The Medical Basis for Radiation-Accident Preparedness: Medical Management

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Chapter 1
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Joseph J. Krol, Jr.

Chapter 2
International Framework for Emergency Preparedness and Response to Radiation Emergencies
R. Martincic, E. Buglova, and F. Baciu

Abstract
The impact of any nuclear or radiological emergency with off-site consequences rapidly becomes of regional and global concern. The need for prompt international notification, information exchange, and cooperation (as well as international assistance in cases when the capabilities of a country Might be exceeded) calls for an international focal point and coordination mechanism. In addition, effective emergency response requires an appropriate international framework and efficient national emergency management systems that are built on international standards and guidelines. The International Atomic Energy Agency plays a central role in facilitating these requirements.

Chapter 3
Medical Management of the Consequences of the Fukushima Nuclear Power Plant Incident
Makoto Akashi, Takako Tominaga, and Misao Hachiya

Abstract
The Great East-Japan Earthquake measuring 9.0 magnitude on the Richter magnitude scale struck the northeast coast of Honshu Island of Japan at 14:46 on March 11, 2011, triggering a tsunami with more than 10-m-high waves hitting the area. The earthquake was followed by sustained numerous aftershocks. The earthquake and aftershocks left 15,861 people dead and 3,018 missing (as of June 6, 2012). The earthquake affected the Fukushima nuclear power plants (NPPs) of Tokyo Electric Power Company, causing serious damage to the NPPs and resulting in large amounts of radioactive materials being released into the environment. Damage was caused to the cooling systems of the NPPs, although they automatically shut down after the earthquake. The trouble with the cooling systems led to core meltdown and hydrogen explosions. The major nuclides released on land were iodine-131, cesium-134, and cesium-137. The deposition of these radioactive materials on land resulted in an elevated ambient dose of radiation around the NPPs, especially within a 20-km radius. Therefore, almost 170,000 people had to be evacuated or stay indoors. Besides affecting the NPPs and the telecommunication system, the earthquake also affected infrastructure, such as the monitoring system for radiation.

The National Institute of Radiological Sciences dispatched its Radiation Emergency Medical Assistance Team to the local command center (which was located 5 km from the NPPs) 17.5 h after the earthquake. However, the local command center was not functional because community lifelines, such as the water supply and electricity, were severely damaged by the earthquake and tsunami. Therefore, even simple countermeasures for decontamination, such as removing clothes and wiping the skin with wet towels, could not be performed by evacuees at the shelters. Furthermore, the local hospital system, including that for radiationemergency medicine, was adversely affected. Hospitals that had been designated as radiation-emergency facilities were not able to function because of earthquake and tsunami damage and because they were also located in the evacuation areas. Local fire department personnel were also asked to evacuate. Their lack of knowledge prevented these personnel from being able to transport contaminated workers from the NPPs. In addition, hospitals not designated as radiation-emergency facilities would not receive patients from the NPPs because of their concerns about the health effects of radiation. In this respect, it was fortunate that no workers from the NPPs or residents around the site required treatment for radiation exposure. We have learned from this disaster that basic knowledge of radiation and its effects is extremely important for health care providers and that the potential for damage to lifelines as well as the monitoring systems for radiation by an earthquake requires intense focus and vigilance. There is an urgent need for a "combined disaster" strategy, which should be emphasized for current disaster planning and response.

Chapter 4

Recommended Approach for Use of Multi-Parameter Biodosimetry

William F. Blakely

Abstract

The need to rapidly assess radiation injury in mass-casualty and population-monitoring Scenarios has prompted an evaluation of (1) suitable biomarkers that can provide early diagnostic information after radiation exposure and (2) effective prioritization processes. We advocate use of a multiple-parameter-bioassay approach based on molecular, hematological, and cytological biomarkers that are rapid and scalable for high-throughput analysis. These biomarkers need to be validated in suitable radiation-model systems. Our approach is based on research studies using ex vivo human blood, murine, and rhesus macaque (Macaca mulatta) in vivo radiation models as well as experience from recent management of human-radiation accidents. Herein, we highlight our research results as applied to the development of a strategy to prioritize the selection of suspected radiation casualties for cytogenetic chromosome-aberration dose assessment. In addition, insights on a strategic approach to fill the critical biodosimetry gap will be discussed.

Chapter 5

Evidence-Based Recommendations for Clinical Management of Radiation-Associated Injury to the Bone Marrow

Nicholas Dainiak and Nicolas Gent

Abstract

Diverse clinical practices have been used to manage individuals with acute injury to the hematopoietic system from ionizing radiation. To assess these practices, a panel of experts was convened in Geneva by the World Health Organization. The panel ranked the evidence for medical countermeasures for management

of hematopoietic syndrome (HS). English-language articles were identified in MEDLINE and PUBMED. Studies included case series and case reports of acute radiation syndrome, randomized controlled trials (RCTs) of relevant interventions used to treat nonirradiated individuals, reports of well-controlled studies in irradiated animals, and prior recommendations of subject-matter experts. Studies were extracted with the Grading of Recommendations Assessment Development and Evaluation (GRADE) system. In cases where data were limited or incomplete, a narrative review of the observations was made. The panel assessed the quality of evidence and classified recommendations as strong or weak. No RCTs of medical countermeasures have been completed for individuals with HS. The use of GRADE analysis of countermeasures for injury of hematopoietic tissue was restricted by the lack of comparator groups in humans. Based upon (1) GRADE analysis and narrative review of survival among individuals with HS who were treated with various countermeasures, as published in descriptive case series and case reports; (2) the recommended clinical use of these countermeasures to treat patients who are not irradiated; (3) observations in controlled irradiated animal experiments that were designed to assess the efficacy of these countermeasures; and (4) recommendations of prior expert panels, a strong recommendation was made for administration of granulocyte colony-stimulating factor or granulocyte macrophage colony-stimulating factor, and a weak recommendation was made for the use of erythropoiesis-stimulating agents or hematopoietic stem cell transplantation.

