THE MEDICAL ASPECTS OF RADIATION INCIDENTS

The Radiation Emergency Assistance Center/Training Site

REAC/TS
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Oak Ridge, TN 37831
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The Radiation Emergency Assistance Center/Training Site (REAC/TS) has provided the Department of Energy with expertise related to the medical management of radiation accidents since 1976. REAC/TS maintains a 24/7 national and international radiation emergency response capability that includes a staff of physicians, nurses, and health physicists experienced in treatment of radiation injuries/illnesses, radiation dose evaluations, and decontamination. The REAC/TS Cytogenetic Biodosimetry Lab (CBL) has the capability to perform dicentric and other chromosomal analyses for radiation biodosimetric purposes. REAC/TS also maintains a radiation accident registry and manages the use of DTPA and Prussian Blue for the Department of Energy. Additionally, REAC/TS provides continuing medical education in its field of expertise through regularly scheduled in-house courses and specially designed off-site courses.

REAC/TS is a response asset of the U.S. Department of Energy/National Nuclear Security Administration (DOE/NNSA). REAC/TS provides treatment capabilities and consultation assistance on a 24-hour basis, and can be reached by calling Dr. 865-576-3131 (days), or after normal business hours via the DOE Oak Ridge Operations Center at 865-576-1005. Leadership for REAC/TS is provided by Dr. Albert L. Wiley, MD, PhD (Director) and Dr. Doran M. Christensen, DO (Associate Director).

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Contents

Section 1 – Introduction and Radiation Basics

Medical care providers are expected to provide care to patients due to a multitude of scenarios. One of those scenarios involves the patient who has been exposed to and/or contaminated with radioactive materials. This document is intended to provide basic information to physicians and other healthcare professionals necessary for the proper medical management of individuals who fall into this category.

The most important consideration in the medical evaluation of people involved in a radiation event is the medical stability of the affected individuals. The relative magnitude of the situation and the resources needed to address the emergency are also important considerations.

> **Small-scale** events are those occurring in laboratories, hospitals, nuclear power plants, etc., involving small amounts of radioactive materials with the potential exposure and/or contamination of one or a few individuals.
> **Large-scale** events are those involving relatively large quantities of radioactive materials and the potential exposure or contamination of large numbers of people**,** e.g., terrorist attacks with radiological weapons, nuclear weapons detonation, and large-scale nuclear power plant disasters.

High-level acute external doses of ionizing radiation typically pose the greatest danger to people. Low-levels of internal or external contamination with radioactive material generally pose little risk. As with all emergency response situations, safety of the responder is a primary concern. A site known to be radiologically contaminated should be assessed before general entry and responders should be advised to limit their time in high dose-rate areas. There is minimal hazard typically associated with handling a radiologically contaminated casualty. See Section 6 for guidance related to decontamination techniques.

The National Council on Radiation Protection Report No. 138 (2001), Management of Terrorist Events Involving Radioactive Material, discusses various events by which personnel could be exposed to radiation or contaminated with radioactive materials. Below are generally accepted categorizations of some of the varying radiological terrorist threats.

- **Radiation Exposure Device (RED)**: radioactive material, in a sealed source or within a container, and intended to expose people in the vicinity of the device to a high-level external dose. Some materials used in commercial equipment contain radioactive sources that could function as an RED. Industrial radiography sources as pictured (bottom, right), are found in the civilian sector and could be used as a RED. Brachytherapy sources (top, right) are also common.

- **Radiological Dispersal Device (RDD)**: any device that causes intentional dissemination of radioactive material without a nuclear detonation. An RDD can cause internal dose through inhalation or ingestion of released radioactive material and external dose due to surface contamination. An RDD intended to disperse radioactive material by use of an explosive device would likely result in injuries associated with blasts and heat to become contaminated with radioactive material. Additionally, the contaminated environs would likely complicate medical response and/or evacuation.
- **Improvised Nuclear Device (IND)**: defined as a device designed by terrorists to produce a nuclear detonation. At full or partial yield, an IND is physically the same thing as a nuclear weapon: blast, burns, and radiation are the forms of energy and are also the cause of injury. An IND exposes people to high-level external dose, trauma, inhalation and ingestion of radioactive materials, and skin contamination. Should an IND fail to detonate properly, the high explosives may disseminate the nuclear material around the environment, thus effectively becoming an RDD.

Operations in some radiological areas could result in personnel receiving sufficient radiation dose or radioactive contamination to warrant medical evaluation and decontamination. Significant amounts of radioactive material may be deposited on surfaces after the detonation of a nuclear weapon, use of a RDD, or a nuclear plant accident.

In addition to the above, personnel can be exposed to radiation and/or become contaminated from accidents involving storage or transportation of radioactive materials, use of industrial sources, or during the course of performance of routine functions throughout the nuclear industry.

Planning
The US EPA has established recommendations for mission-specific risk-based dose limits that include life-saving activities. This guidance can be found in EPA 400-R-92-001, Manual of Protective Action Guides and Protective Actions for Nuclear Incidents. The manual states that workers may receive up to 10 rem (0.1 Sv) to protect valuable property and up to 25 rem (0.25 Sv) for saving a life. They also state that greater than 25 rem (0.25 Sv) can be received for life saving if the responders volunteer, are non-pregnant adults, and are fully aware of the risks involved. These emergency doses are for a once-in-a-lifetime exposure and are not added to occupational dose. ICRP Pub. 103 recommends no dose restrictions for life saving if the benefit to others outweighs the rescuer's risk (informed volunteers). For other *urgent* rescue operations, upper dose recommendations are 1000 mSv (100 rem) or less. Other rescue operations have recommended limits of less than 100 mSv (10 rem).

