Ionizing Radiation and Health

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Although such tragedies as the atomic bombings in Hiroshima and Nagasaki in 1945 should never be repeated, these unfortunate experiences have greatly enhanced our knowledge of the health effects due to ionizing radiation.

Studies on the late health effects of ionizing radiation among the atomic bomb survivors have been conducted since 1947 by the Atomic Bomb Casualty Commission (ABCC) and its successor, the Radiation Effects Research Foundation (RERF) which is equally funded by the two governments of Japan and the United States.

The results thus far obtained up to the present can be classified into the following three categories:

(1) The effects for which a clear increase has been found include malignant neoplasms, cataracts, chromosomal aberrations, small head size and mental retardation among the in utero exposed.

(2) A suggestive increase has been found in the several sites of cancers and immunological abnormalities.

(3) No difference has been observed between the exposed and the non-exposed in some types of leukemia, osteosarcoma, accelerated aging, sterility and hereditary effects.

Atomic bomb survivors, Fixed population, Late health effects

Ionizing radiation is a fact of life and has always been with us, but after Roentgen discovered X-rays in 1895, man was first faced with the problems of radiation induced damage, primarily to the skin and eventually to other organs and systems. Although such tragedies as the atomic bombings in Hiroshima and Nagasaki in 1945 and the Chernobyl nuclear power plant accident in 1986 should never be repeated, it is true that these unfortunate experiences have greatly enhanced our knowledge of the health effects due to ionizing radiation.

At present, besides these episodes, a number of data from various sources are available for health risk estimation of human populations exposed to ionizing radiation (Table 1). These data are derived from, for example, nuclear weapon experiments, medical therapy and diagnosis, and occupational hazards, but as far as the long term health effects are concerned, information from Hiroshima and Nagasaki still remains the most important throughout the

Table 1 Exposed Human Populations for Risk Estimation**ATOMIC BOMBS**

- Japanese Survivors
- Marshall Islanders

MEDICAL THERAPY

- Pelvic Radiotherapy (cervix)
- Spinal Radiotherapy (ankylosing spondylitis)
- Neck and Chest Radiotherapy (thyroid)
- Scalp Irradiation (tinea capitis)
- Breast Radiotherapy
- Radium Treatment

MEDICAL DIAGNOSIS

- Multiple Fluoroscopies (breast)
- Prenatal Irradiation
- Thorotrast Injections

OCCUPATIONAL

- Uranium Miners
- Radium Ingestion (dial painters)

NUCLEAR POWER PLANT

- [• Chernobyl Accident]

world. It should be emphasized that, although there are many other episodes of radiation exposure, these data can not be used for estimation of health risks unless the denominator and nominator populations are epidemiologically well defined.

Before discussing the long term health effects of ionizing radiation, the acute health effects of the atomic bombings will be briefly mentioned here. The effects of the atomic bombs consist of a combination of blast, heat, and radiation. The energy released was mostly in the form of blast and heat, accounting for 50% and 35%, respectively. Radiation accounted for only 15% of the total energy, something like a “by-product”. For the Hiroshima bomb, the blast waves extended to a distance of 4 km and heat to 3.5 km. On the other hand, gamma rays reached out only to about 2 km and neutrons to a much shorter distance.

The energy distribution of the blast, heat, and radiation of the Nagasaki bomb was similar to that of the Hiroshima bomb. However, the respective components traveled 0.5 or 1 km farther than in Hiroshima because the Nagasaki bomb was more powerful than the Hiroshima bomb. The radiation released by the Nagasaki bomb was characterized by a smaller proportion of neutrons.

The populations of Hiroshima and Nagasaki at the time of the atomic bombings were said

to be about 330,000 and 250,000, respectively. The total number of instantaneous deaths and acute radiation deaths until the end of December 1945 has been estimated to be about 1/3 of the total population in both cities.

An important injury caused by the atomic bombing is heat burns. Data from animal experiments suggest that health effects of radiation could be aggravated by a combination with heat burns. One gray radiation plus second degree burns shows a multiplicative effect for mortality (Fig. 1).

Figure 1 Mortality due to radiation and burn (2 degree)
(Dog experiment, Brooks, J.W. et al, 1952)

Epilation occurred at around two weeks after exposure to 3 gray or 300 rad of radiation. The occurrence of epilation among those exposed at the time of the Chernobyl nuclear power plant accident indicates that there had been exposure to a similar level of radiation. They were mainly plant workers and firemen.

