2 Survivors exposed in utero

A Microcephaly and intellectual disability

Summary

Actively dividing cells are known to be more susceptible to ionizing radiation effects than cells that have completed division or seldom undergo division. For that reason, fetuses are believed to be generally more susceptible to radiation effects than adults. ABCC and RERF have focused on research on in utero-exposed A-bomb survivors, specifically radiation effects on the central nervous system, engaging in many such studies. Effects of in-utero radiation exposure have been investigated on the basis of three indices of brain damage: (1) severe mental retardation, (2) intellectual quotient (IQ), and (3) school performance. Such research has led to the observation of increased frequency of brain damage such as severe mental retardation and decreased average IQ scores and/or school performance among A-bomb survivors exposed in utero at 8-15 weeks and 16-25 weeks after conception. On the other hand, no evidence of effects of radiation leading to brain damage has been observed in those exposed in utero at less than 8 weeks or at 26 weeks or later after conception. Research into effects of in-utero radiation exposure on occurrence of seizures revealed an increased risk in survivors exposed in utero at 8-15 weeks after conception. Biological mechanisms of ionizing radiation-induced abnormalities in the brain remain unclear, but magnetic resonance imaging (MRI) of the brains of some mentally retarded in utero-exposed survivors has revealed changes in brain structure—such as ectopic gray matter suggestive of abnormality in neuronal migration. Study of radiation effects on small head size among in utero-exposed survivors showed an increased risk not only among the survivors exposed in utero at 8-15 weeks after conception, but also in those exposed in utero at 0-8 weeks after conception, a group in which increased risk of brain damage such as mental retardation had not previously been reported. With regard to in-utero radiation exposure, it was suggested that there is an embryological difference in development between small head size and mental retardation on the grounds that the period of risk increase for small head size was different from that for brain damage such as mental retardation and that there was no apparent threshold value. In the in-utero exposed with only small head circumference unaccompanied by mental retardation, growth retardation has been observed, but there was no significant difference in mean IQ score compared against the entire study population.

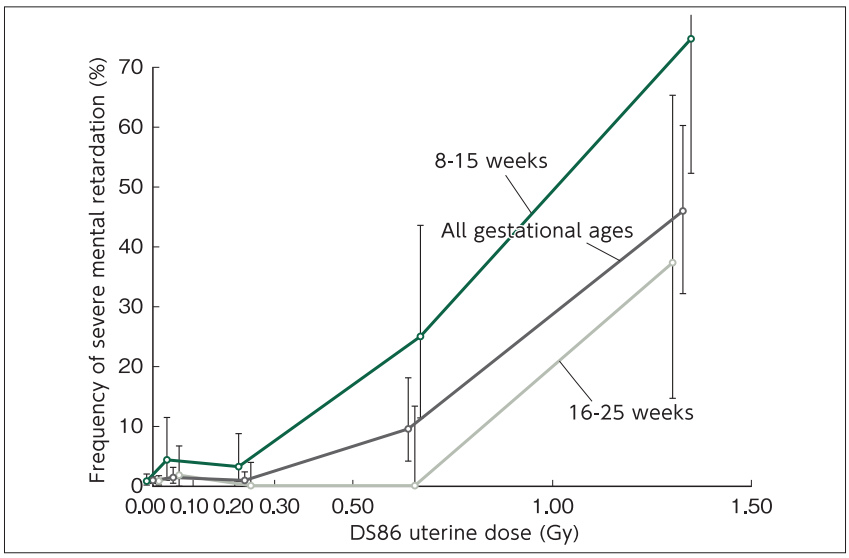

Fig. 1 DS86 uterine absorbed dose and severe mental retardation frequency with 90% confidence intervals (by week of gestation)
(Otake M et al, Severe Mental Retardation among the Prenatally Exposed Survivors of the Atomic Bombing of Hiroshima and Nagasaki: A Comparison of the T65DR and DS86 Dosimetry Systems, Technical Report RERF TR 16-87,1987)