Types of Radiation

The five types of radiation of primary importance:

- **Alpha particles**: charged particles made up of two protons and two neutrons emitted from heavy nuclei including U, Pu, and Am. Alpha particles cannot travel far (about an inch in air) and penetrate no more than a few μm in skin (basically, the dead layer of the skin). Thin clothing, or even a sheet of notebook paper, is an effective shield for alpha particles. Radionuclides that emit alpha particles are therefore a negligible external hazard but can be important in an inhalation or ingestion incident. Due largely to their relatively large size and charge alpha particles are efficient at creating ionization, thus potential biological damage. Therefore, regulatory limits on intakes of radioisotopes emitting alpha particles are typically significantly more restrictive.
- **Beta particles**: electrons emitted from the nuclei of isotopes such as tritium and ^{90}Sr. Beta particles can travel a short distance in tissue (a few millimeters) and up to a couple of meters in air. Most beta particles can be shielded by a thin layer of plastic. The clear face-piece of full-face respirator is an effective shield for many beta particles. Large quantities of beta emitting radioactive materials deposited on the skin can damage the basal layer and cause what are commonly referred to as radiation burns. Beta emitters are also important if inhaled or ingested.
- **Gamma rays**: non-particulate electromagnetic radiation (with wavelengths shorter than UV) capable of creating ionization that are emitted from various

radioisotopes. Gamma rays originate in the nucleus. They are highly energetic and can pass through matter easily, indicating that they are not extremely efficient at creating ionization (compared to alpha particles, for instance). Regulatory limits on intakes of gamma emitting radionuclides are typically much less restrictive than those of alpha emitting radionuclides. Because of its high penetrability, gamma radiation can result in exposure to the internal organs from external sources resulting in damage to them, and are thusly a concern for external irradiation. Dense materials such as lead are used to shield gamma rays.

- **X-rays**: different from gamma rays only in their point of origin: outside of the nucleus as opposed to within it.
- **Neutrons**: uncharged particles, important because they are emitted during the fission process and in some nondestructive testing procedures. They are not as commonly encountered as the other four types of radiation discussed. Neutrons can have from 3 to 20 times more risk of future effects associated with them than gamma rays. Neutrons are the only type of the five discussed that have the ability to make something else radioactive (neutron activation).

Means of Exposure

An individual may receive radiation dose from an external source, by loose radioactive material deposited on the skin or equipment, or by ingesting or inhaling radiological particulates. Ingestion or inhalation of radioactive material may cause internal dose to the whole body or to a specific organ over a period of time, but dose levels received in this manner have historically not normally been acutely lethal.

Irradiation vs. Contamination

A person is irradiated when they are "exposed" to ionizing radiation in much the same way a person is "exposed" to light when someone shines a flashlight on them. In the case of irradiation there is no material transferred. This means that an irradiated patient has no radioactive material on them and poses no radiological hazard to the treatment team.

When people have radioactive materials on/in them they are said to be contaminated. Note that a person is not contaminated with alpha particles, for instance, but with materials such as ^{241}Am that emit alpha particles. A good way to think of this is to imagine a sealed container of radioactive baby powder (This one emits gamma rays!). One can hold the container and be exposed to the gamma rays penetrating through the walls of the container without getting the baby powder on his hands. Should a leak develop around the lid allowing some of the material to

escape, the person may have the powder on his hands, thus resulting in contamination of the individual.

Controlling radioactive contamination is very similar to controlling the baby powder that leaked above. A common sense approach should be taken to limit the spread of the material. This is usually done by proper utilization of protective clothing, controlling entry and exit to/from a contaminated area, minimizing the amount of material dispersed into the air, and proper personnel monitoring. There are other methods one can employ to control the spread of contamination (use of negative pressure, avoid actions that may resuspend the material, covering or removing unnecessary items from the area, etc.), but typically, contamination control is a process that, although important, needn't be overly complicated.

Units

The basic unit of radioactivity used in the US is the curie (Ci) and is defined as 3.7 x 10^{10} becquerels (Bq). The becquerel, one disintegration per second, is the basic SI unit (from the French *le Système International d'unités*). One Ci is equal to 37 gigabecquerels (GBq) and one GBq is equal to 27 millicuries (mCi). Activity is the concept used to quantify the amount of radioactive material present. Conventional units such as ounces, grams, etc. should not be used to quantify the amount of radioactive material present. For instance, one gram of cobalt-60 is a little over 1,100 Ci (~40,000 GBq) while one gram of uranium-235 is about 2.1 μCi (~ 78 kBq).
Some useful activity conversions are:

1 Ci = 37 GBq 1 mCi = 37 MBq 1 μCi = 37 kBq
1GBq = 27 mCi 1 MBq = 27 μCi 1 kBq = 27 nCi
Where:
G = giga (1 x 10^{9}), M = mega (1 X 10^{6}), k = kilo (1 x 10^{3})
m = milli (1 x 10^{-3}), μ = micro (1 x 10^{-6}), n = nano (1 x 10^{-9})

The amount of time it takes for the activity to decrease to ½ of its original value is called the half-life. It cannot be altered by outside forces.

Exposure is a quantification of the amount in ionization in air. The units are the roentgen (R) in the US and coulombs per kilogram in SI units. Since these units are "ionization in air" they are not extremely medically significant since, technically, the energy has not yet been deposited into tissue. Once energy is deposited into tissue it is known as absorbed dose.

The concept of absorbed dose is a measure of the energy deposited in tissue by ionizing radiation. The US unit is the rad. One rad is equal to 100 ergs (10^{-7} joules) of

energy deposited into one gram of tissue. The SI unit for absorbed dose is the gray (Gy) which is equal to one joule of energy deposited into one kilogram of tissue. For relating acute medical effects, it is widely considered that the most appropriate unit to use is the rad or Gy since the acute effects (discussed in Sections 3 and 4) are largely driven by the amount of energy deposited into a particular tissue.

