Medical Considerations for Post-Emergency Response of Radiation Accidents

Panel Discussion Presented by the Radiation Emergency Assistance Center/Training Site (REAC/TS)

Ronald E. Goans, PhD, MD
Richard E. Toohey, PhD, CHP
Shirley A. Fry, MB, BCh, MPH
Robert C. Ricks, PhD; Director, REAC/TS

INTRODUCTION

In the initial evaluation of a radiation accident, it is crucial to estimate the maximum credible accident that has occurred since reliable health physics data may take days to accumulate. Radiation effects usually take hours to days to even weeks to manifest and there is always time to formulate a plan of management and enlist the aid of appropriate medical and surgical sub-specialists. However, because of the evolving nature of radiation-induced lesions, this means that most of the definitive care takes place outside of the Emergency Department. Since management of a radiation accident also can involve medical and surgical complications, it is important to resolve these issues first.

It is important to evaluate population radiation dose in perspective in order to deal with radiation accidents in an informed manner. Average background radiation dose to the population is approximately 0.36 cSv/year (1), dose from a PA and lateral chest film is approximately 0.006-0 02 cSv, and dose from a pelvic or skull CT is 1.5-4.0 cSv/slice. This may be viewed in contrast to the current occupational limit of 5 cSv/year. In contrast, the acute whole body dose for lethality of 50% of a population (LD_{50}) is approximately 4 Gy, somewhat dependent on the state of health of the patient, dose rate, and the availability and sophistication of medical resources. For an exposed population, the dose for 5% mortality may differ from the dose for 95% mortality by only 2-3 Gy. Therefore, an increase in dose by only a factor of 2 may represent the difference between total survival of an individual and essentially total mortality.

DISCUSSION

It is possible to subdivide radiation accidents into four categories: (1) body surface contamination with or without wounds; (2) whole-body irradiation; (3) acute local injury; and (4) internal contamination. The injured patient may exhibit only one or a combination of these effects.

Wound or Intact Skin Contamination

Decontamination of a minor wound or intact skin is relatively straightforward, is commonly practiced and has been presented in detail elsewhere (2). Generally, decontamination procedures

start with the mildest agents possible (soap and water) and progress to more aggressive techniques as indicated. In decontamination of intact skin, it is important not to irritate the skin, thereby disrupting the skin's normal protective barrier and possibly increasing transdermal absorption of any deposited radionuclides. The most important consideration of decontamination of wounds and lacerations is copious irrigation of the area under sterile conditions. Surgical debridement of contaminated areas may also be of help in some cases.

Acute Effects of Whole-body Irradiation (Acute Radiation Syndrome)

It is instructive to look at early deterministic effects of whole-body irradiation:

(1) < 10 cGy, whole body - No detectable difference in exposed vs. non-exposed patients.

(2) ~ 20 cGy, whole body - Detectable increase in chromosome aberrations. No clinical signs or symptoms.

(3) ~ 20-100 cGy, whole body - Detectable bone marrow depression with minor lymphopenia, leukopenia and thrombocytopenia.

(4) ~ 100-800 cGy whole body - Bone marrow depression with dose-related depression of all blood elements.

The Acute Radiation Syndrome (ARS) is an acute illness, which follows a roughly predictable course over a period of time ranging from a few hours to several weeks after exposure to ionizing radiation. ARS has classically been subdivided into component syndromes as follows:

(1) Hematopoietic .....100 - 800 cGy
(2) Gastrointestinal ...800 - 3000 cGy
Cardiovascular/Central Nervous System... > 3000 cGy

The ARS is characterized by the development of groups of signs and symptoms which are manifestations of the reactions of various body systems to irradiation of the whole body or to a significant portion of it. Prodromal signs and symptoms include anorexia, nausea, vomiting, diarrhea, fever, conjunctivitis, and skin erythema. The latter is especially observed if there has been a dose to a localized portion of the body. The higher the whole-body dose, the more quickly one expects to see the prodromal symptoms of nausea and vomiting.

