible association between aging and radiation exposure, should be investigated. Because of their advanced ages, the AHS participants are becoming an excellent cohort for an aging study. Designing an optimal examination program involves developing specific research questions and assigning priority to diseases and conditions of interest, that is, to (1) conditions with known strong associations with radiation, (2) conditions with weak or potential associations, (3) common causes of morbidity and mortality in the Japanese population, and (4) issues of social importance.
2. Improving the participation rate in the biennial health examinations

In all age groups the participation rate has been decreasing, but especially in the elderly. To raise the participation rate, the participants should be provided useful feedback, such as information provided through telephone or mail contact. Feedback methods should be formally evaluated to determine their effects on participation.

3. Decrease the contact interval for AHS subjects to less than 2 years

Most of the AHS follow-up information is obtained from biennial health examinations, but this information is not sufficient. Although the vital-statistics death certificates are regularly retrieved, only 20% of the cases of stroke and coronary heart disease are ascertained thereby. The exact examination interval should be tailored to priority AHS issues. For some research questions that require physical measures or biological specimens, annual or more-frequent examinations may be required. For other research questions, telephone or mail contact may be sufficient. Differing approaches to various age groups should be considered as well. Contact with random samples may suffice for other questions. Additional pilot studies should be used to test these approaches. A combination of methods and modes of contacts would be useful.

For the nonparticipants, it is hoped that, at a minimum, information on their present health status, survival status, and results of medical examination at medical institutions will be obtained by mail or telephone. If they are being examined at medical institutions, a cooperative system for collecting necessary information from the medical institutions should be established by consulting with the medical associations and hospitals.

Health examinations by home visits require time and manpower. Also, procurement of a small motor vehicle to facilitate ECG examinations and blood collection should be considered.

4. Review the content of current examinations

Deletion of some items in the current examination should be strongly considered. Each item, specimen, and measurement in the examinations should be evaluated according to the following criteria: (a) time required; (b) scientific rationale and potential value; (c) standardization, validation, and comparability both over time within the AHS and, secondarily, to other studies; and (d) potential for adverse consequences. The potential psychological problems and medical consequences of positive findings obtained through unproven screening procedures should be evaluated, eg, ultrasound for pancreatic and uterine disease.

The following items should be considered for inclusion in future examinations.

a) Assessment of physical function through questionnaires: Activities of Daily Living (ADL) Questionnaire, Instrumental Activities of Daily Living
Questionnaire (IADL), and performance testing and other physiologic measures reflecting age-related changes.

b) Concise measures of social, cognitive, and mental health
c) Sigmoidoscopy
d) Mammography
e) Ankle/arm blood pressure
f) Bone-mineral density and body-fat distribution using DEXA scan (quality control between DEXA and dual-photon absorptiometry is necessary).
g) Upper GI endoscopy and pepsinogen I & II and helicobacter pylori measures.

5. Improve the surveillance system for detecting morbidity and mortality

This recommendation should include the previously recommended shorter contact interval. To expedite systematic data collection from clinics and hospitals, an appropriate system for cooperation with the medical associations and major hospitals should be established. Access to medical records is essential for a surveillance system. Therefore, a workshop should be organized to discuss these matters. Furthermore, we should consider how to promote joint research with cooperative organizations and should recognize the necessity of a budget for data collection. Contact with family and police doctors should be considered for sudden and unattended deaths. Nursing home contacts should also be considered.
Active Research Protocols by RERF Program

As of 1 January 1993

Life Span Study

**RP 2-61** Study of mortality in children exposed in utero
- **1-75** Research plan for RERF study of life span of A-bomb survivors, Hiroshima and Nagasaki
- **6-88** Comparative analysis of the LSS population and a cohort of 265,000 Japanese men and women
- **4-91** Mail survey on epidemiologic factors in the Extended Life Span Study sample, 1991

Adult Health Study

**RP 2-75** Research plan for RERF Adult Health Study, Hiroshima and Nagasaki

Immunology

**RP 36-63** Blood groups in Adult Health Study and in utero ATB subjects Hiroshima and Nagasaki
- **6-78** Hb antigen changes in relationship to radiation exposure, liver cancer, and liver cirrhosis in the Adult Health Study, Hiroshima and Nagasaki—A prospective study
- **16-81** Establishment of specific reagents for detection of human cancers through in vitro immunologic and biochemical assays
- **2-87** Autoimmunity and autoimmune diseases in the Adult Health Study, Hiroshima and Nagasaki
- **3-87** Cellular immune function and its relationship to in vitro T-lymphocyte radiosensitivity and MN blood group locus mutation frequency in A-bomb survivors: Precursor frequency analysis of mitogen- and antigen-responsive blood lymphocytes
- **1-88** Study on the titers of anti-Epstein-Barr virus antibodies in the sera of atomic bomb survivors
- **7-88** Study of somatic mutations at the glycoporphin A locus in erythrocytes of atomic bomb survivors
- **7-89** Screening of stem cell mutation in lymphoid lineage among A-bomb survivors and its characterization
### Appendix

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<td>Establishment of a method for HLA-DQ and DP gene typing using the polymerase chain reaction</td>
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### Special clinical studies

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<td>6-92</td>
<td>Establishment and operation of a system for collecting and storing leukemia cells</td>
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**Annual Report 92–93**

