Medical Treatment of Radiological Casualties: Current Concepts

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The threat of radiologic or nuclear terrorism is increasing, yet many physicians are unfamiliar with basic treatment principles for radiologic casualties. Patients may present for care after a covert radiation exposure, requiring an elevated level of suspicion by the physician. Traditional medical and surgical triage criteria should always take precedence over radiation exposure management or decontamination. External contamination from a radioactive cloud is easily evaluated using a simple Geiger-Müller counter and decontamination accomplished by prompt removal of clothing and traditional showering. Management of surgical conditions in the presence of persistent radioactive contamination should be dealt with in a conventional manner with health physics guidance. To be most effective in the medical management of a terrorist event involving high-level radiation, physicians should understand basic manifestations of the acute radiation syndrome, the available medical countermeasures, and the psychosocial implications of radiation incidents. Health policy considerations include stockpiling strategies, effective use of risk communications, and decisionmaking for shelter-in-place versus evacuation after a radiologic incident. [Ann Emerg Med. 2005;■■:■■■.]

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INTRODUCTION

Many physicians and other health care providers are unfamiliar with the medical treatment of radiologic casualties. The recent emphasis on the threat of a terrorist attack using nuclear or radiologic weapons, including radiologic dispersion devices, makes it imperative that clinicians understand the key concepts surrounding appropriate health and medical interventions for patients potentially exposed to radiation. In this article, we review current doctrine surrounding medical treatment of radiologic casualties and outline the most recent expert consensus on medical countermeasures.[1-4]

BACKGROUND

Global nuclear war is less likely than in the past, but terrorist use of radiologic weapons is an ongoing threat. Radioactive materials have been confiscated from sellers on various international black markets, making it more than a possibility that they might become available in the United States. In addition, inadequate controls on radioactive materials and the possibility that they might become available create a credible risk that terrorists might acquire and attempt to use such materials.[5] Authorities have also expressed concern that improvised nuclear weapons might be developed and used as weapons of mass destruction.

A terrorist nuclear detonation is the worst-case scenario. Even the smallest detonation (or criticality event) would cause damage comparable to or exceeding the damage caused by the attacks of September 11, 2001. Casualties whose radiation dose is most amenable to treatment will be those who receive between 2 and 6 Gy (200 to 600 rad). Without medical treatment, nearly all casualties who receive more than 4 Gy will die within 30 days.[6] In the absence of medical treatment, the midlevel lethal radiation (dose that will kill 50% of the population within 30 days) for humans has been estimated to be approximately 3.5 Gy, with mortality for untreated patients increasing sharply at higher doses. The primary goal of medical therapy is to shift the survival curve to the right by about 2 Gy.[7] Most casualties whose doses exceed 6 to 8 Gy will also have significant blast and thermal injuries that will preclude survival when combined with their radiation insult.

By contrast, a radiologic dispersion device (''dirty bomb'') is constructed from available radioactive material, which is then dispersed by conventional explosives or other means. Because material is distributed widely, the dose rate at any given location

Table 1. Findings of the prodromal phase of acute radiation syndrome.

Symptoms and Medical Response	ARS Degree and the Approximate Dose of Acute WBE, Gy				
	Mild (1–2 Gy)	**Moderate (2–4 Gy)**	**Severe (4–6 Gy)**	**Very Severe (6–8 Gy)**	**Lethal (>8 Gy)***
Vomiting					
Onset	2 h after exposure or later	1–2 h after exposure	Earlier than 1 h after exposure	Earlier than 30 min after exposure	Earlier than 10 min after exposure
Incidence, %	10–50	70–90	100	100	100
Diarrhea	None	None	Mild	Heavy	Heavy
Onset			3–8 h	1–3 h	Within minutes or 1 h
Incidence, %			<10	>10	Almost 100
Headache	Slight	Mild	Moderate	Severe	Severe
Onset			4–24 h	3–4 h	1–2 h
Incidence, %			50	80	80–90
Consciousness	Unaffected	Unaffected	Unaffected	May be altered	Unconsciousness (may last seconds/minutes)
Onset					Seconds/minutes
Incidence, %					100 (at >50 Gy)
Body temperature	Normal	Increased	Fever	High fever	High fever
Onset		1–3 h	1–2 h	<1 h	<1 h
Incidence, %		10–80	80–100	100	100
Medical response	Outpatient observation	Observation in general hospital, treatment in specialized hospital if needed	Treatment in specialized hospital	Treatment in specialized hospital	Palliative treatment (symptomatic only)

ARS, Acute radiation syndrome; *WBE,* whole-body exposure.
*With appropriate supportive and marrow resuscitative therapy, individuals may survive for 6 to 12 months with whole-body doses as high as 12 Gy. Adapted from International Atomic Energy Agency, Diagnosis and Treatment of Radiation Injuries, Safety Report Series No. 2. Vienna; 1998.[29]

would be comparatively low. For most victims, contamination with radiologic particles would be the primary problem. All victims of a radiologic dispersion device event should initially be considered externally contaminated and may receive skin β-radiation injury if not promptly decontaminated. They should also be assessed for the presence of significant internal contamination when conditions permit. Recommendations about treatment of internally contaminated individuals are made case by case in consultation with a health physicist.