Chapter 6

Electron Spin Resonance in the Diagnosis of Acute Radiation Syndrome: The State of the Art

A. Romanyukha, R.A. Reyes, F. Trompier

Abstract

Electron spin resonance (ESR) is one of a very few techniques capable of directly measuring free radicals induced by radiation. Generation of free radicals is a primary effect of radiation exposure that occurs immediately upon ionization. It is not affected by stress, wounds, burns, or medical treatment. These circumstances give ESR a unique role in advanced diagnosis of acute radiation syndrome at the time when clinical symptoms (such as nausea, vomiting, and diarrhea) have not yet occurred. Two types of tissue are known to be good sources for detection of ionizing radiation exposure by ESR: calcified (teeth and bones) and keratin-based (nails and hairs) tissues. Tooth enamel has the best ESR dosimetric properties because of the high stability of the radiation-induced radicals. During the past decade, ESR dosimetry in teeth has made considerable progress towards becoming a routine dosimetric method. Further, recent instrument developments have made it possible to do in vivo ESR dose measurements in teeth. ESR in fingernails, toenails, and hair is less developed but promises much easier sampling and simplified equipment for dose measurements. Principles, advantages, drawbacks, and examples of applications of ESR dosimetry are presented and discussed.

Chapter 7

SAMÖ2011—A Major Nuclear Power Plant Emergency Exercise with Tragic Relevance

Leif Stenke

Abstract

The emergency exercise SAMÖ-KKÖ 2011 is a current example of how society's capacity for dealing with a multitude of consequences of a serious nuclear power plant emergency can be exercised and assessed. This Swedish exercise, involving more than 6000 persons from more than 60 national and international

organizations at all levels of society, was conducted in three phases between February and April 2011, with a follow-up and evaluation at the end of 2011. The simulated scenario started with an emergency, including a fire, at a nuclear power plant in the southeast of Sweden, resulting in disruption of services and fallout of radioisotopes. The short-term and long-term consequences of the simulated emergency were extensive, with large parts of society being affected, including many critical infrastructure services. Simulated medical issues involved decisions on prophylactic iodine intake, evacuation of large groups of the population, and the medical management of three firemen exposed to ionizing radiation and developing signs of the acute radiation syndrome. Lessons learned from SAMÖ2011 involved a strengthened awareness of the need for regular exercises and international preparedness collaboration. The relevance of this Swedish exercise was drastically underlined within a month of its initiation by the tragic earthquake, subsequent tsunami, and power plant emergency in Fukushima, Japan, in March 2011.

Chapter 8
Recollections: The Accident at Three Mile Island, Unit II
Harold Denton

Chapter 9
Overview of Methods for Establishing Dose to Individuals for Managing Large-Scale, Unplanned, Clinically Significant Exposures to Ionizing Radiation
Harold M. Swartz, Ann Barry Flood, Benjamin B. Williams, Roberto J. Nicolalde, and Alla Shapiro

Abstract
Following an exposure of large numbers of individuals to levels of ionizing radiation that could potentially lead to acute radiation syndrome (ARS), it is essential to have a means to identify those individuals who would benefit from being brought into the medical-care system and to guide medical care. Analyses of the existing guidelines for responses to such events indicate that these guidelines are unlikely to achieve the needed differentiation. The solution to the problem will require both (1) a better understanding of the existing data from exposures of human subjects to ionizing radiation and (2) the development of new methods to establish absorbed dose at the level of the individual under the circumstances associated with a large-scale radiation exposure event. Emerging biodosimetric methods can fill this critically important niche in response to unplanned exposures to radiation involving large numbers of people because they can provide essential after-the-fact information on individual doses.

There are two related but different functions in the response plans where accurate and timely estimates of acute exposures are needed: (1) for initial point-of-care screening of the large population at risk of having received clinically significant radiation exposure, to enable the response system to cope effectively and efficiently in deciding whether to triage them into or out of immediate medical care for ARS and (2) after initial entry into the medical-care system, to facilitate decisions about clinical management of individual patients with significant risk for ARS. To perform the first function, measurements need only to be sufficiently accurate to achieve appropriate triage decisions for each individual. Biodosimetry, which estimates dose to an individual based on physical changes reflecting the amount of radiation absorbed and/or biological consequences of such exposure, is likely to play a key role for performing both functions, but this paper is focused particularly on the first.

