REVIEW ARTICLE

Medical Lessons Learned From Chernobyl Relative to Nuclear Detonations and Failed Nuclear Reactors

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ABSTRACT

The Chernobyl disaster in 1986 involved the largest airborne release of radioactivity in history, more than 100 times as much radioactivity as the Hiroshima and Nagasaki atomic bombs together. The resulting emergency response, administrative blunders, and subsequent patient outcomes from this large-scale radiological disaster provide a wealth of information and valuable lessons for those who may find themselves having to deal with the staggering consequences of nuclear war. Research findings, administrative strategies (successful and otherwise), and resulting clinical procedures from the Chernobyl experience are reviewed to determine a current utility in addressing the appropriate protocols for a medical response to nuclear war. As various myths are still widely associated with radiation exposure, attention is given to the realities of a mass casualty medical response as it would occur with a nuclear detonation.

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Key Words: Chernobyl, radiation, birth defects, prodromal syndrome, thyroid cancer, radiation-induced cancer, potassium iodide

It is widely accepted that the classification of nuclear war victims will be expedited by hemodynamic evaluations[1]; the Chernobyl experience has now added another, low-technology approach: time of onset of the prodromal syndrome.[2] The rapid decline in blood lymphocytes induced by significant radiation exposure has been well recognized for decades, and this also was seen at Chernobyl. Declines in lymphocyte counts were inversely correlated with treatment outcomes, in that there were marked declines in patients who did not survive and milder declines in survivors. An inverse correlation also was noted between granulocyte levels and outcome, aside from the initial postexposure spike in all but the most severely irradiated patients. For lower level exposures, platelet measurement was found to be useful at Chernobyl but was less useful for distinguishing between the groups that had higher exposure.[3]

MEDICAL DEMOGRAPHICS OF LARGE-SCALE AIRBORNE RELEASE OF RADIOACTIVITY

A very interesting finding was noted in the Chernobyl cleanup workers who were highly exposed to radiation (known as liquidators). The survivors were far more likely to have a latent period of more than 4 hours between the initiation of exposure and the onset of vomiting and diarrhea; those who did not survive (due to radiation exposure) were found to have latent periods of less than half an hour.[2] This finding would be highly useful in the rapid assessment of thousands of exposed victims in a nuclear war setting, especially when hemodynamic parameters are not available or are of questionable quality. If both are available, they can be used to validate each other for the designation of patient categories. The health care provider must be careful in using vomiting as a parameter for categorizing patients, however, as many patients will present with this symptom for psychological reasons (ie, stress, fear, from observing the distress or injuries of others).[3]

Management of internally displaced residents was a major issue at Chernobyl, and would be similarly demanding following a nuclear war event, in which thousands to as many as several million could be displaced from their homes for lengthy periods. These people will need to be sheltered, fed, given potable water, nonfood items, and basic health care such as immunizations or medicine. Security will need to be provided in adequate numbers to protect people from theft and from sexual assault, both of which reach alarming rates during crisis situations worldwide.[3] According to the federal interagency *Planning Guidance for Response to a Nuclear Detonation*,[4] state and local agencies should establish a registry system as early as possible after a nuclear event. The registry would be used to contact people who require short-term medical follow-up as well as long-term monitoring.

MYTH AND REALITY OF BIRTH DEFECTS FROM ENVIRONMENTAL RADIATION

One of the most entrenched concepts concerning radiation is the fear of birth defects induced by radiation exposure. While it has been shown that intense radiograph exposure has produced birth defects in humans, only a limited amount of defects were reported in Hiroshima and Nagasaki atomic bomb survivors. In an ambitious, wide-ranging study that involved respected investigators from around the world and available data sets,

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the World Health Organization concluded that the rates of mental retardation and emotional problems were no different in Chernobyl radiation-exposed children than in corresponding controls.[4] Support for these findings has also been reported in a study of evacuee children in Kiev, with no significant differences in neuropsychological performance or school grades, based on in utero exposure,[5] and in a comparative study of cognitive functioning of a large population of children, including those in utero at the time of exposure, from Gomel (one of the highest exposure areas), Mogilev, and Kiev (moderate exposure) and from unexposed control areas.[6] A Harvard review on in utero outcomes from Chernobyl also concluded that there was no substantive proof regarding radiation-induced teratogenic effects from the Chernobyl accident.[7] Similar results have been cited for Western Europe by the EUROCAT group in an analysis of the congenital abnormality registers for 16 European regions; they concluded that in retrospect the widespread fear in the population about the possible effects of exposure on the unborn fetus was not justified.[8]