The easiest weapon to devise is surreptitious public placement of an unshielded high-level radioactive industrial device. The individual's exposure time, any intervening shielding, and distance from the source would determine the dose received. The vast majority of exposed persons will be asymptomatic, but this population group could be large enough to demonstrate significant stochastic effects (ie, possible eventual malignancies) over time.

BASIC PRINCIPLES OF ACUTE RADIATION INJURY

Radiation injury is caused by deposition of energy in tissue.[8] This energy promotes free-radical formation, which may damage DNA or other cellular structures and processes. The risk of adverse effects is proportional to the total absorbed dose a person receives and the rate at which that dose is delivered. Cellular repair mechanisms are effective at low dose rates but tend to fail when the same dose is delivered quickly. Thus, acute, rather than protracted, exposures are more likely to lead to cell death or malignant transformation. At high radiation doses, some parenchymal cells will die. The clinical effect may be insignificant if the cells are not critical to the survival of the individual. However, if a large number of cells are killed or if they are essential to proper organ function, clinical symptoms may become apparent. In general, rapidly dividing cells (such as those of the intestinal mucosa and bone marrow) are the most sensitive to cell killing by radiation. At radiation doses less than 1.0 Gy (100 rad), most damage is modest, and the majority of cells will survive, although they may be subject to subsequent malignant transformation.[9]

Whole-Body Radiation Exposure

A large single exposure of penetrating γ radiation (ie, high-energy γ rays of sufficient energy to cause significant organ dose) can result in various forms of the acute radiation syndrome (Tables 1, 2, and 3). The absorbed dose can initially be evaluated on the basis of symptoms and refined with laboratory studies. The presence and timing of nausea and vomiting is an excellent screening tool to detect those who require urgent medical investigation.[10] Serial CBCs will identify those who have medically important radiation doses. If there is

Table 2. Findings of the critical phase of acute radiation syndrome.

	Degree of ARS and Approximate Dose of Acute Whole-Body Exposure, Gy				
	Mild (1–2 Gy)*	**Moderate (2–4 Gy)**	**Severe (4–6 Gy)**	**Very Severe (6–8 Gy)**	**Lethal (>8 Gy)**
Onset of signs	>30 d	18–28 d	8–18 d	<7 d	<3 d
Lymphocytes, G/L	0.8–1.5	0.5–0.8	0.3–0.5	0.1–0.3	0.0–0.1
Platelets, G/L	60–100	30–60	25–35	15–25	<20
	10–25%	25–40%	40–80%	60–80%	80–100%†
Clinical manifestations	Fatigue, weakness	Fever, infections, bleeding, weakness, epilation‡	High fever, infections, bleeding, epilation‡	High fever, diarrhea, vomiting, dizziness and disorientation, hypotension	High fever, diarrhea, unconsciousness
Lethality, %	0	0–50	20–70	50–100	100
		Onset 6–8 wk	Onset 4–8 wk	Onset 1–2 wk	1–2 wk
Medical response	Prophylactic	Special prophylactic treatment from days 14–20; isolation from days 10–20	Special prophylactic treatment from days 7–10; isolation from the beginning	Special treatment from the first day; isolation from the beginning	Symptomatic only

GL, international parlance (SI units) for concentration and refers to Giga per Liter/or 10 to the 9th (a billion) of the items per liter.
Adapted from International Atomic Energy Agency, Diagnosis and Treatment of Radiation Injuries, Safety Report Series No. 2. Vienna; 1998.[29]
*One Gray=100 rad.
†In very severe cases, with a dose >50 Gy, death precedes cytopenia.
‡Hair loss.

a significant decrease in lymphocytes in the first 6 to 48 hours, prolonged and intense medical treatment will likely be required (Table 4).[11]

At dose levels greater than 30 Gy (3,000 rad) of whole-body penetrating radiation, the cardiovascular/central nervous system syndrome occurs primarily as a result of hypotension and cerebral edema. There is almost immediate nausea, vomiting, prostration, hypotension, ataxia, and convulsions. These casualties should receive palliative treatment only because death invariably occurs within several days. Events that have produced this dose level are extremely rare, having occurred in only a handful of accident victims worldwide.

The gastrointestinal syndrome occurs from acute whole-body doses of approximately 6 to 20 Gy (600 to 2,000 rad), primarily because of death of intestinal mucosal stem cells. In this syndrome, there is prompt onset of nausea, vomiting, and diarrhea. There is a latent period of approximately 1 week and then recurrence of gastrointestinal symptoms, sepsis, electrolyte imbalance, and ultimately death.