1 Gy = 100 rad 1 centigray (cGy) = 1 rad

The differences in the future risk (i.e.: risk of future cancer induction, for instance) among the different radiation types are approximated by use of a quality factor (QF, for dose equivalent, used in the US) or a radiation weighting factor (w_R, for equivalent dose, used internationally). Another way to think of this is that it is a comparison of a dose of one type of radiation required to produce a given effect to the dose of a different type of radiation required to produce the same effect. The difference in dose equivalent (uses QF) and equivalent dose (uses w_R) is found in the definitions used by differing ICRP reports. In simple terms, the QF and w_R represent how much more risk is associated with one radiation type versus the standard (gamma, x-ray where the w_R and QF = 1). The dose in Gy times the w_R yields the equivalent dose, measured in sieverts (Sv). The corresponding US unit for the sievert is the rem. The w_R for x-ray or gamma radiation is one, so for pure gamma radiation:

100 rad x 1 = 100 rem, or 1 Gy x 1 = 1 Sv

The w_R for alpha radiation is 20, so one rad (or Gy) due to alpha radiation is equal to 20 rem (or Sv). Beta radiation has a w_R of one, and for neutrons it lies between three and 20, depending on the neutron energy.

Table 1A - Annual Regulatory Limits (US NRC)

	rem	mSv
Non-Occupational Limit		
Members of the public	0.1	1
Occupational limits		
Whole body (internal + external)	5	50
Any individual organ	50	500
Lens of the eye	15	150
Skin	50	500
Extremities	50	500
Fetal dose (declared pregnancy)	0.5	5

Table 1B – ICRP Publication 103 General Recommendations

	rem	mSv
Non-Occupational Limit		
Whole body (internal + external)	0.1	1
Lens of the eye	1.5	15
Skin	5	50
Occupational limits		
Whole body (internal + external)	2	20
Any individual organ	n/a	n/a
Lens of the eye	15	150
Skin	50	500
Extremities	50	500
Fetal dose (declared pregnancy – remainder of pregnancy)	0.1	1

Occupational dose limits, related in rem or Sv, are in place primarily for risk limitation and fall below the normal thresholds associated with acute medical effects. It is sometimes helpful to reference regulatory limits as a comparison point when trying to explain the magnitude of the dose that may have been received by a patient or when in conversations with other interested parties.

Many radiation detection instruments such as the G-M (Geiger-Mueller) detector or ion chamber use the unit Roentgen (R), or a submultiple such as mR. The R is a unit of ionization in air. The ion chamber, for instance, is an air filled detector so the charge generated in the detector by an incoming ionizing event is appropriately measured in roentgens. For gamma radiation, 1 R ~ 1 rad ~ 1 rem. So, even though the units are different, they are often – conversationally – used interchangeably. For beta radiation a multiplication factor is usually applied when using an ion chamber. One's health physicist can help with this.

Specific Gamma Ray Constant

The *gamma constant* for an isotope is the gamma ray exposure rate in R per hour (R/h) at a one meter distance from a one Ci point source (or the SI equivalents). Three common radioisotopes thought to be of interest to terrorist organizations are ^{192}Ir, ^{137}Cs, and ^{60}Co. Following are the approximate gamma constants for these radioisotopes:

^{60}Co: 1.3 R per hr at 1 m per Ci, or 3.51 mSv-cm^2/hr-MBq
^{137}Cs: 0.326 R per hr at 1 m per Ci, or 0.89 mSv-cm^2/hr-MBq
^{192}Ir: 0.48 R per hr at 1 m per Ci, or 1.3 mSv-cm^2/hr-MBq

Aside from the medical assessment, two principles are of paramount importance in the medical management of the irradiated patient: *early estimation of the magnitude of the radiation/contamination event and identification of the radioisotope(s) in question*. These principles strongly influence subsequent treatment decisions.

Event

An individual goes into a construction area where a 100 Ci (3.7 TBq) ^{192}Ir source is lying in the floor. The source, typically used for industrial radiography, was inadvertently left behind by the radiographer. The patient worked 1 m away from the source. He estimated being in the vicinity of the source for 15 minutes. What is his estimated whole-body dose?

Solution

An approximate dose from a small source is the gamma constant multiplied by the activity of the source times the amount of time spent near the source – all divided by the square of the person's distance from the source in meters (or cm, as appropriate). The gamma constant for ^{192}Ir is 0.48 R/h at 1 m per Ci or 1.3 mSv/hr at 1 cm per MBq (gamma constants for selected radioisotopes can be found in Table 2).

$$\text{Dose} = 0.48 \text{ R/h/Ci} \times 100 \text{ Ci} \times 0.25 \text{ hr}/(1 \text{ m})^2 = \text{about 12 rads}$$
$$\text{Dose} = 1.3 \text{ mSv/hr/MBq} \times 3.7\text{E}6 \text{ MBq} \times 0.25\text{hr}/(100\text{cm})^2 = \sim 120 \text{ mSv}$$

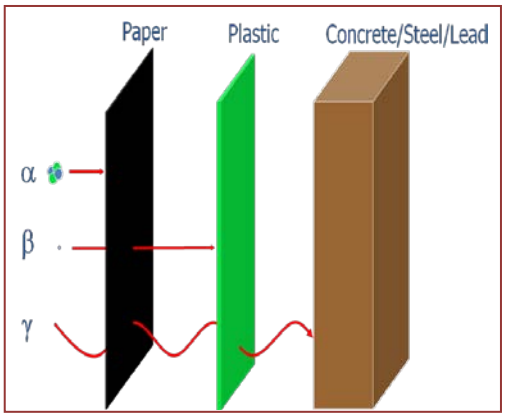
As discussed in Section 3, this incident would result in no significant acute medical consequence to the patient. Reassurance to the patient would likely be in order regarding medical issues. Although this is a rough approximation, it is adequate given the usual uncertainty with the individual's exact distance from the source and the time spent near it. The dose rate for a point source decreases as the square of the distance, so the dose would be substantially smaller at greater distances from the source. This is called the inverse square law, which essentially says, "If you double the distance you quarter the dose." It is therefore important to minimize time near a source and maximize distance from it. For example:

$$\text{At 1 m the dose} = \sim 12 \text{ rad (120 mGy)}$$
$$\text{At 2 m the dose} = \sim 12 \text{ rad} / 2^2 = 3 \text{ rad (30 mGy)}$$
$$\text{At 3 m the dose} = \sim 12 \text{ rad} / 3^2 = \text{about } 1.3 \text{ rad (13 mGy)}$$

