Department of Homeland Security Working Group on Radiological Dispersal Device (RDD) Preparedness

Medical Preparedness and Response Sub-Group

5/1/03 Version

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MEDICAL GUIDELINES
IONIZING RADIATION AND TERRORIST INCIDENTS: IMPORTANT POINTS FOR THE PATIENT AND YOU

1. All patients should be medically stabilized from their traumatic injuries 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 (e.g., 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 four hours may indicate very high (but treatable) external radiation exposures. Such patients will show obvious lymphopenia within 8-24 hours. Evaluate with serial CBC's. Primary systems involved will be skin, intestinal tract and bone marrow. Treatment is supportive with fluids, antibiotics, and transfusions stimulating factors. If there are early CNS 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 is removed by removal of the clothing. Most remaining contamination will be on exposed skin and is effectively removed with soap, warm water, and a washcloth. Do not damage skin by 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 only be handled with instruments such as forceps and should be placed in a protected or shielded area.

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 iodine (KI) is only indicated when there has been 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. Provisions need to be made to potentially deal with thousands of such persons.

9. Radiation doses to people are expressed in Gray (Gy) or Sieverts (Sv). The older units for these are rad and rem. 1 Gray = 100 rad and 1 Sv = 100 rem. An approximation of the relative hazard is given:

Dose	Relative Hazard
About 10 milligray or 10 millisievert (1 rad or rem) or less	No acute effects and only a very small chance of subsequent cancer.
About 0.1 gray or 0.1 sievert	No acute effects, subsequent additional risk of cancer about 0.5%
About 1 gray or 1 sievert	Nausea, vomiting possible, mild bone marrow depression subsequent risk of cancer 5%
Greater than 2 gray or sievert	Definite nausea, vomiting, medical evaluation and treatment required

The amount of radioactivity (contamination) is measured in units of Bequerels (Bq) (1 disintegration per second). Sometimes, it is expressed in counts per minute. Decontamination is usually stopped if the item is reduced to two times the background count rate or if repeated decontamination efforts are ineffective.

10. The principal of *time/distance/shielding* is key. Even in treatment of Chernobyl workers, does to the medical staff were about 10 milligray or 10 millisievert. 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 reduced 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).

MEDICAL GUIDELINES

RADIOLOGICAL PROTECTION FOR FIRST RESPONDERS AND FIRST CONTACT MEDICAL PERSONNEL

2/25/03 Version

Background

The following basic question should drive the actions and precautions of first responders to an RDD event:

- How badly injured are the victims?

RDD events are very unlikely to contaminate victims in a way that will be harmful to responders or caregivers. If a victim is acutely injured, responders should attend to those injuries immediately, regardless of the type or degree of personal protective equipment that is available. Normal barrier clothing and masks should be used if available, but care of patients with life-threatening injuries should not be delayed because first responders lack adequate personal protective equipment Contaminated personnel, equipment, and vehicles can be cleaned later, at little risk to human health or the integrity of the equipment.

In situations involving less-seriously injured victims, or with more time to prepare, greater discretion and attention to personal protective equipment is permissible and in fact recommended.

RDD events, by their nature, disperse radioactive material. There is a risk that finely-divided material may be ingested, inhaled, or absorbed through the skin, although contamination via the latter routes would be uncommon.

Improvised nuclear devices, producing a nuclear detonation, will spread much more radioactive material over a much wider area**.** The precautions that responders must take in this case, however, will be essentially the same.

Radiation is colorless, odorless, tasteless and invisible. The only way to determine whether radioactive material has been involved in an event is to perform *radiological surveys* with specialized equipment. Whenever a hazardous material release is suspected, the incident commander should inform responders of any special precautions that need to be taken.

The three main concerns for first responders to a radiologically contaminated site are, in this order:

- Care of patients with acute traumatic injuries
- Respiratory protection, and
- Skin (barrier) protection.

Respiratory Protection

PPE protection levels are classified A, B, and C, A being the greatest protection level, and C the least. For situations where airborne particulates are the chief concern, such as RDD events, Level C protection is generally sufficient.

There are several approaches to respiratory protection. Fit-tested full or half-mask cartridge-filtered respirators should be used when available. Powered-air purifying respirators (PAPRs) are also useful. Any respiratory protection that is designed to protect responders against chemical or biological agents will likely offer benefits in an RDD event. In fact, concerns for the presence of chemical contaminants at a terrorist event will drive the selection of respiratory protection as they may require a higher level of PPE.

One of the best approaches is also one of the simplest. Ordinary surgical facemasks provide good protection against inhaling particulates, and allow excellent air transfer for working at high breathing rates. If available, high-efficiency particulate air (HEPA) filter masks such as the common NIOSH “N-95” mask provide even better protection. These are standard issue for health care workers who work with patients with tuberculosis and other highly contagious diseases. These masks must be fit-tested to each individual by personnel trained in the OSHA-accepted methods. Under stressful conditions, however, they may cause breathing difficulties, due to their inherently reduced air transfer.

On must always consider other, greater hazards when selecting breathing protection. If authorities suspect that particulates such as anthrax or other such bacterial agents are present, an N-95 mask is required. Neither common surgical nor N-95 masks protect against gases and vapors, however. If chemical agents are suspected, level B or higher protection is required, for both the lungs and the skin. This means fitted, full-face respirators and chemical-resistant coveralls.

Skin Protection

Current weather conditions, as well as the environment at the event, will drive the selection of anti-contamination clothing. Normal barrier clothing and gloves give excellent personal protection against airborne particles. Disposable medical scrub suits, high-density polyethylene coveralls (e.g., Tyvek®), or other close-weave coveralls and hood should be used if they are available.

The choice of clothing will often be driven by other more immediate hazards, such as fire, heat, or chemicals. Protection for these hazards covers any additional threat that radioactive material could pose.

As stated above, transport of the severely injured to available acute care medical facilities should not be delayed due to suspected or confirmed radiological contamination on the patient. If a critically injured but contaminated patient must

be transferred immediately, make preparations for limitation of contamination at the destination facility.

Handling of Bodies

Radioactive materials may contaminate the deceased. Appropriate radiation survey assistance can confirm or rule out such a situation. If a body is known or suspected to be contaminated, personnel engaged in handling of the body should be issued personal protective equipment. As stated above, it is important for responders and mortuary personnel to be aware of other, more acutely hazardous agents that may co-contaminate the remains in question. Appropriately higher levels of protection should be used as needed.

Radiation Dosimetry

Two types of devices may be used. The first type is a clip-on badge containing either film or other radiation-sensitive material (AKA a thermoluminescent dosimeter or TLD). The second type of device is a reusable electronic dosimeter, which can be read visually or by other reading devices. Some devices of this type also "chirp" like the traditional Geiger counter. Radiation protection personnel will distribute and explain how to use such devices.

Cost and Scope Implications

Estimated Cost:

Equipment	Cost per Piece
Surgical mask	$1.00 (less than half that in quantity)
Respirator mask, N-95	$4.00 to $5.00 (as little as $1.00 or less in quantity)
Respirator mask, full-face	$50.00 to $200.00
Surgical scrub suit, disposable	$3.00
Skin protective coverall, disposable	$4.00 to $8.00
Radiation dosimetry, single-use	$5.00 to $7.00 (much less in quantity)
Radiation dosimetry, repeat-use	$150 to$400

Scope of Responders to Receive Equipment

For both a radiological dispersion device and an improvised nuclear device, all responders could reasonably be protected with respiratory and skin protection. Radiation dosimetry will be used as available, but by a minimum of 100-300 of the first responders who work closest to the point of detonation of an RDD or the hypocenter of a nuclear explosion.

References

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MEDICAL GUIDELINES

EVACUATION, SHELTERING, AND OTHER PUBLIC HEALTH MEASURES TO REDUCE/AVERT RADIATION DOSE

2/25/03 Version

Introduction

Terrorist events involving RDDs or INDs may give rise to situations in which the radiation exposure continues after the initiating event. Minimizing additional exposure in such circumstances is critical. Actions or instructions provided to the public in order to accomplish this goal may be termed "interventions." Table 1 gives examples of protective actions. In general, interventions are not justified to avert effective doses of 10 mSv or less, but are almost always justified if potential averted doses are 100 mSv or more.

Table 1 - Examples of Protective Actions (Interventions) for Averting Exposures Via Various Pathways

Route of exposure	Protective action
External irradiation from a source	Control of access, shielding
Radionuclides in air or on ground	Control of access, sheltering, evacuation
External contamination	Protective clothing, decontamination
Inhalation of radioiodine	Stable iodine administration
Ingestion of radionuclides	Restricting contaminated food and water supply, decreasing incorporation into food chain, decontamination

* Criteria and rationale for administration of stable potassium iodide are discussed in another section

There are three general principles that form the basis for making decisions on intervention. First, all possible efforts should be made to prevent serious deterministic health effects (such as bone marrow depression and skin burns). There is no specific dose level at which intervention should be undertaken although, at levels of dose that would cause serious deterministic effects, some kind of intervention would be almost mandatory. The second principle is that the intervention should be justified in the sense that the protective measure should do more good than harm. While this may seem obvious, inappropriate actions have been taken in accidental situations to reduce dose at an extremely high social and monetary cost.

The third principle is that the levels at which an intervention is introduced and at which it is later withdrawn should be optimized. After an intervention is applied (e.g., evacuation or sheltering of a population), there needs to be optimization of the action to determine the scale and duration. Costs and benefits of such

actions will change over time. If people have been relocated and the radioactivity decays sufficiently, the persons may be allowed to go back home.

Guidance for Occupational Exposure in Emergencies

When it is clear that an accident has occurred, it may be necessary to knowingly allow individuals to be exposed to relatively high levels of radiation. This may be necessary to perform an urgent intervention or even to save lives. Values recommended for such circumstances are shown in Table 2.

Table 2 - Guidance for Emergency Occupational Exposure

Type of action	Organ	Level (mSv)
Lifesaving (ICRP)	Whole body *	May exceed 500 effective dose
	Skin	May exceed 5000 equivalent dose
(NCRP)	Whole body (or large part)	May approach or exceed 500
	Skin	5000 equivalent dose
(EPA) (Informed Volunteer)	Whole body	>250 No absolute upper limit
(EPA)	Whole body	250
Urgent (ICRP)	Whole body	500 or less effective dose
	Skin	5000 or less equivalent dose
(NCRP)	Whole body	Annual occupational limits up to 50 effective dose
Limit for protecting valuable property of large populations (EPA)	Whole body	50
Limit for emergency services except lifesaving or protecting valuable property (EPA)	Whole body	100

* Refers to Effective Dose.

An example of use of this table would be to answer the question “How much dose could first responders get in order to recover persons who would otherwise die?” The consensus is more than 250 mSv and probably not a lot more than 500 mSv whole body dose. The rationale for this is than in this dose range there would not be acute radiation sickness but there would be an increased cancer risk of about 1-4% for the responders. Responders should be informed of the risks and exposures voluntary. Allowing persons to get over 1000 mSv would likely result in mild acute radiation sickness of the responders and given the uncertainties in an accident may result in some responder fatalities.

Responders in such situations should have dose rate meters or alarms. General entry to an area is permitted if dose rates are less than 0.1 mGy or mSv/hr and if dose rates of 100mGy or 100mSv/ hr are encountered, responders should turn back for further advice.

Limitation of General Population Doses

Population dose assessment during the early phases of accident management is at best difficult. Early decisions regarding evacuation or sheltering are challenging. Individuals within an affected geographic area can receive widely varying doses. Often it is best to recommend sheltering and showering as an initial intervention until the situation (e.g., source, meteorology) becomes clear. Initial decisions may need to be based upon field measurements.

Sheltering is 10-80% effective in reducing dose depending upon the duration of exposure, building design and ventilation. If there is a passing plume of radioactivity, sheltering may be preferable to evacuation. When sheltering, ventilation should be tuned off to reduce influx of outside air. Sheltering may not be appropriate if doses are projected to be very high or long in duration. Sheltering has the advantage that people have access to food, water and communications. (See Table 3.)

Table 3 – Recommended Values of Averted Dose for Sheltering

Recommending Group	Averted Effective Dose (mSv)	Comments
ICRP	50	
IAEA (up to 2 days)	10	
EPA	10-50	Early phase of a nuclear incident

* If sheltering time is expected to exceed 2 days, other measures such as evacuation should be considered.

One can use this table to answer the question of "Should I recommend sheltering of the public?" If field measurements or predictions are that that population is likely to receive an effective dose in the range of 10-50 mSv sheltering should be recommended. One should not wait until the public has received this dose to take action. As mentioned above, sheltering is an excellent short term but not a long-term solution.

Evacuation is much more disruptive and expensive than sheltering. Care needs to be taken to assess the meteorology and potential changes to avoid moving people into the path of oncoming fallout. Evacuation planning needs to consider schools, hospitals, prisons, food availability, communications and housing. (See Table 4.)