The hematopoietic syndrome occurs from acute whole-body doses of approximately 2 to 10 Gy (200 to 1,000 rad) as a result of bone marrow depression. After prodromal symptoms, there is a latent period of 2 to 3 weeks during which the patient may feel well. During this time, arrangements for medical care at an appropriate center should be coordinated. Lymphocyte depression can occur within 48 hours and is a useful indicator of dose. Maximal bone marrow depression with leukopenia and thrombocytopenia occurs several weeks after exposure; hemorrhage and infection can be major clinical problems.

The correct diagnosis of potential radiation injury is made approximately 85% of the time by a thorough medical history. However, the recent history of radiation medicine shows many cases of delayed diagnosis. In an analysis of 4 major radiation accidents involving lost sources (Mit Halfa, Egypt [May 2000]; Bangkok, Thailand [February 2000]; Tammiku, Estonia [October 1994]; and Goiania, Brazil [September 1987]), the average time from beginning of the accident until definitive

Table 3. Findings of the latent phase of acute radiation syndrome.

	Degree of ARS and Approximate Dose of Acute Whole-Body Exposure, Gy				
	Mild (1–2 Gy)	**Moderate (2–4 Gy)**	**Severe (4–6 Gy)**	**Very Severe (6–8 Gy)**	**Lethal (>8 Gy)**
Lymphocyte, G/L, days 3-6	0.8–1.5	0.5–0.8	0.3–0.5	0.1–0.3	0.0–0.1
Granulocytes, G/L	>2.0	1.5–2.0	1.0–1.5	≤0.5	≤0.1
Diarrhea	None	None	Rare	Appears on days 6–9	Appears on days 4–5
Epilation (loss of hair)	None	Moderate, beginning on day 15 or later	Moderate, beginning on days 11–21	Complete earlier than day 11	Complete earlier than day 10
Latency period, d	21–35	18–28	8–18	≤7	None
Medical response	Hospitalization not necessary	Hospitalization recommended	Hospitalization necessary	Hospitalization urgently necessary	Symptomatic treatment only

Adapted from International Atomic Energy Agency, Diagnosis and Treatment of Radiation Injuries, Safety Report Series No. 2. Vienna; 1998.[29]

Table 4. Expected patient outcome based on absolute lymphocyte count over time after acute penetrating whole-body irradiation.

Minimal Lymphocyte Count Within First 48 h After Exposure	Approximate Absorbed Dose, Gy	Prognosis
1,000–3,000 Normal range	0–0.5	No significant injury
1,000–1,500	1–2	Significant but probably nonlethal injury, good prognosis
500–1,000	2–4	Severe injury, fair prognosis
100–500	4–8	Very severe injury, poor prognosis
<100	>8	High incidence of lethality even with hematopoietic stimulation

diagnosis averaged approximately 22 days. Other accidents, such as the nuclear criticality accident in Tokaimura, Japan, in September 1999, were recognized immediately because of their occurrence in industrial settings with known radiation hazards.

If the patient is aware, radioactive source exposure, description, time of onset of symptoms, and symptom severity should be documented. An early, baseline CBC with differential should be obtained and repeated every 4 to 6 hours to monitor for declines in the lymphocyte and neutrophil count. In addition, blood may be obtained after 24 hours for chromosomal aberration biodosimetry.[12]

After medical stabilization, patients should be assessed for radiation injury on the basis of dose, isotope, and presence of internal contamination. Rapid-sort, automated chromosome biodosimetry and assessment of clinical characteristics such as the time to emesis post event and lymphocyte depletion kinetics estimate radiation dose to a patient involved in a mass casualty incident. Time to emesis, measured from the time of irradiation, decreases monotonically with increasing dose. For time to emesis less than 4 hours, the effective whole-body dose is likely to be at least 3.5 Gy. If time to emesis is less than 1 hour, the whole-body dose probably exceeds 6.5 Gy, and a very complicated and likely fatal medical course may be expected. Lymphocyte depletion follows first-order kinetics after high-level γ and criticality incidents. An estimation of patient radiation dose may be obtained from the medical history, serial lymphocyte counts, and time to emesis using algorithms from the Armed Forces Radiobiology Research Institute's free Biological Assessment Tool, which may be requested on the Internet.[12]

Localized Radiation Exposure

Localized radiation injury occurs from direct handling of intense radioactive sources. The patient often survives, even if local absorbed doses are very high. Because dose rate drops very quickly with distance from the radioactive item, systemic manifestations are less severe than the local injury. In contrast to thermal burns, radiation injury presents with delayed erythema and desquamation or blistering (12 to 20 days postevent).[13] Months to several years after radiation skin burns, vascular insufficiency can cause ulceration or necrosis of tissues that had previously healed.[14]

Treatment of localized radiation injuries includes pain control, prevention of infection, vasodilators, and sometimes plastic surgery, grafting, or amputation. Deterministic thresholds exist as follows for certain clinical signs:

