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Editorial

Acute radiation syndrome and Fukushima: A watershed moment?

As we sit down to write this editorial in late December, it is clear that 2011 has been a very active year for scientists interested in finding better ways to treat radiation-induced injuries. The nuclear disaster that occurred in March 2011 in Fukushima, Japan was the most serious accident since the Chernobyl accident in 1986. Fukushima draws attention to the urgent need to implement measures to prevent such accidents from occurring, but also to develop comprehensive emergency plans to respond to accidental – or intentional – radiation exposure.[1]

We believe that, in the long run, the Fukushima disaster may come to be seen as a watershed moment, as it has increased awareness of the need to better understand how to prevent and treat radiation-induced injuries, including both early effects—acute radiation syndrome (ARS), which primarily affects the blood, skin, and gastrointestinal systems—and late effects, which include genetic damage, cancers, and cataracts. Fortunately, in terms of scientific output, 2011 was a banner year and numerous articles were published on this topic. In this editorial, we highlight some of the most relevant of these publications.

Remarkably, in 2011, three different medical journals, all working independently of each other, published special issues devoted to acute radiation syndrome (ARS) and emergency response measures to be undertaken in the event of a nuclear meltdown and/or detonation.

In March, the journal *Disaster Medicine and Public Health Preparedness* (DMPHP) published a comprehensive assessment of planning and response procedures in the event of a nuclear detonation. The authors emphasize that planning for allocation of scarce resources needs to be well-planned beforehand.[2] We agree. Fortunately, as the authors point out, the U.S. government has prepared a comprehensive web site, called the Radiation Emergency Medical Management site (http://www.remm.nlm.gov/). The aim of the web site is to provide just-in-time, evidence-based guidance for health care providers about clinical diagnosis and treatment of radiation injury during radiological and nuclear emergencies. Another web site, the Radiation Injury Treatment Network (http://www.ritn.net/), provides similar information.

In April, the journal *Clinical Oncology* published a special issue entitled "*The Radiobiological Consequences of the Chernobyl Accident 25 Years On*",[3] in which they assess how the Chernobyl experience has led to the identification of high-risk groups and the use of specialized techniques to collect information on diagnosis, treatment and follow-up. One of the papers in that issue focuses on how the study of affected populations has provided important new data on the association between low dose radiation and late effects, primarily the risk of thyroid cancer,[4,5] as the data show a dose-related increase in thyroid cancer in children and adolescents exposed to radioiodines, with the greatest risk to younger children. The authors also report other interesting findings, including an increased risk of cataracts, leukemia and other hematological diseases, and a possible greater risk for cardiovascular disease in Chernobyl survivors. This information is valuable not only for a better understanding of the effects of radiation, but also to develop measures of radiation protection. The knowledge acquired from the Chernobyl experience is valuable data that can be used in monitoring and treating Fukushima survivors.

In July, the present journal – Reports of Practical Oncology & Radiotherapy – published a special issue (edited by the authors of this editorial) which explored in depth all relevant aspects of ARS, including radiobiology, biodosimetry and dose assessment, medical management, decontamination, and prevention.[6–11] The purpose of that special issue was to present a comprehensive report of the latest understanding of ARS and to provide guidelines for emergency treatment.

In addition to the 3 special issues discussed above, several reports addressed the issue of new treatments for ARS. Because randomized controlled trials of ARS are not possible in humans (due to obvious ethical issues), our current approach is based mainly on data obtained from treating and observing survivors of radiation incidents and accidents and from data generated through laboratory research on animals. The special issue carried out by DMPHP concluded that, in the treatment of ARS, scientific evidence was strong for prophylactic serotonin-receptor antagonist administration when exposure is >2 Gy and topical steroids, antibiotics, and antihistamines for skin damage (burns, ulcers, blisters). Other

interventions with strong evidence include removal and grafting of ulcers or necrosis with persistent pain, supportive care for individuals with neurovascular syndrome, and electrolyte replacement therapy and sedatives for patients with significant burns, hypovolemia, or shock.

Unfortunately, as discussed above, current treatments for extreme radiation sickness are rather limited. However, a number of new treatments may be on the way. Several new therapies are being investigated, some partially or wholly financed by the US government through the Project BioShield Act.[12] One such study is investigating a drug called CBLB502, under development by Cleveland BioLabs.[13] This drug, which was granted fast track approval by the US Food and Drug Administration (FDA), binds an immune protein to activate a cell survival pathway (the Toll pathway). Another study in phase I is testing a drug designed to interrupt proteins (such as p53) involved in cell apoptosis. Another group is working on a technique to use bone marrow to create a stem-cell-based treatment that would help repair organ damage incurred as a result of radiation exposure. The direct infusion of blood stem cells into the bloodstream to increase the number of white blood cells is also being investigated. Yet another group is working on a small molecule to reduce inflammation and oxidative stress in acute radiation syndrome. Researchers have also investigated interventions to prevent or alleviate radiation lung injury. Inhibitors of angiotensin converting enzyme (ACE), have been found to be among the most effective mitigators of lung injury. One study found the ACE inhibitor captopril to be effective in mitigating lung damage when administered up to 1 week following radiation exposure.[14] Transfusion of myeloid progenitor cells has been evaluated in an animal model of ARS, with promising results: this technique has proven effective in protecting animals exposed to lethal doses of radiation.[15] Other areas of research include the search for ways to detect genetic alterations caused by ionizing radiation based on DNA damage-induced gene expression[16] and energy metabolism.[17] Several other interesting papers on the subject of ARS were also published in 2011.[18–20]

To conclude, it seems that the Fukushima incident, together with growing concerns about a potential terrorist attack, have provided a strong impetus for the development of emergency response plans and new research to identify drugs capable of ameliorating the effects of ARS. In addition, researchers are already preparing studies of the long and short-term effects of radiation on the population in the area of Fukushima.[21] We believe that 2011 represents a tipping point in efforts to prevent further nuclear accidents and to develop new approaches in the treatment of radiation sickness.

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