Table 4 – Recommended Values of Averted Dose to Consider Evacuation and/or Relocation

Recommending Group	Averted Effective Dose (mSv)	Comments
ICRP (up to one week)	500	
	5000	Equivalent dose to skin
	1000	5-15 mSv per month for a prolonged period
IAEA (up to one week)	50	
	30 in 1st month and 10 in subsequent month	Temporary relocation
	1000 in a lifetime	Permanent resettlement
EPA	10-50 mSv	Early phase of nuclear incident

* If the radiation problem is not resolved within a week, so that the population may return, other measures such as temporary or permanent resettlement need to be considered.

It should be noted that if persons are outside and there is a major release of radioiodine or radioactive particulate material, they should be instructed to make use of any possible respiratory protection such as folded wet handkerchiefs or towels. When they reach shelter, they should change clothes and if possible shower.

Individual dose assessment is usually not possible in the early phases of a terrorist event. Individual doses may only be approximated in the first few hours or days. Relatively accurate individual dose estimates may take up to a month or more and are retrospectively performed based upon physical dosimetry, accident reconstruction or biological markers and clinical examination. Intake of long-lived radionuclides poses additional problems. Doses are often calculated in terms of "committed dose". This usually refers to the dose an individual would be expected to receive from that intake over the next 50 years. While this may make sense for a young worker, it has little relevance to workers with less than an additional 50-year life expectancy. Another issue is that doses from intakes of radionuclides are often calculated on the basis of models. There may be significant individual deviations from these estimates. With significant exposures, individual information should be used. This is particularly important if there has been an intervention (such as administration of potassium iodide) that substantially affects the clearance and biological half-life of the radionuclide. This text does not deal with the protection of the public in situations of prolonged radiation exposure (for example months or years). Since internal doses are hard to project, it is necessary to limit intake of radioactivity in foodstuffs based on the radioactivity that they contain (see Table 5).

Table 5 - Recommended Activities (Bg/Kg) Regarding Restriction of Foodstuffs

ICRP	Averted Dose	Activity in Any Foodstuff
Restriction of a single foodstuff	10 mSv (in 1 year)	1,000-10,000 Bq kg^{-1} beta/gamma emitters) 10-100 Bq kg^{-1} alpha emitters
IAEA		
Restricting foods containing	General consumption	Milk, infant foods, water
Cs-134,Cs-137,Ru-103,Ru-106, Sr-89	1000 Bq kg^{-1}	1000 Bq kg^{-1}
I-131		100 Bq kg^{-1}
Sr-90	100 Bq kg^{-1}	
Am-241,Pu-238, Pu-239, Pu-240, Pu-242	10 Bq kg^{-1}	1 Bq kg^{-1}

* These are generic guidelines and account needs to be taken of the specific accident circumstances. For example, food and water restriction depends upon alternative supplies being readily available.

Cost and Scope Implications

Estimated Cost

Cost of some interventions (such as administration of potassium iodide) are discussed elsewhere. Sheltering costs are primarily due to disruption of normal work patterns and productivity. Costs of evacuation can be much greater (several millions of dollars) even though many people will self-evacuate by private vehicle. There are costs to control the evacuation, supply food, water, clothing, and housing. Restriction of the food supply will also have a cost in discarded foodstuffs.

Scope of Population Sheltered/Evacuated

The number of people sheltered or evacuated can range from several thousand for an RDD up to hundreds of thousands for an IND or major nuclear power plant core breach. Several hundred thousand persons were evacuated or permanently relocated after Chernobyl.

References

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MEDICAL GUIDELINES
IMMEDIATE MEDICAL MANAGEMENT
2/25/03 Version

Medical Triage
- It is necessary to assess traumatic injury and medical conditions prior to consideration of radiation exposure. In some cases, mass casualties may overwhelm health care resources and adaptable triage methods will be indicated.

Rapid Radiological Triage
- Time to vomiting < 4hours: Refer for immediate evaluation.
- Time to vomiting > 4hours: Refer for delayed evaluation (24-72 hours) if no concurrent injury.

DOSIMETRY RESULTS (GAMMA, CRITICALITY)		
	Time to Vomiting	
	< 4 hours	**> 4 hours**
25% (Gy)	2.5	0.5
Median Dose (Gy)	3.6	0.9
75% (Gy)	6.0	1.7

Patients who experience radiation-induced emesis within one hour after a radiation incident require extensive and prolonged medical intervention, and an ultimately fatal outcome is expected in many cases. The median dose is found to be 6.5 Gray (Gy) with an interquartile (25%-75%) range of approximately 5-11 Gy.

Initial Medical Considerations
- Early triage and stabilization
- Immediate removal of contaminated clothing
- Radiological decontamination of skin and wounds
- Medical history and physical examination
  - Note timing of prodromal signs and symptoms (e.g., nausea, vomiting, diarrhea, transient incapacitation, hypotension, and other signs and symptoms suggestive of high-level exposure)
- Nasal swabs to evaluate for internal contamination
  - Nasal swab activity represents ~5% of lung deposition
- Cytogenetic biodosimetry, if medically indicated
- Initial complete blood count and repeat every 4-6 hours to evaluate lymphocyte depletion kinetics
- Treatment for internal contamination, if indicated

Dermal Manifestations of Radiation Dose

Dose	Clinical Findings	Days Post-Exposure
3 Gy	Epilation beginning	14-21
6 Gy	Erythema	(transient initially, primary erythema occurs 14-21 days post-exposure)
10-15 Gy	Dry desquamation	2-3 weeks
20-50 Gy	Wet desquamation	2-3 weeks
> 50 Gy	Overt radionecrosis and ulceration	>4 weeks

Acute Radiation Syndrome (Whole-Body or Extensive Partial-Body)

Dose	Clinical Status	Description
0-1 Gy	Generally Asymptomatic	White blood count normal or minimally depressed below baseline levels at 3-5 weeks post-accident
1-8 Gy	Hematopoietic Syndrome	Main prodromal signs and symptoms include anorexia, nausea, vomiting, and, occasionally, skin erythema, fever, mucositis, and diarrhea. Laboratory analysis in cases with whole-body exposure greater than 2 Gy can show an initial granulocytosis, with pancytopenia evident 20-30 days post-accident. Subsequent systemic effects of the hematological phase of acute radiation syndrome include immunodysfunction, increased infectious complications, possible hemorrhage, sepsis, anemia, and impaired wound healing.
8-30 Gy	Gastrointestinal Syndrome	Symptoms may include early, severe nausea, vomiting, and watery diarrhea, often within hours post-accident. In severe cases, the patient may present with shock, and possibly renal failure and cardiovascular collapse. Death from gastrointestinal syndrome usually occurs 8-14 days post-accident. Hematopoietic syndrome occurs concomitantly.
>20 Gy	Cardiovascular/ Central Nervous Syndrome	Patients may experience a burning sensation within minutes of exposure, nausea and vomiting within the first hour post-accident, prostration, and neurological signs of ataxia and confusion. Death is inevitable and usually occurs with 24-48 hours.

Cost and Scope Implications

Estimated Cost

- Not applicable

Scope of Patients Treated

- For a radiological dispersion device, <1,000 patients could require evaluation and treatment.

- For an improvised nuclear device, >100,000 patients could require evaluation and treatment.

References

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MEDICAL GUIDELINES
PATIENT DECONTAMINATION
2/25/03 Version

Skin or wound contamination is almost never immediately life threatening to the patient or to medical personnel. Therefore, treating conventional trauma injuries is the first priority. Decontaminate the patient only after medical stabilization.

Ideally, emergency medical services personnel will decontaminate patients at the scene of an incident prior to transport. As this will not always occur, decontamination procedures should be part of the operational plans and procedures of all health care facilities. Removal of outer clothing and shoes can reduce contamination by as much as 90%. Assess for radiological contamination by slowly passing a radiation detector over the entire body, insuring that the same distance is maintained in subsequent surveys. Cover open wounds prior to decontamination of surrounding skin. Remove contaminated clothing and place it in marked plastic bags, moving it to a secure location within a contaminated area. Wash bare skin and hair thoroughly, and if practical, secure and appropriately dispose of the effluent.

Skin Decontamination
Decontaminate skin to decrease the risk of acute dermal injury, lower the risk of internal contamination, and reduce the potential of contaminating medical personnel and the environment. After the patient's clothing is removed, washing the patient with soap and water is 95% effective because soap emulsifies and dissolves contamination. Gentle brushing dislodges some contamination physically held by skin protein and removes a portion of the horny layer of the skin. The stratum corneum of the epithelium is replaced every 12-15 days, so contamination that is not removed and is not absorbed by the body will be sloughed within a few days. The goal of decontamination should be to gently remove as much contamination as possible, without damaging the skin. Since it may prove difficult to remove all contamination, decontaminating to two times background radiation level should suffice. If after the third attempt, this goal is not reached, and further attempts reduce the contamination by less then 10%, cease further efforts and handle the patient following standard blood borne precautions to minimize the possible spread of the contaminant. To avoid survey errors, insure that the same meter to skin distance is used in all surveys.

<u>Decontamination Techniques</u>
Avoid unnecessary damage to the skin; cease washing before abrasion occurs. If washing will not remove stubborn hand and distal extremity skin contamination, wrap the contaminated area, and over time, sweating will decrease contamination. To decontaminate hair, use any commercial shampoo without conditioner. Conditioners bind material to hair protein, making contamination

removal more difficult. Consider clipping hair to remove contaminants. Avoid removing eyebrows since they may not grow back.

Recommended Cleaning Solutions
For skin and wound decontamination, use a cleaning solution. Suggested solutions are:

- Soap and water or normal saline;
- Povidone iodine and water; and
- Hexachlorophene 3% detergent cleanser and water.

Wound Decontamination

Wound characteristics affect the absorption and decontamination of radioactive substances.

- Abrasions disrupt the skin barrier and increase absorption potential. They are usually easy to decontaminate due to easily accessible contaminants.

- Lacerations are easy to decontaminate because the contaminated tissue can be excised.

- Puncture wounds are difficult to decontaminate because of poor access to the contaminants and difficulty in determining the depth and degree of contamination. Standard water picks have been used with success in the past.

Solubility, acidity/alkalinity, tissue reactivity, and particle size affect the absorption of wound contaminants (e.g., the more soluble the contaminant, the greater the absorption rate). Smaller particles may be phagocytized in the tissues and thus internalized more rapidly.

Following the detonation of a radiologic dispersal device, some victims may have wounds containing radioactive shrapnel. Metallic shrapnel should be handled with forceps and, if found to be radioactive, placed in a lead container or at least six feet from personnel. When an extremity is severely contaminated and adequate shrapnel removal is not possible, amputation may be necessary. It is rarely indicated unless the injuries are so extensive that functional recovery is unlikely or the radiation dose is likely to result in necrosis in the extremity.[1] Decisions about amputation should be postponed until long-term risks are clearly defined. In other words, decontaminate but do not mutilate.

[1] NCRP Report 65, *Management of Persons Accidentally Contaminated with Radionuclides*, National Council on Radiation Protection and Measurements, Bethesda, MD, 1980.

Internal Decontamination Treatment

Immediate Care

Immediate care should focus primarily on preventing internal contamination. As discussed earlier, skin or wound contamination is almost never immediately life threatening to the patient or to medical personnel. Therefore, treating conventional trauma injuries is the first priority. As soon as the patient's condition permits, take steps to determine whether internal contamination has occurred. Nasal swab samples for radioactivity should be obtained as early as possible. However, under some circumstances, inhalation exposures may not yield a positive nasal swab. If contamination is present, especially in both nostrils, inhalation of a contaminant may be assumed. Collect urine and feces specimens to help determine whether internal contamination has occurred.

Treatment Procedures

The reason to treat persons with internal contamination is to reduce the radiation dose from absorbed radionuclides and thus the risk of long-term biological effects (i.e., cancer). Minimize internal contamination by 1) reducing the absorption of radionuclides and their deposition in target organs, and 2) increasing excretion of the radionuclides from the body. A number of procedures are available for respiratory and gastrointestinal contamination. The benefit of removing the radioactive contaminant using modalities associated with significant side effects must be weighed against the short and long-term effects of contamination without treatment. The radioactivity and toxicity of internalized radionuclides must also be considered. Risk estimates combine professional judgment with the statistical probability of radiation-induced diseases occurring within a patient's lifetime. Immediate potential treatments include:

1. Oral *potassium iodide* (KI) for appropriate populations, if radioiodine is suspected as a potential contaminant.

2. *Gastric lavage* until washings are free of radioactive material (no more than two times background radiation or repeated lavage does not result in further reduction of contamination). This is only effective if done within 1-2 hours of ingestion and should only be used for large single intakes of radioactive material.

3. If radionuclides are ingested, *antacids* (such as over-the-counter aluminum hydroxide/magnesium carbonate-containing formulas) are indicated to reduce gastrointestinal absorption. Aluminum containing antacids are especially effective in reducing uptake of strontium; reduces uptake by 50-85 percent.