1. 3-Gy (300 rad) threshold for epilation, beginning 14 to 21 days postaccident
2. 6-Gy (600 rad) threshold for erythema, soon postaccident and possibly again 14 to 21 days thereafter
3. 10- to 15-Gy (1,000 to 1,500 rad) threshold for dry desquamation of the skin secondary to radiation to the germinal layer
4. 20- to 50-Gy (2,000 to 5,000 rad) threshold for wet desquamation (partial-thickness injury) at least 2 to 3 weeks postexposure, depending on dose
5. For doses significantly greater than 50 Gy (5,000 rad), overt radionecrosis and ulceration resulting from endothelial cell damage and fibrinoid necrosis of the arterioles and venules in the affected area (a cutaneous syndrome, arising from high-level whole-body along with local injury, has also been described)[1]

OVERVIEW OF MEDICAL TREATMENT FOR RADIATION INJURY

There is significant clinical experience with persons who have received large amounts of external body radiation.[1,2] In general, medical treatment is necessary only for persons who have received external exposure with absorbed doses in excess of 1 Gy (100 rad). Antibiotics used to treat radiation-exposed patients are commonly available and, in most cases, will not be required during the initial 7 to 10 days. Many of the antibacterial agents that would be used in this setting are maintained in the Strategic National Stockpile or its vendor-managed inventory system.[7] Other drugs that would be required include antibiotics used to treat drug-resistant organisms, antiviral medications used to treat opportunistic viral infections, and antifungal medications used to treat *Aspergillus*, candidiasis, and other fungal infections arising in patients with depressed cell-mediated immunity. General objectives in approximate order of importance for emergency management of seriously injured and contaminated patients are as follows:

1. First aid and resuscitation
2. Medical and surgical stabilization
3. Definitive treatment of serious injuries
4. Prevention/minimization of internal contamination
5. Assessment of external contamination and decontamination
6. Treatment of other minor injuries
7. Containment of the contamination to the treatment area and prevention of contamination of other personnel
8. Minimization of external radiation to rescue and treatment personnel
9. Assessment of internal contamination

10. Treatment of internal contamination (this could be concurrent with many of the above)
11. Assessment of local radiation injuries/radiation
12. Counseling of patients about expected long-term effects and risks
13. Long-term follow-up of patients with significant whole-body irradiation or internal contamination

DECONTAMINATION, PREVENTION OR MINIMIZATION OF INTERNAL CONTAMINATION, AND MANAGEMENT OF CONTAMINATED WOUNDS

Skin or wound contamination is seldom life threatening to the patient or to health care personnel. Ideally, the patient will have been decontaminated before transport or before being brought into the emergency department. In the wake of the September 11, 2001, attacks and the dissemination of anthrax through the US mail, most large health care facilities have incorporated procedures for decontamination into their emergency operations plans, although few, if any, have the capability to decontaminate the large number of patients that would present after the detonation of a radiologic dispersion device.

As a general rule of thumb, removal of outer clothing and shoes should reduce the level of external contamination by approximately 90%. Residual contamination can be assessed by passing a radiation detector held a constant distance from the skin over the entire body. Subsequent decontamination of the skin and hair with soap and warm water and gentle brushing to dislodge radioactive particles bound to skin proteins will significantly reduce the remaining contamination. The goal of decontamination should be to remove as much radioactive material as possible without damaging the skin. Open wounds should be covered so as to minimize the risk of internal contamination. The level of contamination should then be reassessed using the same technique and distance from the skin as in the primary survey. The goal of decontamination is to reduce the level of contamination to less than 2 times background radiation or until subsequent attempts reduce the level of contamination by less than 10%.

The cleaning of contaminated wounds will depend on the nature of the injury. Abrasions can be cleaned using standard decontamination techniques, whereas lacerations may require excision of the contaminated tissue if irrigation alone is not effective. Contaminated puncture wounds have sometimes been cleaned successfully using oral irrigators or water jets but typically are difficult to decontaminate because of poor access to the contaminants. Wounds containing radioactive shrapnel must be handled with special care (it has occasionally been necessary to amputate heavily contaminated extremities when radioactive shrapnel could not be removed). All contaminated wounds can increase the level of internal contamination through absorption of radioactive materials directly into the circulatory and lymphatic systems.

If ingestion (as opposed to inhalation) of radioactive material is suspected, administration of aluminum hydroxide or magnesium carbonate antacids is indicated to reduce gastrointestinal absorption. Aluminum-containing antacids should be administered if there is reason to believe that strontium isotopes have been ingested. If ingestion has occurred no more than 1 to 2 hours before evaluation, gastric lavage may be performed to reduce internal contamination. For large ingestions, cathartics (including enemas) may be administered to decrease gastrointestinal transit time.

