

IRPA 10

TOPICAL SESSIONS Reports of Co-Chairmen for Highlight Sessions

T-7: Genetic Risk and Radiation Exposure *Monday, 15 May 2000*

Chair and Keynote: G. Streffer

Co-Chair: N. Nakamura

Unfortunately, two papers were canceled and we had only three presentations, one keynote address related to genetic instability and genetic predisposition for development of cancer, and two papers, one is related to childhood leukemia at the nuclear sites and the other adaptive response. These three papers cover a wide range of current interests, while no presentation was available for the genetic risk of radiation that was the title of the session.

First, **Dr. Streffer** (Germany) gave the **keynote speech** entitled "Genetic predisposition and implications for radioprotection." In brief,

- He introduced evidence for individual variation in radioresponses among radiotherapy patients.
- These individuals, possibly genetic variants to be radiosensitive, are not taken into account in radiation protection that is related to general population thus far.
- However, in recent years, more emphasis is given to these rare individuals.
- He listed human genetic disorders related to cancer proneness.
- Some of these syndromes are characterized by genetic instability.
- The mouse strain that he used, Heilingerberger (HLG), was found to be prone to develop malformation after irradiation of zygotes (early stage of embryogenesis), this stage is usually insensitive for the induction of malformation in other strains of mice.
- In this particular HLG strain, the malformation occurs not only during the embryogenesis immediately following the radiation exposure but also during the embryogenesis in subsequent generation, thus it is described as induction of genetic instability.
- Studies in F₁ hybrid animals after crosses with a resistant strain, C57BL, suggested that the instability is inherited as a recessive Mendelian trait.
- Gene mapping and identification of the responsible gene are now in progress.
- Current data suggest that the gene may be involved in the stability of DNA imprinting or DNA methylation.
- Data from genetically modified animals as well as genetically predisposed patients who underwent radiotherapy suggest that these cancer-prone individuals are also sensitive for the development of radiation-induced malignancy, in accord with Knudson's theory.
- The 21st century will witness the development of molecular technologies, such as DNA chips, for large-scale screening of genetically predisposed individuals in general population.

- However, it is cautioned that the ethical consideration will be one of the most important issues for such a study.

Dr. Slovak (United Kingdom) gave his talk entitled “Transgenerational risks of ionizing radiation: Advances in epidemiological knowledge since IRPA9”. His concern is the issue of childhood cancer, especially the leukemia. He summarized recent progress in the thoughts to explain the increased risk of childhood leukemia at nuclear sites, namely, a shift from parental radiation exposure (genetic event) to population mixing (possible infection). In brief,

- Although epidemiologic data showed a significant correlation with radiation dose to the fathers, occupational exposures are difficult to explain the results.
- The headline statements in UK official report (Committee on Medical Aspects of Radiation in the Environment) are; the excess risk of leukemia is continuing in Seascale, environmental radiation exposure could not account for the excess, occupational radiation exposure is very unlikely to account for the excess, unable to find any convincing explanation, and a mechanism involving infection may probably be a factor.
- As for the last idea of “infection”, “population mixing” might be the key element.
- This hypothesis acquired good support from other studies as well.
- UK Nuclear Industry Family Study shows that the incidence of childhood cancer and leukemia is similar to that in the general population.
- Data from US Hanford workforce population indicate that the study is negative for childhood cancer outcome related to paternal pre-conception irradiation.
- Data from French nuclear complex at La Hague is reported to offer some convincing evidence for a causal role for environmental radiation exposure...but several questions remain.
- Studies on younger patients treated by radiotherapy or Thorotrast were uniformly negative for the increased risk of leukemia in their children.
- While stillbirth data at Sellafield received recent attention, stillbirth is too amorphous an end-point in reproductive studies. The risk is not compatible with the findings in offspring to atomic bomb survivors in Hiroshima and Nagasaki.
- Nonetheless, debates may outbreak anytime.

Dr. Mortazavi (Iran) presented his paper entitled “Synergistic effect versus radioadaptive response: Possible implications of such a response in the estimation of risk of low-level radiation can be more problematical.”

- First, the adaptive response is defined as the change of cellular conditions that are cause by a small priming dose, usually on the order of a few centi-Gray, so that the cells become resistant to the subsequent exposures.
- He used chromosome aberrations as the endpoint of adaptation and identified one apparently healthy individual whose blood lymphocytes did not show any adaptive response but inversely the cells became sensitive by the prior exposure to small priming dose.
- Following repeated tests of the same donor, he found that the degree of the response varied with time, but the cells were consistently devoid of the adaptation.
- Any known factors to affect the adaptive response, such as physiological conditions of the cell culture, genetic constitutions, and aging, could not explain the results.
- In the future, it would be an important task to understand the frequency of

individuals with no adaptation.

- However, curiously, when the priming dose is absent, the case was not radiosensitive but rather radioresistant in response.
- This indicates that screening of individuals with ordinary single-dose exposure would fail to detect such adaptation negative individuals. The screening should include priming dose.
- Finally, how to take into account the presence of such individuals will be a challenge in the future, especially in terms of the risks at low dose and low dose rate. In other words, such individuals are rather radioresistant after single-dose exposure but are radiosensitive after priming dose plus test dose.