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**Histopathology**

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<th>Pathology studies in Hiroshima and Nagasaki: revised research plan</th>
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<td>Senile changes of the brain in Hiroshima and Nagasaki A-bomb survivors</td>
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<td>Analysis of radiation sensitivity mechanism in the severe combined immunodeficient (SCID) mouse</td>
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<td>1-92</td>
<td>Radiation dose estimates using tooth samples. Part 2. Use of electron spin resonance on tooth enamel from Hiroshima atomic bomb survivors</td>
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<td>Tumor suppressor gene alterations in lung tumors from Japanese mustard gas workers and atomic bomb survivors</td>
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<td>Molecular analysis of the p53 tumor-suppressor gene in breast cancers of atomic bomb survivors (with addendum)</td>
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**Biochemical genetics**

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<td>Study to develop methods of DNA analysis for detection of mutations in children of atomic bomb survivors</td>
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**Cytogenetics**

| RP 2-66 | Somatic cell chromosome analysis of exposed individuals Hiroshima and Nagasaki |

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<td>Cytogenetic study of in utero exposed individuals in the Adult Health Study population, Hiroshima and Nagasaki (addendum to RP 2-66)</td>
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<td>Fragile-site-expression assay in peripheral-blood lymphocytes: Pilot study of reproducibility and radiosensitivity in atomic-bomb survivors</td>
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### F<sub>1</sub> studies

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<thead>
<tr>
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<tr>
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<td>Research plan for RERF studies of the potential genetic effects of atomic radiation; Hiroshima and Nagasaki. Part 1. Mortality study of children of atomic bomb survivors</td>
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<td>Collection of surgically removed cancer tissues from A-bomb survivors: Special reference to thyroid and breast cancers</td>
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<td>Ultrasonographic screening of Adult Health Study participants to detect cancer and other diseases</td>
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<td>Guidelines for the conduct of site-specific cancer incidence studies among A-bomb survivors, Hiroshima and Nagasaki</td>
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<td>1-90</td>
<td>Breast cancer incidence study among atomic bomb survivors, Hiroshima and Nagasaki, 1950–85</td>
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RP 5-90  Primary liver cancer incidence study among atomic bomb survivors, 1958–87
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8-86  Ionizing radiation for medical reasons reported by Adult Health Study participants, Hiroshima and Nagasaki
8-87  Organ doses from medical x-ray exposures (addendum to RP 8-84)
5-91  Radiation-therapy-related cancer among Life Span Study subjects (addendum to RP 7-81)

Tumor registry; and tissue registry
RP 18-61  Tumor registry study in Hiroshima and Nagasaki
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RP 6-83  A case-control study on colorectal cancer
3-84  Response of human thyroid cells in culture to neutron irradiation
      (addendum to RP 18-81)
10-85  Nutrients in relation to cancer risk: A prospective epidemiologic
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12-85  Epidemiologic case-control study of thyroid cancer in Hiroshima
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1-86  Study on the mechanism of carcinogenesis among A-bomb survivors. 1. Detection
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3-86  Host variation of radiosensitivity among A-bomb survivors: An in
      vitro study using peripheral T-cells
9-86  Pathology review of lung cancer among atomic bomb survivors and
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6-87  X-ray radiosensitivity of lymphocytes in vitro from A-bomb survivors. Part 2:
      Micronucleus induction (addendum to RP 3-86)
4-89  ABO phenotype association with risk factors of cardiovascular
      disease in the Adult Health Study and its relation to radiation
      exposure, Hiroshima and Nagasaki
Directors, Supervisors, and Scientific Councilors

As of 31 March 1993

Permanent Directors

Chairman: Itsuzo Shigematsu, former director, Department of Epidemiology, National Institute of Public Health
Vice chairman: J.W. Thiessen, former deputy associate director, Office of Health and Environmental Research, U.S. Department of Energy
Permanent director (chief of research): Seymour Abrahamson, former chairman, Zoology Department, University of Wisconsin
Permanent director: Yutaka Hasegawa, former director, Chugoku-Shikoku Regional Medical Affairs Bureau, Ministry of Health and Welfare
Permanent director: Mortimer L. Mendelsohn, former associate director for biomedical and environmental research, Lawrence Livermore National Laboratory
Permanent director (chief of the Secretariat): Tomoyuki Kono, former chairman, Social Insurance Training Institute, Ministry of Health and Welfare

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Shigefumi Okada, professor emeritus, University of Tokyo
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Clark W. Heath Jr., vice president for epidemiology and statistics, American Cancer Society
Leonard A. Herzenberg, professor of genetics, Stanford University School of Medicine
John B. Little, James Stevens Simmons Professor of Radiobiology, Harvard University
Arno G. Motulsky, professor of medicine and genetics, School of Medicine, University of Washington

Consultants

As of 31 March 1993

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Haruo Ezaki, Hiroshima Thyroid Clinic
Kohei Hara, professor, 2nd Department of Internal Medicine, Nagasaki University School of Medicine
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Yutaka Hosoda, chief, Radiological Epidemiology Center, Radiation Effects Association
Michito Ichimaru, director, Sasebo Municipal General Hospital
Katsuhide Ito, professor, Department of Radiology, Hiroshima University School of Medicine
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Shigenobu Nakamura, professor, 3rd Department of Internal Medicine, Hiroshima University School of Medicine

Yukio Nishimoto, director, JR Hiroshima Railway Hospital

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Kozo Ohama, professor, Department of Obstetrics & Gynecology, Hiroshima University School of Medicine

Hajime Orimo, professor, Department of Geriatrics, Tokyo University Faculty of Medicine