4. If large ingestions are suspected, *cathartics* to decrease residence time/radiation dose of materials in the bowel. A biscodyl or phosphate soda enema will empty the colon in a few minutes and should be given

primary consideration. Oral agents of suppositories can be used but take one or more hours to act. Magnesium sulfate can be used to produce insoluble sulfate compounds with some radionuclides (such as radium).

5. Radionuclide specific therapies:

Radionuclide	Therapy
Tritium	Force fluids
Cesium	Prussian Blue (currently investigational)
Plutonium and transuranics	Chelating agents such as Calcium or Zinc diethylenetriaminepentaacetate (DTPA) (currently investigational)
Strontium ingestion	Oral aluminum phosphate or barium sulfate

6. Pulmonary lavage is rarely indicated. It should only be considered after inhalation of very large amounts of long-lived insoluble radionuclides that would be likely to result in major pulmonary compromise if not removed.

Cost and Scope Implications

Estimated Cost

- The cost of decontamination solution is negligible but the process of decontamination can be labor intensive.

  Note: A four-person team can decontaminate approximately 6 non-ambulatory patients an hour. About 20 ambulatory persons could be decontaminated per showerhead per hour.

Scope of Patients Treated

- For a radiological dispersion device, >1,000 patients are likely to present for decontamination.

- For an improvised nuclear device, >100,000 patients are likely to present for decontamination.

MEDICAL GUIDELINES
PATIENT RADIOLOGICAL ASSESSMENT

2/25/03 Version

Treatment of life-threatening injuries always takes precedence over measures to address radioactive contamination or exposure. Individuals with such injuries should be stabilized, if possible, and immediately transported to a medical facility.[2]

Introduction

The radiological assessment of injured individuals includes radiation measurements and collection of information that is relevant to the decontamination and treatment of the patient. *Do not release a medically stable patient to ambulance personnel before a radiological survey has been performed. If contamination is confirmed, a preliminary decontamination should be attempted.* The instrument used to perform the survey should be sensitive to both penetrating and non-penetrating radiation (e.g. a Geiger-Mueller tube with a thin wall or entrance window). Care should be taken not to contaminate the probe by contact with the patient or any other potentially contaminated surface. If they are medically stable and conditions at the site permit, patients should be removed from contaminated areas prior to assessment. The distribution of radioactivity should be recorded for each patient along with other relevant information such as the location of wounds. A nasal swab is recommended to detect inhalation of radioactive contaminants.

The following administrative information should also be recorded:

- Name of the patient
- Name of the individual conducting the survey
- Time, date, and location at which the survey was performed
- Serial number and type of instrument used

Record the results of the radiological survey and proceed to decontaminate the patient. When finished repeat the radiation survey and record the final results.[3]

Physical Dosimetry for First Responders

Pencil or pocket direct reading dosimeters (DRDs), thermoluminescent devices (TLDs), and film badges may be used to provide an estimate of individual absorbed dose.

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[2] NCRP Report 138, *Radiation Protection and Terrorism,* National Council on Radiation Protection and Measurements. Bethesda, MD, 2001.

[3] Adapted from NCRP Report 138, *Radiation Protection and Terrorism,* Sec. 4.3.2 “Patient Radiological Assessment,” National Council on Radiation Protection and Measurements. Bethesda, MD, 2001.

DRDs are easy to use and provide an instant measure of the accumulated exposure, but they do not provide a permanent record and may go off scale by being dropped or bumped against a hard surface. Their accuracy is less than that of TLDs or film badges.

TLDs and film badges do not provide an instantaneous readout and absorbed doses are ascertained only after the fact. TLDs can store information for months and are reusable, but they do not provide information about the energy of the incident radiation. Film badges are not as sensitive as TLDs, but they provide a permanent record and can give some estimate of the incident radiation energy as well as the absorbed dose. Film badges and TLDs must be protected from direct exposure to contaminated patients.

In most radiation accident management situations, it is prudent to wear both a DRD and either a TLD or film badge.[4]

Rapid Dosimetry

The number of unaffected but worried individuals presenting for evaluation after an intentional or accidental radiation release makes it reasonable to consider the use of Geiger-Mueller detectors with thin end-window (or pancake) probes or doorframe and/or portal monitors as a quick-sort triage tool. Where available medical resources are greatly exceeded, the evaluation of persons with no evidence of external contamination can be temporarily deferred. It is important to note that Geiger-Mueller detectors with side-window counters and other devices historically distributed as part of civil defense programs are insufficiently sensitive and thus inadequate.

Dose assessment for affected individuals is based upon physical dosimetry, accident reconstruction, biological markers, and clinical examination. At doses in excess of 0.25 Gy to the whole body and in excess of 1.0 Gy to the extremities, patient management ultimately depends on biological dosimetry and tissue response (e.g., time of onset, severity of skin burns, marrow depression). If the nature of the radiation source can be accurately identified, the history of the exposure may be sufficient to give a reasonable dose estimate.

Goans has demonstrated that time to first emesis decreases with increasing absorbed dose according to the power function:

$$y = ax^{-b}$$

y = the time to emesis post-irradiation,
x = the whole-body dose in Gy,

[4] Kelsey CA, Mettler FA. Instrumentation and Physical Dose Assessment in Radiation Accidents. In Gusev IA, Guskova AK, Mettler FA, Eds. *Medical Management of Radiation Accidents, 2nd Edition*. CRC Press, Orlando, FL, 2001.

a = 4.47±0.16, and
b = -0.57±0.04.[5]

DOSIMETRY RESULTS (GAMMA, CRITICALITY)		
	Time to Vomiting	
	< 4 hours	**> 4 hours**
25% (Gy)	2.5	0.5
Median Dose (Gy)	3.6	0.9
75% (Gy)	6.0	1.7

As shown above, patients who vomit greater than 4 hours post-accident are likely to have, at worst, a mild acute radiation syndrome. From these data, the time to vomiting would appear to be a useful triage instrument in circumstances where a large number of patients are anticipated.

In cases where the number of victims significantly exceeds the available medical resources, patients reporting vomiting less than 4 hours post-exposure can be directed for immediate further testing while the treatment and evaluation of radiation exposure for other patients may be temporarily deferred.

Dose Range	Absolute Lymphocyte Count 8-12 Hours Post Incident
< 1 Gy	Normal – 2500/mm^3
1-5 Gy	1700-2500
5-9 Gy	1200-1700
> 10 Gy	<1000

In recent research[6], a simple prediction algorithm was presented to estimate effective whole-body dose within 8-12 hours after moderate and high-level gamma accidents and after criticality accidents. The algorithm is based on the observation that lymphocyte depletion follows first order kinetics after high-level gamma accidents. Using historical data from both gamma accidents and nuclear criticality accidents, lymphocytes are observed to follow approximately an exponential decline in time within the first 24-48 hours. Utilizing an absolute lymphocyte count taken approximately 8-12 hours after an incident, an estimate for whole-body dose may be obtained from the table above. The technique described here is designed to be a triage mechanism applied in the early phases

[5] Goans, RE. Clinical Care of the Radiation Accident Patient: Patient Presentation, Assessment, and Initial Diagnosis. In Ricks RC, Berger ME, O'Hara FM, Eds. *The Medical Basis for Radiation-Accident Preparedness. The Clinical Care of Victims.* Proceedings of the Fourth International REAC/TS Conference on the Medical Basis for Radiation-Accident Preparedness, March 2001, Orlando, FL. The Parthenon Publishing Group, 2002.
[6] Goans, RE, Holloway, EC, Berger, ME, and Ricks, RC. *Early Dose Assessment in Criticality Accidents.* Health Phys. 81(4): 446-449, 2001.

of a radiation accident and should be considered along with the presence or absence of radiation-induced emesis.

If the nature of the event is such that it is difficult to obtain serial lymphocyte determinations, a conservative rule of thumb is that a lymphocyte count < 1×10^3 μL^{-1} within 24-48 hours in a patient without known prior lymphocytopenia suggests that the patient has received at least a moderate (> 2 Gy) absorbed dose of radiation.

Biodosimetry Assessment Tool

The Armed Forces Radiobiology Research Institute (AFRRI) has developed a Biodosimetry Assessment Tool (BAT) software application that equips health care providers with diagnostic information (e.g., clinical signs and symptoms, physical dosimetry) relevant to the management of human radiation casualties. Designed primarily for prompt use after a radiation incident, the program facilitates the collection, integration, and archiving of data obtained from exposed persons. Data collected in templates are compared with established radiation dose responses obtained from the literature to provide multi-parameter dose assessments.

The program archives clinical information (e.g., extent of radioactive contamination, wounds, infection) useful for casualty management, displays relevant diagnostic information in a concise format, and can be used to manage both military and civilian radiation accidents. An integrated, interactive human body map permits convenient documentation of the location of a personal dosimeter, radiation-induced erythema, and radioactivity detected by an appropriate radiation detection device. In addition, the program archives information for later use in radiation protection analyses. The executable code and supporting graphics files fit on a single CD-ROM and require standard 32-bit Windows operating systems.

BAT may be downloaded from
http://www.afrri.usuhs.mil/www/outreach/batpage.htm.

Biological Dosimeters

Numerous biological dosimeters have been identified. Chromosome exchanges resulting in unstable aberrations such as dicentrics, rings, acentric fragments and other asymmetrical rearrangements may by measured using the technique of fluorescence *in situ* hybridization (FISH), which is currently the assay of choice for definitive biodosimetry. Limitations of the technique include the high cost of the probes and the fact that scoring is highly labor intensive. So-called fast-FISH techniques are currently under development and may alleviate some of these concerns.

Measurement of radiation-induced apoptosis in human lymphocytes may ultimately prove to be the most sensitive, reproducible biodosimeter but requires more research and validation.[7, 8] Counting the frequency or number of micronuclei in the cytoplasm of irradiated cells, electron spin resonance detection of free radical formation in tooth enamel, and measurement of serum biochemical markers such as amylase, IL-6, iron, cholesterol and apolipoprotein levels have also been investigated as potential techniques for determining radiation dose.[9]

Evaluation of Neutron Exposure

Neutron exposure is an element of criticality accidents. A quick-sort method has been developed for estimating the dose received in rad.

$$D = 1.1^{K/M}$$

D = equals first collision neutron dose in rad

K = the count per minute (cpm) for a Geiger tube instrument (calibrated to indicate a response of 3200 cpm in a 1 mR/h radiation field from a gamma source) held against the abdominal area

M = weight of exposed person in kilograms

This technique may be used for pure external gamma or neutron exposures (i.e., where there is no contamination). Neutron activation of metal objects carried by the victim can also be assessed. To translate the activation data to personal exposure, determine the neutron energy range, the activation cross-section for that energy, and the neutron flux.

Hair and blood specimens from exposed patients should be preserved for analysis of ^{24}Na levels in blood and ^{32}P deposition in hair. With the inhomogeneity of exposure in most accidents, few physical methods other than electron spin resonance and ^{32}P activation will provide accurate estimates.[10]

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[7] Boreham DR, Gale KL, Maves SR, Walker JA, Morrison DP. Radiation-induced apoptosis in human lymphocytes: potential as a biological dosimeter. Health Phys 1996; 71:685-91.
[8] Menz R, Andres R, Larsson B, Ozsahin M, Trott K, Crompton NE. Biological dosimetry: the potential use of radiation-induced apoptosis in human T-lymphocytes. Radiat Environ Biophys 1997; 36:175-81.
[9] Chambers DB, Phillip HA. The Current Status of Biological Dosimeters. In Gusev IA, Guskova AK, Mettler FA, Eds. *Medical Management of Radiation Accidents, 2nd Edition*. Orlando, FL, CRC Press, 2001.
[10] Mettler FA, Voelz G. Evaluation of Neutron Exposure. In Gusev IA, Guskova AK, Mettler FA, Eds. *Medical Management of Radiation Accidents, 2nd Edition*. Orlando, FL, CRC Press, 2001.

Internal Contamination

The International Commission on Radiological Protection (ICRP) and National Council on Radiation Protection and Measurements (NCRP) have developed models for the deposition, retention, and dosimetry of inhaled radionuclides.[11, 12] The ICRP recommends that material-specific rates of absorption should be used where reliable human or animal experimental data exist. It must be cautioned that these models rely on numerous assumptions and that the degree of variability in uptake, absorption, transfer coefficients, organ distribution, and excretion among individuals is not known. The NCRP has estimated that effective dose coefficients may vary by a factor of 2-10 for groups of healthy adult males, with even greater uncertainties for other populations.[13] In the acute setting, the need for quick decisions will often preempt the use of such models.

