

## NEED AND IMPORTANCE OF FURTHER RESEARCH IN THE FIELD OF RADIATION

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### Introduction

It would be very difficult to summarise and do justice in a small report the work done in radiation research and the support that it received from various governments and other financing agencies during the last century. It is, however, sad that its support during the later part of the twentieth century and in the present century has been decreasing. In the beginning few decades of the twentieth century, the results of radiation studies were mainly presented and discussed at meetings of medical radiology. In the second half of the century it was realized that further progress in the understanding of biological effects of ionizing radiation could only be obtained from studying these effects at all levels of biological systems, from molecules, cells, organs to the whole organism in a multidisciplinary manner. Consequently, meetings and discussions amongst physicists, chemists, biologists and clinicians led to the development of radiation research as a field as we know it today.

### Contributions of Radiation Research

Radiation research has contributed to a better understanding of action mechanisms not only of ionizing radiation but also of other toxic agents on cells and other living organisms. By such studies fundamental life processes have been discovered; DNA repair and the cycle of cell proliferation were observed and defined by radiobiologists. Through radiation research, many contributions have been made for the understanding of the mechanisms and regulation of these processes. Molecular and cellular biology in general have stimulated the understanding of these processes also with respect to radiation effects. The primary physical effects, radiochemical effects and biological consequences have always been studied simultaneously and quite often in interdisciplinary groups. Our understanding of biology and its principles owes a great deal to the use of radiation as a tool. Recognising this, the Nobel Committee has bestowed a large number of Nobel Prizes to scientists for their work directly or indirectly involving radiation. A cursory look at the web site of the Nobel Committee ([www.nobel.se](http://www.nobel.se)) makes the point obvious that a very large number of Nobel prizes in Physics went to the credit of 'radiation'. It is sad that the boom that set-in in the radiobiology research in 1950s, peaking around 1970s to 1980s, is gradually but significantly showing a declining trend across the globe in 1990s. India is no exception.

Due to technological advancements, radiation is increasingly becoming more useful in medical diagnosis and therapy than in the past opening new vistas of success in medicine. On the other hand, radiations are also finding desirable as well as undesirable uses in industries, in maintaining human safety (e.g., x-ray scanner at airports, etc.) and in warfare (nuclear devices and weapons of various kinds). It is also a futuristic substitute for conventional fuels (viz., nuclear powered industries, aircrafts, ships, submarines, etc.). A new dimension of radiation was revealed when Hiroshima and Nagasaki cities perished under the impact of atom bombs. Further, a series of accidents at different nuclear

power plants in the world, from Three Mile Island in USA to Chernobyl, in former USSR, exposed human populations to high doses of radiation. Human misery that followed in terms of immediate impact of radiation triggered destruction left lasting *albeit* negative impression on human minds about radiation. The late effects of radiation, some of which are still being evaluated, seemed not so drastic as was expected. In the heightened threat perception of the world in the present century wherein terrorist could use nuclear or 'dirty' devices to achieve their sinister goals has further accentuated the fear of radiation. Thus, human concerns on radiation safety of the population have increased significantly. Needless to say that historical experience with radiation, including its diagnostic and therapeutic potentials and tragedies, have been mixed. However, the potential usefulness of radiation in cancer diagnosis, radiotherapy and other medical applications remain high which is constantly growing with technological advancements.

In the times to come as well, as long as mankind lives in an environment with radiation exposure from natural and man-made sources, it is necessary to improve the understanding and estimation of radiation risk. Radiation research has a very high social impact for life throughout the world. The production of energy by nuclear power, the use of ionizing radiation for medical diagnosis as well as tumour therapy are very important factors for living standards in our countries worldwide. Under the circumstances it is very necessary that radiation research continues to get financial support from governmental as well as non-governmental agencies.

#### **Needs of developing countries**

Coming to the special problems of developing countries like India, unnecessary fear of radiation causes many problems. It is very well known that in many developed countries generation of power through nuclear energy is achieved from 35 to 75 per cent. They do not perhaps need more power plants but in

countries like India it is of utmost necessity but it is opposed by the general public for fear of radiation risk. The assumption of a linear dose-effect curve without a threshold in the low-dose range has been made on a scientific basis by the UNSCEAR for reasonable precaution in radioprotection. However, at least for carcinogenesis, the deleterious effect of very low dose of radiation it has not been proven yet. But it has led to the misunderstanding that very small radiation doses are also very deleterious to the human health, hence and opposition for power production through nuclear power plants. India has a large natural laboratory where the radioactivity measured in the 55 km long and 0.5 km wide belt is primarily due to the largest thorium (and its decay products) ranging from 8-10 %, which is the largest anywhere in the world. The radiation levels in the region vary widely from 1 mGy to 35 mGy/year. The size and density of population also in this region is also the largest anywhere in the high background areas of the world. Historically, human population has been living in these areas for over 1000 years. Computer-based cytogenetic studies along with dosimetry studies; chromosomal breakage and non-disjunction, which can be monitored as micronuclei in binucleated lymphocytes blocked at cytokinesis on over 10,000 newborns, on an analysis of 850,000 cells at metaphase have shown no difference between babies born in normal as well as high background areas. Further continued work in this area is very necessary.

