United States-Russian

Workshop on the

Stochastic Health Effects of Radiation

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This Report is Dedicated to the Memory of Dr. Edward Shoemaker

As a major force in the International Cooperative efforts of the U.S. Nuclear Regulatory Commission, Dr. Shoemaker worked tirelessly with the scientists participating in this workshop. His enthusiasm and competence, his humanity and sensitivity, all contributed to making this workshop effective, significant and a first step to the beginning of a long term collaborative research program between our two countries.

WE SHALL NOT FORGET HIM

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FORWARD

In August 1988, two years after the Chernobyl accident, the United States and the Soviet Union signed an agreement to sponsor a Joint Coordinating Committee on Civilian Nuclear Reactor Safety, (JCCNRS). A range of tasks were to be performed, including one on Environmental Transport (7.1) and on Health Effects (7.2). In Working Group 7.2, there were several tasks, one of which was to sponsor a workshop on the stochastic effects of radiation.

The Soviet Union agreed to provide some information on late effects of radiation exposures and to attempt to add some new insights into low dose and low dose rate radiation consequences. At that time, it had just been revealed that significant radiation exposures had occurred in the South Ural Mountains, associated with the early years of operation of the MAYAK nuclear complex.

The need to be able to better predict the long term consequences of overexposures, such as occurred with the Chernobyl accident, was a major factor in organizing this workshop. We decided to invite a small number of experts from the Soviet Union, who had direct knowledge of the situation. A small group of American experts was invited to help in a discussion of the state of knowledge of continual low level exposure. The experts and expertise included:
- aspects of basic theoretical radiobiological models,
- studies on experimental animals exposed to chronic or fractionated external or internal radiation,
- studies on populations exposed to chronic intake and continual exposures,
- workers exposed to low or high continual levels of radiation.

The intent was to begin a dialog on the issue of a better understanding of the dose rate effect in humans. No detailed conclusions could be reached at this first interaction between our two countries, but a model was prepared which seems to support a range of what are known as low dose and dose rate effectiveness factors. A beginning of an evaluation of the role of radiation dose rate on leukemia risk was also accomplished.

There was no requirement to prepare formal papers, and some of the Americans brought reprints of earlier publications, or figures from their published work. Because there was little knowledge of the Soviet experience and data, we asked our Russian visitors to prepare informal briefing papers to assist in understanding their experience. We have included all of their papers as well as a few of the American papers which had been prepared for this Workshop. We spent much of the final hours preparing an executive summary as a distillation of our efforts.

The Soviet team was led by Dr. Igor Filyushkin, and Professor Marvin Goldman led the American side. Drs. Ginevan, Shomaker and Yaniv not only represented their sponsoring agencies, but actively participated in all aspects of
the meeting. The co-chairs gratefully thank the sponsors and the scientists and their staff for their dedication and assistance in making this a most interesting, challenging and thought provoking interaction. In the years that have followed, the interactions that began at Davis have expanded, and a new, longer-term research collaboration is beginning which will continue the work begun at this meeting.

for the Russian side

Igor Filyushkin

Davis, California
December 1994

for the American side

Marvin Goldman
Attendees

RUSSIA

L.A. Buldakov, Moscow, Ministry of Health, Biophysics Institute
I.M. Petojan, Moscow, Ministry of Health, Biophysics Institute
I.V. Filyushkin, Moscow, Ministry of Health, Biophysics Institute
M.O. Detegteva, Chelyabinsk, Ural Research Center for Radiation Medicine
M.M. Kossenko, Chelyabinsk, Ural research Center for Radiation Medicine
N.A. Koshurnikova, Chelyabinsk-65, Branch 1, Biophysics Institute, Ministry of Health

UNITED STATES

M.E. Ginevan, US Department of Energy
C.E. Land, National Institutes of Health
E.J. Ainsworth, Armed Forces Radiobiology Research Institute
R.J. Catlin, University of Texas-Houston
R. L. Ullrich, University of Texas-Galveston
E. S. Gilbert, Pacific Northwest Laboratories
R.E. Albert, University of Cincinnati
S.S. Yaniv, US Nuclear Regulatory Commission
E. Shoemaker*, U.S. Nuclear Regulatory Commission
M. Goldman, University of California-Davis

Technical Assistance

S. Hendrickson, Lawrence Livermore National Laboratory (Administrative)
M. Maculans, University of California-Davis (Administrative)
M. Wasserman, Chicago (Interpreter)
S. Wainson, Moscow (Interpreter)

* deceased
Executive Summary

This report addresses one of the tasks agreed upon in the area of Environmental Transport and Health Effects (Working Group 7.2) of the JCCCNRS, i.e. to hold a workshop on the topic of the role of radiation dose rate effects on stochastic risks for low LET radiation.

