

SUMMARY REPORT

1. Introduction

WHO continues to develop a network of its collaborating centres for radiation emergency preparedness and assistance (REMPAN).

The primary purpose of this network is to promote amongst the WHO Member States medical preparedness for radiation accidents and to provide advice and medical assistance in case of a radiation accident, in particular under the International Convention on Assistance in the Case of a Nuclear Accident or Radiological Emergency.

The second task of the network is to study long-term medical effects of such accidents

The network started with three centres in France, Russia and the USA and increased by the collaborating centres in Argentina, Australia, Brazil, Germany and Japan to provide a broader worldwide emergency coverage. In this way REMPAN facilitates a coordinated response in radiation emergency involving more than one assisting centre.

Five coordination meetings of WHO collaborating centres on radiation emergency medical preparedness and assistance have so far been held. The first of them took place in Le Vésinet (France) and Southampton (UK) between 30 March and 2 April 1987. The second one was held in Oak Ridge (Tennessee, USA) between 17 and 19 October 1988. The third one was organized in then Leningrad (St Petersburg, the former USSR) between 21 and 24 May 1990. The fourth meeting was held in Ulm (Germany) between 1 and 4 December 1992. The fifth one was convened in Paris (France) from 5 to 8 December 1994.

The sixth and present meeting of the collaborating centres was hosted by the WHO Collaborating Centre at the Radiation Effects Research Foundation (RERF) and held in its Hiroshima Laboratory (Hiroshima, Japan) from 23 to 25 October 1995. The programme of the meeting and the list of participants are given in Annex I and II, respectively.

2. Description of the meeting

DAY 1: Monday, 23 October 1995

The meeting was opened by Dr W. Kreisel, Executive Director of WHO. The participants were then welcomed by Dr I. Shigematsu, Chairman of RERF and President of Hiroshima International Council for Health Care of the Radiation-exposed (HICARE), Mr Y. Fujita, Governor of Hiroshima Prefecture, and Mr T. Hiraoka, Mayor of Hiroshima City. Incidentally, the welcome address of Mr Fujita was read by Mr N. Kubo, Vice Governor.

On the first day, three special reports were presented. Dr R. Ricks served as rapporteur.

Special report (1): Radiation emergency medical preparedness and assistance at international level (Speaker: Dr G. Souchkevitch, Moderator: Dr Y. Hasegawa)

Dr Souchkevitch reflected on the use of nuclear radiation and accident experience. He mentioned 380 major radiation accidents were documented worldwide and that 430 nuclear power plants were currently in operation with another 55 under construction. Dr Souchkevitch pointed out that nuclear weapons continue to be produced and that about 1900 weapon tests have occurred worldwide. He cited these facts as a continuing potential for radiation accidents and the obvious need for international response as provided by REMPAN. He reviewed current protective measures and intervention criteria as well as guidelines for use of stable iodine in the event of nuclear power plant accidents. Dr Souchkevitch reviewed the current status of thyroid cancer in the Chernobyl affected areas and stressed the need for continued follow-up projects related to research and technology transfer. He concluded with announcements regarding new collaboration centres in China, the Urals (Russian Federation) and a consideration for a centre at the Institute of Biophysics in Moscow (Russian Federation). He also stressed the importance of post-

Chernobyl scientific conferences in Geneva (Switzerland), Minsk (Belarus), and Vienna (Austria) which will be held in the next six months.

Special report (2): Emergency response systems for real-time prediction of local and global impacts due to nuclear accidents (Speaker: Dr M. Chino, Moderator: Dr Y. Aoki)

Dr Chino reported the emergency response systems to predict local and global impacts due to nuclear accidents. These capabilities were established in Japan following the TMI accident in the USA and are named SPEEDI and WSPEEDI respectively. These computerized programmes use meteorology, topography, and calculated radionuclide release to predict external dose and dose from inhalation. These models are similar to those used in other countries and intercomparison studies have been carried out. Future plans are to construct a worldwide data network between SPEEDI and other systems to enhance intercomparison studies and validate the Japanese system.

Special report (3): Historical medical review of Japanese fishermen exposed to fallout in 1954 (Speaker: Dr T. Kumatori, Moderator: Dr I. Shigematsu)

Dr Kumatori presented a review of the Lucky Dragon accident resulting from fallout related to a nuclear weapons test in the Pacific and its medical follow-up. Dr Kumatori reflected that the Lucky Dragon accident was the first one due to a nuclear test from which humans received high levels of contamination resulting in significant medical consequences. Dr Kumatori presented information on fallout characteristics, radiochemical analysis of particles, external dosimetry, internal contamination, skin reactions, radionuclide excretion, thyroid doses and extensive medical follow-up. Haematological, cytogenetic, and data regarding oligospermia were reviewed. The 1985 follow-up data demonstrated residual skin lesions, slightly sub-normal haematopoiesis, chromosome aberrations, and the absence of cataract. Fifteen of the men involved are alive today.

Following the presentations of these three reports, a tour of respective laboratories at the RERF was arranged for REMPAN participants.

DAY 2: Tuesday, 24 October 1995

[Morning session]

In the morning of the 2nd day of the meeting, three special reports were presented and Dr S. Solomon served as rapporteur.

Special report (4): An accident of exposure to ¹⁹²Iridium source in Chiba: Angiopathy 22 years after exposure (Speaker: Dr M. Akashi, Moderator: Dr A. Akanuma)

Dr Akashi described an interesting case of angiopathy, developed 22 years after accidental exposure to an industrial radiography source. The exposure occurred from an ¹⁹²Ir source of 5.25 Ci, misplaced from shipyards in 1971. The subject of this report was one of 6 workers exposed to the source over a period of some days. The average whole body absorbed dose was estimated from chromosomal analyses to be 1.3 Gy and the absorbed dose to finger, determined from the surface dose rate of the source, was in the range 26-90 Gy.

The clinical findings in the period following the exposure were summarized. In the week following the exposure the subject developed erythema with swelling in the palm and fingers of both hands. The radiation burns were healed by antiseptic treatment, but following discharge repeated ulcer appeared and there was contracture of some fingers.