DOSIMETRY TECHNIQUES FOR SELECTED ISOTOPES:[14]

Nuclide	Radiation	Measurement Methods		Effective $t^{1/2}$	Critical Organ
		External	Internal		
^{241}Am	Alpha, Gamma	A, BG(SP), S	IVC, F, NS, U	139yr	Bone
^{60}Co	Beta, Gamma	BG, S	BC, F, U	10d	Total Body
^{137}Cs	Beta, Gamma	BG, S	BC, F, NS, U	70d	Total Body
^{3}H	Beta	BG(SP), S(LS)	U	12d	Total Body
^{131}I	Beta, Gamma	BG, S	BC, IVC, U	8d	Thyroid
^{192}Ir	Beta, Gamma	BG	BC, U, F, NS	74d	Lung
$^{238,239}Pu$	Alpha, Gamma	A, BG(SP)	IVC, F, NS, U	69-197yr	Bone
^{226}Ra	Alpha, Gamma	A, BG, S	BC, B	44yr	Bone
^{90}Sr	Beta	BG, S	U, IVC, F	15yr	Bone
$^{235,238}U$	Alpha, Gamma	A, BG	BC, IVC, U	15d	Kidney

[11] International Commission on Radiological Protection. Human Respiratory Tract Model for Radiological Protection. ICRP Publication 66. Pergamon Press, 1994.
[12] NCRP Report 125, *Deposition, Retention and Dosimetry of Inhaled Radioactive Substances,* National Council on Radiation Protection and Measurements, Bethesda, MD, 1994.
[13] NCRP Commentary 15, *Evaluating the Reliability of Biokinetic and Dosimetric Models and Parameters Used to Assess Individual Doses for Risk Assessment Purposes,* National Council on Radiation Protection and Measurements, Bethesda, MD, 1998.
[14] Adapted from NCRP Report 65, *Management of Persons Accidentally Contaminated with Radionuclides*, National Council on Radiation Protection and Measurements, Bethesda, MD, 1980.

Notes

External

A	Alpha counting techniques
BG	Beta-gamma counting and detection techniques. Start with detector unshielded
BG(SP)	Special attention to select low-energy monitoring techniques
S	Smear or swipe sample counted in laboratory
S(LS)	Liquid scintillation counting of samples

Internal

B	Breath analyses for gases
BC	Whole body count (standard gamma detection methods), including nuclear medicine counters
F	Feces sample analysis
IVC	Special in vivo counting techniques useful for low energy counting
NS	Nose swipe counted in laboratory if inhalation suspected
U	Urine sample analysis

Cost and Scope Implications

Estimated Cost

Physical Dosimetry Devices:

- Direct Reading Dosimeter (DRD) - $75-400 each
- Film Badge - $1-3 each in bulk
- Thermoluminescent Device (TLD) - $2-8 each in bulk

Radiation Detection Tools:

Equipment	Estimated Cost	Patients/Hr
Geiger-Mueller detector with thin end-window probe (Note: side-window probes would be inadequate for an RDD or IND event)	$300-600	30-60 patients/hr
Door frame monitors	$10,000	60-120 patients/hr
Portal monitor	$15,000	60-120 patients/hr
Biodosimetry Assessment Tool (BAT)	Free Download	12 patients/hr
Fluorescence *In Situ* Hybridization (FISH)	$2,200 per patient	1 patient/2 days

Scope of Personnel/Patients Treated

- For all first responders, a DRD and TLD should be provided to ensure their ability to immediately detect presence of radiation and to record their total exposure over time.

- Many more “patients” will present for treatment than actually need it. For example, in 1987 there was an accidental radiation release that contaminated several houses in Goiânia, Brazil. An estimated 140,000 “worried well” well inundated the health care system. Plans need to be in place to clear the “walking well” quickly through use of portal monitors or other radiation detection monitors.

- Of those patients with confirmed radiation exposure, it is not feasible to use biological dosimeters on all of them due to the cost and labor intensiveness of the process.

MEDICAL GUIDELINES

GUIDELINES ON DEALING WITH DECEASED PERSONS FOLLOWING RADIOLOGICAL TERRORISM

2/25/03 Version

General

A radiation dispersal device or improvised nuclear weapon may cause both radiation exposure and/or radioactive contamination of persons who have died at the site of detonation or a health care facility. This summary provides guidance on safe handling of the deceased as well as issues related to post-mortem examinations, and burial or cremation. Persons dealing with these issues would be considered to be occupationally exposed and are subject to the "occupational" effective dose limit of 50 mSv per year (.05 Gy per year X Quality Factor).

A deceased person who has been externally exposed to a lethal amount of radiation does not become radioactive as a result of the exposure. No special precautions are needed. For example, cancer patients who die after external radiotherapy do not need special handling precautions.

Special precautions are necessary when patients are contaminated and have radioactive material on them or in them. It is imperative to determine the presence of significant radioactivity and the dose rate with a Geiger or ionization type meter before recovering or removing potentially radioactively contaminated bodies. It may be necessary to remove the body from a radiation area to determine whether the body is truly contaminated. When dealing with any contaminated body, it is essential to have protective clothing (e.g., gloves, mask and gown or jumpsuit), a personal dosimeter, and if possible, somebody with radiation protection expertise. Before removing a contaminated body from the scene, there should be an appropriate radiation tag placed.

Radioactive contamination may occur in three ways as a result of a terrorist incident:

1. External contamination with radioactivity on the clothing or skin. Deaths are not likely as a result of a non-explosive RDD, but an RDD or IND with associated explosion, or fallout from a weapon or reactor would likely result in significant external contamination. The external contamination would not only be on the body but also on the ground. The dose rate from this contamination may preclude entry into the area and recovery of bodies may have to wait until some of the radioactivity has decayed or shielding can be arranged.

   Based on the Chernobyl experience, once a person has been removed from the radiation area, it is very unlikely that particulate radioactivity or radioactive fallout will result in a significant hazard to attendants who are

wearing protective garb. Doses received by Chernobyl attendants were in the range of 10 mSv (0.01Gy). The most effective quick method of reducing external contamination and decreasing attendant exposure is removal of the external clothing. This should be done as soon as practical. The clothing should be bagged and tagged.

2. *Internal contamination* is loose radioactive material that has gotten into the body through inhalation, wounds, skin, or rarely ingestion. Experience with radiotherapy patients who have received large amounts of unsealed radionuclides has shown that there is little hazard to providers as long as protective clothing is worn. Pathologists performing autopsies on internally contaminated patients have received less than 5 mSv (.005Gy).

3. *Radioactive shrapnel* is a major potential hazard for attendants. Some radioactive shrapnel may emanate from very radioactive metallic sources or reactor cores. These sources will likely be emitting penetrating gamma radiation. Highly radioactive cadavers will most likely be near the center of an explosion. In such areas, the radiation dose rate must be measured as outlined above. The radiation dose to attendants is a direct function of distance from the body and in some circumstances could exceed occupational dose limits. Evaluation by radiation safety personnel is essential before handling such highly contaminated bodies. Metallic radioactive items should never be handled directly, only with instruments. If such sources are removed from the body, they should be placed in a shielded container in a secure location.

Mass Casualties

In the event of a mass casualty, the Department of Homeland Security may activate the Federal Response Plan and the National Disaster Medical System (NDMS). NDMS assets include Disaster Mortuary Operational Response Teams (DMORTs). A DMORT is a Federal response team designed to provide mortuary assistance in the case of a mass fatality incident or cemetery-related incident. A DMORT works under the local jurisdictional authorities such as Coroner/Medical Examiners, Law Enforcement and Emergency Managers. There are 10 Regional DMORT Teams, one in each of the 10 FEMA Regions. In addition there is one Weapons of Mass Destruction (WMD) DMORT, which can decontaminate between 5 to 50 deceased persons per hour in the field.

Autopsies

Autopsy of minimally radioactively contaminated cadavers does not require precautions other than contamination control and protective clothing. Autopsies of highly radioactive cadavers should be restricted to the absolute minimum. When measured dose rates near the surface of the body are in the range of 0.1-1.0 mGy/hr it may be advisable to split the task among several persons.

Burial/Cremation

Embalming a cadaver by simple injection method generally is not a hazard to the embalmer if an autopsy has not been performed. Embalmers should wear protective clothing and it is advisable to have radiation safety staff present. Issues related to both burial and cremation are a function of the amount and type of radioactive material that remains in the body. Burial is typically not an issue unless there are extremely long-lived radionuclides present that may ultimately find their way into the environment in concentrations that exceed regulatory limits. Whether cremation is allowed depends on what type and amount of radioactive materials are released to the environment by incineration or by disposal of ashes. If the radionuclide has a short half-life it may be possible to wait a few weeks before cremation occurs. There are a few guidelines in other countries regarding cremation that indicate that cremation may occur with a wide variety of radionuclides if the activities in the body do not exceed 400 mBq. For activities in excess of these amounts radiation safety advice is indicated.

Cost and Scope Implications

Estimated Cost

There is little additional cost in handling a deceased radioactive person. Response and recovery teams, pathologists, and mortuary attendants already use the protective clothing needed to prevent transfer of radioactive contamination. The only extra cost involves the presence of radiation safety staff and personal dosimeters.

Scope of Patients Treated

It is unlikely that an RDD without explosives would result in contaminated bodies unless persons died from some incidental cause such as a heart attack or auto accident. With an incident involving conventional explosives that also contain radioactive material, there could be tens to hundreds of contaminated bodies. In the event of an IND or small weapon, the number could be in the tens of thousands. It is likely that many bodies would have minimal contamination, though a small percentage could have enough to represent a serious radiation hazard.

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PSYCHOLOGICAL ASPECTS OF A RDD/IND EVENT
PSYCHOLOGICAL AND BEHAVIORAL CONSEQUENCE MANAGEMENT AFTER RDD/IND EVENTS

2/25/03 Version

Introduction

An attack involving the release of radiation will create uncertainty, fear, and terror. Following the detonation of a Radiation Dispersal Device (RDD) the management of acute psychological and behavioral responses is likely to be as important and challenging as the treatment of RDD-related injuries and illnesses.

Radiation, an invisible, odorless, and poorly understood threat, has been a cause of extreme public anxiety in the past, as demonstrated by the public's response to the Three Mile Island, Chernobyl and Goiânia, Brazil accidents. In the aftermath of an event, the public must rely on health care providers and scientists to determine who has been contaminated. The effects of radiation exposure can manifest years after the causative exposure and may have consequences for future generations. Those who have been exposed or anticipate possible exposure may experience feelings of vulnerability, anxiety, and lack of control. Lack of consensus among experts can increase public fear and anger. Because it is such an unknown, then, radiation stimulates worst-case fantasies.

Terrorists, by definition, strive through their actions to provoke severe psychological reactions in the general public. Affected individuals fall into one of three groups: those who are distressed; those who manifest behavioral changes; and those who may develop psychiatric illness. Where radiation releases are concerned, distress will be common and manifest as sadness, anger, fear, difficulty sleeping, impaired ability to concentrate, and disbelief. Psychological distress after a radiologic incident may also manifest as nonspecific somatic complaints (a presentation sometimes referred to as "MIPS", Multiple Idiopathic Physical Symptoms). General health care providers should manage these patients. Some individuals may exhibit behavioral changes such as decreasing travel, staying home, refusing to send children to school, and increasing substance use and abuse. Fortunately, 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. While Acute Stress Disorder (ASD) and Post-Traumatic Stress Disorder (PTSD) are the disorders most people think of in connection with trauma, major depression, increased substance use, family conflict, and generalized anxiety disorder are also encountered.

It is important to remember that people with no prior history of psychiatric illness are vulnerable to psychiatric illness after a terrorist exposure. In the aftermath of

the Oklahoma City bombing, nearly 40% of those who developed PTSD and depression had no previous psychiatric disorder. Persons at high risk of developing psychiatric disorders include:

- Those directly exposed (e.g., people near the blast and those participating in rescue and recovery operations of people and remains),
- Those who were more vulnerable before the event due to existing mental illness,
- Those who suffered resource losses and disruption of their social supports after the event.

Prior technological disasters, terrorist attacks, and use of novel weapons in the context of war suggests that healthcare providers' offices, medical clinics, and hospitals will be deluged with symptomatic and asymptomatic patients seeking evaluation and care for possible contamination following a radiation event. Some of these patients may be diagnosed as having acute radiation sickness, while others will have diagnosable conditions unrelated to radiation, and a large number will be found to have symptoms for which no etiology can be found. A very conservative estimate of the ratio of unexposed to exposed patients seen in medical settings is 4:1, and the Goiânia, Brazil accident suggests that this ratio may be substantially higher after detonation of an RDD. In the acute aftermath, many unexposed patients will fear that they have been exposed because they will misattribute signs and symptoms of autonomic arousal to radiation. In the longer term, patients will present to primary care providers with multiple somatic complaints for which no etiology can be determined. Attachment A suggests strategies for managing these patients.

Healthcare Providers and Mental Health Care after a Radiation Event

Following a radiologic event, people will likely turn to healthcare providers for information and guidance. Following the 2001 anthrax attacks, for example, 77% of a representative sample of Americans reported that in seeking a reliable source of information they would trust their own doctor most.

Healthcare providers would likely play a key role in determining how patients and the general public respond to a radiological terrorist event. A well-organized, effective medical response will instill hope and confidence, reduce fear and anxiety, and support the continuity of basic community functions.