Most radiation accidents involve doses under 100 cGy and are therefore subclinical. However, for higher doses, the hematopoietic syndrome is the symptom complex most commonly seen. The etiology of the hematopoietic component of the ARS basically arises from destruction of radiosensitive bone marrow stem cells and a consequent decrease in circulating white cells and platelets. Clinical stigmata of this syndrome include immunodysfunction, increased infectious complications, hemorrhage, anemia, and impaired wound healing. Significant neutropenia can

develop some 20-30 days post-exposure, depending on the magnitude of the whole-body dose. The radiosensitivity of circulating lymphocytes has formed the medical basis for an improved technique to estimate total body dose after a severe accident involving low LET radiation (3,4).

As in all accidents, medical management of a severe whole-body exposure includes a complete history and physical examination. Besides the classical components of the medical history, it should also include time of exposure if possible, time of onset and severity of prodromal symptoms, as well as possible exposure to toxic chemicals. A hematological profile (CBC with differential) should be obtained every 2-4 hours following exposure to monitor any initial fall in lymphocyte count. Cytogenetic dosimetry is also an important adjunct to retrospective accident analysis and accident reconstruction involving time and motion studies.

Post-emergency management of the ARS includes treatment of infections (bacterial, viral, fungal, CMV, HSV), trauma surgery as indicated for conventional trauma or thermal burns, and surgical management of radiation-induced skin injuries. Immediate treatment of ARS includes supportive care, platelet transfusions as indicated, psychological support, infection control, and, most importantly, stimulation of the hematopoietic system. The primary goal of radiation casualty management involves therapy to correct radiation-induced bone marrow aplasia and infection from opportunistic pathogens.

Hospital care of mild cases (< 2 Gy) involve triage by prodromal symptoms and by lymphocyte depletion kinetics, evaluation of biological and physical dosimetry, emergency surgery if indicated during an appropriate early time window, and close observation of the patient with frequent hematologic profiles. It is also appropriate to consider management of residual skin contamination and medical management of internal contamination, if present. For the more severely injured patient (2-5 Gy), reverse isolation techniques are appropriate, GI tract decontamination with antibiotics, growth factor therapy to reverse marrow aplasia, and viral prophylaxis. If the patient exhibits a febrile neutropenia, then antibiotics and urine and blood cultures are appropriate. For a patient with whole-body dose beyond the LD_{50}, it is important to utilize aggressive growth factor therapy with transfusion of peripheral blood progenitor cells (PBPC) or cord/placenta blood progenitor cells (CBPC). These cells are transfused after mobilization and *ex vivo* expansion by cytokines. Examples of hemopoietic cytokines currently either in use or in development are GM-CSF, G-CSF, IL-6,11, PIXY321, MGDF, and Erythropoietin.

Clinical cases involving the gastrointestinal syndrome (GIS; 800-3000 cGy) or the cardiovascular/central nervous syndrome CV/CNS) are rare and effective treatment modalities do not exist, especially for the CV/CNS syndrome. Effects resulting from the GIS include malabsorption, Ileus, fluid and electrolyte shifts, dehydration, acute renal failure, cardiovascular collapse, GI bleeding, and sepsis. Typically the patient dies within 5-9 days post-exposure. The Cerebrovascular / CNS Syndrome (CV/CNS; > 3000 cGy) generally exhibits vomiting and diarrhea within minutes, confusion and disorientation; severe hypotension, hyperpyrexia,

convulsions, and ultimately coma. The literature contains very few of these cases, but they have all been fatal within 24 to 48 hours.

Acute Local Injury

Acute local injury is seen reasonably frequently in industrial settings, typically after handling high-level sources at small distances. Common sources inducing local radiation injury are ^{192}Ir, ^{60}Co, and ^{90}Sr. Local injury was also seen in the weapons testing program from fission product betas, and is seen currently in industrial radiography and in misuse of X-ray machines, X-ray diffraction units and X-ray fluorescence units. Since these are deterministic effects, certain approximate thresholds with common signs are observed:

(1) 300 cGy threshold - Epilation, beginning around day 17.
(2) 600 cGy threshold - Erythema; developing minutes to weeks post-exposure, depending on dose.
(3) 1,000 - 1,500 cGy - Dry desquamation.
(4) 2,000 - 5,000 cGy - Wet desquamation, 2-3 weeks post-exposure, depending upon dose.
(5) >>5,000 Gy - radionecrosis with deep ulceration.