The treating physician and assisting health physicist should maintain open communications to ensure the dose calculations and the anticipated medical signs/symptoms somewhat agree. In the event the medical ramifications do not agree with what was predicted by the dose estimations, time and distance estimates may be at fault. Effort should be made to resolve these types of issues. It is not uncommon

for the incident investigation to uncover new facts or for initial recollections of an event to change as time goes on.

Personnel Protection



ALARA (As Low As Reasonably Achievable) is the underlying philosophy associated with protecting people from ionizing radiation. It basically means that one should not unnecessarily expose themselves to radiation without the benefit outweighing the risk. Time, distance, and shielding are widely considered to be the primary concerns. At REAC/TS we like to add a fourth item to the list – quantity. All four of these concepts are used concurrently with the others. For instance, if one were to increase the distance from a radioactive source they are actually adding more shielding (yes, air is a shield). To spend less time in an area one moves farther away from the source (distance, and thusly, shielding). When one minimizes the quantity of radioactive material in an area they are moving the source farther away. As one can see, protecting oneself from ionizing radiation is nothing more than using good common sense: minimize the time around the source, increase the distance from the source, put "stuff" between the target and the source, and/or simply remove the source.

Appropriate personnel dosimetry should be used to monitor external doses to ensure they are maintained ALARA. Dosimeter types include film badges, thermoluminescent dosimeters (TLD), and optically stimulated luminescent dosimeters (OSLD). Additionally, direct read-out dosimeters (DRD) are available. Whereas TLDs, OSLDs, and film badges must be read by special equipment, DRDs allow the user to continually track their accumulated dose. Dosimetry types should be researched and the appropriate type selected for one's individual needs.

Areas of contamination could result not only from industrial or medical sources, but also from the use of an RDD, detonation of a nuclear device, or other reasons. External contamination by radioactive materials can occur when an individual traverses a contaminated area without appropriate protective clothing. If, for instance, an event occurs causing the radioactive materials to become airborne or the individual is wounded while in the contaminated area, he/she could possibly become internally contaminated. Radiologically contaminated patients generally pose no danger to health care personnel due to irradiation. Medical providers must therefore be prepared to provide prompt treatment of conventional trauma complicated by ionizing radiation or radioactive contamination.

Protective clothing is used to protect the medical provider from external contamination. The purpose of protective clothing is simply to keep the radioactive material off of your skin or personal clothing. Paper coveralls, cloth coveralls, and surgical garb, for example, are acceptable forms of protective clothing. Concerns for heat stress should be taken into account since most people are not likely used to working in extra layers of clothing. Medical personnel should be monitored for contamination and, if necessary, decontaminated following treatment and decontamination of contaminated patients.

Standard issue particulate protective masks (respirators) afford excellent protection from inhalation and ingestion of most radioactive material. Since these respiratory protection devices are typically designed to filter particulates, radon and tritium gas will pass through the filters. However, short exposures to these nuclides are not usually medically significant. Keep in mind that surgical masks are not intended for respiratory protection – they are used to protect the patient.

Section 2 – Initial Medical Response

Initial Medical Response

Medical triage should be conducted based on traditional surgical and medical considerations (see REAC/TS patient treatment algorithm in Appendix A). Once the individual is medically stable, radiological dose magnitude estimation and treatment planning to address the ramifications of the anticipated dose can begin. In order to prepare an effective treatment plan, an early estimation of the dose magnitude is needed. As previously discussed the use of the appropriate gamma constant is an easy way to estimate the dose at a distance. All one needs to know is the source activity (A), the isotope and corresponding gamma constant (Γ), the distance the victim was from the source (m or cm), and the time in the area (t). The following formula can be used to determine the dose. Be sure to keep the units straight between US units and SI units.

$$\frac{(A)(\Gamma)(t)}{(m)^2}$$

To estimate contact dose rates, Table 6 of Appendix B in NCRP Report No. 40 can be used. Below is an excerpt from the table.

Table 2A – Dose Information

Nuclide	Gamma Constant	Surface R/min per Ci*	1 cm Tissue Depth R/min per Ci
Cs-137	0.326 R/Ci-hr at 1 m	770	28
Co-60	1.30 R/Ci-hr at 1 m	3100	114
Ir-192	0.480 R/Ci-hr at 1 m	1200	43

** includes ~50% increase to account for electron production in a thin stainless steel capsule wall. Multiply by 0.667 to remove this factor.*

Table 2B – Dose Information

Nuclide	Gamma Constant	Surface Gy/min per TBq*	1 cm Tissue Depth Gy/min per 37 GBq*
Cs-137	0.89 mSv/MBq-hr at 1 cm	140	0.28
Co-60	3.51 mSv/MBq-hr at 1 cm	560	1.14
Ir-192	1.30 mSv/MBq-hr at 1 cm	220	0.43

** includes ~50% increase to account for electron production in a thin stainless steel capsule wall. Multiply by 0.667 to remove this factor.*

For externally irradiated patients without trauma, patients receiving a high whole body dose can be distinguished from those with a dose < 1 Gy using two criteria: the neutrophil/lymphocyte ratio (N/L) and whether emesis has occurred. A triage score, T, is assigned as follows:

$$T = N/L + E, \text{ where } E = 0 \text{ if no emesis; } E = 2 \text{ if emesis.}$$

In a normal, healthy human population, the N/L ratio from a CBC with differential has been found to be ~2.21. For time > 4 h post-event, T is significantly elevated for dose > 1 Gy. One study has shown this scoring technique to have a sensitivity of 89% and a specificity of 93% to separate those with dose < 1 Gy from those with higher dose (N=250 controls, N=36 radiation cases; median dose 3 Gy: REAC/TS Radiation Accident Registry). A cut-point of 3.7 has been chosen to maximize sensitivity and specificity. If T > 3.7, the patient should be referred for further evaluation. This technique is useful for times up to two weeks post event.

