LOW-LEVEL RADIATION HEALTH EFFECTS: PROGRAMS AND PANEL DISCUSSION

Cosponsored by the Biology and Medicine, the Education and Training, the Enviromental Sciences, the Isotopes and Radiation, and the Radiation Protection and Shielding Divisions

Session Organizer: Jim Muckerheide (Comm Mass)

All Papers Invited

1. Health Effects of Russian Nuclear Accidents: What Can We Learn? *Richard Wilson, Alexander Shlyakhter (Harvard)*

NUCLEAR ACCIDENTS IN THE USSR

The goal of this summary is to draw attention to a number of data sets concerning the health effects of ionizing radiation, which were collected by the scientists in the former USSR. The Chernobyl accident of 1986 was only the most recent and the most publicized nuclear accident. The report of the Soviet Union to the International Atomic Energy Agency experts' meeting in Vienna August 25 to 29, 1986, was very impressive, both in the amount of detailed work that went into it and in the release of information unprecedented for the Soviet (or any previous Russian government). However, data on the earlier accidents were until recently classified.

In the late 1950s Americans became aware of nuclear activities and some serious accidents near Chelyabinsk in the Ural Mountains. The U-2 aircraft of Gary Powers was shot down trying to photograph the area. Foreigners were not permitted to visit Chelyabinsk or even be on airplanes stopping at the airport. But scientists, notably Professor Frank Parker, were able in the 1970s to figure out much of what happened from published data on radioactivity in Siberian rivers.

In 1990 an article appeared in the Soviet popular science journal *Priroda* detailing the increases in cancer among the workers in the MAYAK plant at Kyshtym (near the city of Chelyabinsk), where plutonium had been produced in reactors and separated for bomb production for ~40 yr (Ref. 1). This was followed by a series of articles describing the Kyshtym accident and its consequences.[2] By filling the missing data with plausible assumptions, we were able to show that the increase in mortality was about three times less than would be estimated from an immediate application of the Hiroshima/Nagasaki data. The reduction was presumably due to the reduced effects at low dose rate.

THE DATA SETS

In the former USSR there are several data sets that are comparable to the Hiroshima/Nagasaki cohort and are potentially as valuable:

1. The 300 plant workers and firemen at Chernobyl who suffered acute radiation sickness and 200-rem dose: Of those we expect up to 50 to develop cancers due to radiation.

2. The 25 000 people evacuated late from the Chernobyl area who had an average of ~40-rem dose: Among these we expect to identify perhaps 500 cancers.

3. Other members of the population.

4. The 600 000 clean up workers (liquidators) who received an average of 25 rem (first year) and 10 rem (later years).

5. The estimated 3000 early workers at the plutonium production reactor and chemical facility at the MAYAK plant: Some of them received up to 400 rem for 1 yr.

6. About 30 000 villagers who used water contaminated with ^{90}Sr from the Techa River and received an average dose of 50 rem. It appears that the cancer rate is increased about 15% (in this group).

7. About 11 000 residents exposed at the time of the explosion of the holding tank with nuclear waste at Kyshtym in September 1957; 1150 of them received an average of 52 rem (Ref. 3).

8. The population in the Altai krai exposed to the radioactive fallout from the Semipalatinsk test site.

RESULTS OBTAINED SO FAR

The Russians have been studying cohorts 5, 6, and 7 for 30 yr and have several reports thereon. An increase of leukemia has been found in cohorts 5 and 6, but in each case it seems that the number is less than given by the Hiroshima/Nagasaki results without a dose-rate reduction.[4]

Data related to exposure of population after the Kyshtym accident are collected and studied at the Urals Center for Radiation Medicine. For the Chernobyl accident, the data are now spread with little coordination among three former Soviet republics: Belarus, Russia, and Ukraine. In Belarus, a leukemia registry is being developed for the first time in history, but no increase in leukemia has been found 7 yr after the accident (none have been found in Russia or the Ukraine either). In Belarus, thyroid cancers began to appear among children in 1991. These have now appeared in Russia and the Ukraine also.