Medical management of local injury generally involves history and physical exam, laboratory tests as indicated, slit lamp ophthalmoscopy, and documentation of the evolution of the lesion(s) with serial color photos. One significant problem with the management of local radiation injury is that the actual dose is rarely known when the patient is first seen. The radiation dose is estimated after the lesion has run its course (usually over several weeks). Mock-up of the accident from a retrospective scenario is quite often helpful and medical management often is supervised by a plastic or reconstructive surgeon.

Internal Contamination

Exposure situations involving internal contamination are more common than accidents involving acute whole-body irradiation. Potential workplace accidents involve stages of the nuclear fuel cycle, fabrication of fuel elements, reactor operation and repair, decommissioning, reprocessing, and waste disposal, and accidental intake with radioactive sources in the medical and industrial sectors. Environmental uptake associated with accidental or intentional releases of radioactivity (e.g., reactor accidents, terrorist activity) is also possible. Pathways of contamination include inhalation (particularly likely with explosion or fire), absorption from wounds, and ingestion. In inhalation incidents, the size of the aerosol particles determines the region of the respiratory tract where most are deposited. The fate of inhaled particles is dependent on their physico-chemical properties and highly insoluble particles can remain in the lung for long periods of time. As in all radiation accidents, it is important to attempt to determine the maximum credible accident.

Nasal swabs taken within a few minutes post-exposure can aid in nuclide identification and estimation of the maximum credible accident. Whole body counting is an important adjunct

modality to estimate internal deposition for those nuclides that emit penetrating x or gamma rays. It is also useful for nuclides, such as ^{90}Sr, which emit energetic beta particles; these nuclides can often be detected by the bremsstrahlung radiation given off as electrons slow down in soft tissue. In internal contamination incidents, 24-hour urine and fecal bioassay is usually necessary to estimate intake using various, well-accepted biokinetic models.

CONCLUSION

General principles of treatment of internal contamination include: minimizing intake, reducing and/or inhibiting absorption, blocking target organ uptake, isotopic dilution, promotion of excretion, altering the chemistry of the substance, displacing the isotope from receptors, or utilizing chelation therapy. It is important to remember that radioactive isotopes deposited internally metabolize in the same manner as their stable counterparts. It is instructive to consider some selected examples:

(1) Tritium - ^{3}H; follows pathway of water in the body; penetrates skin, lungs, and GI tract, either as tritiated water (HTO) or in the gaseous form. Single exposures are treated by forcing fluids. This has the dual value of diluting the tritium and increasing excretion. Forcing fluids to tolerance (3-4 L/d) will reduce the biological half-life to 1/3 to ½ of the normal value (10 days).

(2) Uranium- exists in various solubility classes; inhalation is the usual occupational exposure. Overall biological half-life is 15 days and 85% of retained U resides in bone. Kidney toxicity is the basis of occupational exposure limits. Oral doses or infusions of sodium bicarbonate are the treatment of choice and should be administered in a dosing schedule to keep the urine alkaline.

(3) Radioiodine - The dominant internal exposure after a reactor accident, nuclear weapons test, or any incident involving *fresh* fission products is likely to be ^{131}I. The thyroid is the target organ and medical management involves blocking the thyroid by stable iodine, either by KI tablets or SSKI (Saturated Solution of Potassium Iodide).

(4) Radiocesium - ^{137}Cs (physical half-life, 30 years; biological half-life 109 days) is the dominant radioisotope in *aged* fission products. Cesium distributes in body fluids similarly to potassium. The most effective means for removing radioactive cesium is the oral administration of the ion-exchange resin, ferric ferrocyanate, commonly called Prussian blue

(5) Actinides - Plutonium, Americium, Curium, and Californium (all have long biological half-lives). Inhalation is approximately 75% of industrial exposures and these accidents are generally seen in the DOE complex or in universities supporting weapons research. Ca-D TPA and Zn-DTPA chelation therapy is the treatment of choice.

(6) Additional Chelating agents - Chelation has an active history in radiation medicine and much research is still directed toward developing better chelating agents. For example, Dimercaprol (BAL) forms stable chelates with mercury, lead, arsenic, gold, bismuth, chromium, and nickel. It

may therefore be used for the treatment of internal contamination with radioisotopes of these elements. Deferoxamine (DFOA) has been effective in treatment of iron storage disease and may be used for chelation of ^{59}Fe. Penicillamine chelates copper, iron, mercury, lead, and gold. It is superior to BAL and Ca-EDTA for removal of copper (Wilson's Disease).