In spite of these widely accepted conclusions concerning the lack of congenital abnormalities related to Chernobyl exposures, a number of studies were reported with data that alleged various degrees of radiation-induced reproductive effects. These reports were not accepted in the aforementioned studies due to lack of transparency in sampling, testing, or dose reconstruction methods, or to lack of statistical control. These reports included studies of intellectual reasoning, intelligence, or emotional problems[9,10] and birth defects.[11,12] Calls have continued for additional study[9,13] and for a new claim of abnormalities.[13] An overall analysis of the Chernobyl accident after 20 years concluded that it was not possible to separate the claims of Chernobyl-related congenital abnormalities from elevated incidences in the region to various other known causes.[14]

Indeed, the most definitive Chernobyl health impact in terms of numbers was the dramatic increase of deliberately induced pregnancy terminations near and at significant distances from the accident site. This increase was due to "nuclear phobia," lack of information, and inadequate official guidance that led to anxiety regarding possible fetal radiation effects and a panic among expectant mothers about giving birth to an abnormal child.[7] As a result, increase in abortions was significant.[15,16] Even in countries far from the significant radiation zones, including Denmark,[17] Norway,[18] Italy,[19] Hungary,[20] and Greece,[21] a reduction of births was noted.

It is critical for health care practitioners, policy makers, administrators, public health thought leaders, and media spokespersons to be informed about the myths and realities of radiation-induced birth defects. Current scientific consensus is that widespread airborne dissemination of more than 100 times as much radioactivity as Hiroshima and Nagasaki combined (ie, Chernobyl) did not result in documented congenital abnormalities, and that terminating pregnancy for fear of birth defects is not medically justified.

LONG-TERM EFFECTS: CANCER

One of the most feared long-term effects of radiation exposure is the subsequent development of cancer. By tracking the survivors of the Hiroshima and Nagasaki atomic bomb attacks, it has been determined that there is a long latent period followed by a definite increase in the incidence of radiogenic cancers.[22] Some cancers (eg, breast and bone marrow) are relatively radiation sensitive, while others (eg, prostate, pancreas, and uterus) are relatively resistant to radiation induction.

After the Chernobyl accident, thyroid cancer was the most definitive cancer found. In 2000, the United Nations Scientific Committee on the Effects of Atomic Radiation review reported 1800 cases in Belarus, Ukraine, and Russia,[23] and a widely quoted review 20 years after the accident reported 4000 cases.[24] Following the Chernobyl nuclear accident, a much shorter latent period for thyroid cancer was noted in children, starting as soon as 4 years after the accident, as opposed to 15 years after the atomic bomb attacks on Japan.[25] A meta-analysis of the thyroid cancer data concluded that there were a few cases earlier than 5 years that did not meet statistical significance, but the risk was significant starting 5 to 9 years after exposure.[26] It is possible that the much higher doses of radioiodine at Chernobyl versus those that occurred after Hiroshima and Nagasaki might be responsible for the shorter latent period. It may be simpler to attribute this finding to the fact that because the Chernobyl exposures were so large, it is more feasible to detect an earlier onset. Indeed, it must be remembered that the radiation exposure to fallout after Chernobyl was very different from the whole-body radiation after the atomic bomb attacks.[27]

It is well established that a number of nonthyroid cancers occurred in the survivors of the atomic bomb attacks on Hiroshima and Nagasaki, starting with leukemia after 6 years, lymphomas after 9 years, lung cancer after 15 to 20 years, and breast cancer after 20 years.[28,29] In addition to usually being the earliest onset (except at Chernobyl), leukemia is one of the most well-established radiation-induced cancers.[30] However, extensive follow-up studies of the thousands of significantly exposed people in the Chernobyl region have not definitively established any nonthyroid cancers that can be attributed to radiation exposure.[14,2324,30,31] Outside of the former Soviet Union, there also is no evidence of an increase in cancer.[23,24,32] Therefore, the Chernobyl experience tends to significantly diminish the expectation of cancer incidence due to the airborne dispersion of radionuclides, which would have an impact on the anticipated use of pharmaceutical intervention for radiation exposure.