In 1993, the subject revisited NIRS with right finger pain. The skin of two fingers was infected and necrotic and the right thumb was atrophied. There was a significant decrease in the density of some bones. Angiography showed complete occlusion of the palmar digital and dorsal pollical arteries and the narrowing of a radial index artery. The condition of the hand necessitated the amputation of two fingers and replacement of the thumb with a toe. It was concluded that the delayed effects observed were caused by slowly developing angiopathy.

In the discussions following the presentation, Dr Ricks questioned the estimates of skin dose; he observed that the exposure rates were consistent with thin encapsulation and that dose estimate may be low; this was consistent with the nature of the lesion on the left buttock which he felt was more consistent with a surface dose in excess of 500 Gy.

Dr Jammet observed that over-exposure due to ^{192}Ir was not uncommon and that he had prepared in 1986 a document on the safe use of such sources. This document had still not been adopted.

Dr Gusev spoke of two such cases in Russia, with follow-up ultrasound measurements of blood flow. The ultrasound measurements have not been correlated with biological changes, but a large increase in flow in damaged region was observed in the period 1 to 3 months post-exposure.

Special report (5): Effects of radiation accidents in South Urals (Speaker: Dr S. Shalaginov, Moderator: Dr K. Mabuchi)

This report provided a comprehensive overview of the radiation exposures and medical impact associated with contamination arising from the facilities at Chelyabinsk. Vast areas of south and middle Urals were contaminated and the exposed populations were divided into six groups. These groups have had medical follow-up over a period of 30 years by the Ural Research Centre.

The sequence of contamination of the area was detailed, covering discharges to the Techa River between 1949-1956, an incident with radioactive waste in 1957 and an incident with contaminated lake water in 1967. These incidents resulted in high contamination along a 300 km corridor. Steps were taken to protect the population, including resettlement of populations along the river Techa, but there was a delay in the implementation of the special sanitary protection regulations and a proportion of the population along the river received large doses.

Estimates of average population doses from the sources of radiocontamination over the period 1948-1967 were given. For the Techa river group, doses from both external and internal irradiation were in the range of 0 to 3 Gy, with a mean dose of 0.4 Gy. The health effects of these exposures have been studied and a registry of all people living near the river during the releases was established. The present study includes 28,000 exposed between 1950-1953 and follow-up studies were carried out. A group of 940 residents near the Techa River were identified as having chronic radiation sickness, with a range of radiation reactions and no single specific symptom. A range of symptoms were noted and these persist for more than 30 years. An increase in both leukaemia incidence and mortality rates among the exposed residents was observed. These rates were 2-3 times lower than those derived from A-bomb survivors. The incidence of birth rate and fertility indicated normal reproductive function; a somewhat increased mortality rate in children and an increase in both medical and spontaneous abortions were noted.

In the discussions, Dr Mabuchi commented that RERF is interested in dose rate effects; but there is some uncertainty in dosimetry and the control groups may not be comparable. He pointed out that these studies have been reported in an issue of *Science* (Vol. 142, No. 1,2, March 1994, Elsevier).

Dr Bebeshko asked how many patients with chronic radiation syndrome were identified in first 5-10 years. Dr Shalaginov replied that there were 940 cases from beginning to now.

Special report (6): Radiation accident in Estonia (Speaker: Dr I. Gusev, Moderator: Dr H. Jammet)

This report described the exposures associated with a radiation accident in the former Soviet Republic of Estonia. The exposure arose from a ^{137}Cs source from a radiation sterilization assembly. Estonia does not have a high level radiation repository and this source was placed in concrete pit containing mostly low level medical radioactive waste. The assembly had been placed on the surface of the pit and there was no identification of isotopes at the time of burial. The report described in some details the accident event sequence; as much as it could be reconstructed. There was exposure to 3 brothers as well as 3 individuals in the house to which the source was taken. Exposure extended over a period of some weeks, although the largest local doses were received in the first period of handling

The response to the accident was initially handled by the local Estonian radiation authorities, with the Russian Institute of Biophysics being called in almost one month after the knowledge of the accident. Dose assessments were made using physical calculation methods (reconstruction and measurement) and ESR measurements of clothing. The source was believed to be ^{137}Cs with an activity of 90 Ci. One victim was assessed as receiving a local dose to the thigh of the order 2000 Gy. This victim died after admission to hospital. No detailed medical tests were carried out at the time. The other victims had varying degrees of acute radiation syndrome, local radiation injuries and bone marrow syndrome, but all fully recovered.

This case had large complications due to the loss of information due to lack of expertise on the part of local authorities. There was a lack of information of the radiation source and the request for aid was delayed. There was no specific training for physicians in responding to radiation injuries; there is a need to look to training in this area.

The full texts of the above six special reports are included in Annex IV.

[Afternoon session]

In the afternoon of the 2nd day, a panel discussion took place.

Panel discussion (1): New activities of WHO collaborating centres involved in REMPAN and radiation emergency medical preparedness at national level (Moderator: Dr G. Souchkevitch, Rapporteur: Dr R. Drummond)

The moderator opened the session indicating that the panelists were either the director of a WHO collaborating centre or his delegate. Each was requested to make a presentation reporting upon: 1. the current situations within their centres and the new activities since the last REMPAN meeting in Paris in 1994 and 2. the information on medical preparedness for radiation emergencies at a national level within their countries.

Presentations

1. Dr J. Skvarca, Argentina

Dr Skvarca reported his major activities in this last year as

- a) Developing rapid communication and links between branches of responsible authorities and hospitals within Argentina.
- b) Forging links between centres in other adjacent Latin American countries.
- c) Practical training for medical staff.

He described the relationship between, and organization within existing institutions which are responsible for medical preparedness for radiation accidents within Argentina including the agreement between them signed in 1984 called SAMARI.

The aspects of SAMARI function at a national level include distribution of roles to the various institutions, formulation of a plan for responding to radiation accidents and identification of hospitals and personnel for their role in medical preparedness. The aim is to have one or two physicians trained, with one room equipped, in each designated hospital, capable of managing a radiation victim. It is anticipated that in 1996 an institute of radiological medicine will be created as a central facility for the study of radiation effects.

As another major activity related to Argentina's role in the region, considerable effort was placed in establishing direct links with institutions in neighbouring countries like Chile, Peru, Paraguay, and Uruguay. A formal agreement with Paraguay will be signed in November and similar agreements with the others by the end of year. This will enable planning for medical preparedness, training programmes for medical and other personnel, and information exchange to occur at a regional level.