Healthcare providers are also subject to fear and terror. Absenteeism, flight, refusal to see patients, and dereliction of responsibility have been reported during infectious disease outbreaks (such as the outbreak of pneumonic plague in Surat, India) and in environments where new or unfamiliar life-threatening agents are thought to be present. Many of those who abandon their responsibilities do so because they feel they need to protect or evacuate their families.

Ensuring that health care providers understand radiation, how to protect themselves, and the available medical countermeasures can minimize role abandonment. Perhaps most importantly, health care providers are more likely to provide patient care if they believe that their families will be taken care of in their absence – e.g. are given potassium iodide where appropriate, etc. The availability of ongoing telephone contact with families and dedication of personnel to assist health care provider's families will be reassuring to health care providers and help them focus on their mission.

Triage and Initial Disposition

Triage and disposition is challenging. For example, in the 1987 Cs-137 accident in Goiânia, Brazil, 8.3% of the first 60,000 people screened, presented with signs and symptoms consistent with acute radiation sickness: e.g., skin reddening, vomiting, diarrhea, although they had not been exposed.

The term "worried well" and similar disparaging terms should not be used to describe such patients. Patients thus labeled may feel stigmatized and that their health concerns have not been taken seriously. The use of such labels contributes to mistrust of the medical community and may damage the credibility of individual providers. Non-stigmatizing terms such as "high risk", "moderate risk", and "minimal risk" convey continued concern and imply continued monitoring, both of which are reassuring to patients.

Mental Health professionals including psychiatrists should be an integral part of the teams that perform initial screening and triage. Patients referred to a mental health specialist may feel stigmatized. The patient may feel that the physician has missed some important clue of contamination and is dismissing him or her prematurely.

Where feasible, the establishment of an "Emergency Services Extended Care Center" (ESECC; a term first developed by the Rush Chicago Medical Center) may offer an important means of monitoring patients who remain fearful and are not reassured by negative findings. Patients with minor physical problems who cannot return home can also be referred here. In the event that a patient is misdiagnosed, the patient can be accompanied back to the Emergency Department. Ideally, there would be simple tasks that the patients can perform while in the ESECC to help them transition out of the patient role and restore their sense of control.

Early Psychological Interventions

Early psychological interventions (psychological first aid) are provided in the first hours, days, and weeks after exposure to a traumatic event. The most important element of psychological first aid is good medical care. Other important aspects of psychological first aid are listed below. "Debriefing", an often-recommended

technique, is actually a controversial acute intervention. Appendix B discusses this controversy in more detail.

Principles of Psychological First Aid

- Reduce physiological arousal – encourage rest, sleep, normalization of eat/sleep/work cycles
- Provide food and shelter in a safe environment
- Orient survivors to the availability of services/support
- Facilitate communication with family, friends, and community
- Assist in locating loved ones
- Keep families together and facilitate reunions with loved ones
- Provide information and foster communication and education.
- Observe and listen supportively to those most affected
- Decrease exposure to reminders of the traumatic event
- Advise decreasing watching/listening to media coverage of overly traumatic images and sounds (e.g., people jumping out of buildings, victim stories)
- Educate patients to check rumors with available information resources
- Use established community structures to encourage social conduct and education (e.g., faith-based institutions and businesses)
- Encourage talking to and involvement with the patient's natural social supports such as family, friends, neighbors, and coworkers (this will promote discussion of fears, interpersonal support, and early detection of persistent symptoms)
- Offer reevaluation if symptoms persist.
- Educate about the expected natural recovery that occurs for most people over time.

Health Care: Evaluation and Diagnosis

Addressing psychological and behavioral issues following a radiation release from an RDD may be far more challenging, in terms of the number of people affected, than addressing the consequences of radiation exposure in the affected population. Symptoms of depression, bereavement, family conflict, and somatization will be much more common than posttraumatic stress disorder (PTSD). Increased smoking and increased alcohol use can be expected, at least in the short run. Sleep disturbance, hypervigilance, decreased concentration, and uncertainty are other early symptoms of psychological distress. Patients presenting with multiple somatic complaints may have physical illness, or their presentation may be an expression of distress, depression and/or demoralization. Accurate differential diagnosis and management of these individuals will require education of primary care providers. Physicians caring for patients presenting with medically unexplained physical symptoms (MUPS) should:

- Carefully assess and record the specifics of the patients' concerns

- Make arrangements for follow-up rather than instructing patients to “return if there’s a problem”
- Listen for patient fears and concerns
- Consult colleagues as appropriate

It should be pointed out that patients do not process or remember information well when they are frightened. Many people will be unsure if they have radiation-related illness (up to 50% of those in contaminated areas), and others will be anxious that the exposure has caused genetic damage that will be passed on to future generations. As time passes, the lack of baseline health data in exposed populations may lead to the misattribution of illness to radiation exposure by individuals and communities. Handouts on radiation that summarize key points and tell patients how to get follow-up may be helpful in minimizing all of these concerns.

Reinforcing self-efficacy and providing information that can be used to protect oneself and ones family decrease distress. Patients trying to cope with negative life events unrelated to the RDD event will, in general, have more psychological distress and psychiatric illness than those not similarly afflicted. Negative life events occurring after an attack or traumatic event increases subsequent risk for psychiatric illness, illness, and injury.

Finally, the psychological value of distributing appropriate medical countermeasures and information about methods of self-protection can be substantial.

Patient Education

Providing accurate information to patients is critical. Many people, as noted above, fear radiation, and the history of nuclear weapons, not to mention the images associated with their use, exacerbate such fears. Repeated education about risks and protective countermeasures will help diminish fear, concern, and distress.

Healthcare providers should let patients know that distress in the immediate aftermath of an event is universal and that common responses include sleep disturbance, loss of appetite, and diminished concentration that should resolve over the course of several weeks. Healthcare providers should also inform patients that if these symptoms persist or have detrimental effects on performance, they should return to their healthcare provider for follow-up. Health care providers should anticipate questions about the safety of their food and water supplies and whether homes are contaminated. Patients should be advised that experts may have conflicting views.

The concept of a “threshold dose” of radiation below which risk is not changed is difficult for many to understand. Similarly the concept of “half life” is not easily transmitted to communities. Simple metaphors or other messages to explain

these complex scientific ideas (such as liquids evaporating at different rates) must be developed for healthcare providers to use with their patients (as well as appearing in mass media campaigns.)

- Fears and preoccupation with cancer will remain high for years. Responding accurately, empathetically and recognizing what is not known is important. Health care providers should understand the basic areas of disagreement about radiation's health consequences and be ready to explain them to patients in a straightforward manner. Uncertainly about health effects should be acknowledged and not minimized in communicating to patients and the public.

- Stigmatization of those exposed or traveling from contaminated areas can be expected. This will affect the relocation and entry of new students into school systems. Outreach health education to school systems, parent-teacher education programs and through school nurse training can allay community anxiety.

Special Issues (Children and Pregnant Women)

- Parental concern for children will be high. This will be true whether or not the children in question were exposed. Reports by parents of child distress, fears, and worries may also reflect the fears of the parent.
- Direct assessment of children and adolescents is important to determine the child's mental health because of the high levels of distress in the parents.
- The concerns of pregnant women and women with small children will be amplified following a radiation incident. Pregnant women may seek abortion to avoid expected or feared possible child malformations. Special education and counseling may be necessary.

Public Health and Mental Health

Responding to the mental health needs of the community as a whole raises many challenges. In the immediate aftermath of an event, the affected community is likely to draw together, but over time contaminated communities may manifest anger or reduced cohesiveness, low morale, and decreased social service due to distress and economic losses. Handouts on stress and fear management techniques and activities should be prepared for distribution. Contamination of food supplies create acute and long-term education and potentially health surveillance needs. Public health outreach to senior citizens will be important since their distress may heighten their social withdrawal. Door-to-door contact programs for this group and those with chronic medical needs who stay at home will be needed. Establishment of a clinical registry and appropriate health surveillance may in and of itself have important psychological benefits for affected communities. Patients who have their contact information recorded in a database will feel more assured that follow-up will be available.

Relocation of families out of zones of exclusion is complicated and requires particular attention to familial needs and social justice. Maximizing the choice of families is important. Some (perhaps 10%) will not want to move under any circumstances. Many of those for whom relocation is not recommended will leave voluntarily. Still others, who might prefer to move, will be unable to do so due to reasons of employment or an inability to sell their homes in what is likely to be a depressed real estate market. The perception of inequity in these and other matters will stress social fault lines and may divide communities.

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PSYCHOLOGICAL ASPECTS OF A RDD/IND EVENT

COMMUNICATION BETWEEN PRIMARY CARE PROVIDERS AND PATIENTS: EDUCATION STRATEGIES AFTER AN RDD EVENT

2/24/03 Version

Background

The imperceptibility of low-level radiation exposures may cause many persons to develop persistent health concerns or to arbitrarily link idiopathic symptoms to benign or improbable exposures (even under normal circumstances, a third of primary care patients present for assistance with medically unexplained physical symptoms [e.g., idiopathic fatigue and pain]). Over 90% of the general population will visit their primary care provider each year, making primary care a crucial setting for dissemination of accurate health risk information following suspected community radiological exposures.

Primary Care Communications Triage

In the aftermath of a radiation release, primary care providers should make an effort to determine the degree of exposure suffered by all patients visiting their clinics, regardless of the reason. In some circumstances this determination will be assisted by the use of biodosimetry, but more commonly it will be based simply on the patient's proximity to the event and subsequent location during a critical period of exposure. Based on this initial primary assessment of exposure, the presence or absence of symptoms, and the presence or absence of disease (medical and psychiatric), patients may be assigned to categories for treatment, follow-up, and education. Counseling may be provided on risk, symptoms, and/or disease findings. Assessment for Posttraumatic Stress Disorder (PTSD), depression or anxiety, and altered alcohol or tobacco consumption are important.

After a radiation release, it may be useful for primary care clinics to routinely assess the degree of concern about exposure-related illness, separate from actual exposures. This process can be facilitated by asking, "Is your visit today related to terrorism or radiation concerns?" at the beginning of every visit. Patients who respond "yes" or "maybe" to this question or who express concern about exposure-related illness should receive extra primary care assessment to elucidate the nature of the patient's concerns and his/her expectations of and goals for the medical visit. These concerns and expectations can then guide medical triage and the intensity of risk communication efforts.

Often the primary care provider will have the most difficulty in communicating with those who are:

1. Possibly exposed but unconcerned and with no symptoms or disease;

2. Either exposed or unexposed with a high level of concern but asymptomatic (no symptoms or disease): or

3. Either exposed or unexposed with a high level of concern and unexplained symptoms.

The last group of patients is often categorized as having MIPS (Multiple Idiopathic Physical Symptoms).

Communication Interventions for Critical Primary Care Groups

- P*ossibly exposed but unconcerned with no symptoms or disease* – Many patients will deny or neglect personal medical needs. Assuming medical needs are subacute, careful contact information should be obtained and entered into a local registry to facilitate follow-up to ensure patient has attended appropriately to injuries and exposures.

- *Either exposed or unexposed with high levels of concern but asymptomatic* – Some patients amplify concerns and repeatedly resist clinician reassurances. In a mass casualty situation, these patients can disrupt delivery of critical medical care, so it may be helpful to plan for such patients by dedicating staff and an area to their care. Development of a careful contact registry with dedicated efforts to provide follow-up contact and care is one way of communicating compassion and concern without succumbing to risky or unnecessary testing. Research suggests that a negative test offers only transient reassurance and can sometimes increase illness concerns, especially when false positive results occur. Discussing the basis for patient concerns and exploring what tests the patient thinks he or she might need prevents many patients from feeling that such concerns have been ignored. Time-contingent follow-up (planned rather than as-needed visits) reduces illness worry, increases satisfaction with care, and may mitigate downstream litigation conflicts and concerns.

- *Either exposed or unexposed with high levels of concern and unexplained symptoms (no disease, MIPS)* – As with the asymptomatic concerned patient, the patient with idiopathic symptoms can disrupt delivery of critical medical care. These patients may invoke more clinician anxiety because unlike the patient with isolated concerns, these patients are often visibly suffering and their symptoms may sound potentially catastrophic (e.g., chest pain and sweating).

  In addition to a dedicated area, staffing, contact registry, and redoubled primary care follow-up efforts, intervention for patients concerned with unexplained symptoms should involve brochures, fact sheets, and literature about self-management approaches to medically unexplained symptoms. In the acute crisis, it is helpful to triage these patients to an area distinct from the area used to care for acutely ill individuals, but the area should not be labeled or perceived as a “psychiatric care” area for “worried well” patients because of the sense of stigmatization that such labels generate. Many patients in this group will fear that their symptoms represent a harbinger of impending

medical catastrophe. Resentment on the part of patients who feel that their complaints are being ignored can result in a “contest” in which patients report progressively severe symptoms in a quest for legitimization. Patients with unexplained symptoms should therefore receive early and frequent validation from the clinician that symptoms are important and will be followed up quickly and carefully. The care of patients with unexplained symptoms is frustrating for primary care physicians, especially if the physician feels that “minor problems” are distracting them from more acute care.