ADVANCES IN PHARMACEUTICAL INTERVENTIONS FOR RADIATION EXPOSURE SINCE CHERNOBYL

Considerable development has occurred in pharmaceutical intervention strategies for radiation exposure, including the removal of internally deposited radionuclides (decorporation) and the amelioration of radiation-induced health effects. In making the decision to actually use one or more of the decorporation agents, a general rule is that when the cumulative exposure dose is less than the annual limit of intake (ALI) set for a worker occupationally exposed to radiation, no attempt at decorporation is warranted. If the cumulative dose is greater than 10 times the ALI, decorporation therapy is indicated.[22] Doses in between these values require a more considered risk-benefit analysis.[33] The specificity of decorporation agents varies between individual radionuclides, which deposit in different tissues (ie, radiocesium in muscle, plutonium and radiostrontium in bone, radioiodine in thyroid). Prussian blue is useful for ingested cesium, thallium, or rubidium. The chelating agent diethylenetriaminepentaacetic acid (DTPA) binds to plutonium, and the chelated plutonium is then removed from the body. If DTPA is given within an hour of exposure, more than 80% of internally deposited plutonium can be removed, even from bone. Deposition of radioactive iodine into the thyroid is blocked by administering potassium iodide (KI), which saturates the thyroid, thus preventing the absorption of radioactive iodine from the circulation into the thyroid gland. Elimination of uranium can be increased by alkalinizing the urine.[22]

One of the management tragedies of the Chernobyl accident was the critical, and inexcusable, delay in the administration of potassium iodide to highly exposed children in the immediate vicinity of the accident. Because the Soviet command structure (Gorbachev was the Soviet leader at the time) did not announce the reactor accident for 3 days, pharmaceutical intervention was critically delayed beyond the point at which it was capable of being useful.[22,29,34] Administering KI in these exposed patients more than 72 hours after the initiation of exposure proved to be ineffective, as evidenced by the thousands of thyroid cancers in Belarus, Ukraine, and Russia. To be useful in blocking the uptake of radioiodine in the thyroid, KI must be administered within 4 hours of exposure, and preferably within 1 hour.[22,29] Additional studies have been done with pectin[35] in humans and insoluble Prussian blue in livestock[36] for the removal of cesium 137 as a result of the Chernobyl disaster. For humans, it was thought that oral administration of Prussian blue would reduce the effective cesium dose by 29%, and simulation inferred that hemoperfusion or hemodialysis might be able to reduce the internally received dose by up to 50%.[36]

If the course of therapy for acute radiation sickness and cutaneous radiation syndrome is long, substances such as cytokines and cell growth factors cause surviving stem cells and progenitor cells to speed up division and maturation, and for blood cell elements to be released into the systemic circulation. The compound WR-2721, or amifostine, has been shown to inhibit radiation damage in protected tissues in patients undergoing radiation therapy, and has reduced the risk of carcinogenesis in animal studies. Treatment of emesis in irradiated casualties is improved by anti-emetic agents, preferably 5-HT3 antagonists (ondansetron, granisetron). After Chernobyl, physicians empirically used probiotics such as *Bifidobacteria* and *Lactobacillus* to suppress pathogenic overgrowth over the gut epithelium and to encourage growth of normal flora involved in this suppression. Although the likelihood of survival was not demonstrably increased, survival time was, and stool cultures for pathogenic bacteria were negative.[22]

Stem-cell transplantations have been used with success in patients with certain hematologic malignant conditions, but their record in radiation-accident victims is much less impressive.[22] Stem-cell transplants were attempted on some of the most highly exposed emergency responders at Chernobyl, and 11 of 13 of these patients died; medical evidence indicates that the 2 survivors reconstituted their own bone marrow and probably did not benefit from the transfused tissue.[34] As a result of the Chernobyl experience and due to the great cost in resources, it is not anticipated that allogeneic stem-cell transplants would have much of a role in radiation mass casualty events.