2. *Dr S. Solomon, Australia*

The collaborating centre in Australia is made up of two institutions; the Australian Radiation Laboratory (ARL) and the Peter MacCallum Cancer Institute. Activities in the last year consisted of training activities, environmental monitoring programmes and acquisition of a new high quality spectroscopy system for monitoring lung exposure.

Dr Solomon described the responsible organizations within Australia for dealing with a radiation emergency and the role of ARL at a national level. Currently the response capability is small.

Activities in the coming year will be directed toward increasing training for medical and nursing staff, working with the states to develop plans for medical preparedness at that level, and improving and upgrading the existing radiation accident register. It is of great assistance to Australia to draw on the knowledge and experience of the other WHO collaborating centres in developing effective plans for radiation emergency medical preparedness for Australian and the region

3. *Dr C. Oliveira, Brazil*

The activities of the Institute of Radiation Protection and Dosimetry and the establishment of its emergency assistance service (SAER) were described. The medical response is provided by the Reference Centre for the Evaluation and Assistance of Radiation Victims (CRAAR). The current procedure for responding to a radiation accident was outlined.

Brazil has 1,856 radiation installations with 1,303 in south east Brazil. In 1990 a central register of radiation incidents was begun. 176 events have been reported to the end of 1994. Approximately 10% of these had the potential to be a serious accident.

A national system for medical assistance in radiation emergencies has been developed and will soon be introduced federally by the governmental regulation. It comprises 3 levels of organization:

- 1) Local - pre hospital, at scene intervention
- 2) Loco-regional - assistance in closest hospital; internal and external decontamination
- 3) National Reference Centre - specialized assistance for severe radiation injuries.

The role of the Institute of Radiation Protection and Dosimetry in supporting this plan at each level was described.

In discussion of this presentation Dr Ricks and others congratulated Brazil on their significant achievement in the high level of training and organization of medical preparedness for radiation emergencies they had reached since the Goiania accident in 1987.

4. *Dr H. Jammet, France*

The International Centre for Radiopathology was established in 1985. Its main areas of research in the last year have been in the treatment of skin radiological burns with enzyme therapy, cataract formation after radiation and the effects of various types of non-ionizing radiation, such as ultraviolet radiation, medical laser beams and electromagnetic field.

France is dependant on atomic energy for its power and has over 50 atomic reactors. As such, it has a responsibility to be able to deal effectively with radiation accidents both for its own benefit as well as the neighboring countries. The International Centre for Radiopathology has developed a network including the main civil hospitals and all the specialized military hospitals. The network can respond with technical intervention and health or medical intervention, in case of radiation accidents. Hospitals with special expertise are identified and available to receive accident victims at short notice when their services are required. The International Centre for Radiopathology will

provide advice, mobile response teams or care within the centre, as required. The Centre is available to provide assistance internationally if requested through WHO or IAEA

5. *Dr D. Densow, Germany*

The WHO collaborating centre comprises the University of Ulm and the Institute for Applied Knowledge Processing.

Activities in this last year include:

- 1) Research - in occupational radiation protection and haematological effects of chronic low dose irradiation
- 2) Monitoring of occupationally exposed
- 3) Training - training physicians in hospitals and those working at nuclear reactors

In planning medical preparedness for a radiation emergency, there are 2 scenarios: incidents involving less than 10 people or more than 10 people

The plans for dealing with both scenarios were outlined. Medical assistance is provided on site or at the local designated hospital. More specialized care is available at the Regional Radiation Protection Centre in relation to a small number of victims

In the case of large accidents, federal authorities are responsible for crisis management. The regional radiation protection centres will need to direct victims to appropriate hospitals for their care. There are 12 regional radiation protection centres across Germany. 67 hospitals are identified as willing to accept radiation accident victims. 14 hospitals can do bone marrow transplantation. There is a recognized need to train more medical staff to manage radiation accident victims.

6. *Dr Y. Hasegawa, Japan*

The terms of reference of the WHO Collaborating Centre for Radiation Effects on Humans at RERF were presented. Its major role in REMPAN is in the follow-up of effects on irradiated humans. The Centre has continued the activities defined in its terms of reference. The additional activities in the last year have been participation in WHO conferences and hosting this meeting.

Dr A. Akanuma, Japan

The National Institute of Radiological Sciences is involved in planning for radiation disasters at a national level. The history of developing a plan for medical preparedness was outlined. The three categories of medical facilities and their capabilities were discussed. The NIRS has the definite care hospital and accepts acutely injured and severely contaminated patients. It has 3 different medical teams to respond to particular aspects of radiation accidents.

NIRS also registers and follows up exposed people, conducts life science research, and education and training for medical personnel as well as acting as a reference centre.

In the discussion, the importance of equipping the medical dispatch team to support themselves in a disaster area was emphasized.

7. *Dr V. Komar, Russian Federation*

The WHO collaborating centre is based upon the radiology and radiobiology part of the Central Research Institute of Roentgenology and Radiology, St Petersburg.

Activities in the past year include -

- 1) studies on the health status of Chernobyl victims.
- 2) cytogenetic and lymphocyte studies looking at the relationship between proliferation rate of lymphocytes and chromosome abnormalities.
- 3) chromosomal analysis to establish leukaemia risk in children from Chernobyl.

The organization of medical assistance in case of nuclear accidents was presented in outline. There are 6 principal centres for dealing with medical assistance for radiation effects in Russia. The local medical institutions must provide the first aid.

Dr I. Gusev, Institute of Biophysics, Moscow, was invited to describe his centre and the facilities available to support its medical preparedness for radiation accidents. He acknowledged the support of Dr Jammet and the International Centre for Radiopathology (France).

In the discussion, the philosophy of dispersing radiation casualties to many hospitals to avoid overloading any one hospital was recommended. Dr Gusev said that there was a need to decentralize the medical care. He also commented that the experience of the general disaster medicine teams would be useful for the training of radiation response teams.

8. *Dr R. Ricks, REAC/TS, USA*

Dr Ricks outlined REAC/TS activities since the last meeting of REMPAN under the following headings.