Major Medical Issues

- Victims of radiological terrorism or industrial events require prompt diagnosis and treatment of medical and surgical conditions as well as conditions related to radiation exposure and/or radioactive contamination. Medical and nursing personnel have never received a medically significant acute radiation dose when providing patient care to radiation casualties. Although this has not been

documented, the possibility of occurrence should be considered in medical planning.

- Radiation dose can not only be estimated early post-event by health physics calculations, but from evaluation of serial blood counts and the medical history (i.e.: the timing and severity of symptom complexes, the time to emesis, etc.). A medically significant dose may be subsequently confirmed/discounted with chromosome-aberration bioassay, the current gold standard in radiation biodosimetry.
- Obtain an initial baseline CBC with differential, if possible, and repeat q 6 h. Lymphocyte depletion follows dose-dependent, first-order kinetics after high-level gamma and criticality incidents, while the neutrophil/lymphocyte ratio (N/L) increases over the first few days post-exposure. Both are sensitive indicators of radiation dose.
- For time to emesis (TE) < 2 hours, the effective whole-body dose is likely to be at least 3 Gy. If TE < 1 hour, the whole body dose most probably exceeds 4-6 Gy. Conversely, if the patient has not vomited within 8-10 hours post-event, the whole-body dose is likely < 1 Gy. This can be reassuring to the patient. Note that vomiting due to radiation dose tends to be persistent while psychosomatic vomiting will likely cease once the patient is reassured the radiation dose is of minimal medical concern.
- Medical management of patients with acute, moderate to severe radiation exposure (effective whole-body dose > 3 Gy) should emphasize the rapid administration of colony-stimulating factors (CSF) to enhance hematopoietic recovery. All of these compounds decrease the duration of radiation-induced neutropenia and stimulate neutrophil recovery, albeit with some variability.
- Currently, the only hematopoietic CSFs with FDA marketing approval for management of treatment-associated neutropenia are recombinant forms of granulocyte-colony stimulating factor (G-CSF, Neupogen®), granulocyte-macrophage-colony stimulating factor (GM-CSF, Leukine®), and the pegylated form of G-CSF (Neulasta®). Recommended dosages are given in Section 3 (ARS).
- Adherence to the current Infectious Disease Society of America (IDSA) guidelines for high-risk neutropenia is recommended for patients developing febrile radiation-induced neutropenia.

Required Initial Labs (Field or ED)

- CBC with differential and repeat q 6h in order to evaluate lymphocyte kinetics and to calculate the neutrophil/lymphocyte ratio.
- Serum amylase (baseline and qd after 24 h): A dose-dependent increase in amylase is expected after 24 h in the event of significant radiation exposure.

Important Labs to Obtain (If Feasible)

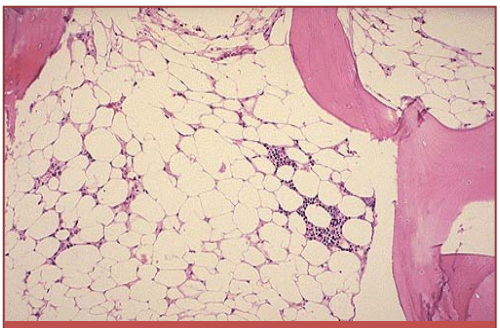
- Blood FLT-3 ligand levels – Marker for hematopoietic damage
- Blood citrulline – Decreasing citrulline indicates GI damage
- Interleukin-6 (IL-6) – Marker increased at higher radiation dose
- Quantitative G-CSF – Marker increased at higher radiation dose
- C-Reactive Protein (CRP) – Increases with dose; shows promise to discriminate between minimally and heavily exposed patients
- Cytogenetic studies with overdispersion index to evaluate for partial body exposure

Recommended Anti-Emetic Dosages

The following dosages of selective 5-HT_3 receptor antagonists are recommended for radiation-induced emesis:

- **Ondansetron**; Zofran®, Zofran ODT® – Initial: 0.15 mg/kg IV; A continuous IV dose option consists of 8 mg followed by 1 mg/hr for the next 24 hours. Oral dose: 8 mg q 8 h as needed.
- **Granisetron**; Kytril® – oral dosage form (tablets): Dose is usually 1 milligram (mg) initially and repeated in twelve hours after the first dose. Alternatively, 2 mg may be taken as one dose. IV dose is based on body weight; it is typically 10 micrograms (mcg) per kilogram (kg) (4.5 mcg per pound) of body weight.

Section 3 – Acute Radiation Syndrome


Stem cells damaged by radiation

Acute Radiation Syndrome results from external exposure to radiation doses greater than one Gy delivered to the whole body, or a major portion of it, over a short time period (high dose rate). The whole body, in this instance, can be considered to be from the knees up and elbows in. Dose reconstruction, time to emesis, lymphocyte and neutrophil kinetics, clinical history noting the timing and sequence of signs/symptoms, and several biochemical markers can be used for early dose estimation. Medical and surgical urgencies require preferential attention before radiation and/or decontamination concerns rise to a level of priority.