Lymphocytes are the most sensitive tissue in the body to radiation exposure, and a continual and sustained decline is indicative of the dose that was received. Neutrophils spike shortly after acute radiation exposure before dropping, so a high neutrophil/lymphocyte ratio 4 hours or so after exposure is a useful determinant of significant radiation exposure.[1] In connection with the time to emesis indicators related previously, several medical reports determined that time to emesis was 2 hours or more, 1 to 2 hours, greater than 1 hour, and less than 30 minutes, for doses of 1 to 2 sieverts (Sv), 2 to 4 Sv, 4 to 6 Sv, and greater than 6 Sv doses, respectively.[4,34,37,38] Mechanistically, radiation-induced emesis at low, survivable doses is due to the effect of serotonin and histamine released by irradiated tissues on the vomiting and chemoreceptor trigger zones, respectively, in the brain. If, in extreme situations, laboratory dosimetry information is not available, the general rule of emesis beginning within the first 4 hours (median dose of approximately 2 Sv [200 rem]) can be used to start therapy.[3]

Transfusions have proven to be highly important in radiation casualties. Several Chernobyl casualties were treated with anticoagulants such as heparin. It is not generally considered a fundamental tenet of radiation casualty treatment currently; however, there is empirical evidence in the former Soviet Union medical community, particularly from Chernobyl, for the use of anticoagulants in severe radiation injuries. It would appear reasonable to test casualties for elevated fibrin split products, prolonged prothrombin time, prolonged partial thromboplastin time, and prolonged bleeding time (platelets will be depressed anyway); if disseminated intravascular coagulation is present, it should be treated with anticoagulant or other therapy.[22]

From the Chernobyl experience of fatalities in the first month after acute radiation exposure, a majority of casualties had skin injuries from radiation. These injuries ranged from erythema to epilation to desquamation, both dry and moist, and ulceration with eventual fibrosis. The appropriate therapy from this experience and others is to use steroid ointments for relatively intact skin, topical antibiotics with dressings if blistering is present, and other emollients. Silver sulfadiazine is indicated in cases of moist desquamation or ulceration. One of the most important consider-

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ations is to debride the burns thoroughly to control infection and inflammation, as infection can be expected to result in almost half of the subsequent deaths of burn victims. This finding is true for radiation burns and thermal burns, both of which will be seen in a nuclear weapon medical response.[22]

PSYCHOSOCIAL IMPACTS OF ENVIRONMENTAL RADIOACTIVITY

The fear of radiation in the public, and in most health care workers, is visceral and tends to become an extreme reaction under conditions of stress. As a result, among the anticipated outcomes for the general public will be fear of invisible agents and contagion, magical thinking about radiation, anger at perceived inadequacies by government entities, scapegoating, paranoia, social isolation, demoralization, and loss of faith in social institutions.[6] In fact, one of the most lasting and widespread effects of Chernobyl has been mental health issues. The conclusion of the Chernobyl forum report[39] was that "the mental health impact of Chernobyl is the largest public health problem unleashed by the accident to date."

As indicated, the combination of fear of birth defects and lack of appropriate medical guidance led to thousands of unwarranted pregnancy terminations based strictly on incorrect expectations of radiation-induced effects in utero. It is likely that similar fears will drive many thousands of uninjured, low-risk, or virtually no-risk people to clog emergency departments and hospital facilities in the event of a nuclear attack. It was an interesting feature of the Chernobyl evacuation that people in the immediate vicinity of the burning reactor were relatively calm during the first few days after the accident, when they knew something was definitely wrong but before they were told of its exact nature. In the city of Pripyat, a model Soviet city populated almost exclusively by people directly associated with the nuclear power industry, people watched smoke coming out of the reactor from their balconies, ensuring a near maximal exposure to the airborne radionuclides. When the Soviet government finally announced the dangers involved 3 days after the accident, there was a panic and an abrupt exodus of people from their homes, most of them never to return.[40] This extremely poor management approach is a warning to us in the future; withholding needed information to the public in radiation-related disasters is only going to worsen the impact of the announcement when it inevitably is released.[41]

Chernobyl remains, 25 years later, as the largest airborne release of radioactivity into the atmosphere after the atomic bomb detonations in Japan. Therefore, it continues to be a compelling laboratory of the medical, social, and economic impacts of large amounts of radioactivity released into the environment. While the medical response was not exemplary by any measure, a number of valuable lessons were learned for the eventual repeat of this unfortunate scenario in the future. In particular, the rapid evaluation of radioactively exposed populations is of paramount importance. A dramatic increase in planning needs to be incorporated into mass casualty plans for urban areas in the event of a nuclear attack or nuclear reactor malfunction. It is remarkable that so little progress has been made in planning, training, and exercise outcomes for radiation- and nuclear-related disasters, in spite of distinctive warnings from the experience of Chernobyl and the recent Fukushima crisis.

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