Studies on the late health effects of ionizing radiation among the atomic bomb survivors have been conducted since 1947 by the United States Atomic bomb Casualty Commission (ABCC) in cooperation with the Japanese National Institute of Health, and its successor, the Radiation Effects Research Foundation (RERF) which is equally funded by the two governments of Japan and the United States.

The program of the ABCC-RERF studies consists of three groups (Table 2). First is the follow-up of a fixed population of atomic bomb survivors which had been established in 1950. This includes the Life Span Study for the survey of life span and causes of death, the Pathology Program for the elucidation of causes of disease by autopsy and other means, the Adult Health Study to identify the health status and detect diseases in the participants by periodic health examinations, and the In Utero Study of those who had been exposed during the pregnancy of their mothers.

Table 2 Major Research Programs

Studies	Number of Subjects	Year of Base Population	Year Commenced
Life Span Study (LSS)	120,000	1950	1958
Pathology Study	70,000	1950	1961
Adult Health Study (AHS)	20,000	1950	1958
In Utero Study	2,800	1945-46	1956
<u>Genetics Study (F₁)</u>			
Mortality	77,000	1946-	1960
Cytogenetics	33,000	1946-	1967
Biochemical Genetics	45,000	1946-	1975
<u>Specific Studies</u>	<u>Components</u>		
AHS			
Cardiovascular disease	Incidence, risk factor		1965
Aging study	Osteoporosis, menopause, senile dementia		1970
Somatic cell study	Immunology, immune competence, mutation		1981
Cell biology	Radiation sensitivity, radiation carcinogenesis		1979
Cytogenetics	Chromosome aberrations		1965
LSS			
Cancer study	Case-control study, site-specific cancer studies		1979
Reassessment of A-bomb Radiation Dosimetry	US-Japan Joint study		1981

Second is the study of the offspring of atomic bomb survivors. This includes the Mortality Study, Biochemical Genetics Study, and Cytogenetic Study of the Children.

Third includes other studies, such as studies of cardiovascular diseases, cancers, experimental pathology and immunology studies. Efforts were also made from the earliest period to develop accurate estimates of individual radiation doses, and recently the DS86 (Dosimetry System 1986) became available for use. Reanalyses of all relevant epidemiological data have been carried out based on this new dosimetry system, and it has been suggested that health risks or radiation might be several times higher than before.

Various methods have been adopted for following the exposed population for late health effects. The Japanese family registration system enables almost complete follow-up of deaths and their causes. The tissue registry system is unique, and the tumor registries in Hiroshima and Nagasaki have the longest history in Japan.

The results thus far obtained to the present can be classified into three categories (Table 3):

Table 3 Late Effects of Radiation (1950 to date)

INCREASE CONFIRMED	INCREASE SUGGESTED	NO INCREASE (to date)
Malignant Tumors: Leukemia, thyroid cancer, breast cancer (female), colon cancer, lung cancer, stomach cancer, multiple myeloma, ovarian cancer Cataract Microcephaly and mental retardation (in utero exposed) Delayed growth and development (exposed at young age) Chromosome abnormalities in lymphocytes Somatic mutations in erythrocytes and lymphocytes	Malignant Tumors: Esophageal cancer, urinary cancer, malignant lymphoma, salivary gland tumor Hyperparathyroidism Specific (humoral or cell-mediated) changes in immunologic competence	Malignant Tumors: Chronic lymphocytic leukemia, osteosarcoma *Mortality from diseases other than malignant tumors *Acceleration of aging (including cardiovascular diseases) Infertility F ₁ : Congenital abnormalities, mortality, chromosome aberrations, and biochemical variants

*Unresolved

The effects for which a clear increase has been found include malignant neoplasms such as leukemia, cancers of thyroid, breast, colon, lung, stomach and ovary, and multiple myeloma. Cataracts and chromosomal aberrations developed in the relatively early period. Small head size and mental retardation have been observed in those who were exposed in utero. Delay in growth and development was seen in those exposed during infancy.

The periods when the radiation-induced deaths developed after the atomic bombing can be shown schematically (Fig. 2). Acute deaths due to atomic bomb radiation had occurred within 4 months after the bombing. Leukemia began to increase from the second or third year after exposure and reached the peak at the sixth year. All other cancers started to increase from the tenth year after exposure and is still continuing its increasing tendency.