- 1) Emergency response
- 2) Training
- 3) Participation in conferences
- 4) International assistance for IAEA training

Details of the above are included in his summary.

In addition, REAC/TS took part in a major training exercise conducted by the Department of Energy in Yorktown. The DOE is the responsible authority for responding to radiation emergencies at a national level. The DOE emergency response assets were described. REAC/TS provides the medical input for this emergency response capability both nationally and locally to support other parts of the system.

9. *Dr S. Ali, India*

India has 160,000 radiation workers. Medical preparedness for radiation accidents is based around the atomic reactor sites. At the reactor sites, decontamination and minor medical procedures are handled. The site hospital is away from the plant and manages radiation injury and/or physical trauma. The Bhabha Atomic Research Centre (BARC) is the central hospital for the system accepting patients with exposure dose of 2-10 Gray. BARC facilities were described. Bone marrow transplantation is available at the TATA Memorial Hospital.

The other major activity is conduct of training courses for medical staff which has been done yearly for the last 5 years.

Dr Kreisel raised concern about coping with an accident occurring far from Bombay. Dr Ricks commented that deploying assets in large countries was difficult. He feels that radiation accidents are not true medical emergencies. Training of medical staff in this and ensuring that they know where to get advice are the best way to manage casualties, i.e., to let the local medical officer manage the problem and support them with expert advice. Only cases of very high exposure need transfer to a central facility.

Dr Jammet disagreed. There is an urgency for investigation. There are only 6 hours to obtain material for bone marrow matching.

Dr Souchkevitch also considered that there was urgency to treat the exposed person.

Dr Gusev mentioned the importance of observing the immediate effects so that this could be used to triage victims into exposure level groups.

General discussion

1. There was discussion of nonionizing radiation and its effects and the increasing importance this was assuming in many countries; Dr Jammet described the deterministic and stochastic effects of UV, laser, microwave and EMF radiation.

2. Dr Yasumoto raised the problem of medical doctors who refused to be involved in medical treatment of radiation casualties. It was recognized that this was a widespread problem seen in Japan, USA, Brazil, Russia and Germany. There was discussion about overcoming this attitude. Education of doctors and nurses, providing financial inducements and emphasis on duty to society were all considered useful approaches.

Conclusion

Dr Souchkevitch thanked all the WHO collaborating centres for their work and thanked the speakers for addressing both requests. However, despite the combined efforts there were still many gaps in medical preparedness for radiation actions.

There was a need for different plans for different countries as they had different circumstances.

1. countries with nuclear power plants
2. countries which have a country or countries with nuclear power plants in their neighbourhood
3. countries far from any nuclear power plant

He felt sure that future activities will solve the problems in improving medical preparedness.

Medical preparedness at a national level is particularly important and serves as a basis for international assistance.

The format of REMPAN meetings should be more flexible. They may be held sometimes in a form of workshops, e.g. in order to develop recommendations on particular issues.

The full texts of the above nine presentations will be found in Annex IV.

DAY 3: Wednesday, 25 October 1995

On the third and last day of the meeting, two panel discussions took place. Afterwards, Dr Kreisel made a concluding presentation and Dr Hasegawa closed the meeting. Dr Akanuma served as rapporteur for all these sessions.

Panel discussion (2): Medical care of acute radiation symptoms and injuries (Moderator: Dr H. Dohy)

Presentations

1. Dr M. Ohtani, Faculty of Medicine, University of Hiroshima: Planning and treatment for human radiation injuries

Guidelines for the radiation emergency planning were presented where (1) radiation source, (2) type of radiation, (3) distance from the source, (4) time from the onset, (5) whole body or a part of body, and (6) internal or external contamination have to be taken into consideration. Severity was considered according to the exposed dose.

With about 50 Gy, patients will be fatal and 8-10 Gy was considered severe exposure. With 1-2 Gy, patients may have intermediate symptoms. Traumas, haematocrit and acute radiation syndrome have to be closely observed. Treatment for acute radiation syndrome was explained. (1) fluid and electrolyte supplementation, (2) antibiotics administration, (3) platelet transfusion, (4) granulocyte transfusion, (5) red blood cell transfusion, and (6) bone marrow transplant were considered. Principles for decontamination of an exposed patient were described. Necessity of radioactive waste disposal was stressed.

Thermal injury was then described. 1st, 2nd and 3rd degree burns corresponding to dermal layers were explained. Examples of full burns and chemical burns were displayed. The phases of burn injuries were then described. Resuscitation phase is important. Pathophysiology of the burn shock is as follows; 1. burn edema, 2. dermal changes, 3. systemic hemodynamic changes, and 4. haematologic changes. Hematologic changes include 1. hemoconcentration, 2. haemolysis, 3. leucocytosis, and 4. hypocoagulation. Practical approaches for treatment were described. At first, no glucose will be added in resuscitation fluid. Instead, lactate and colloids will be given. Menus for children and adults are different. For monitoring purposes, blood pressure, pulse rate, urine volume, ECG, temperature, blood gas and pulmonary artery wedge pressure will be used. For poor ventricle function, low dose dopamine administration may be effective. In post resuscitation phase (48 hours after), low salt glucose will be used. Potassium and protein will be added. In case of smoke inhalation, to secure airway is important. Management of burn wounds includes cleaning, pain control and debridement. In the inflammation-infection phase, provision of adequate nutrition, lung infection control and minimizing risks of ARDS are important. For infection control, topical antibiotics application was recommended.

In the discussion, Dr Jammet commented that enzyme treatment was effective for local deep radiation burn. Dr Gusev stated that fetal cells would be good for beta ray burns. The moderator responded that it would not be possible in Japan. Dr Ali commented that potato skin would be applicable to the burns, but most of the participants were not convinced. Dr Bebeshko asked the reason why children were classified according to the body surface burned area (below and above 40%). The reason was that the requirement of fluid was different. Dr Jammet asked whether a computer assisted system was employed or not. The answer was no.