Etiology

Radiation damage to cells occurs within microseconds of exposure. Cellular damage is generally most severe in rapidly reproducing cell types, such as intestinal crypt cells

and stem cells, or cells with a large nucleus such as lymphocytes. As one can see, damage to cell lines such as these can result in a myriad of clinical signs and symptoms. Stem cells damaged by radiation (dose > 2 Gy) are shown to be pyknotic in the image above.

ARS and Dose

The Acute Radiation Syndrome (ARS) is an acute illness that varies in onset from a few hours to weeks. The illness typically follows a pattern of prodromal signs/symptoms, a latent period, and a period of manifest illness, followed by recovery or death. Each phase varies in length relative to the radiation dose received. Organ/tissue involvement is related to various radiation dose thresholds as described in Table 3.

Prodromal signs and symptoms of high-level radiation exposure include anorexia, nausea and vomiting, diarrhea, and mild fever. Conjunctivitis, if the radiation dose is near the eyes, and possible skin erythema may also be encountered due to the skin entrance dose that oftentimes accompanies large acute whole body exposures.

The ARS includes a subclinical phase (< 1 Gy) and three sub-syndromes resulting from whole-body irradiation or irradiation to a significant fraction of the body. The clinical syndromes that result from radiation exposure occur within a predictable range of doses after whole-body or significant partial-body exposure. These thresholds can be used to approximate the radiation dose based on the patient's signs/symptoms. Below are general thresholds associated with various radiation dose thresholds.

- Hematopoietic syndrome (> 1 Gy),
- GI syndrome (> 6-8 Gy), and
- Cardiovascular/CNS syndrome (> 20 Gy).

Lymphopenia, neutropenia, and perhaps pancytopenia due to bone marrow aplasia may result in sepsis, hemorrhage, and impaired wound healing.

Hematopoietic Syndrome

Because of their rapid cell turnover, the progenitor cells in the bone marrow are among the most radiation-sensitive cells in people. The mature lymphocytes are also very sensitive to the effects of ionizing radiation due to their large nuclei. The threshold for hematopoietic syndrome is considered to be > 1 Gy, but it is not until greater than 2 Gy that clinically significant hematologic-related illness likely develops. The clinical manifestations will typically occur over the next few weeks following the

event. This is because the mitotically active hematopoietic progenitors are unable to divide after a whole-body exposure > 2-3 Gy. At doses beyond the 2-3 Gy range, involvement of various organs can significantly complicate patient management. Lymphopenia, followed by diminution of other blood elements, allows bleeding and infection, thus leading to increased morbidity and mortality.

Table 3 - Radiation Effects				
Dose (Gy)	20 and above	**> Bone Marrow Suppression**	**Neurovascular Syndrome onset**	Multiple organ failure Probable death
	11			
	10			Consider stem cell transplants
	9			
	8			
	7			$LD_{50/60}$ with supportive care
	6		**GI Syndrome onset**	
	5			$LD_{50/60}$ without treatment
	4			
	3			
	2			~100% survival without treatment
	1		**Hematopoietic Syndrome onset**	
	0			

The need for hematologic support may be prolonged and include blood products, hematopoietic growth factors, and antibiotics. Keep in mind that combined injuries – acute radiation illness in the presence of physical trauma such as burns and/or wounds – exhibit a synergistic relationship between the radiation dose and the trauma. Concomitant physical injuries complicate treatment of ARS and can lead to prolonged recovery time and increased mortality. Conversely, ARS patients with burns and/or wounds often suffer from poor wound healing, bleeding, and infection because of hematopoietic suppression.

Modern supportive care is capable of changing survival of $LD_{50/60}$ doses (50% of the population surviving at 60 days) from 3.5-4 Gy (without medical care) up to 5-6 Gy with supportive care such the use of transfusions and antibiotics. Supportive care is intended to maintain the patient until surviving islands of stem cells can be stimulated to resume blood cell (neutrophil and platelet) production. The addition of colony stimulating factors (CSFs) and ICU care may raise the $LD_{50/60}$ to 6-8 Gy. The highest survival rates will come from those with 6 Gy doses, or less, without physical trauma.

Gastrointestinal Syndrome

Although relatively mild, GI symptoms may be experienced around 6 Gy. In the dose range beginning around 8 Gy the GI syndrome becomes more symptomatic with onset of severe nausea, vomiting, and diarrhea. The time to onset of signs/symptoms is dose related, with a more rapid onset indicating a higher dose.

Additional clinical issues with the gastro-intestinal syndrome can include significant fluid and electrolyte shifts, malabsorption of nutrients, GI bleeding, and sepsis from loss of integrity of the crypt cells of the intestinal villi. Once there is depletion of the epithelial cells lining the lumen of the gastrointestinal tract, bacteria can gain free access to the body, often serving as the impetus for gram-negative sepsis. In addition, there can be significant hemorrhage through the denuded areas. Although death from radiation illnesses in the 8 Gy range have historically occurred within several weeks of the incident, the survival period can be extended considerably with state-of-the-art intensive care.

Although not associated with the GI syndrome, it is worth noting that penetrating radiation doses to the torso in the 6-8 Gy range – and higher – will likely have adverse affects on the pulmonary system.

Cardiovascular/CNS Syndrome

The cardiovascular/CNS syndrome occurs at doses exceeding 20 Gy. Nausea and vomiting within minutes and early transient incapacitation has occurred from doses in this range. Following the early incapacitation there may be a short period of return of some functionality from a few hours up to a few days, followed by a deterioration of the patient's status, the signs/symptoms of which include hyperpyrexia, prostration, and decreased blood pressure. This will likely be followed by decreasing consciousness, vascular instability, and death. Convulsions may or may not occur. Cerebral edema and multiple organ pathology are often seen during necropsy.