Pulmonary lavage may be considered after significant inhalations of insoluble radionuclides but in general is rarely indicated.

MEDICAL COUNTERMEASURES

Medical countermeasures for radiation fall into 3 broad classes. Radioprotectants are drugs that prevent radiation-induced cellular and molecular damage, radiation mitigators are drugs that accelerate recovery or repair after radiation injury, and radionuclide eliminators are drugs that discorporate or block absorption of internalized radionuclides.

Numerous candidate radiation countermeasures have been identified (Table 5). Radioprotectants currently licensed or under investigation include the phosphorylated aminothiols amifostine and phosphonol, Tempol and other membrane-permeable nitroxides, keratinocyte growth factor, the angiotensin-converting enzyme inhibitor captopril, the isoflavone genistein, the nonandrogenic steroid androstenediol, and the vitamin E analogue α-tocopherol succinate. Radiation mitigators currently under investigation include the colony-stimulating factors, androgenic steroid androstenediol, glutamine, and pentoxifylline. Radionuclide eliminators currently licensed or under investigation include potassium iodide, ferric hexacyanoferrate (Prussian blue), calcium and zinc diethylenetriaminepentaacetate (Ca- and Zn-DTPA), bicarbonate, barium sulfate, calcium gluconate, penicillamine, the aluminum antacids, and sodium alginate.

Colony-Stimulating Factors (Cytokines)

Colony-stimulating factors are endogenous glycoproteins that induce bone marrow hematopoietic progenitor cells to proliferate and differentiate into specific mature blood cell types. Three recombinant colony-stimulating factors (filgrastim, pegfilgrastim, and sargramostim) are licensed for use in patients with neutropenia resulting from myelosuppressive chemotherapy.[15] Filgrastim and sargramostim have been used in radiation accident victims and anecdotally appear to hasten recovery of neutrophil counts, but experience is limited and it is impossible to draw conclusions about the clinical effectiveness of colony-stimulating factors in this setting. Numerous studies, however, demonstrate shortening of the duration of severe neutropenia when colony-stimulating factors are administered early (1 to 2 days) postirradiation to Cobalt-60 irradiated rhesus macaques.[16] The Radiation Studies Branch at the Centers for Disease Control and Prevention recently developed an investigational new drug protocol for the use of colony-stimulating factors in patients exposed to high doses of ionizing radiation.

Table 5. Specific therapies for internal contamination.

Radionuclide	Therapy
Tritium	Dilution (force fluids)
Iodine-125 or 131	Blocking (SSKI or potassium iodide) Mobilizing (antithyroid drugs)
Cesium-134 or 137	Blocking (Prussian blue)
Strontium-89 or 90 ingestion	Decrease absorption (aluminum phosphate gel antacids) Blocking (strontium lactate) Displacement (oral phosphate) Mobilization (ammonium chloride or parathyroid extract)
Plutonium and other transuranics	Chelating (Zn or Ca-DTPA; investigational)
Unknown ingestion	Reduce absorption; consider emetics, lavage, charcoal, laxatives

SSKI, Saturated solution of potassium iodine.

In a recent review, Waselenko et al[7] proposed a set of triage protocols for the administration of colony-stimulating factors to victims of radiologic terrorism. They recommended the initiation of cytokine therapy in healthy individuals with no other injuries who receive exposures in excess of 3 Gy and in persons with multiple injuries or burns who receive exposures in excess of 2 Gy. (The upper limits of exposure are determined largely by the scale of the event and available resources.) The authors also recommended initiating therapy with filgrastim at 5 μg/kg per day or sargramostim at 250 $\mu g/m^2$ per day administered subcutaneously as soon after exposure as possible and continuing therapy until the absolute neutrophil count exceeds 1,000. Alternatively, 6 mg of pegfilgrastim can be administered subcutaneously once weekly to adults and adolescents greater than 45 kg.

Role of Stem Cell and Bone Marrow Transplantation

The toxic effects of ionizing radiation on the hematopoietic system are well documented.[17,18] Ionizing radiation causes dose-dependent declines in circulating cells by direct toxic effects on the bone marrow and induction of apoptosis in mature formed elements of the blood. The mechanisms of this toxicity are complex and may involve direct effects on DNA, effects on gene expression, the activation of apoptotic pathways, and the so-called bystander effect in which radiation induces pathophysiologic effects in unirradiated cells. The radiation level causing irreversible failure of the hematopoietic system varies among individuals and undoubtedly reflects genetic and individual physiologic differences, as well as the circumstances of the exposure (direction, duration, presence of partial shielding, and so forth). For persons with persistent marrow failure who do not respond to marrow stimulation, allogeneic stem cell transplantation would appear to be a therapy that could reestablish hematopoiesis. Unfortunately, this same patient group would likely have other severe irradiation effects.