Shozo Sawada, professor, Research Institute for Nuclear Medicine and Biology, Hiroshima University

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Koji Yoshizawa, professor, Department of Hygiene, Hiroshima University School of Medicine

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Tasuku Honjo, professor, Department of Biochemistry, Kyoto University Faculty of Medicine

Leonard S. Lerman, senior lecturer, Massachusetts Institute of Technology
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Michio Oishi, professor, Institute of Applied Microbiology, University of Tokyo

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Yoshiyuki Sakaki, professor, Human Genome Analysis Center, Institute of Medical Science, University of Tokyo

Masao Sasaki, professor, Radiation Biology Center, Kyoto University

Eiichi Soeda, senior research scientist, Institute of Physical & Chemical Research, Wakoshi, Saitama

Toshio Sofuni, chief, Laboratory of Cell Variants, Department of Mutagenesis, National Institute of Hygienic Sciences, Tokyo

Michihiro Yoshida, professor, Chromosome Research Unit, Faculty of Science, Hokkaido University, Sapporo

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Michael A. Bean, director, Pacific Northwest Research Foundation, Seattle, Washington

Max D. Cooper, professor, Howard Hughes Medical Institute, Birmingham, Alabama

Kiyohiko Dohi, professor, 2nd Department of Surgery, Hiroshima University School of Medicine

Akihiro Itoh, professor, Research Institute for Nuclear Medicine and Biology, Hiroshima University

Kokichi Kikuchi, president, Sapporo Medical College

Yasushi Okumura, professor, Department of Immunology, Juntendo University School of Medicine, Tokyo

Hiroshi Shiku, professor, Department of Oncology, Nagasaki University School of Medicine

Tomio Tada, professor, Department of Immunology, University of Tokyo Faculty of Medicine

Nobuo Takagi, assistant professor, Research Center for Molecular Genetics, Hokkaido University, Sapporo.

Hiraku Takebe, professor, Department of Experimental Radiology, Kyoto University Faculty of Medicine, and Director, Radiation Biology Center, Kyoto University

Norihide Takeya, professor emeritus, Hiroshima University (concurrent assignment)

Epidemiology

Suminori Akiba, professor, Department of Public Health, Kagoshima University Faculty of Medicine
Takashi Aoyama, professor, Experimental Radiology, Shiga University of Medical Science
Takeshi Hiyayama, director, Institute of Preventive Oncology, Tokyo
Hiroo Kato, director general, National Institute for Minamata Disease, Minamata, Kumamoto
Masafumi Kimura, former Welfare Ministry technical official, Department of Health Population, Institute of Public Health, Tokyo
Takashi Maruyama, research officer, National Institute of Radiological Sciences, Chiba
Otsura Niwa, professor, Research Institute for Nuclear Medicine and Biology, Hiroshima University
William J. Schull, director and professor, Graduate School of Biomedical Sciences, Center for Demographic and Population Studies, University of Texas
Norihide Takeya, professor emeritus, Hiroshima University
Kazuo Uemura, professor, Ryutsu Keizai University, Kyugasaki, Ibaraki

Statistics
Yasunori Fujikoshi, professor, Department of Mathematics, Hiroshima University Faculty of Science
Akio Kudo, professor, Department of Developmental Technology, Tokai University, Numazu, Shizuoka
Masaki Munaka, professor, Research Institute for Nuclear Medicine and Biology, Hiroshima University
Sumiyasu Yamamoto, director, International Institute for Natural Sciences, Kake International Center for Academic Exchange, Kurashiki, Okayama

Epidemiologic Pathology
Robert E. Anderson, professor and chairman, Department of Pathology, University of New Mexico
Koki Inai, professor, 2nd Department of Pathology, Hiroshima University School of Medicine
Hideyo Itakura, professor, Department of Pathology, Institute for Tropical Medicine, Nagasaki University
Nanao Kamada, professor, Research Institute for Nuclear Medicine and Biology, Hiroshima University
Koji Namba, professor, Hiroshima University Faculty of Integrated Arts and Sciences
Takashi Saku, professor, Department of Oral Pathology, Niigata University School of Dentistry
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Takashi Taguchi, professor, 2nd Department of Pathology, Nagasaki University School of Medicine
Eiichi Tahara, professor, 1st Department of Pathology, Hiroshima University School of Medicine

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Secretariat
Hisashi Kodama, director, N'IT Hiroshima Central Health Management Clinic
Shun-ichiro Michitsuji, lecturer, Department of Neuropsychiatry, Nagasaki University School of Medicine

Expert Advisory Panels

As of 31 March 1993

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Kingo Fujimura, assistant professor, Research Institute for Nuclear Medicine and Biology, Hiroshima University

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Koichi Tatsumi, chief, Department of Biostatistics, National Institute of Radiological Science

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Elaine Ron, research scientist, U.S. National Cancer Institute, Bethesda, Maryland
Statistics

Takashi Yanagawa, assistant professor, Department of Mathematics, Kyushu University Faculty of Science
Richard Sposto, statistician, EMMES Corporation, Potomac, Maryland
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Desmond E. Thompson, assistant professor, George Washington University, Washington, D.C.