There are two basic types of biodosimetry with different and often complementary characteristics: those based on changes in biological parameters, such as gene activation or chromosomal abnormalities, and

those based on physical changes in tissues [detected by techniques like electron paramagnetic resonance (EPR) or luminescence]. The advantages of biologically based parameters are their potential sensitivity for assessing an individual's dose and their potential to predict the biological consequences of the absorbed dose. Disadvantages include that they may vary over time and among individuals; that they require biological processing before changes can be observed; and that they may be affected by prior physiological and pathophysiological states and perturbations, including those that are likely to be associated with an acute event, such as stress, wounds, and burns. Physically based biodosimetric methods, because they do not assess biological responses, are not subject to these limitations. Because the physical changes occur virtually simultaneously with the exposure, these changes can be assessed at any time after the event. Results based on EPR use non- or minimally invasive sampling techniques, and dose estimates potentially are available within 5 min of the start of measurement. However, physically based dose estimates do not reflect the individual's actual biological responses. They therefore cannot fully predict the implications of exposure, which are most important for the second function (i.e., determining what medical management is needed).

Biodosimetry methods in general should also be useful for a third function: identifying individuals with lower doses who may not need immediate care but who should be followed for evidence of long-term consequences.

Session Two: Advances in the Diagnosis and Management of Acute Radiation Syndrome, Cutaneous Radiation Syndrome, and Acute Local Radiation Injuries

Daniel Flynn

Chapter 10

Diagnosis and Management of Cutaneous Radiation Syndrome and Local Radiation Injuries

Viktor Meineke

Abstract

Cutaneous radiation syndrome (CRS) is among the earliest clinical signs and symptoms of high-dose accidental radiation exposure in the event of whole-body or significant partial-body exposure, such as in a nuclear scenario. CRS therefore plays an important role both as an early indicator of exposure and as a prognostic indicator of the development of radiation-induced multi-organ interactions and multi-organ failure. Current understanding of the contribution of CRS to the pathophysiology of whole-body radiation reactions is more and more a systemic perspective. This view has a tremendous impact on CRS management. Local radiation injuries (LRIs) are a common denominator in many accidental radiationexposure incidents in industry, such as unintentional exposure to orphaned radiation sources. Time courses of development depend on exposure conditions, mode, degree, and clinical pictures of tissue damage that are different from CRS after high-dose and wholebody exposure. Systemic inflammatory reactions at the tissue and organ levels are the link between CRS and LRI. Therapeutic strategies must consider similarities and differences between the management of more-local vs. systemic skin reactions after accidental radiation exposure. The current and up-to-date standards of diagnosis and management are reviewed.

Chapter 11

Mesenchymal Stem Cell Therapy in Local Radiation Injuries: A Japanese Approach

Sadanori Akita, Hiroshi Yoshimoto, Kozo Akino, Akira Ohtsuru, Kenji Hayashida, Akiyoshi Hirano, Keiji Suzuki, and Shunichi Yamashita

Abstract

Local radiation injury can lead to fatal injuries when vital organs and tissues are involved. Sometimes it takes a very unfavorable clinical course, such as intractable and prolonged wounds. There is clinical evidence that the local somatic stem cells are expressed adjacent to the wounds even in local radiation wounds. Such cells are resistant to radiation and may contribute to subsequent tissue repair and regeneration. Stem cells are used for treatment of local wounds, and implanted cells proliferate and maintain their capacity to differentiate into needed cells and tissues. Among such somatic stem cells, adipose-derived regenerative cells (ADRCs) or adipose-derived stem cells (ADSCs) are expected to be a cell source because the donor-site morbidity is minimal. That is the widely accepted expectation in plastic and aesthetic surgical procedures like liposuction, and minimal morbidity results in very fast and easy cell processing in a closed circuit in a clinical setting. The ADRC/ADSC demonstrates at least similar cell-surface antigen expressions to those of well-studied bone-marrow-derived stem cells with high cell proliferation and differentiation capacity towards multiple lineages (such as bone, cartilage, blood vessel, neuron, muscle, liver, epithelium, and fat). Nagasaki University was selected as a global strategic center for radiation health risk control by the Japan Ministry of Education, Culture, Sports, and Technology from FY 2007 to 2011. It has been exploring therapeutic regimens to prevent radiation injuries and potential medical and surgical therapies for regenerating radiation-injured tissue by using patients' own ADRCs.

From December 2008 to June 2011, 11 consecutive clinical studies were conducted to treat chronic local radiation injuries in patients aged 47 to 89 years (63.9 ± 14.2 years) more than 30 years after sequentially fractionated radiation doses of more than 50 Gy that produced radiation-induced wounds and contracture. Treatment with ADRC/ADSC renitiated regenerative wound healing and local tissue regeneration, including regeneration in tendon, bone, fat, muscle, and skin. Seven of the 11 cases had wounds, and all cases regenerated and healed within 2 to 10 weeks (6.6 ± 3.2). No recurrence was observed in the follow-ups that extended postoperatively to 2 years, 10 months. In addition, there was no continued abnormal wound healing or regeneration. We therefore recommend this easy and safe method as the first choice of therapy for intractable radiation-induced local injuries.

