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## “Late Effects of Exposure to Ionizing Radiation and Age on Human Thymus Morphology and Function”

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### Study Findings

This study suggests that age-associated thymic involution\* was accelerated among A-bomb survivors, including those exposed to a relatively low dose of radiation, and that thymopoiesis\*\* was reduced among them for years after exposure when compared to non-exposed controls. These results are considered useful for developing a model to predict changes in thymic function due to natural aging as well as in response to therapeutic radiation or accidental exposure.

\* Age-dependent reduction in the cell density of the thymus tissue.

\*\* The function of the thymus, i.e., the activity to produce thymocytes that differentiate into mature T cells.

### Explanation

T cells are the key component to mediate immune response, and the thymus is essential for T-cell maturation, which enables them to respond to newly encountered antigens. Thus, the thymus plays an important role in proper development and maintenance of a T-cell repertoire. This study reviewed changes in thymic function due to radiation exposure and aging, using archival thymus tissues collected from A-bomb survivors.

#### 1. Study Purpose

An abundance of evidence indicates that age-related deterioration in T-cell mediated immunity accelerates among A-bomb survivors, suggesting that radiation exposure may adversely affect the function and formation of the thymus and thereby promote age-related deterioration in immunocompetence. This study examined the long-term effects of radiation on thymic function using valuable thymus tissue samples that collected from A-bomb survivors and preserved.

#### 2. Study Methods

We made a comparative review of thymus tissues collected from pathological autopsies of 165 A-bomb survivors. These tissue samples were stained using hematoxylin and eosin (H&E),\* immunohistochemical staining,\*\* and immunofluorescence staining.\*\*\* Multiple pathologists then conducted microscopic observations and scored active thymus areas that were classified according to cell types including CD1a+ immature thymocytes. Based on these scores, we statistically analyzed associations with age (age at exposure and age at sample collection), sex, and radiation dose.

\* Hematoxylin and eosin staining, which marks cell nuclei and cytoplasm with different colors, is the most common histological staining method.

\*\* Immunohistochemical staining uses antibodies that are identifiable with dyes.

\*\*\* Immunofluorescence staining uses antibodies that are labeled with fluorescent dyes.

#### 3. Study Results

Thymic involution was accelerated in those exposed to either relatively low (5–200 mGy) or relatively high (>200 mGy) doses of ionizing radiation, compared with the rate of involution in non-exposed individuals. Sex-related differences were observed when the analysis was restricted to individuals less than 60 years of age at the time of sample collection; among those less than 60, females underwent slower involution than males. However, such differences were not observed when

reviewing the entire population; the extent of increased involution was similar between males and females in the study participants aged 60 or older.

These findings suggest that even low-dose radiation exposure can accelerate age-related thymic involution and adversely affect T-cell production for a prolonged period of time after radiation exposure.

### **Study Significance**

Autopsy tissue samples, stored at RERF over an extended period of time, were useful for a review of histological changes due to radiation exposure and aging. This study suggests that radiation exposure might affect the pivotal role of the thymus in the formation of the T-cell immune system. Since this study was based on a limited number of tissue samples that were autopsied after death and preserved, it is possible that cause-of-death bias or other types of bias might arise. It is therefore crucial to take this issue into account with regard to the effects of low-dose radiation exposure. Based on the results of this study, it is possible to predict functional changes in the human thymus caused by natural aging and radiation exposure other than that from the atomic bombings, including radiotherapy.

**The Radiation Effects Research Foundation** has studied A-bomb survivors and their offspring in Hiroshima and Nagasaki for around 70 years. RERF's research achievements are considered the principal scientific basis for radiation risk assessment by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and for recommendations regarding radiation protection standards by the International Commission on Radiological Protection (ICRP). RERF expresses its profound gratitude to the A-bomb survivors and survivors' offspring for their cooperation in our studies.

<sup>§</sup>***Radiation Research***, which is an official monthly journal of the Radiation Research Society, publishes original peer-reviewed papers and review articles on radiation effects and related issues in the fields of physics, chemistry, biology, and medicine. (Impact factor in 2015: 3.022)