Epidemiologic Pathology

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Megumu Fujiwara, acting chief, Department of Pathology, Hiroshima Red Cross–A-bomb Hospital
Toshiyuki Fukuhara, chief, Department of Pathology, Hiroshima Prefectural Hospital
Aya Hanai, supervisor, Epidemiology and Investigation Section, The Center for Adult Diseases, Osaka
Yuzo Hayashi, senior chief, Department of Clinical Laboratories, Hiroshima Asa Citizens Hospital
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Masao Kishikawa, assistant professor, Medical Materials Center for Atomic Bomb Casualty, Atomic Disease Institute, Nagasaki University School of Medicine
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Takeshi Matsuo, assistant professor, 1st Department of Pathology, Nagasaki University School of Medicine
Hiroo Matsuura, chief, Department of Pathology, Hiroshima Citizens Hospital
Osamu Takahara, chief, 2nd Department of Clinical Laboratories, and chief, Pathology Division, Nagasaki Red Cross–A-bomb Hospital
Nobuo Tsuda, assistant professor, Department of Clinical Laboratories, Nagasaki University School of Medicine

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As of 31 March 1993

Operating Committee chairman
Itsuzo Shigematsu, RERF chairman

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- Yutaka Hasegawa, permanent director
- Mortimer L. Mendelsohn, permanent director
- Tomoyuki Kono, permanent director and chief of the Secretariat
- Katsutaro Shimaoka, associate chief of research, Nagasaki Laboratory
- Akio Awa, chief, Department of Genetics
- Richard D. Sperry, business administrator, Secretariat
- Yasukiyo Hirano, operations administrator, Secretariat
- Tadashi Nakaoka, chief of administration, Secretariat, Nagasaki Laboratory

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As of 31 March 1993

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Committee deputy chairman
Katsutaro Shimaoka, associate chief of research, Nagasaki Laboratory

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- Kenjiro Yokoro, senior consulting scientist
- Hideo Sasaki, assistant chief, Department of Clinical Studies
- Yoshiaki Kodama, research scientist, Cytogenetics Laboratory, Department of Genetics
- Toshio Seyama, chief, Cell Biology Laboratory, Department of Radiobiology
- Seishi Kyoizumi, research scientist, Immunology Laboratory, Department of Radiobiology

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Norio Takahashi, division chief, Radioisotope Facilities
Yukiko Shimizu, senior scientist, Department of Epidemiology
Dale L. Preston, chief, Department of Statistics
John B. Cologne, research scientist, Department of Statistics
Jill L. Ohara, chief, Research Information Center
Yasukiyo Hirano, operations administrator, Secretariat
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John B. Cologne, research scientist, Department of Statistics

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Yuko Hirai, associate senior scientist, Immunology Laboratory, Department of Radiobiology
Yasuhiko Yoshimoto, associate senior scientist, Department of Epidemiology
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Yukiko Shimizu, senior scientist, Department of Epidemiology
Tetsuo Imada, chief, Computer Section, Research Information Center
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  Ai Yokoyama, unit supervisor, Library, Library and Archives, Publication & Documentation Center

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Committee chairman
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Deputy chairman
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  Akio Awa, chief, Department of Genetics
  Nori Nakamura, assistant chief, Department of Radiobiology
  Shizuo Inoue, assistant chief, Secretariat
  Tadashi Nakaoka, chief of administration, Secretariat, Nagasaki Laboratory
Executive secretary
Shun-ichiro Matsuoka, assistant chief, External Affairs Section, Secretariat

Professional and Supervisory Staff

As of 31 March 1993

Research Departments
Seymour Abrahamson, chief of research
Shoji Tokuoka, senior consulting scientist

Hiroshima Laboratory
Department of Clinical Studies
Kazunori Kodama, department chief
Hideo Sasaki, assistant department chief
Ken-ichiro Ishii, administrative assistant department chief
Noboru Ueda, attached to the department

Division of Medicine
Kazuo Neriishi, division chief
Saeko Fujiwara, research scientist (associate senior scientist)
Michiko Yamada, research scientist
Masaharu Nobuyoshi, research scientist
Shizuyo Kusumi, research scientist (concurrent assignment)

Division of Radiology
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Yumiko Sano, assistant chief of technicians
Hiromichi Fukuchi, assistant chief of technicians

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Toyoko Nakamura, assistant chief of nurses
Yayoko Hirofuji, assistant chief of nurses
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Iitsuji Okibayashi, section chief
Iwao Osaki, assistant section chief
Hiromi Sakaguchi, assistant section chief
Naoya Kagimoto, Clinical Counselling Unit supervisor
Masahiro Wada, Medical Record Unit supervisor
Yasuko Bo, Administration Unit supervisor

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Kanjuro Hidaka, section chief
Minoru Aihara, assistant section chief
Miyoko Kamisako, Scheduling Unit supervisor
Midori Kamouchi, Contacting Unit supervisor
Taeko Kuwabara, Contact Records Unit supervisor

Department of Genetics

Akio Awa, department chief
Chiyoko Satoh, assistant department chief

Cytogenetics Laboratory

Akio Awa, acting laboratory chief
Kazuo Ohtaki, research scientist
Mimako Nakano, research scientist
Yoshiaki Kodama, research scientist
Sadayuki Ban, research scientist
Masashi Hiramoto, chief of technicians

Biochemical Genetics Laboratory

Chiyoko Satoh, acting laboratory chief
Jun-ichi Asakawa, research scientist (senior scientist)
Mieko Kodaira, research scientist
Norio Takahashi, research scientist (concurrent assignment)
Yasukazu Kimura, chief of technicians
Junko Kaneko, assistant chief of technicians