Figure 2 Health effects after A-bombing

According to the attributable risk percents to radiation for all causes of death among the survivors during the past 35 years, excess deaths are observed mainly in cancer and few in other causes of death (Fig. 3).

The breakdown of attributable risk percents for cancer deaths by site indicates that, although the actual number of deaths is small, 55% of leukemia deaths are attributable to atomic bomb radiation, followed by 33% of multiple myeloma, 23% and 22% of urinary and breast cancer, respectively (Fig. 4). In colon and lung cancer 15% and 11%, respectively, are attributable to atomic bomb radiation.

According to the relative risks of cancer deaths by site at 1 Gy of radiation, leukemia shows the highest relative risk, followed by multiple myeloma, and breast and urinary cancers (Fig. 5).

Figure 3 Attributable risk for major causes of death
 ≥ 0.01 Gy/0 Gy (1950-85)

Figure 4 Attributable risk for major sites of cancer death
 ≥ 0.01 Gy/0 Gy (1950–85)

Figure 5 Relative risk for major sites of cancer death at 1 gray (1950–85)

Figure 6 Incidence of mental retardation by intervals after conception

One of the most important findings obtained from the In Utero Study is that the frequency of mental retardation was highest among those exposed during the 8th to 15th week of gestation, followed by those in the 16th to 25th week of gestation (Fig. 6). No cases have been reported among those exposed during other periods of gestation.

A suggestive increase has been found in the several sites of cancers such as oesophagus, urinary tract and salivary gland, malignant lymphoma and immunological abnormalities. Further observation may prove some of these to be definitely increased.

No difference has been observed between the exposed and the non-exposed in some types of leukemia, osteosarcoma, accelerated aging, sterility and genetic effects such as birth defects, mortality, chromosomal aberrations and biochemical variants in the F1 generation. Although no effects have been observed in all the genetic programs up to the present, more sophisticated study such as DNA analysis is now in progress. It should also be noted that the children of the survivors will attain the cancer-prone age hereafter.

As mentioned above, excess deaths among the survivors were observed mainly in cancer and few in other causes of death. These are the recent results of the Life Span Study which suggest that other causes of death such as cardiovascular diseases may be more frequent in those highly exposed than in those non-exposed. Furthermore, dysfunction and non-cancerous disease such as hyperthyroidism and benign thyroid tumor seem to be more prevalent in the exposed than in the non-exposed according to the recent Adult Health Study. These findings are very important if they are truly related to radiation, so that a careful review is now being made of all relevant data.

According to the survival status of the exposed in Hiroshima and Nagasaki during the past 35 years which is compared with that of the non-exposed by sex, more than 60% of the survivors are still alive except for males in Hiroshima. The percentage of survivors among the exposed is not so different from that of the non-exposed (Table 4).

Table 4 Survival Status by Sex during 1950–1985 Life Span Study**MALE**

City	Exposed	Non-exposed
Hiroshima	54%	56%
Nagasaki	63	61

FEMALE

City	Exposed	Non-exposed
Hiroshima	65%	67%
Nagasaki	68	70

Since the ABCC-RERF fixed population does not include those persons who died between the time of the atomic bombings and 1950, it has been presumed that this may have resulted in the inclusion of individuals who were more resistant to radiation. However, this fact has not been proved yet.

Finally, the following seven points should be considered in future research on atomic bomb survivors.

1. Continuation of follow-up studies of the aging atomic bomb survivor population, because unsuspected health effects might become evident in association with the aging phenomenon.
2. Cancer risk estimates are necessary for the young cohort now entering the "cancer-prone age".
3. Evaluation of interactive environmental effects which might be confounded with radiation-induced effects is important.
4. Molecular biology study should be encouraged to promote the clarification of radiation carcinogenesis.
5. Organ functional change should also be studied.
6. Improved genetic risk estimates are required by applying more advanced techniques.
7. International cooperative studies are necessary, particularly for revealing the health effects of low dose exposure to radiation.

I would like to take this opportunity to express sincere appreciation to the survivors and their families for their cooperation in the studies by ABCC-RERF. I also wish to thank Dr. Aoki and the Organizing Committee Members of this Meeting for providing this opportunity to present my paper.