Medical Management of ARS

The management of ARS is focused mainly on support and recovery of the hematologic system. Early onset of anorexia, nausea, vomiting, and malaise are indications of higher doses. Two major aims of medical management are efforts to prevent neutropenia and sepsis as heralded by fever. As neutropenia worsens, the risk of infection increases – especially as the absolute neutrophil count drops below $100/mm^3$.

Radiation-induced emesis may be confused with psychogenic vomiting, especially if others are vomiting. Radiation-induced vomiting tends to be more persistent and is best treated by granisetron or ondansetron. Early oral feeding is preferable to IV

feeding in order to maintain the physiologic integrity of the gut.. Careful history and group observation may help in differentiation. An early collection of blood samples for CBC with differential repeated every 6 - 12 hours will allow calculation of the absolute lymphocyte count (ALC) and absolute neutrophil count (ANC), a rapid and deep the decrease in the ALC indicating a high dose. The ALC and neutrophil/lymphocyte ratio, along with time to emesis, can be used to estimate the severity of the radiation dose and resulting triage score (see Section 2 and the sample problem below).

Radiation induced emesis is best treated by granisetron or ondansetron. Early oral feeding is preferable to IV in order t maintain the physiologic integrity of the gut.

Neutropenic infections are common, but great variability occurs in gram negative and gram positive infectious organisms over time with any one patient and among institutions. Keeping in mind the ARS patient's weakened immune system, antiviral and antifungal medications should also be considered. Selection of treatment regimens for infections should follow current recommendations of the Infectious Disease Society of America (IDSA).

Filgrastim (Neupogen®) is a granulocyte colony-stimulating factor (G-CSF) as is its longer-lasting pegylated form (Neulasta®). Sargramostim (Leukine®) is a granulocyte-macrophage colony-stimulating factor (GM-CSF). These are hematopoiesis stimulators that shorten the time to recovery of neutrophils and macrophages. Maximum effectiveness is accomplished with these medications via administration early after exposure, preferably within 24 to 72 hours. Daily injections should continue until the absolute neutrophil count reaches 1000/mm^3.

Cytokines: Recommended Dosages

The following cytokines are available for patients expected to experience severe neutropenia:

- Filgrastim (G–CSF) 2.5–5 μg/kg/d QD subcutaneously or the equivalent (100–200 μg/m^2/d)
- Sargramostim (GM–CSF) 5–10 μ g/kg/d QD subcutaneously or (200–400 μ g/m^2/d)
- Pegfilgrastim (pegG-CSF) 6 mg once subcutaneously

Hospital Management Issues for ARS

- Antibiotic, antiviral, and antifungal agents
- Early cytokine therapy
- Early wound closure

- GI decontamination
- Minimization of invasive procedures
- Barrier isolation
- Reverse isolation for patients with whole body doses greater than 2-3 Gy
- Strict environmental control, including isolation, strict hand washing, surgical scrubs and masks for staff, and possibly laminar flow
- Avoid antacids and H_2 blockers to maintain gastric acidity, sucralfate to avoid stress ulcers
- Oral feeding is preferable to IV, if possible (only cooked foods, no root crops)
- Meticulous oral and nail hygiene
- Povidone-iodine or chlorhexidine for skin and hair

Clinical Example – ARS Triage

Event

An individual was brought to your emergency department after entering the irradiation chamber of an industrial irradiator with the source in the up position. He had just entered the area when he noticed the unsafe situation and immediately exited the room. Your patient has normal vital signs and a normal primary and second survey, but has vomited repeatedly, beginning approximately 2 hours after he exited the area.

Solution:

Using the simple scoring system from Tab 1, the neutrophil to lymphocyte ratio is given for the times below:

Time Post-event	N/L
2 h	1.32
4.5 h	15.2
9h	9.78

A CBC with differential has been obtained. N is obtained from WBC x (% neutrophils) and a similar equation for lymphocytes. From the differential, N/L= (% neutrophils)/(% lymphocytes) since the WBC value cancels in the ratio. Assigning 2 points for emesis gives values of T=3.32 at two hours, 17.2 at 4.5 hours, and 11.78 at nine hours post exposure. Because the score was greater than 3.7 at 4 hours, the patient should be referred for more extensive hematological evaluation. Clinical data in this example is from a real patient evaluated at Oak Ridge Associated Universities in 1971. The patient was found to have a 3.5 Gy acute gamma dose from a 7700 Ci (285 TBq) ^{60}Co source.

Conclusion

Early ARS with whole body or significant partial-body irradiation calls for the institution of supportive measures and cytokine therapy as medically indicated. Monitor for impending neutropenia/ neutropenic fever and consult IDSA guidelines for antibiotic therapy when appropriate. For doses exceeding 1,000 rads (10 Gy), or so, early lung issues may also arise. As one can see, consultations with a hematologist, radiation oncologist, and possibly others should be considered since these specialties will likely be able to provide valuable insight into the treatment of radiation induced illness/injury.

Section 4 – Medical Management of Local Injury

Dose and Clinical Signs

Acute local irradiation events may occur separately or co-exist with ARS. It is a common radiation injury in the civilian sector where many radiation devices are in industrial use. Deterministic thresholds exist as follows for certain clinical signs:

- **3 Gy: Epilation**, typically beginning 14-21 days post-incident.
- **6 Gy: Erythema** is often transient soon post-incident, with secondary erythema 14-21 days thereafter. The pathophysiology for erythema includes arteriolar constriction with capillary dilation and local edema. Erythema may occur in a few hours post-accident (primary erythema) or come and go in waves.
- **10-15 Gy: Dry Desquamation** of the skin secondary to radiation to the germinal layer is usually seen approximately 20 days post-incident. Dry desquamation results from response of the germinal epidermal layer to radiation. There is diminished mitiotic activity in cells of the basal and parabasal layers with thinning of the epidermis and desquamation of large macroscopic flakes of skin.
- **20-50 Gy** for wet desquamation (partial thickness injury) at least 2-3 weeks post-exposure, depending upon dose. In moist desquamation, microscopically, one usually finds intracellular edema, coalescence of vesicles to form macroscopic bullae, and a wet dermal surface, coated by fibrin. Potential radionecrosis as the dose increases.
- **For skin dose >> 50 Gy**, overt radionecrosis and ulceration secondary to endothelial cell damage and fibrinoid necrosis of the arterioles and venules in the

affected area. A cutaneous syndrome, arising from high-level whole-body along with local injury, has also been described by various authors.