The use of an onsite “ombudsman” or “advocate” who can help patients with unexplained symptoms overcome perceived barriers to care helps to defuse patient notions that “no one cares” and affords clinicians a way to reduce the pressure to meet these patients’ needs. The ombudsman can make special efforts to ensure that symptoms are acknowledged, embraced, and carefully discussed. As with concerned but asymptomatic patients, time-contingent follow-up is key. If symptoms persist and explanations for symptoms remain unclear, some of these patients may develop mistrust in clinician motives and develop improbable “conspiracy theories”. Advocacy for these individuals may reduce the likelihood of eventual litigation including class action lawsuits.

PSYCHOLOGICAL ASPECTS OF A RDD/IND EVENT

THE DEBRIEFING DEBATE

2/25/03 Version

Physical safety and security of victims and relief workers must take first priority. After safety is assured, other interventions such as debriefing may begin. Debriefing is a popular, early intervention following disasters in which small groups of people involved in the disaster, such as rescue workers, meet in a single lengthy session to share individual feelings and experiences. The effectiveness of debriefing in preventing later mental health problems is much in debate. As a minimum the following should be considered if debriefing is included as part of an intervention plan.

- Rest, respite, sleep, food and water are critical early interventions.
- Encourage natural recovery processes. Advise participants to talk to fellow workers, spouses and friends. This can decrease isolation and therefore facilitate identification of persistent symptoms and increase the chances of early referral.
- Debriefing has not been shown to prevent PTSD. For some, it may relieve pain, restore some function and limit disability, however, further study is needed.
- There are a number of early approaches other than debriefing (e.g., continue to follow and reevaluate, case management and problem solving, couples emotional support training, sleep medication, intermittent psychotherapy, advice giving/education). These should be considered in an intervention plan.
- Debriefing during an ongoing traumatic event may be particularly problematic.
- Debriefing is an opportunity for education about responses to trauma such as emotional reactions to disaster, somatic reactions, violence, substance abuse, and family stress.
- During a debriefing, there is an important opportunity to identify and triage people who are in need of additional assistance/intervention.
- Ongoing groups are more helpful than a one-time meeting.
- Talking in homogeneous groups (e.g., firefighters) may be more helpful than in heterogeneous (stranger) groups.
- Individuals dealing with the death of a loved one may have difficulty if placed in a group with others who have survived a death threat. Therefore it is generally important not to mix those who have experienced a loss and those who have experienced life-threatening exposures.
- Debriefing groups with individuals having different levels and types of exposures may “spread” exposure from those with high trauma exposure to those with low trauma exposure resulting in more symptoms in low exposure individuals.

- Different people have different stories and concerns. Groups often tend to want to all agree on a single perspective. In a heterogeneous group this may lead to isolation and stigmatization of some participants. [15]

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PSYCHOLOGICAL ASPECTS OF A RDD/IND EVENT
GUIDANCE FOR MANAGING STRESS IN FIRST RESPONDERS

Version 2/25/03

The magnitude of death and destruction in the disasters and terrorist attacks places a heavy burden on the society, particularly those who have the gruesome job of recovering and identifying the bodies of the victims and on those who supervise the process.

First and foremost, these workers must be assured a relatively safe and secure physical environment in which they are at minimal risk of injury, work-rest cycles that are not over-taxing, and appropriate management procedures. To be effective and efficient, recovery teams must have sensitive and consistent supervision. Supervisors must be aware of inevitable jurisdictional issues, which will not be easily resolved due to conflicts between investigative and recovery tasks. Competing issues of jurisdiction often lead to conflicting instructions to workers, tasks that must be repeated unnecessarily, and messages to the public that the procedure is not being handled professionally. Supervisors also must provide a management and tracking system to direct workers to where they are needed and to provide hands-on supervision. One of the risks with a task of this magnitude is that workers digging through the rubble amidst the general chaos of heavy debris-moving equipment and other activity can lost contact with their supervisor and literally "get lost" with no one knowing who or where they are.

It is difficult to predict the kinds of psychological problems an individual may develop as a result of recovering bodies. However, the following management suggestions-developed by the Center for Traumatic Stress of the Uniformed Services University of the Health Sciences -- can help minimize later problems:

Guidance for Supervisors

- In order to diminish surprise and anticipatory anxiety, supervisors and personnel going off shift should prepare the workers on the new shift for what they will see, hear, smell, feel, and touch.

- When body search and recovery missions include children, it diminishes psychological stress if visible reminders of the children (e.g., toys, drawings) can be removed first. If not, rescue workers and body recovery personnel are subjected repeatedly to the stress of thinking about dead and injured children.

- Persons who have emotional difficulty with the recovery task often do not want to be dismissed, which may contribute to a sense of failure in an activity for which they felt a "calling." Assign them to another task in which

they can contribute, but do not use the individual's desire to continue work as the sole factor determining assignment of duties.

- Send workers home for food and sleep whenever possible.

- Pair workers with a buddy to help combat potential overwork and provide mutual, ongoing support.

- Every individual has different motivations and a different way of approaching the task of recovering bodies. Supervisors should not require the same actions of everyone.

- As much as possible, allow people to work in an area of their choosing and, if desired, to vary their tasks so they can adjust their exposure to the stress of finding and removing bodies.

- Provide some immediate change of clothing, such as socks, t-shirts, and underwear.

- Workers may fearful of radiological contamination and diseases that might be carried by the remains. Supervisors should discuss protective measures against radiological hazards as well as protection from diseases.

Guidance for Medical Care Providers of First Responders

- Monitor the length of exposure to the dead and to the scene. Recommend rest periods for volunteers and professionals. Do not allow an individual to work longer than a 12-hour shift except in an emergency.

- Watch for workers who become overly zealous or dedicated to the task of recovery, working to exhaustion; they are at increased risk for later disability.

- Provide a rest area with food and beverages, shade with facilities for rest, washing and showering, and protection from news media and onlookers.

- Encourage workers literally to get off their feet during breaks.

- Moderate stress by engaging workers in conversation of their choosing - not necessarily about their feelings or the scene. Talking about the events of life-not death--is central to health.

- Encourage workers to develop a mindset in which they do not personalize the bodies they are recovering or identify with them. Dealing with personal

effects of victims-family photographs in a purse, for example, is one of the most difficult aspects of body recovery especially if people personalize or identify with the victim.

- Advise workers--especially those who have volunteered for the task with minimal training-- not to personalize or identify with the bodily remains of victims or with the circumstances or environment in which the tragedy occurred. Human faces and hands tend to evoke strong personalization, therefore, it is better for recovery personnel to focus their gaze on other parts of the body such as the chest.

- There should be a medical follow-up procedure for all workers to check for signs of disease or effects of known and unknown hazards and, most important, to learn of workers' concerns about such effects.

- Psychiatric assessment should initially be part of the overall medicine outbrief in primary care. Follow-up at three months for those with continued symptoms is indicated.

- Individuals should be advised that reminders of the dead may be disturbing to them.

- Opportunities to educate supervisors and spouse/significant others about the experience of those working in the mortuary will increase the opportunity for talking and support.

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MEDICAL COUNTERMEASURES
AMIFOSTINE

2/25/03 Version

Background

Amifostine (WR-2721), a phosphorylated aminothiol, is the first agent approved by the Food and Drug Administration as a radioprotectant. In mammals, the active metabolite (WR-1065) is a free radical scavenger that protects cell membranes and macromolecules such as DNA from radiation-induced free radicals. Amifostine has been shown in animal and cell systems to protect against cell death, carcinogenesis, and mutagenesis.[16,17,18]

Amifostine (Ethyol®) has also been shown to protect certain tissues in cancer patients undergoing fractionated radiotherapy and/or chemotherapy. Amifostine significantly decreases radiation toxicity (i.e., xerostomia and mucositis) in patients receiving radiotherapy for head/neck cancer when200 mg/m^2 is given intravenously 15 to30 minutes prior to each radiation fraction.[19] However, use of the drug is limited by its side effects, which include significant hypotension, nausea, and vomiting. Other clinical trials have demonstrated decreased radiation esophagitis, pneumonitis, and bone marrow depression, with similar side effects.[20, 21, 22]

Recent small clinical trials with subcutaneously administered amifostine (500 mg/m^2 in 2.5 cc), given 20 minutes before each fraction of radiotherapy, demonstrate similar benefits with much less nausea, vomiting, and hypotension.[23] It is not known whether amifostine given prior to a single dose of intense radiation would protect normal tissues, but clinical studies with fractionated radiotherapy suggest that possibility. Significantly, there is no

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clinical evidence that amifostine offers any protective value when given after exposure to ionizing radiation, and it therefore would seem to be of no value to victims of a radiation dispersion device (RDD).

Interestingly, amifostine given prior to gamma and neutron radiation exposure in animal and cell systems also seems to reduce carcinogenesis and mutagenesis.[24,25,26] This observation raises the theoretical possibility that giving the drug to first responders prior to entering a RDD exposure area might reduce their stochastic (cancer, mutation) risks.

Summary

The advance administration of amifostine subcutaneously to first responders might have value if it is anticipated that the responders will be exposed to doses of radiation in deterministic ranges. In most RDD scenarios, however, such exposures would be highly unlikely. Whether or not administration of amifostine could provide a reduction in the stochastic risks such responders would face is speculative, but would seem to be an important area for further research. In summary, based on current clinical data, amifostine does not appear to be of practical value as a medical countermeasure in most RDD scenarios.

Cost and Scope Implications

Estimated Cost

The estimated cost is approximately $475 - 1,400 per intravenous dose. The subcutaneously administrated drug is an investigative and a price is not yet available. Each patient would probably be given only one dose within an hour prior to exposure.

Scope of Patients Treated

- For a radiological dispersion device, <10 patients would reasonably be treated with this countermeasure.

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MEDICAL COUNTERMEASURES

BICARBONATE ($NAHCO_3$)

2/25/03 Version

Background

Although uranium is not considered to be a likely component of an RDD, sodium bicarbonate ($NaHCO_3$) would be a useful, safe medical countermeasure for RDD victims exposed to certain chemical forms of natural, depleted, or enriched uranium. This drug is readily available to the public in oral and IV forms from many pharmacies. $NaHCO_3$ is also an important intervention to prevent "crush syndrome" which may be associated with blast injury.

Chemical Pharmacology

The chemical form and particle size of a uranium inhalation exposure are important factors in determining the clinical effectiveness of $NaHCO_3$ treatment. In general (unless the uranium is more than 5-8% enriched ^{235}U) the hazard is more chemical than radiological. For example, kidney damage, acute tubular necrosis (ATN), is possible from an exposure of only 0.058mg U/kg because in the usual acid urine pH, the UO_2^{2+} ion binds to kidney tubules. Renal damage is prevented by urine alkalinization. $NaHCO_3$ should be administered either orally or IV and the urine pH followed frequently to ensure alkalinity. Alkaline urine forms a non-toxic uranium carbonate complex that is promptly excreted by the kidney.

Treatment

Oral administration of 4 g initially (650 mg tablets are usually available in pharmacies) and 2 g every 4 hours is recommended until a urine pH of 8 to9 is obtained and maintained. Alternatively, 2 ampules of sodium bicarbonate (44.3 mEq each; 7.5%) in 1000 cc normal saline @ 125 cc/hr can be given IV. Pediatric doses vary from 84-840 mg/kg/day, p.o. in divided doses, every 4 to 6 hours. Therapy can be monitored and guided by collecting 24-hour urine and fecal specimens and analyzing for uranium content as well as for chemical toxicity (e.g., proteins, microglobulin, casts). Serum renal function tests should also be monitored. If large populations are exposed, it is initially reasonable to do the urine/fecal bioassays (and nasal swabs) on a selected group from the suspect larger population to get an early indication of the magnitude of the problem.

Clinical History

There is minimal actual clinical experience in the treatment of uranium-exposed patients with $NaHCO_3$, but NCRP 65 and some medical experts consider it safe and reasonable therapy.

Cost and Scope Implications

Estimated Cost
The cost of sodium bicarbonate medication is small (about $0.40 for a 4 gm dose). The major expense would be the cost of bioassays and medical care.

Scope of Patients Treated
For either a RDD or up to a 10-Kiloton nuclear explosion involving uranium, the availability of this drug countermeasure would not limit the number of patients that could be treated, however, lack of health care providers could be problematic with mass casualties. The number of doses of bicarbonate needed would vary from only a few to possibly thousands, depending on the size and location of the hypothetical event.

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MEDICAL COUNTERMEASURES
COLONY STIMULATING FACTORS
2/25/03 Version

Background
Cytokines are naturally occurring glycoproteins that induce bone marrow stem cells to proliferate and differentiate into a wide variety of mature cell types. Colony stimulating factors act on hematopoietic cells by binding to cell surface receptors, which in turn, stimulate proliferation, differentiation, commitment, and end cell functional activation.