2. Dr S. Asano, Institute of Medical Science, University of Tokyo Marrow donor programme in Japan

Dr Asano introduced the current status of Japan Bone Marrow Donor Programme (JMDP) in detail. When homeopathic stem cells are damaged, HLA-matched sibling or one HLA-loci mismatched relative should be first searched for preparing the allogenic bone marrow transplantation (BMT). But it may not be sometimes practical. Therefore, the donor programme will be necessary to secure the unrelated HLA-matched donors. JMDP was officially established in December 1991 for this purpose and the first transplant from one of the registered donors was performed in January 1993. The programme has been so far working well since then, but he emphasized several problems. One, the size of potential donor pool is still not large enough. Two, the outcome of UBMT is not satisfactory due to severe GVHD, etc. Namely, it is still at a investigational stage. Three, of most importance among the future directions will be to use the frozen-stored stem cells by the ex-vivo stem cell expansion technology. Many investigators have been engaged in this research subject, and some promising data are coming with a combined use of soluble IL-6R plus SCF in animal models

Discussion

Dr Bebeshko asked about the risk of viral contamination of the transplants. Dr Asano replied that, because the donors are to be repeatedly examined and ultimately only negative donors are selected, there is no problem.

Dr Souchkevitch asked about transplantation for myelodysplastic syndromes. Dr Asano answered that in Japan the favourable results had been so far obtained with HLA-identical sibling BMT and the outcome of UBMT seemed to be the case, too.

Dr Jammet commented that he first made a bone marrow transplantation to an acutely exposed patient in 1958 and that in EC the number of registered donors went up to 7,000,000.

Dr Akashi asked how those exposed patients could be provided the chances of bone marrow transplantation, because there was now a long waiting list in most transplantation centres. Dr Asano responded that he had no answer to the question of Dr Akashi, and thought that the policy aiming at establishing many small transplantation centres was wrong. Several big BMT centres which have educational programmes will be urgently needed for its solution.

Dr Gusev commented that, according to the experiences from Chernobyl accident, BMT is not so useful as it was thought. Dr Asano said that he agreed with the opinion of Dr Gusev. BMT should be considered only after the administrations of haematopoietic factors such as G-CSF and also only in rare cases without any risk of severe infection.

Dr Jammet commented that the cases from Chernobyl accident were special. The transplant is useful for a case of pure external exposure.

Dr Asano added his opinion that stem cell growth factors without any adverse effect will be also beneficial. The search for these factors will be important.

3. Dr S. Nagataki, Faculty of Medicine, University of Nagasaki: Iodine prophylaxis for the accident of nuclear power stations

Nuclear weapon tests were performed by US and USSR until 1963 and after 1963 France and China continue the tests. The fall-out increased environmental radiation levels and the contamination was found in cattle thyroids even after 1963. The Chernobyl accident also increased the environmental radiation level in Japan, but in Ulm the increase rate was 106 times higher than in Japan. The Time Magazine in August 1995 showed on the front page the scene of Nagasaki right after the nuclear explosion. In its middle shown was the destroyed Nagasaki Medical School which was located at 500 metres from the hypocentre. In Nagasaki, autoimmune hypothyroiditis is confirmed even 45 years from the explosion though the occurrence of thyroid cancer was confirmed much earlier. The acute exposure to thyroid at even 6-8 rad increases the incidence of thyroid cancer, which has been verified among the natives of Rongelap, Sifo and Utirik where the exposed group of 253 people was compared with the control group of 227 people. Short-lived iodines seem to deposit in thyroid more than iodine-131. It is not clear yet which nuclide caused the thyroid cancer. Cesium seems not to be related to it. The estimated iodine distribution does not coincide with the thyroid cancer incidence distribution. The medical use of iodine-131 with therapeutic or diagnostic purposes did not show to increase the thyroid cancer incidence. Therapeutic use of iodine delivered the dose of 20 to 88 Gray and diagnostic use delivered 0.4 to 1.6 Gray to thyroid. The animal experiments show a significant increase in the thyroid cancer incidence with irradiation.

Since there is no method to prevent the occurrence of cancer after exposure, it is important to prevent the exposure to thyroid. As far as thyroid the followings are considered and planned in the medical preparedness for radiation emergency. It is said that in nuclear plant accidents the release of radioactive materials can be predicted and be announced 30 hours prior to the onset. Carcinogenesis in thyroid is highly dose-dependent. This fact has been confirmed by the data from Hiroshima and Nagasaki, Bikini Atoll and Chernobyl. Children and pregnant women should be evacuated from the contaminated area as soon as possible without administration of iodine. With irradiation to thyroid TSH increases and T4 decreases. WHO recommends daily 25 mg of iodine for 1-3 year old children, 50 mg for 3-12 year old children, 100 mg for 12 years old or above. People with Grave's disease or thyroiditis and those with allergy to iodine are susceptible and have to be evacuated. The side effects are studied in Poland where potassium iodide tablets were administered. Up to now no side effects were yet reported. The recommended administration for the prophylaxis is as follows. Within one hour or before the release of radioactive iodine, 30, 50 or 100 mg of iodine tablets are given first. 30 mg appears sufficient though 100 mg is recommended in many countries. Those who have to continue working in a contaminated area have to have the daily repeated administration.

Clinical observations revealed that long term administration of daily 30 mg iodine provokes side effects. Serum T4 decreases. TSH increases. Serum thyroglobulin increases. The size of thyroid gland also increases. Dietary intake of iodine in Japan seems to be in the range of daily 100 microgram to 20 mg. Not all kinds of sea weeds have high contents of iodine.

In summary, the speaker recommends the following administration of iodine in radiation emergency. People at risk should be evacuated. Those with no risk should take 30 to 50 mg iodine. Workers in a contaminated area should take 30 to 50 mg iodine daily.

Discussion

Dr Kreisel asked whether the thyroid cancer was found among children who were born after the accident. The speaker responded stating that no thyroid cancer has been found among them, and moreover in the area within 30 km the thyroid cancer did not increase significantly.

Dr Gusev commented that the first day is important. Iodine-131 can be easily absorbed through the skin.

Dr Jammet commented that according to some literatures the thyroid cancer can be induced also by the external exposure. Dr Mabuchi commented that the studies in literatures have a sufficient number of observations.

Dr Souchkevitch asked whether there is any evidence of the increase in thyroid cancer incidence in Poland. The speaker answered that there was no evidence yet.

Dr Bebeszko asked why thyroid cancer is induced so soon compared with other radiation induced cancers. The speaker responded that there was no experimental evidence.