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Post-emergency Response: Epidemiological Considerations

Shirley A. Fry, M.B., B.Ch, M.P.H.

Oak Ridge Associated Universities

INTRODUCTION

During the three decades following the nuclear explosion in Japan, radiation accidents worldwide generally were contained within secured and often remote environments, involved small numbers of active participants, and with a few notable exceptions, had little or no impact on the public health. More recently however, accidents such as those originating at the Three Mile Island and Chernobyl nuclear power generating plants, at metal processing facilities in Juarez, Mexico and in Taiwan, and at medical facilities in Goiania, Brazil and Indiana, Pennsylvania had, or were perceived to have the potential to affect the health of members of the general public in addition to those at the accident site. The potential for similar situations to occur in the future raises questions about the need or desirability to follow groups of individuals for epidemiological purposes, and how to prepare for such eventualities. Such questions are likely to be relevant or applicable in the case of non-radiological emergencies.

DISCUSSION

Reasons for implementing epidemiological follow-up of groups of persons 'at risk' after an emergency event include:

1. To identify adverse health effects in the 'at risk' group, and to determine if the risk of such effects is greater relative to some comparable 'non-exposed' group or population.

2. To determine if increased risks that may be identified are associated with exposure to known agents (e.g., radioactive materials, released in the emergency).

3. To determine if the increased risks observed are related to or influenced by other factors associated with or independent of the emergency.

4. To add to the scientific basis for establishing or modifying protection standards for workers and the public.

Outcomes of the first three of these follow-up objectives potentially can benefit individuals in the 'at risk' group by:

1. Identifying a need for medical awareness of verified or suspected exposure to potentially hazardous agents.

2. Identifying the need to include 'at risk' persons in medical monitoring or screening programs that are known to be effective in early detection of diseases inducible by the agent involved in the emergency, so that interventions can be implemented to avoid or minimize future morbidity.

Implementation of actions to achieve these objectives are likely to reassure the individuals and groups that: 1) something is being done; 2) they will know if they are or are not at increased risk for developing exposure – related diseases in the future; and if so 3) appropriate actions to prevent or minimize the effects of the increased risk can be implemented.

Although increasing the scientific basis for protection standards may not be of direct benefit to the individuals in the 'at risk' groups, it may contribute to improved protections for others at risk of similar exposures in the future.

Unfortunately, implementing such follow-up programs is not without its technical or scientific difficulties and limitations, the first of which is 'who should be included?' Other practical considerations included: 1) whether or not the exposure is known to cause an unique disease; 2) what 'measures of exposure' are available; how certain are they?; and 3) is there likely to be a definitive answer in the short-term. Factors that can affect or influence the interpretation of the results of epidemiological studies include: 1) whether the population or number of individuals available for inclusion or the follow-up program, and the exposure levels are sufficient to identify an effect of the exposure of interest, if any exists. This is especially important when the outcome is not uniquely caused by the exposure part as in the case of radiation and cancer. In these cases, attribution of the increased risk to the exposure must rely on statistically significant differences between the risk of the outcome (disease) in the 'exposed' compared with a 'non-exposed' group. Large populations generally are needed to achieve this objective. The interval between an exposure and an exposure-related health outcome, such as cancer, especially is long, so that long periods of follow-up may be necessary before a valid result is available. Also, human health is inevitably affected by inherent genetic and life-style factors that must be considered in interpretation of results. Such factors would include the stresses of the emergency itself, such as evacuation, loss of economic support, and the benefits that may accrue to the 'exposed' population such as increased medical attention, or improved diets.

CONCLUSION

Proper consideration of issues relating to epidemiological follow-up is appropriately included in the planning for radiation and other potential emergencies to the benefit of the public health. Such planning should include capabilities to immediately and adequately document persons impacted by the emergency so as to permit their follow-up directly by contact, or indirectly

through national records systems such as the Social Security Administration or State Drivers' License Bureaus.

It is likely that there will be emergency or accident situations in which epidemiological follow-up of the 'survivors' is not justifiable on scientific grounds but in which socio-economic and political considerations necessitate implementation of a follow-up program. Being prepared to act effectively in either situation is to the advantage of the responders and in the interests of the public health.

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