Chapter 12

Ultrasound and Thermography for Diagnosis of the Extent and Magnitude of Acute Local Radiation Injury

Ronald E. Goans, Carol J. Iddins, and Doran M. Christensen

Abstract

Local radiation injury (LRI) is difficult to diagnose early, both in severity and extent, because of the prolonged time for the development of clinical signs and symptoms. A 12-MHz linear-array ultrasound transducer has been used clinically at the Radiation Emergency Assistance Center/Training Site (REAC/TS) in conjunction with a thermography system capable of imaging skin lesions in the 6- to 14-μm infrared spectrum. This combination of techniques has enabled early detection of subcutaneous pathologic changes not visible clinically. Three current REAC/TS-patient histories are presented, along with animal studies undertaken in both Yorkshire pigs and Wistar rats, in an attempt to elucidate basic science issues associated with LRI.

Chapter 13

Regenerative Medicine for the Medical Management of Local Radiation Injury: From Bench to Bedside

M. Benderitter, R. Tamarat, M. Prat, A. Chapel, J.F. Bottoliers-Depois, J.J. Lataillade, and E. Bey

Abstract

From 2003 to 2007, the Institut de Radioprotection et de Sûreté Nucléaire (IRSN) published the preclinical proof of concept of the therapeutic benefit of mesenchymal stem cell (MSC) injections for the treatment of severe radiological injuries. IRSN together with the Centre de Transfusion Sanguine des Armées and the Percy Military Hospital made the clinical transfer of this innovative medical treatment for the first time to two patients in 2007. At this point, seven patients exhibiting severe radiological burns weeks to months postirradiation have been treated in France. All these patients received radiation doses higher than 25 Gy, which is considered the lower threshold for skin and underlying muscle necrosis. These patients came from different countries, mainly from South America and Africa, as the result of requests to the International Atomic Energy Agency for medical assistance after radiological accidents. MSC therapy was given to the patients after dosimetry-guided surgery to resolve established tissue necrosis. This clinical application was legally authorized by the Agence Française de Sécurité Sanitaire des Produits deSanté as a compassionate treatment. Patients were injected with autologuous MSCs and received repetitive local injections. The clinical follow-up of these patients shows at least a rapid disappearance of pain after MSC injection; a beneficial and significant wound healing of musculo-cutaneous radiation-induced lesions; and a reduction of the inflammatory-necrotic recurrences, which are frequently observed after radiation injories. To date, no longterm side effects have been observed with these patients. Regenerative therapy for radiation disease is in an important phase. Breaking down the traditional barriers among individual areas of specialization will be challenging but necessary if we are to move beyond stem cell biology toward the development of truly beneficial regenerative therapy for severe radio-induced sequelae. To foster this multidisciplinary collaboration, effort is needed to bring academic science in close contact with clinicians.

Chapter 14

Evidenced-Based Support for the Treatment of a Potentially Lethal Hematopoietic Acute Radiation Subsyndrome

Thomas J. MacVittie and Ann M. Farese

Abstract

Medical countermeasures (MCMs) against current radiological and nuclear threats are an urgent requirement to protect a vulnerable America. This matter of national security was addressed by the National Biodefense Science Board (NBSB) at the request of the Health and Human Services Assistant Secretary for Preparedness and Response. The NBSB, a federal advisory committee authorized in December 2006, provided a review (NBSB 2010) of the Public Health Emergency Medical Countermeasure Enterprise (PHEMCE). This review, entitled *Where Are the Countermeasures?* Protecting America's Health from CBRN Threats, provided an unbiased account of MCM development within the PHEMCE for chemical, biological, radiological, and nuclear (CBRN) agents (NBSB 2010). The successful development and (U.S.) Food and Drug Administration (FDA) approval are still being sought for the initial MCMs to treat potentially lethally irradiated personnel from either subsyndrome within acute radiation syndrome (ARS) or the delayed effects of acute radiation exposure. There are no FDA-approved MCMs against the hematopoietic or gastrointestinal (GI) subsyndromes or lung injury, a noted delayed effect of acute radiation exposure. The MCMs closest to FDA approval are those approved for other indications related to chemotherapy-induced myelosuppression [e.g., granulocyte colony-stimulating factor (G-CSF), granulocyte/macrophage colony stimulating factor (GM-CSF), and polyethylene glycol granulocyte colony-stimulating factor (peg-G-CSF)].

Chapter 15
Practical Medical Applications of Dose Magnitude Estimation
Stephen L. Sugarman and Richard E. Toohey

Abstract
In the event of a radiation incident, it is essential that medical-care providers are able to obtain a quick estimate of the radiation dose that a patient may, or may not, have received so that proper treatment can be planned. The information needs to be easily obtained and able to provide a realistic potential of dose magnitude. Various techniques can be employed to help gather the necessary information. Evaluation of nasal swabs and wound counts can help ascertain the potential for significant intakes of radioactive materials, and mathematical dose estimations can help determine the potential magnitude of external doses. With a good incident history and other data, health physicists and physicians can develop a strategy for providing proper medical care to individuals who may have been involved in a radiological incident.