4. Dr S. Araki, Faculty of Medicine, University of Tokyo: Chelation therapy in Japan: A report based on 25-year use of CaEDTA in occupational medicine

Dr Araki presented his experience in chelation therapy. He is chairing the Department of Public Health of the University of Tokyo and has much experience in treating lead poisoned patients, in particular, in EDTA intravenous administration for lead and other heavy metal poisonings. In Japan DTPA is not yet recognized as a drug for medical use. In application of chelating agents, due consideration has to be given to several factors that include mobilization efficacy into serum, urine vs. plasma relation in concentration, hydration and adverse effects. These will be discussed later.

IAEA once published a report titled "Medical Handling of Accidentally Exposed Individuals." This report describes a number of chemical compounds which enhance the excretion of metals from a body by chelation. DTPA is more effective in removing transuranium elements and Zn-DTPA is less toxic than Ca-DTPA. Therefore, for a long term fractionated therapy Zn-DTPA is more advantageous. No serious toxicity from Zn-DTPA administration within recommended dose is reported in man. DTPA is an investigational new drug in the United States.

The mobilization of heavy metals by Ca-EDTA has been clinically studied by the speaker who infused 20 mg/kg of Ca-EDTA to lead poisoned patients. The blood lead concentration was 22 to 59 ug/dl which is 13 times higher before the administration. For mercury there was no increase. Zn was mobilized 11 times more. Cd was 3.4 times more. Cu was 1.3 times more. Mn was 3.8 times more. And Cr was 1.1 times more. In lead poisoning, the yield became the highest both in urine and serum between one and two hours after EDTA administration. And within 24 hours about 14% of body burden of chelatable lead was excreted into urine. The half life is 3.3 years. The blood lead concentrations and the body burden of chelatable lead showed a logarithmic linear relation. The speaker treated about one hundred patients but no adverse effects were noted.

Discussion

Dr Jammet stated that he had a case of plutonium intoxication who had 150 injections of DTPA for three years and 85% was excreted.

Dr Bebeshko asked on the change of methaemoglobin and enzyme changes in tissues and also on late effects. The speaker answered that methaemoglobin was not measured. In regular clinical studies no significant change in enzyme values was noted. Up to now no significant late effects have been noted.

Dr Ricks commented that in the US about 800 cases of DTPA treatments have been registered 25% of them had such complications as fever, pain in site and bone pain. Two cases of metal fume poisoning had bone pain, but after stopping the administration the symptoms disappeared. No long term health effects were reported.

Dr Bebeshko commented that EDTA might cause hepatitis and enzyme studies are important.

The texts of the above four presentations are included in Annex IV.

Panel discussion (3): Case registries and follow-up (Moderator, Dr S. Solomon)

Presentations

1. Dr R. Ricks, REAC/TS: Case registries in the USA

Dr Ricks talked about the registry and follow-ups for last 20 years in REAC/TS. He explained the system and incidences using tables. The registration was not intended first to include medical data but now they may be included if available. The registry generates training materials. Critical radioisotope accidents are not many. Majority are radiation device accidents which indicates the requirement of more training for technicians. Fatal cases (death within 2 years) were 26 in the States and 77 in other countries. In 26 US fatal cases, 9 non-radiation deaths were included. 21 cases were caused by medical mal-practices.

IAEA initiated to construct a database of the unusual radiological events. However, little information has thereafter been released. The Oak Ridge Institute for Science and Education (ORISE), of which REAC/TS is a part, signed a formal agreement with the Biophysics Institute of the Russian Federation in July 1995 to develop an ARS database of the clinical department of the Institute which is different from the one in Ulm. Dr Fliedner also has an agreement with the Biophysics Institute. Dr Ilyin, Director of the Biophysics Institute of Moscow, hopes that DOE will continue this project. Therefore, the same data will be stored in three different places.

Discussion

Dr Kindler stated that there was no formal contract, but a written memorandum of understanding with the Moscow Institute under which terms the Ulm University contributed the efforts and money. Dr Ricks responded that since there is a transboundary act in the States, a formal contract is required.

Dr Jammet commented on the database in the International Centre of Radiopathology, which was supported by Dr Souchkevitch who stated that the database of the WHO collaborating centre in France is important.

Dr Ricks stated that the data are an intellectual property of the No. 6 Hospital in Moscow.

2. Dr H. Kindler, University of Ulm: International computerized database

Dr Kindler presented the Ulm system of ARS registration which was initiated by Professor Fliedner. Its goal is to prepare a complete documentation of ARS, to follow-up patients and to develop a clinical guideline to treat these patients. Acute phase data and follow-up data have been contributed from all over the world. The database has now complete histories of 264 cases and incomplete records of 277 cases. Demonstrations were made on how to access

the database. Also, sample summaries were given of drug administration, skin burns, primary symptoms and serum amylase changes. Examples of questionnaires were also shown.

Discussion

Dr Solomon commented that the data accessibility seems technically satisfactory.

Dr Souchkevitch asked whether the easy access may have risks to be destroyed. Dr Kindler responded that the backup system is sufficient.

Dr Jammet commented that the definition of ARS is a problem. There is no problem in whole body exposure cases but in partial body exposure ones.

Dr Bebeshko stated that 100 cases of ARS are being followed and studied in Ukraine and these can be incorporated.

3. Dr C. Oliveira, Institute for Radioprotection and Dosimetry: Follow-up of Goiania accident cases

Dr Oliveira talked about the radiological accident in Goiania in which 19 gram of cesium-137 was dispersed in the downtown of Goiania. 16 days later the accident was realized and massive screening and decontamination were performed. 112,800 people were monitored and 249 people were suspected to be contaminated. 129 (later 151) persons were internally contaminated. In vivo measurements of the internal contamination were difficult because some patients were heavily contaminated and the range of measurements varied widely. A special measurement apparatus was developed by the Goiania General Hospital. The ages of patients whose internal contamination were measured ranged from 2 month old baby to 73 year old man and 800 people were measured. For the treatment Prussian blue was given. Three adult and three adolescent patients underwent daily 10 gram administration. The effectiveness was 41%. Mean half life was 21 days. A woman who was internally contaminated and was exposed with 1.3 Gy had been pregnant and her baby was also contaminated. Another woman who was also internally contaminated and exposed with 2 Gy became pregnant 4 years after the accident and her baby was not contaminated. Some people rubbed the skin with the radioactive powder where more burns were observed.