Department of Radiobiology

Mitoshi Akiyama, department chief
Nori Nakamura, assistant department chief
Kyoko Ozaki, administrative assistant department chief
Michiko Takagi, assistant section chief
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Takashi Itoh, research scientist
Terumi Mizuno, research scientist
Keisuke S. Iwamoto, research scientist

Immunology Laboratory
Mitoshi Akiyama, acting laboratory chief
Seishi Kyoizumi, research scientist
Yuko Hirai, research scientist (associate senior scientist)
Yoichiro Kusunoki, research scientist
Seigo Teraoka, research scientist
Noriko Abe, chief of technicians
Kazumi Tanabe, assistant chief of technicians

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Yukiko Shimizu, research scientist (senior scientist)
Yasuhiro Yoshimoto, research scientist (associate senior scientist)
Thanne P. Rose, research scientist
Marc T. Goodman, research scientist
Charles E. Land, visiting research scientist
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Akiko Tamagawa, Administration Unit supervisor

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Toshio Miyoshi, assistant section chief
Kyoko Nakaya, Master Files Unit supervisor
Michihiro Matsuo, Records Unit supervisor

Coding Section
Miyuki Kurose, section chief
Suzuka Kikkawa, unit supervisor

Field Investigation Section
Shigeyoshi Michitsuji, section chief
Tsunemaro Ohmoto, assistant section chief
Masashi Sakurai, Investigation Unit supervisor
Masatsugu Yuki, Data Collection Unit supervisor
Department of Statistics
  Dale L. Preston, department chief
  Masanori Otake, assistant department chief
  Shoichiro Fujita, research scientist (senior scientist)
  Eiji Nakashima, research scientist
  John B. Cologne, research scientist
  Fumiyoshi Kasagi, research scientist
  Michael Væth, research scientist
  David J. Pawel, research scientist
  Donald A. Pierce, research scientist

Department of Epidemiologic Pathology
  Kiyohiko Mabuchi, department chief (concurrent assignment)
  Takako Okita, Administration Unit supervisor

Pathology Laboratory
  Kiyohiko Mabuchi, acting laboratory chief
  Masayoshi Tokunaga, visiting research scientist
  Chiyoko Omoto, assistant chief of technicians

Tumor & Tissue Registry Office
  Yukiko Shimizu, office chief (concurrent assignment)
  Masayuki Morita, section chief
  Morito Dote, assistant section chief
  Yukinobu Nakata, unit supervisor
  Nobuko Hoshino, unit supervisor

Research Information Center
  Jill L. Ohara, Center chief

Information Systems Laboratory
  Mensah Solomons, research scientist
  Scott Pohlman, research scientist
  Robert L. Allen, research scientist

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  Tetsuo Imada, section chief
  Tsumeyuki Isaka, assistant section chief
  Kyoko Katagami, Operations Unit supervisor
  Mieko Koda, Management Unit supervisor
Appendix

Publication and Documentation Center
Mioko Miyasaki, Center chief
Takashi Okita, assistant Center chief

Administration and Support Section
Kimiko Ono, section chief
Kimiko Ono, Administration and Records Unit supervisor (concurrent assignment)
Tokiko Himori, unit supervisor
Eiko Ishizaki, unit supervisor

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Beth A. Magura, section chief
Junso Takayama, assistant section chief
Reiko Sasaki, assistant section chief
Reiko Sasaki, Production Unit supervisor (concurrent assignment)
Beth A. Magura, English Publications Office chief (concurrent assignment)
Robert H. Masterson, research scientist
Kimiko Ono, Japanese Publications Office chief (concurrent assignment)
Junso Naruto, Printing–Photography Unit supervisor

Library and Archives
Mioko Miyasaki, acting curator of library
Kayoko Arakawa, Archives Office unit supervisor
Ai Yokoyama, Library Office unit supervisor

Radioisotope Facility
Norio Takahashi, division chief

Secretariat
Tomoyuki Kono, chief
Richard D. Sperry, business administrator
Yasukiyo Hirano, operations administrator
Shizuo Inoue, assistant chief of Secretariat
Takahiko Saeki, assistant chief of Secretariat

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Takeo Murata, section chief
Akiko Enami, assistant section chief
Tadaaki Watanabe, General Affairs Unit supervisor
Jun-ichi Nakamura, Archives and Document Unit supervisor
External Affairs Section
Shun-ichiro Matsuoka, section chief
Shun-ichiro Matsuoka, Acting International Relations Unit supervisor (concurrent assignment)
Shun-ichiro Matsuoka, Public Relations Unit supervisor (concurrent assignment)
Junko Houta, Administrative Unit supervisor

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Hirokichi Tominaga, section chief
Tadataka Kuribayashi, assistant section chief
Fujiko Naito, Personnel Unit supervisor
Tadataka Kuribayashi, Payroll Unit supervisor (concurrent assignment)

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Torao Sasaki, section chief
Akio Ihara, Accounting Unit supervisor
Torao Sasaki, Receipts and Disbursements Unit supervisor (concurrent assignment)

Supply and Property Section
Takeshi Abe, section chief
Yofu Sato, assistant section chief
Toyoshi Matsumura, assistant section chief
Yofu Sato, Supply Unit supervisor (concurrent assignment)
Toshikazu Ohmori, Maintenance Unit supervisor
Toshiharu Ueno, foreman

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Yoshihiro Kurakawa, section chief
Katsuko Fukuba, assistant section chief
Takumi Okita, Operations Unit supervisor
Katsuko Fukuba, Welfare Unit supervisor (concurrent assignment)
Toshiko Takata, Food Service Unit supervisor