The Chernobyl Nuclear Power Plant accident in April 1986, released a very large quantity of radionuclides, and the populations, were exposed primarily to low LET radiation, from $^{131}I$, $^{134}$, $^{137}Cs$ and $^{90}Sr$. Carcinogenic risk resulting from low level/low LET radiation exposure, has never been observed. There is very little epidemiological information on the risks to population from low level radiation exposure. Our major data base, which strongly influences all international and national quantitation of radiation risk, is derived from the study of the survivors of the atomic bombing of Hiroshima and Nagasaki, a situation in which the dose was delivered instantaneously and the dose rate was essentially infinite. Other widely known human studies are generally to fractionated high dose rate exposures or to continual exposure to high LET radionuclides.

Problems of extrapolation of data derived from long term, low LET radiation exposure of experimental animals is hampered by the lack of verified scaling factors for time, for pathology and physiology differences and for cancer sensitivity of specific tissues.

While the weight of fragmentary evidence supports the use of a low LET dose rate effectiveness factor of about 2-10 or more, there are few "solid" data in human experiences to confirm the appropriate value. In attempting to anticipate and perhaps forecast potential consequences to Chernobyl exposed populations, this workshop was developed as a first step in reducing the uncertainty about the dimensions of low dose rate effectiveness in induction of stochastic health effects. Newer knowledge of fundamental processes, additional insights into radiation carcinogenesis and the recent availability of new information on Russian populations exposed in the South Urals, provide an opportunity to address this issue. A unique feature of the post Chernobyl accident situation is the presence of internal and external exposures and the non uniformity of tissue absorbed radiation doses.

No information has been published on effects of mixed radiation exposures, and the usual practice has been to determine these independently and add them.

In the recently revealed information on populations in the Urals, who received their exposures primarily some 35 to more than 40 years ago, we have an opportunity to learn more about the role of low dose rate exposures to internal and external low LET radiations. The available information is considered preliminary. Problems in retrospective dosimetry and in epidemiological follow-up have yet to be solved.
The workshop provided an opportunity for radiobiologists and epidemiologists to review and discuss the epidemiological data, the lessons from laboratory studies and reach conclusions on low level risk assessment resulting from the fundamental knowledge and theoretical models.

Brief presentations were made by the attendees, and these are summarized herein. In addition many of the attendees prepared manuscripts which are included in this report.

The discussion centered on a set of questions and insights in to three general areas of low radiation dose rate science: epidemiological, experimental and theoretical.

Epidemiological questions and needs were also discussed. When do exposed people show their cancer effects? With protracted exposure the concept of "latency" is obscured since the exposure time is long. The time of first recognition of the stochastic effect and the time of exposure onset are at least two of the temporal factors. For the exposed Russian populations, (Chernobyl and South Urals [and perhaps others]), comparison of appearance times of cancers with those from the Japanese data base can be used in an attempt to develop a time and age specific "incidence rate." Particular cognizance should be paid to the fact that some stochastic effects (cancers) are not immediately apparent or life threatening.

Dose rate effects revealed in epidemiological observations may be influenced or altered by factors other than radiological. Those should include accounting for the possible role of sex, age at exposure, other environmental or occupational exposures, "cultural" and dietary influences, and the presence of possibly different genetic subgroups; e.g. Russian vs. Tartar.