A device was developed to measure residual radioactive Cs internal contamination. The characteristic X-rays of $K\alpha$ $K\beta$ detection was utilized. 10 patients underwent this measurement. Patient No.1 still had internal contamination of Cs-137. However, his left knee was radiation-negative on this new apparatus, but his right knee was radiation-positive. The spectrometer revealed that it was Cs contamination. Patient No.3 had the same contamination and two locations of contamination on his right thigh were detected. Other 8 patients were radiation-negative. There was some residual Cs radioactivity in the scar tissues from radiation burns. Patient No. 3 showed high values of $K\alpha$ and $K\beta$. All patients showed some values of $K\alpha$ and $K\beta$ except patients No. 5 and 6. In whole body counting patient No. 10 showed no radioactivity.

Discussion

Dr Abrahamson, Vice Chairman of RERF, asked about the counter to check people. The speaker explained that they developed a unit of movable whole body counter to check internal contamination in the fields.

Dr Jammet commented that, according to the classical knowledge, Cs goes all over the body but it accumulates in liver. He asked whether or not quantitative measurements were performed and whether there was any damage in liver. Dr Oliveira answered that there was no phantom to calibrate the dose. Therefore, quantitative measurements were not possible. One patient showed some liver damage three years after the accident and it persisted even now. But he was also a heavy drinker.

4. Dr K. Mabuchi, RERF: Long-term follow-up of atomic bomb survivors in Hiroshima and Nagasaki

Dr Mabuchi talked about what they have learned from the ABCC/RERF studies for the last 50 years. In the life span study 86,572 survivors are registered. Among them 36,572 were exposed below 0.005 Sv and 50,113 were above 0.005 Sv. Currently 50% of them are alive. In 1950 roughly half of survivors who met the conditions within 2.5 km area were registered. Age/sex matched survivors within the area 2.5 to 10 km were also registered. The dose estimate is available in 90% of these registrants.

Cancer incidence statistics since 1958 using Hiroshima and Nagasaki tumour registries are available. The total observed solid cancer cases were 7,578 among 86,572 registrants. The corresponding number of the expected cases is 7,243. Therefore, the excess was 335. Vital statistics according to the age at exposure are available. Solid cancer excess relative risk is fairly constant among exposed age groups of thirties and fifties but those who were exposed in very young ages (teenagers) have a higher relative risk. The risk decreases with time and the excess relative risk comes close to that of higher age groups. Leukemia excess deaths were 86. Cancer incidence excess relative risk is constant among organs. Because the advance in cancer treatments affect the cancer death rate, cancer incidence provides more precise data.

2,800 prenatally exposed survivors were also followed up, but showed no significant increase in the risk compared with their controls, except microcephaly. 77,000 were registered in the F₁ mortality study group. They showed no significant increase in the mortality compared with the control group.

Discussion

Dr Jammet congratulated Dr Mabuchi on his work in cleaning up the complex data. He then asked about the risk in non-malignancy. Dr Mabuchi explained that there were some increase in cardiovascular mortality and incidences of chronic liver diseases and some benign tumours such as myomas and parathyroid tumours.

The texts of the above four presentations will be found in Annex IV.

Concluding session (Moderator: Dr J. Skvarca)

Concluding Presentation

Dr W. Kreisel, WHO: WHO/REMPAN - Its perspectives

REMPAN shall be the well coordinated network of relevant national institutions within the field of radiation emergency medical preparedness and assistance. For this purpose the following should be pursued.

1. To complete designation of national institutions which are in China, India and Russia.
2. To set up E-mail communication among the members.
3. Development of an international database on radiation protectors, on the signs and symptoms of acute radiation sickness, on diagnostic method and treatment of acute and chronic radiation sickness and on teams of specialists.
4. Development of diagnostic and treatment kits with emphasis on the first aids in the nuclear accident.
5. To prepare updated guidelines on medical preparedness for accidents.
6. To support researches.
7. To prepare and disseminate information for the public.
8. To produce training materials
9. To organize training courses.
10. To organize and conduct REMPAN meetings every 2-3 years.

On the basis of the above, he urged to prepare a work plan for the next five years. In order to implement this five year work plan, the following budget would be required:

1.	personnel for network maintenance	US\$50,000
2.	consultants	80,000
3.	meetings	40,000
4.	printing and translation	50,000
5.	training course	60,000
6.	regional or international exercises	20,000
7.	coordination and management	25,000

The first year requires a total budget of \$325,000. For five years the total budget of \$1,500,000 will be required. To raise the necessary funds, the contribution from industries is to be anticipated.

Discussion

On behalf of the participants, Dr Skvarca expressed his gratitude to Dr Hasegawa and other Japanese hosts and then opened discussion.

Dr Jammet stressed the importance of preparing a reference book for physicians. Dr Densow supported Dr Jammet's comment and proposed that he and his institute can be a candidate to promote the work.

Dr Skvarca commented about the next meeting site and stated that the Brazilian Collaborating Centre is prepared to host the next REMPAN meeting. The next meeting will be held in October 1997.

Dr Souchkevitch commented on the scenario of the REMPAN meeting which is to be evolved in process of time. He also commented on the need of support for developing countries. He also said that since psychological impacts are important, he would like to propose to invite to the next meeting in Brazil those who have experience in that aspect.

Dr Kreisel commented on upgrading this meeting.

Closing session

Dr Hasegawa made closing remarks thanking the participants for their invaluable contributions to the meeting and stating that there were many informative presentations in this meeting which made the meeting extremely successful. To further develop REMPAN, however, more efforts would be required including the aspect of the fund raising. WHO asked the Japanese Collaborating Centre at RERF to assist them in preparing the final report. Therefore, he asked the participants to cooperate with him in that work.

Dr Kreisel thanked Drs Shigematsu and Hasegawa for the perfectly organized meeting.