Even if serious damage occurs to most of the hematopoietic system, surviving stem cells can migrate to damaged areas and restore hematopoiesis. Ex vivo expansion of adult human hematopoietic stem cells, an area of current research in transplantation and gene therapy, may play a role in the management of such patients in the future.

The role of bone marrow transplantation in response to radiation injury is limited. Because of the resilience of hematopoietic stem cells, the wide distribution of stem cells in the marrow, the ability of remaining stem cells to repopulate the entire hematopoietic system, and the likelihood of nonuniform radiation in accidental exposure, most individuals can recover hematopoiesis without a bone marrow transplant. Serious radiation injury to the lungs and other organs, as well as burns and physical trauma, will in many cases be of greater consequence than marrow injury. However, bone marrow transplantation may be useful in carefully selected cases.

Amifostine

Amifostine, approved by the US Food and Drug Administration (FDA) in 1999 as the first radioprotectant, is a freely soluble organic thiophosphate cytoprotective agent used to reduce toxicities associated with certain cancer chemotherapy and radiotherapy. It is indicated to reduce the incidence of moderate to severe xerostomia in patients undergoing postoperative radiation treatment for head and neck cancer, in which the radiation port includes a substantial portion of the parotid glands. Amifostine must be administered intravenously and is typically given 15 to 30 minutes before radiotherapy. It is not effective when administered postexposure.

Amifostine also appears to enhance the chemical and enzymatic repair of damaged DNA, and animal studies have suggested that amifostine administered before γ and neutron irradiation may reduce subsequent carcinogenesis and mutagenesis.[19] The potential of amifostine to reduce the long-term consequences of radiation exposure suggests a possible prophylactic role for this compound in protecting first responders entering contaminated areas after a radiologic or nuclear event.[20] However, intravenous amifostine has been associated with significant dose-limiting adverse effects (including severe hypotension, nausea, vomiting, and hypocalcemia), and this inherent toxicity, the limited window of drug-induced protection, and the need to administer the drug by intravenous infusion severely limit the drug's utility in nonclinical settings.[21]

Potassium Iodide

Potassium iodide is the drug of choice to prevent thyroid uptake of radioiodines, but it provides no protection from external irradiation. It must be administered within a few hours of exposure to confer its thyroid-protective benefits.[22] Children are more vulnerable to the effects of radioiodine than adults.[23] The World Health Organization reference levels for the implementation of iodine blockade in different age groups reflect these differences. Potassium iodide therapy in the setting of acute radioiodine exposure is rarely indicated for adults older than 40 years and generally only if there is a projected thyroid dose of 5 Gy or greater. In neonates, infants,

and children, therapy should be initiated to avert as little as 10 mGy of radiation. Potassium iodide has been associated with rashes, allergic reactions, and gastrointestinal symptoms. Persons with underlying thyroid disease are at risk for iodine-induced thyroid dysfunction.

Prussian Blue

Ferric hexacyanoferrate, or Prussian blue, is an insoluble dye that, when administered orally, enhances fecal excretion of cesium and thallium from the body by means of ion exchange. Radioactive isotopes of cesium, particularly cesium-137, are a byproduct of nuclear fission reactions and also have many commercial and medical applications. Cesium-137 is considered ideally suited for acts of radiologic terrorism because of its presence in current or abandoned radiation therapy and industrial devices, its long half-life (30 years), its highly specific activity (88 Ci/g), and its granular nature and solubility (as a chloride salt).[24]

Treatment of internal contamination with cesium-137 is not usually indicated in persons for whom the internal contamination is less than 1 annual limit of intake.[25] An annual limit of intake for cesium-137 is 200 μCi (7.4 MBq) from inhalation and 100 μCi (3.7 MBq) from ingestion. Treating physicians should consult with a qualified health physicist to determine whether the annual limit of intake has been exceeded. At 1 to 10 times the annual limit of intake, the need for treatment is controversial, whereas at estimated intakes exceeding 10 times the annual limit of intake, treatment is usually indicated. Prussian blue generally should be discontinued once less than 1 annual limit of intake remains in the patient. If, after prolonged therapy, greater than 1 annual limit of intake of contamination persists, Prussian blue can also be discontinued at the discretion of the treating physician.

The FDA recommends that adults and adolescents receive 3 g of Prussian blue 3 times a day and children 2 to 12 years of age receive 1 g 3 times a day for a minimum of 30 days. Treatment may be individualized, depending on the level of internal contamination.[26] The most significant adverse effect associated with Prussian blue is constipation. Prussian blue should be used with caution in patients with decreased gastrointestinal motility.

Ca- and Zn-DTPA

Ca- and Zn-DTPA are chelating agents used to treat internal contamination with the transuranic elements plutonium, americium, and curium.[27] Ca- and Zn-DTPA react with these elements to form stable ionic complexes, which are then excreted in the urine. The FDA recommends that therapy be initiated with a single 1.0-g loading dose of Ca-DTPA in adults (14 mg/kg in children younger than 12 years) administered intravenously as soon as possible after exposure. Ca-DTPA is believed to be teratogenic and should not be administered to pregnant women if Zn-DTPA is available.