Session Three: Advances in Assessment and Management of Internal Contamination
Volker List

Chapter 16
The French Armed Forces Health Service and the Medical Management of Plutonium-Contaminated Patients
Jean-Christophe Amabile, Sandra Bohand, Alain Cazoulat, Xavier Michel, Gérald Gagna, Daniel Schoulz, and Pierre Laroche

Abstract
The medical management of a plutonium-contaminated patient could be necessary in the case of a nuclear weapon incident, a civilian work accident in a specialized (i.e., nuclear) facility, or a terrorist attack. These kinds of situations require a special method of organization to deal with numerous victims and special institutional structures like the Center for the Treatment of Radio-Contaminated Wounded (CTBRC). The French Defense Radiation Protection Service (SPRA) is located on the site of the Percy Military Hospital, which is well known for the treatment of radiological contamination and irradiation injuries. SPRA oversees all of the CTBRC in France. During exercises conducted by the French Navy or Air Force, the SPRA provides hygiene and safety support to the Ministry of Defense; advises headquarters; plays the role of arbitrator; and can deploy, by road or air, an expert team and an analysis team with mobile laboratories for radiochemical analysis. The SPRA is also involved in numerous military and civilian training courses coordinated by the French Armed Forces Health Service to teach the principles of medical response to a radiological incident and especially the efficacy of drugs like calcium-diethylene triamine pentaacetic acid. The French Armed Forces Health Service (SSA) fulfils missions mainly for the benefit of the armed forces and, if necessary, for the national public health system. The "operational contract" with the military defines the necessary health support of the armed forces regardless of the location and circumstances, including those related to chemical, biological, radiological, and nuclear (CBRN) risks.

Chapter 17
The French Armed Forces Health Service and the Surgical Management of a Plutonium-Contaminated Patient at Percy Military Hospital, France, 2010
Pierre Laroche, Alain Cazoulat, Sandra Bohand, Virginia Schoen, Eric Bey, Henri Roche, Benoit Quesne, and Jean-Christophe Amabile

Abstract

In February 2010, a technician was contaminated with plutonium during a maintenance operation inside a glovebox. The worker presented with a right forearm wound produced by significant compression of the muscle mass when his arm was caught in a drive belt. This work accident was immediately treated by the Occupational Medicine Service of the facility for external and internal decontamination. The worker was then sent to the Percy Military Hospital (Clamart, France) for a moderate-compartment syndrome associated with radiological contamination of the wound. This case was managed by the emergency unit crew in charge of the Center for the Treatment of Radio-Contaminated Wounded of Percy Hospital with technical support from three experts of the French Defense Radiation Protection Service (SPRA) located at the same site. After repeat radiological evaluation and a repeat clinical examination, a second decontamination process was undertaken. As a consequence of increasing pain, paresthesia, and a decrease in grip strength, the patient was admitted to a special operating room at the Percy Hospital. An indication for a fasciotomy was confirmed, and the decision to excise the surface of the skin, which had fixed contamination, was taken after a briefing between the surgical team and the SPRA. This surgical technique used a dermatome guided by mapping of the surgical area with a radiation probe in real time, leading to complete decontamination of the patient.

Chapter 18

Some Lessons Learned from the Analysis of Severe Internal-Contamination Accidents (with Suggestions on New Methods for Risk Evaluation, Mitigation, and Prevention of Lethal Radiotoxicity)

Albert L. Wiley

Abstract

The clinical effects of internal contamination from radionuclides are generally classified into stochastic (primarily related to cancer risk) and deterministic effects. While some stochastic risk is present from any internal contamination, deterministic risks are typically of the most urgent clinical concern following high levels of internal contamination. In rare instances, internal contamination may even cause various aspects of acute radiation syndrome with associated life-threatening effects. This paper is a brief review and update on the medical management of internal contamination, followed by a brief discussion of all the known lethal outcomes that have been reported from various types of internal-contamination incidents. Some new tools for internal dose and risk assessment, as well as for mitigating and prevention of organ-specific radiotoxicity from severe internal contamination, are also discussed. It was also of interest to ask, "In the light of current knowledge, if similar incidents were to occur in the future, could severe organ damage from internal radionuclide contamination be better evaluated and treated and could potential fatalities now be averted?" So, for discussion purposes, this question was also considered in an analysis of the Radiation Emergency Assistance Center/Training Site Registry of the known and reported lethal internal-contamination incidents.

Chapter 19

The Goiânia Accident (Brazil, 1987, ^{137}Cs): Internal-Dosimetry Aspects

Luiz Bertelli, Dunstana R. Melo, and Carlos A.N. Oliveira

Abstract

The Goiânia incident occurred in September 1987, resulting in internal/external contamination and significant irradiation of several people from a wide range of age groups. In vitro (feces and urine) and in vivo (whole body counting) bioassay measurements were used to monitor contaminated people and to estimate the efficacy of the internal decontamination by Prussian blue, which proved effective when administered above a certain threshold dose. This paper covers the setup of the laboratories, bioassay measurements, and dose assessment for members of the public and for occupationally exposed personnel. It also assesses the efficacy of the Prussian blue administration.