Clinical Pharmacology
Filgrastim is a human granulocyte colony stimulating factor (G-CSF) produced by recombinant DNA technology that is marketed by AMGEN.[27] The Food and Drug Administration (FDA) approved filgrastim in 1991 for use in neutropenic patients receiving myelosuppressive anti-cancer therapy for non-myeloid malignancies. Filgrastim was designed to decrease the incidence of infections that were manifested by febrile neutropenia by stimulating the proliferation, differentiation and function of neutrophils. Pegfilgrastim is the long-acting form of filgrastim and is produced by conjugating the parent molecule with a monomethoxy polyethylene glycol. The conjugated product demonstrates a prolonged plasma half-life and decreased renal clearance. In fact, renal clearance varies with the neutrophil count (i.e., the greater the number of new neutrophils, the faster the clearance of pegfilgrastim).[28]

Sargramostim is a recombinant human granulocyte-macrophage colony stimulating factor (rhu GM-CSF) marketed by Berlex.[29] It is administered to patients with acute myelogenous leukemia to accelerate neutrophil recovery and reduce the incidence of life-threatening infections.

Treatment
- The recommended dosage of filgrastim is 5 mcg/kg/day.
- The dosage for pegfilgrastim is a single subcutaneous (SC) injection of 6 mg.
- The dosage for sargramostim is 250 mgm/m^2/day.
- There are currently no recommended dosing regimens for patients exposed to radiation. . There are no current recommended dosing regimens for patients whose neutropenia is due to radiation exposure. However, based on

[27] Filgrastim is only marketed by AMGEN under the trade name “Neupogen”.
[28] Pegfilgrastim is only marketed by AMGEN under the trade name “Neulasta”.
[29] Sargramostim is only marketed by Berlex under the trade name “Leukine”.

similar paphophysiology, it is anticipated that off-label cytokine therapy would provide similar benefits of decreased infections.

Considerations for Special Populations

Oncologists have used cytokines for pediatric patients with varying degrees of success. Cytokines are used more frequently for primary prophylaxis and less often for uncomplicated febrile neutropenia in this population compared with adults.

High-Risk Patients:

-> 65yrs old
-Existing illness/infection
-Existing malignancy
-History of prior febrile neutropenia
-Hypotension
-Immunocompromised
-Invasive fungal disease
-Open wounds
-Pneumonia
-Pre-existing neutropenia
-Prior chemo-/radiation therapy
-Profound neutropenia (< 100/ul)
-Sepsis syndrome
-Uncontrolled primary disease

Cytokines are generally considered Pregnancy Category C.

Clinical History

Cytokines do not yet have an FDA-approved indication for use in radiation-induced neutropenia. There is no clear evidence that use of cytokines actually reduces mortality.

Cost and Scope Implications

Estimated Costs

- The estimated cost for a treatment course of filgrastim (11 days) is $2,538.
- The estimated cost for a treatment course of pegfilgrastim (1 dose) is $2,950.
- The estimated cost for a treatment course of sargramostim (11 days) is $1400.

Scope of Patients Treated

- For a radiological dispersion device (RDD), <10 patients could reasonably be treated with this countermeasure.
- For an improvised nuclear device, >25,000 patients could reasonably be treated with this countermeasure.

Policy Issues

- There is currently a sufficient supply of these cytokines in the U.S. to respond to multiple mass casualty events involving RDDs, point source attacks, and

most conceivable improvised nuclear devices (IND). The sole manufacturer, Amgen, has already initiated an informal vendor managed stockpiling system based on initial meetings with Armed Forces Radiobiology Research Institute. However, this effort will require prompt attention by the Federal government for continuation.

- Use of these medications for radiation-induced neutropenia after an attack with an RDD or IND would be “off-label”. For the individual physician-patient interaction, this is not a problem. Institutional policy advocating their use or addition to the Strategic National Stockpile would require establishing an Investigational New Drug protocol with Institutional Review Board oversight, adequate monitoring, and informed consent procedures or an exception to policy.

MEDICAL COUNTERMEASURES
DIETHYLENETRIAMINEPENTAACETATE (DTPA)

2/25/03 Version

Background

Ca-DTPA (Trisodium calcium diethylenetriaminepentaacetate) is a calcium salt of DTPA. Zn-DTPA is the analogous zinc salt. Both drugs are Food and Drug Administration (FDA) investigational drugs used in the U.S. and worldwide as chelating agents for plutonium and other transuranic elements such as americium, californium, and curium. Oak Ridge Associated Universities (ORAU) distributes ca-DTPA and Zn-DTPA to co-investigators under contract with the U.S. Department of Energy (DOE). The current supply of Ca-DTPA originates from a German company, HEYL Chemisch-pharmazeutische Fabrik GmbH & Co. KG (HEYL GmbH) .

Clinical Pharmacology

DTPA belongs to the group of chemicals that form stable complexes (metal chelates) with a large number of metal ions. The drug effectively exchanges calcium for another metal of greater binding power (e.g., plutonium, americium) and therefore promotes renal excretion. With repeat dosing, Ca-DTPA may deplete the body of zinc and, to a lesser extent, manganese and other trace elements. Ca-DTPA and Zn-DTPA treatments are efficacious for treatment of internal contamination with soluble plutonium salts, such as the nitrates or chlorides. However, these treatments are ineffective in treating patients contaminated with highly insoluble compounds, such as the high-fired oxide.

Treatment

- DTPA is supplied as 1g in 5 ml of diluent and administered as 1 g daily unfractionated.
- The route of administration may be either slow intravenous push, intravenous infusion, or inhalation in a nebulizer (1:1 dilution with water or saline). Chelating efficacy is greatest within six hours of exposure.
- DTPA should not be considered when inhalation intake is less than one annual limit of intake (ALI). In the range 2-10 ALI, clinical judgment dictates use of DTPA. For intake > 10 ALI, administration of DTPA is highly recommended.

Considerations for Special Populations

- Ca-DTPA is currently contraindicated for children, pregnant women, and patients with nephrotic syndrome or bone marrow depression.
- Zn-DTPA, if clinically indicated, could be administered to children titrated on a mg/kg basis and to pregnant women in all trimesters, although insufficient data exist for both populations.

- Ca-DTPA is classified pregnancy category D and Zn-DTPA is classified pregnancy category C.

Ca-DTPA is thought to be approximately 10 times more effective than Zn-DTPA for initial chelation of transuranics; therefore, Ca-DTPA should be used whenever larger intakes of transuranics are involved. Ca-DTPA is the form of choice for initial patient management unless contraindicated. Approximately 24 hours after exposure, Zn-DTPA is as effective as Ca-DTPA. This comparable efficacy, coupled with its lesser toxicity, makes Zn-DTPA the preferred agent for protracted therapy.

Clinical History

Over 4,600 doses have been administered in 40 years of investigational use. Less than 1% of patients have shown adverse reactions, almost all minor. There are currently 40 U.S. co-investigators.

Cost and Scope Implications

Estimated Cost

The estimated cost per dose is $1.15 per 1g ampule of Ca-DTPA and $1.70 per 1g ampule of Zn-DTPA. These estimates are based on a December 2001, estimate from Heyl GmBH for orders of 100,000-200,000 units (each unit with 5 ampules).

Scope of Patients Treated

- For a radiological dispersion device, <1,000 patients could reasonably be treated with this countermeasure.

- For an improvised nuclear device, <1,000 patients could reasonably be treated with this countermeasure.

Policy Issues

- There is currently an insufficient supply of Ca-DTPA and Zn-DTPA in the U.S. to respond to multiple mass casualty events.

- The only supplier of DTPA is Heyl GmbH, Berlin, Germany. Multiple terrorist events could result in significant radiological exposures both in the U.S. and in Europe. In such a case, it is likely that the German supplier would preferentially meet European needs. Establishing domestic manufacturing capacity is necessary to assure adequate access for U.S. needs.

- DTPA is normally administered intravenously, sometimes in multiple doses, and treatment should begin within 6 hours of exposure. In a mass casualty event, investing in development of a product suitable for oral administration

would significantly increase the number of people who could receive timely treatment. The pharmaceutical industry advises that this is technically feasible. The development of such a product would represent a significant advance for radiation medicine.

References

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- Breitenstein, BD. 1976 Hanford Americium exposure incident: medical management and chelation therapy. Health Phys, 1983; 45:4; 855-66.

MEDICAL COUNTERMEASURES

POTASSIUM IODIDE (KI)

2/25/03 Version

Background

There are a number of radioisotopes of iodine for possible use in a RDD; among these are ^{131}I, ^{125}I, and ^{123}I. Although the short half-life of these isotopes makes them less likely for RDD use, they are readily available since they are in routine use in nuclear medicine for diagnostic (^{123}I) and therapeutic purposes (^{131}I for thyroid therapy and ^{125}I "seeds" for prostrate cancer therapy). Radioiodines are also part of the fission product inventory that may be released from breach of nuclear reactor fuel elements and from nuclear fission explosions. Potassium iodide (KI) is the drug of choice as a medical countermeasure to prevent thyroid uptake of radioiodines; but it must be clearly stated that KI is useful only for protecting the thyroid against radioactive iodine and is not a generic "anti-radiation medicine," as is often implied in popular media. One of the limitations of KI is that its efficacy is dependent on its ingestion soon after exposure. Also, KI would not be protective against fallout skin burns that could result from prolonged contact with iodine-contaminated fallout. There is also controversy and on-going research on the efficacy of KI on patients over the age of 40 (see FDA table below). At this point in time, the guidelines developed by the FDA are recommended.

Clinical Pharmacology and Treatment

Radioactive iodine, like stable iodine can enter the body through the gastrointestinal tract, skin, or lungs and is quickly taken up by the thyroid. Potassium iodide (KI) is a safe, effective, medical countermeasure against radioactive iodine since KI completely prevents thyroid uptake if given <u>prior</u> to exposure. KI, however, is decreasingly effective if given <u>after</u> exposure (only 7% effective if given 24 hours after exposure).

The FDA and EPA have approved the following daily dose schedule for KI tablets, which are available at many pharmacies:

Threshold Thyroid Radioactive Exposures and Recommended Doses of KI for Different Risk Groups[30]				
	Predicted Thyroid Exposures (cGy)	**KI Dose (mg)**	**# of 130 mg tablets**	**# of 65 mg tablets**
Adults over 40 years	≥500	130	1	2
Adults 18 – 40 years	≥10			
Pregnant or lactating women	≥5			
Adolescents 12-18 years*		65	1/2	1
Children 3 – 12 years				
Over 1 month through 3 years		32	1/4	1/2
Birth through 1 month		16	1/8	1/4

* Adolescents approaching adult size (≥70 kg) should receive the full adult dose (130 mg).

The partial tablet doses can be prepared by dissolving one 130 mg tablet in 4 tsp. water and measuring accordingly (i.e., 1 tsp = 32 mg KI). More conveniently for pediatrics, PIMA® cough syrup (per Physician Desk Reference (PDR) dose schedule) is also available by prescription, as well as saturated solution of potassium iodide (SSKI) and Lugol's solution. Delivery of radiostable iodine through the skin using povidone-iodine has been studied in a limited fashion and the initial human study appears promising. These doses should be given daily until the threat of exposure is over, except in pregnant and lactating females who should not be given repeated doses due to the risk of effecting fetal or neonatal thyroid function.

Considerations for Special Populations

The Chernobyl experience has shown that the fetus, neonate, and child are most at risk for radiationinduced thyroid disease (cancer, adenomas, hypothyroidism) following exposure to ^{131}I. Urgent consideration for giving KI to pregnant women (especially 2nd and 3rd trimesters) and children is appropriate (see contraindications below). There is some debate on the need for KI therapy in adults since the Chernobyl data seem to indicate that the risk of thyroid cancer to ^{131}I exposed people over 20 years old is small. KI is contraindicated for people hypersensitive to iodine, or who have dermatitis herpetiformis or hypocomplementemia vasculitis. Possible morbidities include gastrointestinal

[30] Guidance: Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies, USDHHS, FDA (CEDR), December 2001.

disturbance, rashes, allergic reaction, and thyroid function alterations, including thyrotoxicosis, goiter, and hypothyroidism.

Cost and Scope Implications

Estimated Cost
Estimated cost per dose is somewhat variable and dependent on the form of drug administered. For example, the U.S. Postal Service recently purchased it for 18.3 cents per pill, but prices of 71.4 cents per pill are not unusual.

Scope of Patients Treated
For either a radiologic dispersal device containing radioiodine or a 10-kiloton nuclear weapon detonation, radiostable iodine prophylaxis could be used to avert most of the radioiodine dose to the thyroid. Terrorist fission (nuclear) devices, being surface-blast devices, may cause radioiodine fallout. The weather and source term conditions (which dictate the size, shape, and ^{131}I concentration in the resultant plume after an event at a nuclear reactor or an improvised nuclear device), will ultimately determine the population risks. The number of doses of KI potentially needed will therefore vary from a few to millions depending on whether the radioiodine source is an RDD or a 10-kiloton nuclear weapon explosion.

Policy Issues

- The potential use of the drug KI is logistically problematic. KI is available through some pharmacies, but there is a need for a well thought out plan for distributing it to a large population within a few hours of exposure to radioiodine.