#### **Need for further studies in radiation**

Let us take up another area of work in radiation research which is very necessary and would need continues financial support. It is assumed that because of the political pressure and the international situation atomic bombs may not be used in future. The unprecedented terrorist attack on the World Trade Centre on September 11, 2001 and the turn of events across the globe since then have heightened the perception of threat to the civilized world. The fear of a repeat of such events with increased intensity and possible use of nuclear weapons in such acts is not an impossible reality. Prompted by such

possibilities, the scientific communities of the world have started to address the issue of planning appropriate strategies to minimize loss of life and property. One important workshop, 'Interagency Workshop on the Radiobiology of Nuclear Terrorism', was held at Bethesda, USA in December 2001 (Moulder 2002a) to address the nuclear related issues in the post-September 11 era. Incidentally, about one year earlier another workshop, 'Modifying Normal Tissue Damage Postirradiation', also addressed issues relevant to radiation damage (Stone, McBride and Coleman 2002). Both workshop deliberations have many overlaps, understandably due to common concerns, in the domain of the existing knowledge base of the consequences of human exposure to moderate doses (1 - 10 Sv) of radiation. The Bethesda workshop, in addition, outlined possible strategies to be adopted over the next 5 years to improve our ability to diagnose, triage, prevent and treat radiation injuries (Moulder 2002b). While the academic contents and recommendations of these meetings are relevant to the nuclear disaster scenario, one has to keep in mind that in a nuclear tragedy situation, large segments of population are likely to be simultaneously exposed to a range of doses. Therefore, there is need to look into the biological response to different qualities as well as to variable quantities of radiation. Further, the context of discussion in the two meetings mentioned above related to situations in developed countries where medical, paramedical and first-response teams are relatively better trained and the awareness level of the population is relatively high. The circumstance in a large number of under-developed, third world countries, including India, is quite different. The response management and medical infrastructures are relatively poor and the awareness level of the population is low. Thus, it is important that other aspects, including the psychological state of the population in distress, are also discussed and evaluated so that the immediate impact of such a disaster could be kept to a minimum. With this in view, the Indian Society for Radiation Biology (ISRB) took the lead in organising a multinational, multiagency workshop, 'Radiation Risk in the Age of Nuclear Terrorism', in collaboration with the Research Center, Juelich (Germany), Health Canada, Ottawa (Canada)

and School of Life Sciences, Jawaharlal Nehru University (JNU), New Delhi (India).

**Issues of discussion at the workshop:**

The workshop was held on November 16, 2002 at the School of Life Sciences, JNU, New Delhi. The total of 40 participants, included a multinational team of radiation biologists and allied scientists, including scientists from Japan - the solitary country having first hand experience of management of the aftermath of nuclear bombings (for details see ISRB-Participants 2002). Prof. R. N. Sharan, in his opening remarks, highlighted the need and urgency of the workshop and discussed its scope in light of the increasing threat perception of nuclear or 'dirty' devices falling in the hands of terrorists. Professor Emeritus P. N. Srivastava (JNU, New Delhi), in his inaugural address, recalled the chronological events of the past where large segments of population across the globe were exposed to heavy doses of radiation. He impressed upon the participants the need to come up with suitable recommendations, which may form part of the strategies of various governments to tackle radiation emergencies with dexterity. Prof. K. A. Dinshaw (Tata Memorial Center, Mumbai) delivered a lucid thematic talk entitled "'Managing Radiation Emergencies' - a physician's view" covering all aspects of medical and health management during and after a nuclear holocaust. The next four technical sessions covered, in depth, various aspects of the consequences of radiation exposure, new approaches to biological dosimetry, biological responses and radioprotection strategies. Dr. A. Trivedi (Health Canada, Ottawa) presented new strategies for radiation risk assessment in the dose range of 1-10 Sv - doses that may not be lethal but can potentially cause acute effects. Dr. K. P. Mishra (Bhabha Atomic Research Center, Mumbai) detailed the need for more extensive research to elucidate the role of free radicals in the induction of membrane and DNA damage, which may provide better understanding of apoptotic death and bystander effects. Prof. R. N. Sharan (NEHU, Shillong) presented evidence of nucleotide sequence determined vulnerability of