Session Four: Radiation Accidents of Interest: An Overview

Marina Vazquez and Marina Di Giorgio

Chapter 20

Lessons from the Goiânia Radiation Accident

Nelson Valverde

Abstract

On September 13, 1987, in Goiânia, the capital of the State of Goiás in central Brazil, two scavengers removed the head of a radiotherapy device containing a 50.9-TBq cesium-137 source that had been left in an abandoned clinic. Because the source was broken open and sold to a junkyard, many persons were externally irradiated, incurred external and internal contamination, and suffered associated radiological injuries and illnesses. Sixteen days elapsed from the source violation to the recognition of the accident's nature. A pivotal cause of that delay was that local physicians did not recognize the clinical manifestations of the victims as radiation-induced. Twenty persons were hospitalized in Goiânia and Rio de Janeiro, and four died of acute radiation syndrome (ARS). The Goiânia accident was the first opportunity for large-scale use of Prussian blue for radiocesium decorporation and for the use of a bone-marrow growth factor, granulocyte-macrophage colony stimulating factor, in patients with ARS. This experience opened the way for the indication of this drug on a much more rational basis in other radiation accidents. The city cleanup resulted in 3500 m3 of waste, which was initially accommodated in a temporary disposal site and later at a permanent, dedicated site. Even today, victims of the accident are followed up in Goiânia for long-term effects of radiation exposure, but so far no association has been established between exposures at the time of the accident and present medical conditions of the cohort. The Goiânia accident continues to be of relevance because of its magnitude, impacts, and lessons. It also serves as an excellent model for the possible consequences of a malevolent act with radioactive materials.

Chapter 21

The Use of Biological Indicators in the Evaluation of Radiation Injury in Selected Cases: The Dakar (Senegal) and Fleurus (Belgium) Radiation Accidents

Jean-Marc Bertho, Maâmar Souidi, Marc Benderitter, and Patrick Gourmelon

Abstract

The evaluation of radiation-induced damage to vital physiological systems after an accidental irradiation remains difficult, mainly because of unknown radiation conditions: dose, dose rate, and geometry of exposure. Physical dose reconstruction, biological dosimetry with cytogenetic chromosome aberrations, and clinical symptoms are sometimes insufficient in proposing a robust diagnosis and/or prognosis. Thus, the use of biological indicators of radiation damage to specific physiological systems may be useful in delineating the extent and severity of the radiation-induced damage and may help in defining a therapeutic

strategy. We have used such biological indicators to evaluate and follow the evolution of radiation-induced damage in three victims, one from the Fleurus accident (Belgium, March 2006) and two from the Dakar accident (Senegal, July 2006). These three victims received a mean whole-body equivalent radiation dose of 4.5 Gy, 2.3 Gy, and 1.6 Gy, respectively, on the basis of cytogenetic chromosome aberrations. The Flt3-ligand concentration was used to assess the hematopoietic system. Citrulline concentration was used as a biological indicator of damage to the digestive tract. Several oxysterols were measured as hepatic and vascular markers. The Flt3-ligand measurement indicated the occurrence of a hematopoietic syndrome in two of these patients, and the citrulline concentration showed an absence of severe gastrointestinal damage. Oxysterol measurements indicated subclinical damage to the liver and cardiovascular system. These results were correlated with classical biochemical markers, confirming the interest in these new predictive biological indicators. Overall, followup of these three patients demonstrated the value of a multiparametric approach in the evaluation of radiation-induced damage, especially in complex accidental irradiation situations.

Chapter 22

The Accident at Tokai-mura, Japan (1999): Managing the Psychosocial Impact

Kazuo Neriishi

Abstract

On March 11, 2011, a magnitude-9 earthquake and subsequent tsunami cut the supply of off-site power to the Fukushima Daiichi nuclear power plant. In addition, backup diesel generators for the plant's cooling system were damaged by the tsunami. Then, radioactive substances were released to the environment. Residents within a 20-km radius of the nuclear power plant were evacuated, and people within a 30-m radius were asked to remain indoors. However, the environmental contamination and unstable nuclear power plants have caused social anxiety and fear, not only among the residents but also among people all over the world. It is very likely that people will suffer from psychosocial problems long after the accident. In 1999, Japan experienced another nuclear accident in Tokai-mura, Japan. On September 30, 1999, a criticality accident occurred at a uranium-processing plant, and the criticality persisted for about 20 h. Of the three persons who were heavily exposed to neutron and gamma radiation caused by the criticality, two died. Six hundred of the residents within 350 m of the uranium processing plant were evacuated and spent the night at a nearby community center. Among those evacuated, 112 residents were exposed to radiation doses of more than 1 mSv, and some were exposed to as much as 20 mSv. In response, the Japanese Government launched a medical surveillance program with physical checkups for the public to follow their health status, including psychological problems, until 2010. Psychological characteristics are presented in this paper, and actions are suggested for reducing the psychosocial effects following the Fukushima incident.

Chapter 23

The 1976 Hanford Americium Accident: Then and Now

Eugene H. Carbaugh

Abstract

The 1976 chemical explosion of an americium-241 (241Am) ionexchange column at a Hanford Site federal waste-management facility in Richland, WA, resulted in the extreme contamination of a worker with 241Am, nitric acid, and debris. The worker underwent medical treatment for acid burns as well as wound debridement, extensive skin decontamination, and long-term diethylenetriaminepentaacetate chelation therapy for decorporation of 241Am. Because of the contamination levels and prolonged decontamination efforts, care was provided for the first three months at a special Emergency Decontamination Facility, with

gradual transition to the patient's home during another two months. The medical treatment, management, and dosimetry of the patient have been well documented in numerous reports and journal articles. The lessons learned with regard to patient treatment and effectiveness of therapy still form the underlying philosophy of treatment for contamination injuries. Changes in infrastructure and facilities as well as societal expectations make for interesting speculation as to how responses might differ today.