The summaries of the South Urals data were compared with those from the United Nations reports, the U.S. National Academy of Sciences reports, the ongoing occupational studies in the U.S. and some of the animal fundamental and theoretical studies. Some of these are shown in the table.

| TABLE |
| "STUDIES OF POPULATIONS RECEIVING DIFFERENT DOSE RATES" |

An attempt at developing a unifying "schema" on dose rate effectiveness is shown in the figure. The Japanese a-bomb data base, the "ultimate high dose rate," was assigned a value of unity.

| FIGURE |
| "DOSE RATE EFFECTIVENESS FACTORS" |
In considering the dose rate of protracted exposure, the conventional use of total dose or average annual or quarterly dose were considered inadequate. It is necessary to also include some information on the temporal distribution of dose. Since no single parameter seems adequate, a preliminary specification should at least consider the magnitude and duration of peak dose rate. In reality, there is no universal symmetrical temporal model that is acceptable. Perhaps a dose-time product concept incorporating a "full width at half height" of the peak can be helpful. Our focus was on how the cells at risk "saw" the incident fluence of radiation.

In answering the question about whether we can obtain individual dose estimates, the temporal distribution of dose is but one consideration. The data must provide the temporal aspects of both internal and external dose so as to permit a credible estimate of individual organ doses. A technique in which the risk of cancers in individual organs is summed to derive the overall risk has been proposed. In derivation of risk factors for specific organs different models might be used for different organs (e.g. relative or absolute temporal risk projection models). Such an integrated model, which is normalized with regard to organ absorbed doses and "weighted" by organ specific risks coefficients can be an important step in understanding of overall risk.

Tentative conclusions which were developed at the meeting are:

1- Low LET exposures at low doses and/or rates are obviously less effective at producing stochastic health effects than are high, acute doses.

2- For the epidemiological studies for which such dose rate data exist, the lower the dose rate, the greater the apparent amount of reduction of consequences.

3- For radiation-induced leukemias, peak dose rates of about $10^{-5}$ Gy/da have not been associated with an increased risk in US nuclear workers.

4- Preliminary evaluation of a cohort of Russian nuclear workers exposed to peak dose rates of about $10^{-1}$ Gy/da showed an increased risk which was between 20 to 80 % of the risk seen in atomic bomb survivors.

5- Thirty to 70% reduction in comparable risk was seen in populations exposed to radionuclide releases, ($10^{-4}$ to $10^{-2}$ Gy/da peaks), near the Tech River in Russia some 40 years ago.

6- Radiation therapy cohorts have also demonstrated a reduction in risk.

7- Further follow-up of exposed populations is needed as is a more intensive program of retrospective dosimetry.
8- Other cancers may provide similar dose rate relationships. The radium dial luminizer population may be an example of dose rate effectiveness associated with high LET exposures.
Table 1 - Human Radiation Leukemia * and "Peak" Dose Rates

<table>
<thead>
<tr>
<th>Author</th>
<th>Series</th>
<th>Gy/da</th>
<th>Plateau Risk per P<em>Y</em>Gy</th>
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<tr>
<td>UNSCEAR 88</td>
<td>A bomb</td>
<td>∞</td>
<td>2.94 x 10^-4</td>
</tr>
<tr>
<td></td>
<td>spondylitis</td>
<td>~1</td>
<td>2.02 x 10^-4</td>
</tr>
<tr>
<td></td>
<td>cervical</td>
<td>0.1-1</td>
<td>0.61 x 10^-4</td>
</tr>
<tr>
<td>Smith 82</td>
<td>spondylitis</td>
<td>~1</td>
<td>0.54 x 10^-4</td>
</tr>
<tr>
<td>Boice 88</td>
<td>cervical</td>
<td>0.01-1</td>
<td>0.1 x 10^-4</td>
</tr>
<tr>
<td>Koshurnikova 92**</td>
<td>Ural workers</td>
<td>~ 0.01</td>
<td>0.6 - 2.3 x 10^-4</td>
</tr>
<tr>
<td>Kossenko 92**</td>
<td>Techa River series</td>
<td>~ 0.001</td>
<td>~ 0.7 - 2 x 10^-4</td>
</tr>
<tr>
<td>Gilbert 91</td>
<td>US nuclear workers</td>
<td>&lt; 0.00001</td>
<td>~ 0.0 x 10^-4</td>
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*Modified from Filyushkin, **Preliminary estimate
Figure 1 - Radiation Leukemia Series

Dose rate risk reduction relative to A-bomb

Peak dose rate (Gy/da)