- Further clinical research should be encouraged regarding the optimal dose and use of topical iodine as a medical countermeasure. Povidone-iodine has shown promise in blocking thyroid gland uptake and is readily available at hospitals and health care facilities. It does not suffer shelf life problems and is easier to administer than oral preparations. The FDA should consider approving povidone-iodine for this use.

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- NCRP Report 138, *Radiation Protection and Terrorism*, National Council on Radiation Protection and Measurements, Bethesda MD, 2002.

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MEDICAL COUNTERMEASURES

PRUSSIAN BLUE (PB)

2/25/03 Version

Background

Insoluble Prussian Blue (PB), ferric hexacyanoferrate, is a drug that enhances excretion of isotopes of cesium and thallium from the body by means of ion exchange. Insoluble PB has been recommended for years as the drug of choice by national and international radiation protection societies for use in treating internal contamination with radiocesium. It was effectively used in the treatment of patients contaminated with ^{137}Cs in the 1987 Goiânia, Brazil incident.

PB is currently supplied by a German company, Heyl Chemisch-pharmazeutische Fabrik GmbH & Co. KG (Heyl GmbH), under the trade name Radiogardase®. The Oak Ridge Institute for Science and Education (ORISE) administers PB under contract with the U.S. Department of Energy.

Clinical Pharmacology

PB has a very high affinity for cesium and thallium, whose metabolism follows an entero-enteric cycle. Orally administered PB traps thallium or cesium in the gut, interrupts its re-absorption from the gastrointestinal tract, and thereby increases fecal excretion. The biological half-life of thallium and cesium is significantly reduced after decorporation therapy with PB. PB itself is not absorbed across the gut wall in significant amounts.

Treatment

- Initial dose for ^{137}Cs: 1 gm orally three times daily. Insoluble PB is supplied as a 0.5 gram gelatin capsule for oral administration.
- There are essentially no contraindications. PB is effective only if gastrointestinal motility is intact. Patients will experience blue-tinged stool and should be so informed.
- PB should not be considered when intake is less than one annual limit of intake (ALI). In the range 2-10 ALI, clinical judgment may dictate use of PB. For intake > 10 ALI, administration of PB is highly recommended.

Considerations for Special Populations

- The dose of PB for children is 1-1.5 g daily in 2-3 divided doses.
- PB may be given in pregnancy if clinically indicated and is classified in pregnancy category C.

Clinical History

The PB treatment of 46 patients with incorporated ^{137}Cs after the radiological accident in Goiânia, Brazil in 1987 has been described. Patients' ages 4 to 38 years were treated with PB for up to 150 days. Doses generally ranged from 1-10 g daily. In four adult cases, 20 g was administered daily in divided doses. Children were given 1-1.5 g daily in 2-3 divided doses. PB significantly expedited cesium decorporation in these cases. In various human accidents, the effective half-life of the cesium depended on the individual and ranged from 36-124 days. PB accelerated the decorporation of cesium, reducing the average effective half-life from 39 to 16 days. In the 1987 Goiânia, Brazil ^{137}Cs contamination accident, an upper therapeutic range of insoluble PB was established at approximately 10 g orally per day in 3 divided doses. Doses higher than 10 g per day resulted in an increased incidence of gastritis, constipation, and diarrhea.

Cost and Scope Implications

Estimated Cost

The estimated cost per dose is $15.80 per 30 capsule bottle (December 2001 estimate from Heyl GmbH for orders of approximately 100,000 bottles). One bottle of PB is a 5-day supply for one person for dosing at 1g TID.

Scope of Patients Treated

- For a radiological dispersion device, <1,000 patients could reasonably be treated with this countermeasure.

- For an improvised nuclear device, <1,000 patients could reasonably be treated with this countermeasure.

Policy Issues

- There is currently an insufficient supply of Prussian Blue (PB) in the U.S. to respond to multiple mass casualty events. Estimated delivery times for large quantities could range between 12-18 months.

- The only supplier of PB is Heyl GmbH, Berlin, Germany. Multiple terrorist events with ^{137}Cs could result in significant radiological exposures both in the U.S. and in Europe. In such a case, it is likely that the German supplier would preferentially meet European needs. Establishing domestic manufacturing capacity is necessary to assure adequate access for U.S. needs.

Reference

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MEDICAL COUNTERMEASURES
STEM CELL TRANSPLANTATION
2/25/03 Version

Introduction
Ionizing radiation may cause transient disruption of hematopoiesis with whole-body exposures of as little as 0.5-1.0 Gy (50 to 100 rad). As the level of radiation exposure increases, the number of hematopoietic cells in the marrow decreases, the number of cells subsequently available to circulate in the blood is reduced, and the onset of pancytopenia is accelerated. The radiation level that causes irreversible failure of the hematopoietic system varies among individuals and probably reflects both genetic and individual physiologic differences. At effective doses above 5 Gy, the peripheral blood platelet and granulocyte level in many patients will drop precipitously around 14 days after exposure, and the risk of death from bleeding or infection in unsupported patients increases dramatically (LD50 estimated at 4.5 Gy).[31] (LD50 is the dose at which 50% lethality is achieved.) Fortunately, it is possible to support most radiation casualties with cytokines, antibiotics, and routine intensive care. In this sense, patients with myelosuppression related to radiation exposure are comparable to patients undergoing marrow transplantation or suffering from marrow failure related to chemotherapy or aplastic anemia.

While the majority of cells of the hematopoietic system are rapidly replicating and thus exquisitely sensitive to radiation, the system as a whole is quite resilient. The basic biology of hematopoiesis generally protects the system from irreversible damage. The stem cell itself rarely replicates and is very stable, and physical damage, including radiation, to part of the system has no harmful affect on undamaged parts of the system. Most cases of accidental irradiation result in non-uniform exposures, leaving pockets of normal marrow. Even if serious damage occurs to most of the hematopoietic system, surviving stem cells can migrate to damaged areas and restore hematopoiesis. In animal models, a few hematopoietic stem cells can repopulate the entire system. In humans, small infusions of marrow from healthy donors routinely reconstitutes the completely ablated hematopoietic systems of recipients.

Clinical Considerations and Evolution of Transplant Medicine
Marrow or stem cell transplantation from a monozygotic (identical) twin can safely restore hematopoiesis in lethally irradiated patients, but the availability of this type of donor is rare. The use of transplantation from allogeneic (non-self) donors in the setting of radiation exposure is controversial. The additional immunosuppression required to prepare the recipient for the transplant, and then after the transplant to mitigate graft-versus-host disease (GVHD), introduces very

[31] Mole RH. The LD50 for uniform low LET irradiation of man. Br J Radiol 1984; 57:355-69.

serious risks in already immunosuppressed individuals. Moreover, radiation levels that cause severe marrow damage or failure usually produce concomitant life-threatening injury to other organs, particularly the lungs and intestines. Care of patients or casualties who have radiation-induced marrow failure is complicated by these other injuries, and patients who recover marrow function frequently succumb to non-hematopoietic injuries. To date, comparatively few transplants have been performed for radiation casualties and lethally irradiated patients receiving marrow or cord blood transplants have not demonstrated improved survival.

For those casualties with persistent marrow failure, however, allogeneic transplantation is the only therapy that can reestablish hematopoiesis. Because transplantation is a high-risk procedure, transplants should be performed in established transplant centers, using donated marrow or stem cells from matched siblings, matched unrelated donors, or the best available cord blood (currently the latter can be recommended only for children without matched siblings or matched unrelated donors).[32] In recent years, the technology of allogeneic transplantation has evolved rapidly and clinical advances may increase the applicability of transplantation to radiation accident response in the future. New approaches to immunosuppression that greatly reduce the risk of the procedure for elderly and other high-risk patients are under investigation. Reduced-intensity allogeneic transplants (so-called "mini-transplants") are particularly promising in that they have been shown to be significantly less toxic than conventional transplants. Post-transplant GVHD continues to be a significant problem, however.

Indications

Indications for transplant therapy are unclear. Lymphocyte depletion kinetics can provide an early initial estimate of dose for pure gamma or mixed neutron/gamma exposures in the 0.5 Gy < dose < 8-10 Gy range, but for the reasons cited above such estimates cannot definitively identify patients who will subsequently require transplant.[33] Other authors have argued that the reduction of blood granulocytes to levels of less than 200-300/mm^3 on day 5 to6 after exposure indicates that no stem cells remain from which a spontaneous

[32] The National Marrow Donor Program (NMDP) has a roster of nearly 5 million volunteer marrow donors; access to tens of thousands of cord blood units; a laboratory, management, and support infrastructure linking over 500 medical institutions; and oversight and support from the Department of Health and Human Services and the U.S. Navy. The NMDP exercises this system daily through tens of thousands of searches, performs thousands of transplants annually, and maintains availability to respond to radiation emergencies.

[33] Goans RE. Clinical Care of the Radiation Accident Patient: Patient Presentation, Assessment, and Initial Diagnosis. In Ricks RC, Berger ME, O'Hara FM, Eds. *The Medical Basis for Radiation-Accident Preparedness. The Clinical Care of Victims.* Proceedings of the Fourth International REAC/TS Conference on the Medical Basis for Radiation-Accident Preparedness, March 2001, Orlando, FL, The Parthenon Publishing Group, 2002.

regeneration could occur and hence necessitates stem cell transplantation.[34] Following the Chernobyl accident, one transplant indicator used was multiple site marrow biopsies with low cellularity in multiple sites (indicating severe aplasia). Other measures of marrow function, such as the number of circulating $CD34^+$ cells, could also be used. Information about the distance of the exposed individual from the radiation source, tests of chromosomal changes in lymphocytes, demonstrations of change in electron spin resonance in electron spin resonance -sensitive material, and the clinical medical examination of the victim can augment tests of marrow function.

If marrow does not demonstrate ongoing hematopoietic recovery by 1 to 2 weeks following aplasia (day 25-40 following exposure), transplantation of normal hematopoietic cells from a healthy marrow (or stem cell) donor may be required. The earlier the aplastic period begins following exposure, the more likely it is irreversible. Very low granulocyte counts 8 to12 days following exposure indicate a whole body dose in excess of 6 Gy and an increased likelihood of long term aplasia requiring transplantation. If early indicators of potential stem cell failure are present, casualties should be cared for in a medical facility with a transplant center so as to allow the transplant clinical team to assist in the care and evaluation of the patient and to begin the identification of a matched donor either from the family or from an unrelated donor should transplant ultimately be required. It is important to note, however, that exposures in this range are associated with significant and potentially lethal toxicity to other organ systems. Restoration of hematopoiesis is of negligible benefit in persons suffering whole body doses in excess of 10 Gy, who invariably die from gastrointestinal and pulmonary complications.

Limited Current Application

In summary, the role of marrow or stem cell transplantation in contingency response to radiation injury is currently 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 non-uniform radiation in accidental exposure, most individuals can recover hematopoiesis without a 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, marrow transplantation must be available for carefully selected casualties, and its future applicability may change as transplant procedures improve.

Cost and Scope Implications

Estimated Cost

The estimated cost is $150,000-350,000 per transplant.

[34] Fliedner TM, Tibken B, Hofer EP, Paul W. Stem cell responses after radiation exposure: a key to the evaluation and prediction of its effects. Health Phys 1996; 70:787-97.

Scope of Patients Treated

- For a radiological dispersion device, <100 patients would reasonably be treated with this countermeasure.

- For an improvised nuclear device, <100 patients would reasonably be treated with this countermeasure.

APPENDIX A – ACRONYMS

AFRRI	Armed Forces Radiobiology Research Institute
ALI	Annual Limit of Intake
ATN	Acute Tubular Necrosis
BAT	Biodosimetry Assessment Tool
Bq	Bequerels
CNS	Central Nervous Syndrome
CPM	Counts per Minute
CV	Cardiovascular
DNA	Deoxyribonucleic Acid
DOE	U.S. Department of Energy
DRD	Direct Reading Dosimeter
DTPA	Diethylenetriaminepentaacetate
FDA	Food and Drug Administration
FISH	Florescence in situ hybridization
G-CSF	Granulocyte Colony-Stimulating Factor
GI	Gastrointestinal
GM-CSF	Granulocyte-macrophage Colony-Stimulating Factor
GVHD	Graft-Versus-Host Disease
Gy	Gray (unit of measure for radiologic exposure)
IAEA	International Atomic Energy Agency
ICRP	International Commission on Radiological Protection
IND	Improvised Nuclear Device
IRB	Institutional Review Board
NCRP	National Council on Radiation Protection and Measurements
NMDP	National Marrow Donor Program
ORAU	Oak Ridge Associated Universities
ORISE	Oak Ridge Institute for Science and Education
PB	Prussian Blue
RDD	Radiological Dispersion Device

Sv	Sieverts
TLD	Thermoluminescent Dosimeter

APPENDIX B – MEDICAL PREPAREDNESS AND RESPONSE SUB-GROUP MEMBERS

Material provided in this document is a joint effort by those listed below.

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