Chapter 24

Lessons from the 1999 Iridium-192 Accident at Yanango

L.E. Barriga, M. Zaharia, L. Pinillos, A. Moscol, A. Heredia, G. Sarria, J. Marquina, O. Barriga, and C. Picon

Abstract

Since the discovery of ionizing radiation, radioactive sources have been used in medicine, research, agriculture, and industry. Safety precautions are essential to limit the exposure of persons to harmful radiation. Radiation accidents are rare, are often not immediately recognized, and have a very low reproducibility rate. When they do happen, damage has particular features that may delay recognition of the accidental situation, resulting in severe injuries and even deaths. A serious radiological accident occurred on February 20, 1999, at Yanango hydroelectric power plant in Peru (San Ramon District, 300 km east of Lima). A welder found an iridium-192 industrial source on the ground and placed it in the back pocket of his trousers, where it remained for several hours. He thereby received a very high dose from the source. When the patient arrived at the hospital, his dose was calculated by the Medical Physics Department of the National Cancer Institute of Peru; the calculation was based on information provided regarding the time the source was in his pocket. The calculated dose was extremely high and led Peruvian doctors to raise the possibility of a hemipelvectomy as a treatment. However, a decision was made to delay the procedure and to graft over the lesion in an attempt to save the irradiated limb. Peruvian authorities requested foreign assistance, and the patient was hospitalized in France, where the grafting techniques failed and the limb was amputated a few months later. It has been more than 12 years since the accident, and the patient is still alive. He is in all practicality resigned to his fate but with a great psychological deficit. Common sense could have prevented many such accidents that resulted in serious injuries or deaths. Delay in identifying the type of accident results in severe consequences, not only for the patient but also for the family. Radiography cameras need to be designed and constructed in a way that prevents unauthorized or accidental access to the radioactive source. Persons not directly working with radiation sources, but working nearby, should be given appropriate information and may require training. National authorities must stop focusing on bureaucratic concerns and engage in education and supervision.

Session Five: Other Topics of Interest in Radiation Medicine

Doran M. Christensen

Chapter 25

The Internet's Role in Radiation Biodosimetry

Gordon K. Livingston

Abstract

Nuclear and radiological terrorism is considered a threat requiring timely medical intervention to reduce radiation casualties. Timely and optimal medical care, however, depends on knowledge of the victim's radiation dose. In the absence of physical dosimetry data, radiation-specific chromosome-damage studies can be used to estimate the absorbed dose. The dicentric-chromosomeaberration assay is considered the "gold standard" to estimate radiation dose because the dicentric frequency always correlates positively

with the absorbed dose, a fact that has been validated in numerous radiation accidents during the past four decades. Dicentric chromosomes occur at low background frequency in circulating lymphocytes, are independent of age and gender, and are relatively easy to identify. An exposure of 1 Gy increases dicentrics by a factor of 100, and an exposure of 5 Gy increases them by more than a factor of 1000. The dicentric yield curve fits a linear quadratic dose-response function that can be used as a calibration curve. This assay, however, is labor-intensive; a small number of cytogeneticists could easily be overwhelmed by an incident involving hundreds or thousands of persons. The dicentric assay requires cell culture, slide preparation, and chromosome analysis. Nuclear preparedness in the United States could be significantly strengthened by combining laboratory specialists in radiation cytogenetics (few in number) with clinical cytogeneticists (many in number) to conduct training, proficiency testing, and validation exercises. The ratio of these two types of cytogenetic laboratories in the United States is about 1 to 70, which demonstrates a large untapped resource of "chromosome experts" in the country who could assist in a mass-casualty scenario. Our studies have confirmed that visual analysis of electronic images produces scoring accuracy and dose estimations equivalent to visual analysis directly in the microscope. We conclude that combining the manpower and expertise of research and clinical laboratories, coupled with use of the Internet to score images, would significantly strengthen the nation's capacity to respond to a radiation emergency.

Chapter 26

Polonium-210 Contamination in London 2006, the Public Health Response

Jill R. Meara

Abstract

Alexander Litvinenko died from polonium-210 poisoning in November 2006 in London. A public health response was mounted by the Health Protection Agency (HPA) to (1) define if there were an ongoing health hazard, either from residual poison or from secondary contamination, and prevent it by identifying significantly contaminated areas and ensuring that they were removed from public use; (2) identify and advise members of the public who may have been exposed to the contamination and arrange appropriate radiation monitoring, dose assessment, and medical follow-up for these people; and (3) provide reassurance to those exposed and members of the public who were not likely to be at risk. This paper describes the practicalities of the HPA response, including the environmental and people monitoring; summarizes the results of a public survey about the effectiveness of the HPA health protection advice; and discusses factors that are likely to increase pubic reassurance.