CONCLUDING PRESENTATION

WHO/REMPAN - ITS PERSPECTIVES

Wilfried Kreisel
Executive Director
World Health Organization

GOAL

**THE ESTABLISHMENT OF A WELL-
COORDINATED, FULLY FUNCTIONAL NETWORK
OF RELEVANT NATIONAL INSTITUTIONS WITHIN
THE FIELD OF RADIATION EMERGENCY
MEDICAL PREPAREDNESS AND ASSISTANCE**

ACTIVITIES

1. COMPLETE DESIGNATION OF NATIONAL INSTITUTIONS IN CHINA, INDIA AND RUSSIAN FEDERATION (INSTITUTE OF BIOPHYSICS AS WHO COLLABORATING CENTRES IN REMPAN)
2. SET-UP E-MAIL COMMUNICATION BETWEEN NETWORK MEMBERS
3. DEVELOP INTERNATIONAL DATA BASE ON:
 - RADIOPROTECTORS
 - SIGN AND SYMPTOMS OF RADIATION INJURIES
 - DIAGNOSTIC METHODS AND TREATMENT OF ACUTE AND CHRONIC RADIATION SICKNESS
 - TEAMS OF SPECIALTIES
4. DEVELOPMENT OF DIAGNOSTIC AND TREATMENT KITS WITH EMPHASIS ON FIRST AID TO NUCLEAR ACCIDENT VICTIMS
5. PREPARE UPDATED GUIDELINES ON MEDICAL PREPAREDNESS FOR ACCIDENTS TAKING INTO ACCOUNT DIFFERENT GROUPS OF COUNTRIES ACCORDING TO:
 - AVAILABLE TYPES OF NUCLEAR INSTALLATIONS IN A COUNTRY (NPPs or RADIOACTIVE INSTALLATIONS ONLY WHICH ARE USED IN MEDICINE, INDUSTRY, ETC.)
 - SIZE OF A COUNTRY (SMALL, LARGE)
 - DISTANCE FROM COUNTRIES WITH NPPs (NEAR-FIELD, FAR FIELD)

ACTIVITIES (Cont'd)

- 6. SUPPORT RESEARCH INVESTIGATIONS**
- 7. PREPARE AND DISSEMINATE INFORMATION FOR THE PUBLIC ON RADIATION HEALTH EFFECTS AND ACHIEVEMENTS IN TREATMENT OF RADIOLOGICAL CONSEQUENCES**
- 8. PREPARE TRAINING MATERIAL FOR SPECIALISTS, GENERAL PRACTITIONERS AND NURSES**
- 9. ORGANIZE AND CONDUCT TRAINING COURSES/WORKSHOPS**
- 10. ORGANIZE AND CONDUCT REMPAN MEETINGS EVERY TWO-THREE YEARS**

OUTPUT (PRODUCTS)

1. **UPDATED GUIDELINES**
2. **TRAINING MATERIALS**
3. **RECOMMENDATIONS FOR NATIONAL HEALTH AUTHORITIES**
4. **INTERNATIONAL DATA BASES**
5. **RECOMMENDATIONS ON THE DEVELOPMENT OF DIAGNOSTIC AND TREATMENT
KITS**
6. **IMPROVEMENT OF NATIONAL MEDICAL CAPACITY THROUGH TRAINING AND
ORGANIZING INTERNATIONAL EXERCISES OF MEDICAL STAFF**
7. **RE-EXAMINED PLANS FOR RADIATION EMERGENCY MEDICAL PREPAREDNESS**
8. **BROCHURES AND INFORMATION MATERIALS FOR THE PUBLIC**

WORKPLAN

- 1. DEVELOPMENT OF THE DETAILED PLAN OF ACTIVITIES FOR A PERIOD OF 5 YEARS**
- 2. IDENTIFICATION CONTRACTORS CONSULTANTS TO DRAFT GUIDELINES, REVIEWS, APPROVAL, PUBLICATION AND TRANSLATION (WHO OFFICIAL LANGUAGES) OF GUIDELINE**
- 3. DEVELOPMENT OF THE METHODOLOGY FOR INTERNATIONAL AND REGIONAL EXERCISES**
- 4. ANNUAL REGIONAL EXERCISES AND ONCE PER 5 YEARS INTERNATIONAL EXERCISE**
- 5. PREPARATION OF TRAINING PACKAGES**
- 6. CONDUCT INTERNATIONAL TRAINING COURSES**
- 7. PREPARATION AND PUBLICATION MATERIALS FOR THE PUBLIC**
- 8. ORGANIZATION OF TWO REMPAN MEETINGS**

BUDGET REQUIRED (MINIMUM)

	US\$/YEAR
1. PERSONNEL FOR NETWORK MAINTENANCE	50,000
2. CONSULTANTS	80,000
3. MEETING	40,000
4. PRINTING, TRANSLATION	50,000
5. TRAINING COURSE	60,000
6. REGIONAL OR INTERNATIONAL EXERCISES	20,000
7. COORDINATION AND MANAGEMENT	25,000
<hr/>	
TOTAL FIRST YEAR BUDGET	\$325,000
TOTAL FIVE YEAR BUDGET	\$1,500,000

Closing Remarks

Yutaka Hasegawa
Director
WHO Collaborating Centre
for Radiation Effects on Humans
and Permanent Director, Radiation
Effects Research Foundation

Ladies and Gentlemen, now it's the time for closing the meeting.

Thank you very much for the excellent and informative reports and lively discussions which have lasted for these three days and which, I firmly believe, have made this meeting extremely successful.

We have no doubt that the best to do is to prevent any radiological and nuclear accidents. However, as Dr Kreisel indicated, the complete prevention may be impossible and some more accidents may happen in the future.

We therefore have to prepare for such unfortunate events and incidents. Thanks to the WHO's REMPAN programme, the world-wide systematic approach has been developing to deal with such events.

It is obvious, however, that we need to do more.

I do hope that, with the concerted efforts of WHO, WHO collaborating centres and experts involved in the REMPAN, this programme will become much more capable to cope with any radiation accidents in the near future.

As the WHO Collaborating Centre that hosted this meeting, we have been asked by WHO to prepare the report of this meeting. We will do our best, and in the process of the finalization of the report we may contact you for further information on your presentations and additional materials. I would appreciate your cooperation in our work.

I thank you all for coming to Hiroshima in spite of your tight schedule.

I wish you a safe and pleasant journey back to your home country and your home town. I hope to see you again in the near future.

Good-bye!