********

Nagasaki Laboratory
J.W. Thiessen, director of Nagasaki Laboratory
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Kenjiro Yokoro, senior consulting scientist
Department of Clinical Studies
  Katsutarō Shimaoka, acting department chief  
Masazumi Akahoshi, acting assistant department chief  
Tsutomu Nakamura, administrative assistant department chief

Division of Medicine
  Masazumi Akahoshi, acting division chief  
Midori Soda, research scientist (concurrent assignment)  
Kiyosumi Oishi, research scientist  
Hiroaki Nonaka, research scientist (concurrent assignment)  
Masako Tsuruta, research scientist

Division of Radiology
  Yasuko Amazaki, division chief  
Ichiro Koba, chief of technicians

Division of Clinical Laboratories
  Hiroaki Nonaka, acting division chief  
Masako Fukamachi, chief of technicians  
Moritaka Taniguchi, assistant chief of technicians  
Tatsuko Hamaura, assistant chief of technicians  
Akemi Matsuo, assistant chief of technicians

Nursing Section
  Yumiko Yamashita, assistant chief of nurses

Clinical Administration Section
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Noboru Imamichi, assistant section chief  
Miyako Kitagawa, Medical Records Unit supervisor  
Masao Irie, Administration Unit supervisor

Clinical Contacting Section
  Yasutaka Ohgushi, section chief  
Mitsuko Ikeda, assistant section chief  
Ayako Kawazato, Scheduling Unit supervisor  
Hiroyuki Fujinaga, Contacting Unit supervisor  
Nachiko Fukae, Counseling Unit supervisor
Department of Radiobiology
Takeo Honda, department chief
Michiko Hirose, Administration Unit supervisor

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Yoko Urakawa, chief of technicians

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Masumi Abe, research scientist
Hiromitsu Miki, assistant chief of technicians

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Kazuko Dateki, assistant section chief
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Toshiko Tanaka, Records and Archives Unit supervisor

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Osamu Kusumi, assistant section chief
Osamu Kusumi, Field Investigation Unit supervisor (concurrent assignment)
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Midori Soda, assistant department chief

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   Tatsue Taneguchi, assistant section chief
   Koji Nakamura, unit supervisor
   Koki Sonoda, unit supervisor

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   Moritaka Taniguchi, assistant chief of technicians (concurrent assignment)

Secretariat
   Tadashi Nakaoka, chief of administration

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   Takaaki Hashiguchi, section chief
   Kin-ichi Honda, chief of Public Relations Office (concurrent assignment)
   Akihiro Yamauchi, General Affairs Unit supervisor
   Hiroshi Ichoda, Employees Unit supervisor
   Atsuko Nakagawa, Public Relations Unit supervisor

Accounting Section
   Kin-ichi Honda, section chief
   Mitsuo Yutaka, assistant section chief
   Mitsuo Yutaka, Accounting Unit supervisor (concurrent assignment)
   Yasushi Takeda, Supply and Property Unit supervisor
Summary Tables

*April 1992–March 1993*

Family contacting for the Adult Health Study (AHS) and permanent lymphocyte cell-line* establishment

<table>
<thead>
<tr>
<th>Category</th>
<th>AHS subjects allocated for contacting</th>
<th>Appointments made</th>
<th>PLC families allocated for contacting</th>
<th>Appointments made</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hiroshima</td>
<td>2846</td>
<td>2081</td>
<td>77</td>
<td>55</td>
</tr>
<tr>
<td>Monthly average</td>
<td>237.2</td>
<td>173.4</td>
<td>6.4</td>
<td>4.6</td>
</tr>
<tr>
<td>Nagasaki</td>
<td>1376</td>
<td>1227</td>
<td>66</td>
<td>42</td>
</tr>
<tr>
<td>Monthly average</td>
<td>114.7</td>
<td>102.3</td>
<td>5.5</td>
<td>3.5</td>
</tr>
</tbody>
</table>

*RP 5-85: Culture of permanent lymphocyte cell lines (PLC) as sources of biological samples for investigation of genetic effects of radiation on children of atomic-bomb survivors. The study was initiated in Hiroshima in August 1985 and commenced in Nagasaki in September 1986.

Medical clinic visits

<table>
<thead>
<tr>
<th>Category</th>
<th>Total</th>
<th>Scheduled</th>
<th>Others*</th>
<th>AHS</th>
<th>Nonsample</th>
<th>Specimens only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Referral</td>
<td>Return</td>
</tr>
<tr>
<td>Hiroshima</td>
<td>2749</td>
<td>2081</td>
<td>563</td>
<td>97</td>
<td>8</td>
<td>188</td>
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<tr>
<td>Monthly average</td>
<td>229.1</td>
<td>173.4</td>
<td>46.9</td>
<td>8.1</td>
<td>0.7</td>
<td>15.7</td>
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<tr>
<td>Nagasaki</td>
<td>1710</td>
<td>1227</td>
<td>368</td>
<td>110</td>
<td>5</td>
<td>58</td>
</tr>
<tr>
<td>Monthly average</td>
<td>142.5</td>
<td>100.3</td>
<td>30.6</td>
<td>12.3</td>
<td>0.4</td>
<td>4.8</td>
</tr>
</tbody>
</table>

*Return, nonscheduled examination, etc.
## Tumor-registry accessions (malignant tumors only)
### January–December 1992