WHAT CAN WE LEARN FROM RUSSIAN DATA?

The following information seems obtainable by comparison with Hiroshima/Nagasaki studies:

1. dose-rate reduction factor for leukemia
2. dose-rate reduction factor for other cancers
3. dose response for childhood thyroid cancers never before seen
4. clear identification and dose response for chronic radiation sickness.

We must examine carefully the existing studies to verify their reliability and, if appropriate, to improve upon them. It is important to realize that partial information is often useful. Thus an *upper limit* on the number of leukemias at a given dose might tell us that the dose-reduction factor is at least as large as X or that the response at that dose is less than the linear response by an amount Y.

In these studies, we depend on our Byelorussian, Russian, and Ukrainian colleagues who must do most of the work. We must give them all the resources, honor, and recognition that we can.

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2. Current Research on Biological Effects of Low-Level Exposures, *Leonard A. Sagan (Sagan)*

Rather substantial numbers of industrial chemicals, pharmaceuticals, and radiation display U-shaped or seemingly paradoxical dose-response relationships. A limited listing of studies providing examples of data fitting the U-shaped curve has been published.[1] This array suggests that the U-shaped response is broadly generalizable and therefore potentially of considerable significance in the toxicological and public health domains. In fact, in 1992 and 1993, three conferences (Japan,[2] United States,[3] and China) were held exclusively on the topic of the biological effects of low doses of chemicals and radioactivity with particular emphasis on U-shaped curves.

While much research has been limited to descriptive reporting of U-shaped dose-response curves, substantial efforts have also been made to explore the mechanistic underpinnings of such observations. The emerging mechanisms involved in the occurrence of the U-shaped dose-response curve appear to be a highly diversified array of defense mechanisms that are normally active and or inducible at low doses but probably overwhelmed at high doses. For example, at low doses of carbon tetrachloride (CCl_4) tissue repair mechanisms prevent CCl_4 hepatotoxicity, but this protective effect is lost at high CCl_4 doses.[4] A large literature exists on inducible adaptive responses to radiation where a low prior exposure is protective against subsequent higher and normally damaging exposures. In addition, cellular adaptive responses involve the synthesis of proteins such as metallothionein that are now recognized as having antioxidant properties.[5] Likewise, heat stress proteins that are synthesized in response to a wide range of stressors may play a role in a variety of protective mechanisms, including DNA repair and increased cell survival.[6] There are even some provocative data on 2,3,7,8 tetrachlorodibenzodioxin that suggest a protective effect for low levels vis-à-vis breast cancer.[7]

When elevated doses [e.g., those approaching and/or exceeding the mean therapeutic dose (MTD)] result in tissue damage, the subsequent cellular repair may provide a promotional response resulting in an enhanced tumor incidence.[8-11] Since the damage associated with exceeding the MTD does not occur at lower doses, it makes extrapolation to lower and more realistic human exposures less reliable, most likely providing unrealistically high risk estimates. Likewise, the saturation of critical detoxification pathways at high doses may result in the activation of normally unused alternative metabolic pathways, resulting in the production of "novel" metabolites. If these novel metabolites have carcinogenic potential, then the animal bioassay may produce adverse effects at high levels of exposure that would not be expected to occur at lower levels. The implications of such findings for the risk assessment process are likely to be significant and argue for a reconsideration of present practices of adherence to the linear paradigm.[12-15]

A group of scientists representing several federal agencies (Agency for Toxic Substances and Disease Registry, Department of Defense, U.S. Department of Energy, U.S. Environmental Protection Agency, National Center for Toxicological Research, and National Institute of Environmental Health Sciences), the private sector, and academia came together to enhance the study on the biological effects of low-level exposures (BELLE) to chemical agents and radioactivity with consideration given to the range of biological and statistically based hypotheses. The group, known as the BELLE Advisory Committee, has been working together since 1990. It is committed to the enhanced understanding of low-dose responses, whether of an expected nature (e.g., linear and sublinear) or paradoxical nature. The advisory committee is responsible for distributing the BELLE newsletter and conducting workshops and conferences.

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