segments of genomic DNA suggesting that genome instability or inherent radiosensitivity may be, at least in part, determined by the primary sequence of nucleotides. Professor Emeritus M. S. Sasaki (Kyoto University) presented a new model of biological dosimetry. The strategy takes into account the fact that dose distribution is not likely homogeneous in a person exposed to radiation in a nuclear disaster. Thus, the score of chromosome aberration recorded in lymphocytes is spread over a mixed Poisson distribution into dose component to get most probable dose distribution profile and a realistic biological dose assessment. Dr. F. H. A. Schneeweiss (Institute of Medicine, Research Center, Juelich) offered an alternative to this approach in which early cellular response could be assessed by analyses of lymphocyte proteins by two-dimensional differential gel electrophoresis and mass-spectrophotometer coupled with COMET-FISH analysis of DNA damage. Prof. P. Uma Devi (J. N. Cancer Hospital, Bhopal) presented results of extensive research involving prenatal exposures of mice and cancer incidence. Prenatal exposure was shown to significantly increase genome instability. Prof. R. K. Kale (JNU, New Delhi) presented evidence of the xanthine oxidoreductase system producing free radicals in the post-irradiation period suggesting, thereby, that inhibition of the system may reduce radiation damage. Dr. B. S. Dwarkanath (Institute of Nuclear Medicine and Allied Sciences, Delhi) discussed the possible use of minor groove binding DNA ligands, such as Hoechst 33258 and 33342, for protection of radiation induced DNA damage. The Hoechst ligands were shown to scavenge free radicals as well as afford stabilization to DNA superstructure. Dr. A. Chatterjee (NEHU, Shillong) elaborated upon the use of the endogenous radioprotector, GSH, in reducing post-irradiation damage to proliferating cells.

#### **Recommendations of the workshop:**

The final session of the workshop was a round-table plenary discussion with panelists Prof. P. N. Srivastava (India), Prof. M. S. Sasaki (Japan), Dr. F. H. A. Schneeweiss (Germany), Dr. A. Trivedi (Canada) and Dr. Vijaylaxami (USA). The

session was initiated by a short presentation on "Chemical, Biological, Radiological and Nuclear Research & Technology Initiative" by Dr. Trivedi. All panelists and the participants interacted extensively and freely on various aspects of the proceedings of the day and made recommendations to define a strategy to handle a nuclear disaster scenario.

Briefly, the main points of the recommendations were (for details see ISRB-Recommendations 2002):

(a) International Collaborations/Partnerships: Closely interactive joint efforts be initiated and strengthened for free exchange of information and collaborative research among scientists and institutions engaged in radiobiological teachings and research across the globe.

(b) Preparedness: The participants felt strongly that "preparedness" was an essential component of containing the damage of a nuclear disaster scenario. It was felt that special initiatives are needed for school children and public awareness. ISRB should play a pro-active role in the design of such programmes to prevent misinformation and unfounded alarm to children and the public.

(c) First Response Team: First response teams should be created at various locations. The fire brigade, police and paramilitary personnel should be given training and orientation on the effects of radiations and handling radiation accident/disaster situations including decontamination procedures. Preparation of emergency situation 'manuals' for different teams was recommended.

(d) Categorization of Hospitals: Hospitals should be categorized and equipped for handling various categories of patients and different degrees of emergencies. Triage Centers and Teams, Emergency Centers, Definitive Care Centers and Specialized Centers could be some of these categories of hospitals.

(e) Trauma Control Hospitals: Specialized hospitals with psychotherapists and psychoanalysts should be developed for trauma control.

(f) Biological Dosimeters with Field Applicability: Appropriate biological dosimeters, especially with field applicability, need to be developed. National and international initiatives on such research and development programmes and priority funding were recommended.

(g) Radio-modulatory Drugs: New generation drugs for post-exposure treatment, such as endogenous or exogenous radioprotectors, free radical scavengers and nucleotide modifiers, should be developed and tested through international collaborations and priority funding.

(h) Role of Bhabha Atomic Research Center (BARC): Active collaboration and exchange of views between scientists of BARC, Mumbai and Universities should be initiated and encouraged on a large scale.

(i) Role of the Indian Society for Radiation Biology (ISRB): The ISRB should take initiatives to start appropriate contacts programs to achieve the above goals. Prof. Sharan, President, was entrusted with the task of preparing the report and forwarding the recommendations to appropriate agencies in Indian and other participating countries.

The deliberations of the workshop are in press (International Journal of Radiation Biology, 2003)

#### References:

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