<table>
<thead>
<tr>
<th>Category</th>
<th>Total</th>
<th>Total</th>
<th>AHS</th>
<th>F₁, PE86, in utero samples</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hiroshima</td>
<td>8826</td>
<td>873</td>
<td>223</td>
<td>84</td>
<td>7869</td>
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<tr>
<td>Monthly average</td>
<td>735.5</td>
<td>72.8</td>
<td>18.6</td>
<td>7.0</td>
<td>655.8</td>
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<tr>
<td>Nagasaki</td>
<td>5332</td>
<td>183</td>
<td>51</td>
<td>17</td>
<td>5132</td>
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<tr>
<td>Monthly average</td>
<td>444.3</td>
<td>15.3</td>
<td>4.3</td>
<td>1.4</td>
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</tbody>
</table>

### Tissue-registry accessions

<table>
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<th>Year</th>
<th>Hiroshima</th>
<th>Nagasaki</th>
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</thead>
<tbody>
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<td>3249</td>
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<td>10056</td>
<td>4633</td>
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<tr>
<td>1980</td>
<td>10521</td>
<td>6110</td>
</tr>
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<td>1981</td>
<td>12434</td>
<td>6972</td>
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<tr>
<td>1982</td>
<td>13440</td>
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**NOTE:** Tissue registration was commenced in Hiroshima in April 1973 and in Nagasaki in September 1974 with funds provided by the U.S. National Cancer Institute.
Requests for reprints of RERF journal publications by country
April 1992–March 1993

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Total: 486 from 42 countries
RERF Technical Reports Series: peer reviewers

RERF's directors would like to extend special thanks to the persons who during Fiscal Year 1992 donated their time and talents to the peer review of scientific manuscripts submitted for the RERF Technical Report Series. We are deeply indebted to all of you for your efforts on our behalf.

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A.B. Rickinson, University of Birmingham Medical School, Department of Cancer Studies, Birmingham, UK
Masao S. Sasaki, Radiation Biology Center, Kyoto University, Kyoto, Japan
A.D. Tates, Sylvius Laboratories, Department of Radiation Genetics and Mutagenesis, Leiden, The Netherlands
Sheldon Wolff, University of California–San Francisco, Laboratory of Radiobiology, San Francisco, CA, USA
Chronology of Events

1 April 1992–31 March 1993

1992
April

1    Ceremony to welcome new employees
1    Human Investigation Committee meeting
13   Research Protocol Review Committee meeting
13   Meeting of research department chiefs and assistant department chiefs
14   Executive Committee meeting, Operating Committee meeting, staff liaison meeting
14   Long Service Award ceremony, Hiroshima
20   Mitsoshi Akiyama, chief, Department of Radiobiology, became a member of the American Cancer Society
30   Long Service Award ceremony, Nagasaki
30   Human Investigation Committee meeting

May

11   Executive Committee meeting, Operating Committee meeting, staff liaison meeting
11   Research Protocol Review Committee meeting
11   Meeting of research department chiefs and assistant department chiefs
11–15 Audit by Price Waterhouse
13   Fire drill by the in-house fire brigade, Hiroshima
22   RERF Chairman Itsuzo Shigematsu commended by Princess Chichibu, president of the Tuberculosis Prevention Society, for his contribution in preventing tuberculosis at the 43rd National Tuberculosis Prevention General Meeting
22   Kazunori Kodama, chief, Department of Clinical Studies, receives the Award for Prevention of Cardiovascular Diseases from the Japan Heart Foundation at the general meeting of the Japanese Association for Cerebro-cardiovascular Disease Control
29   RERF receives the Chugoku Postal Services Bureau Award for being a postal services cooperative foundation at the 1992 Postal Services Commendation Ceremony
June


5 Human Investigation Committee meeting

7 Late Atomic Bomb Effects Research meeting, Nagasaki

11 Chairman Itsuzo Shigematsu conferred with the title of Fellow of the Royal College of Physicians of London

12 Retirement ceremony for the first half of Fiscal Year 1992, Nagasaki

15 Research Protocol Review Committee meeting

15 Meeting of research department chiefs and assistant department chiefs

16 Executive Committee meeting, Operating Committee meeting, staff liaison meeting

16 Retirement ceremony for the first half of Fiscal Year 1992, Hiroshima

18 9th RERF-National Institute of Radiological Sciences-Research Institute for Nuclear Medicine and Biology Exchange Seminar, Hiroshima

24 Mortimer L. Mendelsohn assumes position as permanent director

24–26 26th meeting of the Board of Directors, Nagasaki

July

1 Party to celebrate RERF Chairman Itsuzo Shigematsu being conferred with the title of Fellow of the Royal College of Physicians of London

1 Research Information Center begins publication of *Computer Hiroba*

7 Human Investigation Committee meeting

10 Hiroshima and Nagasaki Departments of Clinical Studies meet at Hiroshima Laboratory

10 Leukemia registry meeting

15 Crown Prince Naruhito visits Hiroshima Laboratory

20 Research Protocol Review Committee meeting

20 Meeting of research department chiefs and assistant department chiefs

21 Executive Committee meeting, Operating Committee meeting, staff liaison meeting
July
26–31  5th Japan Cerebro-cardiovascular Disease Prevention Seminar was held at the Hiroshima Kosei-nenkin-kaikan (Seminar Honorary President: Itsuzo Shigematsu, RERF chairman; Organizer: Kazunori Kodama, chief, Department of Clinical Studies, RERF)