The recommended maintenance dose is 1.0 g (14 mg/kg in children) of Zn-DTPA administered intravenously once a day, administered over days, months, or years, depending on the level of internal contamination. Ca-DTPA is also effective when administered by nebulizer. Serum levels of trace minerals, including zinc, magnesium, and manganese, should be monitored during therapy.

PSYCHOLOGICAL EFFECTS OF RADIATION INJURY

An attack involving the release of radiation will likely create uncertainty and fear. Once it is revealed that terrorists have used a radiologic dispersal device, the management of acute psychological and behavioral responses will be as important and challenging as the treatment of radiation-related injuries and illnesses. Those who have been exposed or even anticipate possible exposure may experience feelings of vulnerability, anxiety, and lack of control. Signs and symptoms of autonomic arousal such as tachypnea, tachycardia, nausea, and diarrhea occurring in unexposed patients may be misattributed to the effects of radiation. Psychological distress after a radiologic incident may also manifest as nonspecific somatic complaints (a presentation sometimes referred to as multiple idiopathic physical symptoms).[28] Health care providers who do not have a clear understanding of the risks posed by radiation or how to protect themselves from these risks may experience fear and anxiety, resulting in absenteeism, refusal to see patients, and dereliction of duty.

Mental health professionals should be an integral part of the teams performing initial screening and triage of potentially exposed victims. Providing food and shelter in a safe environment, facilitating communication with family and loved ones, limiting exposure to reminders of the event, and directing victims to available services and support are all critical elements of psychological first aid, but the first priority must be the provision of good medical care. Assessing and recording the patient's specific concerns and making arrangements for follow-up (rather than advising the patient to "return if there is a problem") will mitigate the patient's psychologic distress. Providing accurate information about the risks of exposure and available medical countermeasures will also lessen fear, concern, and distress. Some patients, such as pregnant women, the parents of small children, and children themselves, have special needs and may require additional attention. Patients may also be concerned about the long-term risk of developing cancer, and this concern may persist for years after the event in question.

For the vast majority of people, distress and psychological and behavioral symptoms related to the traumatic event exposure will diminish over time. For others, however, symptoms will persist, affect function at home and work, and may result in psychiatric illness. In addition to acute stress disorder and posttraumatic stress disorder, major depression, increased substance use, family conflict, and generalized anxiety disorder are also encountered. People with no psychiatric history are vulnerable to psychiatric illness after terrorism, but those at greatest risk include people directly exposed (ie, near the blast or involved in rescue and recovery of victims and

1. All patients should be medically stabilized from their traumatic injuries, without delay, before radiation injuries are considered. Patients are then evaluated for either external radiation exposure or radioactive contamination.
2. An external radiation source with enough intensity and energy can cause tissue damage (eg, skin burns or marrow depression). This exposure from a source outside the person does not make the person radioactive. Even such lethally exposed patients are no hazard to medical staff.
3. Nausea, vomiting, diarrhea, and skin erythema within 4 hours may indicate very high (but treatable) external radiation exposures. Such patients will show obvious lymphopenia in 8 to 24 hours. Evaluate with serial CBCs. Primary systems involved will be skin, intestinal tract, and bone marrow. Treatment may involve fluids, antimicrobial agents, transfusions, and marrow-stimulating factors. In cases involving explosions, during the emergency department phase of treatment, early hypotension and central nervous system changes from radiation effects may be indistinguishable from trauma-related causes. If there are early central nervous system findings or unexplained hypotension, survival is unlikely.
4. Radioactive material may have been deposited on or in the person (contamination). More than 90% of surface radioactive contamination may be removed by removal of the clothing. Most remaining contamination on exposed skin is effectively removed with soap, warm water, and a washcloth. Do not damage skin by overvigorous scrubbing.
5. Protect yourself from radioactive contamination by observing standard precautions, including protective clothing, gloves, and a mask.
6. Radioactive contamination in wound or burns should be handled as if it were simple dirt. If an unknown metallic object is encountered, it should be handled only with instruments such as forceps and saved in a protected or shielded area for forensic analysis.
7. In a terrorist incident, there may be continuing exposure of the public that is essential to evaluate. Initially suggest sheltering and a change of clothing or showering. Evacuation may be necessary. Administration of potassium iodide is indicated only when there has been a confirmed release of radioiodine.
8. When there is any type of radiation incident, many persons will want to know whether they have been exposed or are contaminated. Provision needs to be made to potentially screen thousands of such persons.
9. Radiation doses to people are expressed in gray (Gy) or sievert (Sv). The older units for these are rad and rem. 1 Gy=100 rad, and 1 Sv=100 rem. Clinically significant acute radiation syndrome seldom if ever occurs in people receiving less than 1 Gy of whole-body radiation. The risk of developing cancer after exposure to radiation is a function of the dose received and begins to accrue even with very low doses (ie, there is no minimum threshold dose). For contaminated patients, the amount of radioactivity present is measured in bequerels (Bq) (1 disintegration per second). Sometimes, it may be also expressed in counts per minute. Decontamination is usually stopped if the item is reduced to 2 or 3 times the background count rate or if repeated decontamination efforts are ineffective at further reducing the count rate.
10. The principles of time/distance/shielding are key. Even in the treatment of Chernobyl workers, doses to the medical staff were only about 10 mGy or 10 mSv. Doses to first responders at the scene, however, can be much higher, and appropriate dose-rate meters must be available for evaluation. Radiation dose is diminished by reducing time spent in the radiation area (moderately effective), increasing distance from a radiation source (very effective), or using metal or concrete shielding (less practical).