Chapter 27

Screening for Radioactive Contamination and Health Monitoring of a Large Population That Does Not Need Hospitalization

Armin Ansari

Abstract

A major radiation incident is likely to have significant short- and long-term impacts on people and the environment. Several chapters in these proceedings address the clinical management of radiation injury and medical response to radiation incidents. An incident involving mass casualties can quickly overwhelm available response resources, especially hospitals caring for the injured (HSC 2010; Coleman et al. 2011). One issue that is often overlooked in preparedness planning is that, after any large-scale radiation incident, there will be people requiring assistance who may be contaminated with radioactive materials

or think that they have been exposed to radiation or contaminated with radioactive materials. Very few among this potentially large population may need hospitalization. However, if adequate planning is not in place to address their needs, many are likely to report to hospitals, further challenging the scarce medical resources that are needed to address the immediate medical needs of the exposed and the injured. A second, often overlooked issue is that of the displaced population. An incident that releases a large amount of radioactive material (such as a nuclear detonation or a major accident at a nuclear power reactor) will cause the displacement of a large population through mandatory and self-directed evacuations. Depending on the population density of the affected region, the number of displaced population may be in the millions, and many will travel long distances from their homes. Again, few among the displaced population may need hospitalization, but providing the basic needs of this refugee population can challenge local response organizations, even at far distances from the site of the incident. In this chapter, the needs of this population that does not need hospitalization are described from a radiation-protection perspective. The burden of providing assistance and meeting these needs is likely to fall on the local authorities who host this displaced population. This chapter also discusses strategies and resources that are available to local public-health and emergency-management officials to plan and become better prepared to meet these needs with, to the extent possible, locally available resources.

Chapter 28
An Overview of Antioxidants and Radiation Injury
Carol J. Iddins

Abstract
Ionizing radiation induces free radicals and the formation of reactive oxygen species (ROS) and oxidative stress. It would be intuitive that substances that reduce ROS and oxidative stress could be good candidates for radioprotectants, mitigators, and therapeutics in radiation injury. In the field of radiation oncology, radioprotectants have been of primary importance. For development of radiation medical countermeasures, both civilian and military entities are seeking substances that may mitigate the effect of a radiation exposure and may be given before the exposure (protectants), during the exposure or prior to symptoms (mitigators), or after symptoms appear (therapeutics). To be effective in a mass casualty incident involving radiological and/or nuclear materials, these countermeasures ideally should be substances that can be given to large numbers of people, have a long shelf life, have minimal side effects, may be given without supervision of a physician, and may be economically feasible to produce. Many antioxidants occur naturally and are part of cellular metabolism and maintenance. There has been much research with these antioxidants. Some areas of research include synthetic antioxidants, superoxide dismutase/catalase mimetics, protease inhibitors, existing medications, and other treatment modalities. Research pioneers have opened doors into many areas that will benefit those undergoing radiation therapy or therapy for radiation injuries as well as other facets of medicine. This chapter is an overview of various natural and synthetic antioxidants that have been or are currently being investigated.

Topics: Radiation Biodosimetry Workshop

- Ionizing Radiation Biodosimetry Through Noninvasive Ocular Monitoring: Preliminary Findings
  N. Menon, J.D. Down, C.C. Tan, and P. Bui
- Radiation Metabolomics: A Solution for Rapid Radiation Biodosimetry
  Diren Beyoğlu and Jeffrey R. Idle

- Pitfalls and Perspective on Gene Expression Profiling of Peripheral Blood to Predict Radiation Status
  Joseph E. Lucas, Sunil Suchindran, Holly Dressman, and John Chute
- Integrated Microfluidic System for Gene-Expression-Based Biodosimetry
  Muriel Brengues, Stanley Smith, Matthew Estes, and Frederic Zenhausern
- Radiation-Induced Changes in Plasma-DNA Concentration for Early Biodosimetry: Fit-for-Purpose Studies in Two Species
  P. Okunieff, L. Zhang, S. Ju, Y. Guo, L. Zhang, M. Zhang, B. Zhang, A. Zhang, S. Yang, Y. Cao, Y. Tian, L. Yin, K. Zhang, S. Swarts, O. Hyrien, A. Baran, P. Keng, R. Howell, S. Vidyasagar, and B. Fenton
- SpinDx™: A Rapid, Point-of-Care Biodosimetry Platform That Uses Peripheral-Whole-Blood Protein and Leukocyte Biomarkers
  Ulrich Y. Schaff, Chung-Yan Koh, Natalia I. Ossetrova, William F. Blakely, and Greg J. Sommer
- Biomarker-Based Radiation-Dosimetry Diagnostics
  George B. Sigal, Eli N. Glezer, John Kenten, Sudeep Kumar, Natalia I. Ossetrova, and William F. Blakely
- Application of the Premature Chromosome Condensation (PCC) Assay in Radiation Dose Assessment
  Daniela Stricklin
- Micronucleated Lymphocytes as a Biodosimeter Following Radioiodine Therapy
  Gordon K. Livingston and Albert L. Wiley
- γ-H2AX Assay as a Biodosimeter for Ionizing-Radiation Exposure: A Study in Nonhuman Primates for Total- and Partial-Body Irradiation
  C.E. Redon, A.J. Nakamura, K. Gouliaeva, A. Rahman, W.F. Blakely, and W.M. Bonner
- The RABiT: A Rapid Automated Biodosimetry Tool
  Guy Garty, Helen C. Turner, Maria Taveras, Oleksandra V. Lyulko, Gerhard Randers-Pehrson, and David J. Brenner
- Integrated Medical Recording for Multiple Radiation Bioassays
  William F. Blakely, David J. Sandgren, Ira H. Levine, Brian E. Livingston, and Ronald E. Goans
- Astronauts' Biodosimetry and Risk Assessment
  Francis A. Cucinotta and Kerry A. George
- Cytogenetic Biodosimetry and Clinical Hematology in the Management of Radiation Injury
  Ronald E. Goans