B Growth and developmental disorders

Summary

ABCC and RERF have studied radiation's effects on growth and development in the in utero-exposed population of A-bomb survivors based on physical measurements of height, body weight, sitting height, chest girth, and head circumference, as well as X-ray imaging of the hand and wrist. The research revealed that average values of physical measurements in such survivors decreased with increasing radiation dose,. Concerning the presence of a difference in radiation effects on these physical measurements by gestational age, a correlation was observed in small head-size cases, but we have yet to obtain consistent results, leaving the issue unresolved. Studies into the timing of epiphyseal closure based on hand and wrist X-ray imaging failed to show clear radiation effects. Due to the limited number of persons exposed to high-dose radiation, it remains unknown whether or not in-utero radiation exposure affected skeletal maturation. On the grounds that the mechanisms behind how ionizing radiation caused growth and developmental impairment??? remain uncertain, and that the possibility exists for such social factors as immediate postwar malnutrition to have contributed to the relevant growth reduction, accurate assessment is difficult.

C Malignant tumors

Summary

The cohort of in utero-exposed A-bomb survivors studied by RERF was established through selection of subjects matched on maternal A-bomb exposure distance, city, sex, and birth date, on the basis of such information sources as birth records for the period 1945-46, basic lists compiled by ABCC, and source material for the supplemental surveys of Hiroshima and Nagasaki taken at the time of the 1960 National Census in Japan. The cohort comprises 3,638 individuals, a population that has contributed to the understanding of radiation cancer risk for individuals exposed to radiation in utero through their participation in longitudinal studies of mortality and cancer incidence.

Such research pointed to the fact that persons exposed to the atomic bombings when young faced a higher cancer risk from radiation than those exposed in adulthood, and therefore risk among in utero-exposed survivors was assumed to be even higher.

Investigation into cancer incidence among a population of subjects with attained ages between 12 and 55 years during the period from 1958 (when local cancer registries were initiated) to the end of 1999 showed that in-utero exposure significantly increased adulthood cancer risk. On the other hand, however, excess relative risk of cancer in the in utero-exposed survivors was observed to be significantly lower than in those exposed in childhood and did not increase with attained age, suggesting that lifetime risk of solid cancers from in-utero radiation exposure is lower than that presumed for childhood exposure. Establishing the veracity of such observations clearly requires further follow up.

Research involving persons exposed in utero to X-rays from maternal obstetric examinations showed such a high excess risk of childhood cancers that the results are controversial. Studies into childhood cancers in those exposed in utero to the atomic bombings, however, have not yielded any evidence supporting the high childhood cancer

risk seen in the research involving those exposed to medical X-rays in utero.

Because the in utero-exposed survivors are just now reaching the ages at which development of cancer is more common and fewer than half of the projected lifetime cancer cases and cancer deaths have materialized as of the present time, understanding risk of cancer development will require follow up of the in utero-exposed survivors for 10 or 20 more years.

D Non-cancer disease and abnormalities

Summary

Few reports exist regarding effects of in-utero radiation exposure on non-cancer diseases. In a report on adolescent blood pressure among in utero-exposed A-bomb survivors in 2007, significant dose effects were observed for systolic hypertension in adolescence as well as for levels of systolic blood pressure in a group exposed in utero in the second trimester of pregnancy. On the other hand, in a follow-up study conducted until the end of 2003 involving adult-onset non-cancer disease, no evidence was found of radiation effects on prevalence of thyroid disease or cataract, or on incidence of hypertension, hypercholesterolemia, or cardiovascular disease (stroke, myocardial infarction). However, no significant difference was observed in radiation risk for all solid thyroid nodules and cardiovascular disease between survivors exposed in utero and those exposed in childhood, a group for which a significant dose response was observed. In the future, increases in various diseases are anticipated as the in utero-exposed survivors age, although the age of the subjects at the time of the previous study was, at less than 60, relatively young. Continued follow-up of this population is expected to clarify radiation effects more fully in the in utero-exposed A-bomb survivors.