Figure. Top 10 key points for medical management of radiation casualties.

remains), those with previous mental illness, and those who experience loss of property or disruption of their social supports as a consequence of the incident.

HEALTH POLICY CONSIDERATIONS

The management of large numbers of patients potentially exposed to radiation raises many policy questions that can be addressed as part of routine planning and emergency preparedness. Many emergency management decisions, such as whether to recommend evacuation or sheltering in place, will be based on multiple variables. It must be clear who has the authority to make decisions; how valid scientific data will be collected, analyzed, and weighted; and how the information will be communicated to the public. With respect to the latter, developing a strong risk communication strategy is critical. Identifying and training personnel who will develop and deliver messages to the media and public after an event has occurred will facilitate the dissemination of critical public health information. Appropriate health-risk communications by a credible medical source can greatly reduce anxiety among victims and responders and direct people to appropriate and effective life-saving therapies.

Another major health policy consideration is whether and how to stockpile medical countermeasures. Threat and vulnerability assessments (which can be conducted at the national, state, regional, and local level), combined with modeling of plausible scenarios, will provide an estimate of the number of persons who might be exposed if an event were to occur, and these estimates can be used to assess the need for stockpiling. In making these determinations, public health officials must bear in mind that the initial distribution of countermeasures may occur in a setting in which it is difficult or impossible to perform accurate dosimetry or bioassays and that many more people are likely to present requesting countermeasures than actually need them. Additionally, it may be necessary to stockpile some countermeasures (ie, drugs such as potassium iodide that must be administered within minutes to hours to be effective) at the local level, whereas others (therapies such as cytokines or Prussian blue

that can be administered after a delay) can be stockpiled regionally or even nationally. If the supply of a countermeasure is limited by production capacity (as is the case with Prussian blue and the DTPA products, each of which currently has a single licensed manufacturer), obtaining additional supplies (or resupply) after an incident may be difficult. Finally, for a stockpiling program to work, activation, distribution, and local incident management systems must all be in place and exercised.

Health policy considerations will also influence the development of plans and procedures for triage of potentially exposed patients, especially when such plans and procedures are developed at the community rather than institutional level. Emergency departments should have current emergency management plans in place to deal with large numbers of well-appearing persons concerned that they may have been exposed to radioactive material. A simple Geiger-Müller survey is generally adequate to rule out significant external contamination. If the patient is uninjured and a brief medical history and physical examination have reasonably normal results, prompt referral to a secondary assessment center distant from the trauma scene will allow for a more comprehensive medical examination, psychological counseling, and detailed health physics analysis to evaluate for possible internal contamination.

In summary, government officials have expressed concern that terrorists may use radiologic or nuclear weapons against civilian populations. Most physicians, however, are unfamiliar with the treatment of patients exposed to radiation. Health care providers must know when to suspect radiation injury and keep several key principles in mind (Figure). Radiation exposure can be external or internal or be combined with nonradiation injuries. Physicians should first triage for traumatic and medical emergencies before attending to radiation injuries. It is also crucial that physicians work with health physicists to gain access to appropriate dosimetry equipment. Multiple medical countermeasures exist, but it is essential to identify the involved internal radionuclide to determine the appropriate treatment. Effective risk communications and psychological support are particularly important in a radiologic incident.

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Short Abstract for TOC

The threat of radiologic or nuclear terrorism is increasing, yet many physicians are unfamiliar with basic treatment principles for radiologic casualties. External contamination from a radioactive cloud is easily evaluated using a simple Geiger-Müller counter, and decontamination is easily accomplished by prompt removal of clothing and traditional showering. Management of surgical conditions in the presence of persistent radioactive contamination should be dealt with in a conventional manner with health physics guidance. To be most effective in the medical management of a terrorist event involving high-level radiation, physicians should understand basic manifestations of the acute radiation syndrome, the available medical countermeasures, and the psychosocial implications of radiation incidents. Health policy considerations include stockpiling strategies, effective use of risk communications, and decisionmaking for shelter-in-place versus evacuation after a radiologic incident.