August
5  Party to bid farewell to Permanent Director and Chief of Research James E. Trosko and to welcome his successor, Seymour Abrahamson, and Permanent Director Mortimer L. Mendelsohn
6  Chairman Itsuzo Shigematsu, Vice Chairman J. W. Thiessen, Permanent Director and Chief of Research James E. Trosko, Permanent Director Mortimer L. Mendelsohn, and Permanent Director Tomoyuki Kono attend Hiroshima City Atomic Bomb Peace Memorial Ceremony
6  Chairman Itsuzo Shigematsu and Permanent Director Yutaka Hasegawa attend the memorial service held by the Hiroshima City Medical Association for its former members and deceased medical workers who perished as a result of the atomic bombing
6  In-house events at the Hiroshima Laboratory to commemorate the anniversary of the atomic bombing of Hiroshima
7  Human Investigation Committee meeting
9  Permanent Director and Chief of Research James E. Trosko, Associate Chief of Research Katsutaro Shimaoka, and Chief of Administration Tadashi Nakaoka attend Nagasaki City Atomic Bomb Peace Memorial Ceremony
10–12 As members of the newly inaugurated RERF New Facility Committee, Chairman Itsuzo Shigematsu, Vice Chairman J.W. Thiessen, Department Chief of Radiobiology Mitoshi Akiyama, and Assistant Chief of Secretariat Shizuo Inoue visit Research Triangle Park, North Carolina, to see some of the most modern laboratories.
13  Chairman Itsuzo Shigematsu, Vice Chairman J.W. Thiessen, and Assistant Chief of Secretariat Shizuo Inoue meet NAS representatives, Washington, D.C.
14  Chairman Itsuzo Shigematsu, Vice Chairman J.W. Thiessen, and Assistant Chief of Secretariat Shizuo Inoue participate as observers in the Japan–US meeting about RERF relocation matters in Washington, D.C.

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**September**

1. Executive Committee meeting
2. 1st meeting of RERF New Facility Committee (basic plan for new facility is discussed)
7. US Ambassador to Japan Michael H. Armacost visits Hiroshima Laboratory
14. Executive Committee meeting, Operating Committee meeting, staff liaison meeting
18. Human Investigation Committee meeting
28. Research Protocol Review Committee meeting
28. Meeting of research department chiefs and assistant department chiefs

**October**

1–7. 43rd National Labor and Health Week, employee strength tests conducted
3–4. Hiroshima Laboratory staff recreational trip to Shimane and Tottori prefectures
3–4. Nagasaki Laboratory staff recreational trip to Yamaguchi Prefecture
6. Executive Committee meeting, Operating Committee meeting, Nagasaki
26. Honorary Secretary-General of the International Atomic Energy Agency Sigvard Eklund visits Hiroshima Laboratory
26. Meeting of research department chiefs and assistant department chiefs
27. Executive Committee meeting, staff liaison meeting

**November**

10. 6th general meeting of ABCC–RERF Retirees Association (Hiroshima Century Hotel)
11. 2nd meeting of RERF New Facility Committee (basic plan for new facility is discussed)
12. Tadashi Nakaoka, chief of administration, attends Nagasaki University Medical School’s Autopsy Memorial Service
16. Research Protocol Review Committee meeting
16. Meeting of research department chiefs and assistant department chiefs
17. Executive Committee meeting, Operating Committee meeting, staff liaison meeting
17. Party at the Hiroshima Laboratory to honor William J. Schull, former RERF vice chairman (1979–80), who received the Third Order of the Sacred Treasure
<table>
<thead>
<tr>
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<tr>
<td>November</td>
<td>25 3rd meeting of RERF New Facility Committee (basic plan for new facility is discussed)</td>
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<tr>
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<td>26 Lecture on fire prevention for National Fire Prevention Week, Nagasaki Laboratory</td>
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<td>December</td>
<td>1 Executive Committee meeting</td>
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<td>2 4th meeting of RERF New Facility Committee (basic plan for new facility is discussed)</td>
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<td></td>
<td>14 Research Protocol Review Committee meeting</td>
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<td></td>
<td>14 Meeting of research department chiefs and assistant department chiefs</td>
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<td>15 Executive Committee meeting, Operating Committee meeting, staff liaison meeting</td>
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<td>16 Retirement ceremony for the latter half of Fiscal Year 1992, Hiroshima Laboratory</td>
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<tr>
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<td>17 Retirement ceremony for the latter half of Fiscal Year 1992, Nagasaki Laboratory</td>
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<td>1993</td>
<td>January 5 Executive Committee meeting</td>
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<td>18 Research Protocol Review Committee meeting</td>
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<td>18 Meeting of research department chiefs and assistant department chiefs</td>
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<td>19 Executive Committee meeting, Operating Committee meeting, staff liaison meeting</td>
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<td></td>
<td>25–27 AHS Health Monitoring Workshop, Hiroshima Laboratory</td>
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<td></td>
<td>28 US–Japan meeting on Cross-National Dementia Study, Hiroshima Laboratory</td>
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<td>February</td>
<td>2 Executive Committee meeting, Operating Committee meeting, Nagasaki Laboratory</td>
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<td>15 Research Protocol Review Committee meeting</td>
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<td>15 Meeting of research department chiefs and assistant department chiefs</td>
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<td>26 Atomic Bomb Dosimetry Assessment Review Committee working group meets, Hiroshima Laboratory</td>
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<td>March</td>
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<td>March 29–31</td>
<td>20th meeting of the Scientific Council, Nagasaki</td>
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