Extensive lesion from Ir-192 source

Clinically, within the first week post-accident (depending on dose), the patient is asymptomatic, with possibly an early wave of transient erythema. Around week 2, true erythema develops along with progressive epilation, suppression of sweating, and diminished sebaceous gland secretion. In week 3, the patient often presents with warm skin that is edematous, painful to touch, with occasional severe pruritis, and symptoms that are generally limited to the radiation field. By week 4, overt dry or wet desquamation has evolved in a dose-dependent manner in skin exposed to the radiation field.

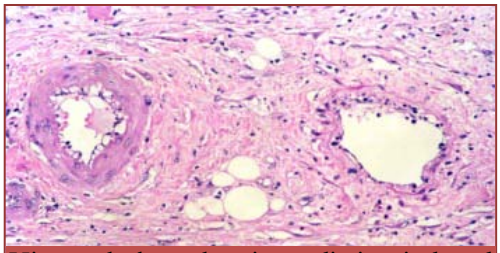
Treatment

The US experience in partial-body exposure has usually been high-level, low linear energy transfer-exposure to relatively small areas of skin, either from sealed sources or from X-ray or accelerator accidents. For a clinically significant lesion to occur generally requires that more than 10 cm^2 of the basal layer of skin have been irradiated. The US CDC has recently published physician guidelines for grading cutaneous radiation injury:

- Grade I: > 2 Gy
- Grade II: > 15 Gy
- Grade III: > 40 Gy

The medical history is particularly important in diagnosis of the extent of partial-body injury since signs and symptoms generally take days to weeks to manifest. In addition, serial color digital photographs are crucial, possibly along with drawings of the lesion. These allow more precise documentation of the evolution of cutaneous necrosis.

In the US, diagnosis of high-level skin dose has generally been estimated by observing the serial evolution of symptoms. However, additional diagnostic tools such as cytogenetic dosimetry, PET scans, MRI, ultrasound visualization of the lesion, and Doppler or laser flow profiles have been used. The key management issues with cutaneous radiation injury are infection control, state-of-the-art wound care, and appropriate pain management. It is often also very helpful to obtain the services of a plastic or reconstructive surgeon early in the clinical course.



Histopathology showing radiation-induced fibrosis of arteriole, Yanango, Peru case

Radiation-induced skin and organ fibrosis and late skin radionecrosis are delayed complications that are usually considered irreversible. Typical medical management includes eliminating local and general aggravating factors and controlling acute and chronic inflammation with steroids.

On the basis of etiology, local radiation injury can be managed by:

(1) Anti-inflammatory treatment with topical corticosteroids,
(2) Vascular therapy with hyperbaric oxygen (HBO) and pentoxifylline (Trental®, PTX) or PTX-vitamin E combination
(3) Wound management and surgical guidance by physicians experienced in the management of chronic vascular injury.

Clinical Example – Multi-Parameter Analysis of Partial- Body Radiation Injury

Event

A ^{137}Cs source (100 Ci, 3.7 TBq) is placed in a restaurant. Unaware of this fact, an individual visits the restaurant, sees a metallic object, and puts it in his pocket. Two days later, he reports to the nearest hospital complaining of redness to his right buttock and mild tingling in the area. As the emergency physician, you see an apparently healthy 26-year-old male with normal initial vital signs. Moderate vomiting begins 2 h later. On history, the patient reports the object. Appropriate officials are notified to investigate the possibility of it being a radiation source.

Blood is drawn for a CBC with differential and q 6h, and the patient is admitted for observation. An initial consult is obtained from a plastic and reconstructive surgeon as well as from a hematologist. It now appears to attending physicians that a major radiation event may have occurred. A medical consult is requested from REAC/TS. Using dosimetric information found in Table 2 and time/motion related questioning of the patient, a rough estimate of the dose magnitude can be derived. Potential whole body radiation doses should also estimated using the specific gamma constant for ^{137}Cs found in Section 2. Repeat CBCs show decreasing lymphocytes and a slightly rising neutrophil count. Consultant physicians order a multi-parameter partial body irradiation blood panel and chromosome biodosimetry as indicated. The patient experiences nausea multiple times, and Granisetron, 1 mg is administered IV q 12 h prn.

A multi-parameter blood panel drawn the next day shows the following results: ↓ Lymphocytes; ↑Amylase x4 (450 IU/L); ↑Neutrophil/lymphocyte ratio; FLT3 – 100 pg/mL (↑x10); ↑CRP 100 μg/mL (↑x100); normal citrulline; ↑x10 IL6; and ↑x30

gCSF; cytogenetic results: estimated 3.5 Gy whole body dose; Poisson dispersion index: 1.35.

The Poisson dispersion index is defined as the variance of the statistical distribution divided by the mean which should equal unity in a perfect Poisson process. This significant deviation is strongly suggestive of non-uniform partial body injury. In the US, analysis of over-dispersion of dicentric chromosomes from the expected Poisson distribution most commonly employs the Qdr technique of Sasaki.

Section 5 – Medical Management of Internally Deposited Radionuclides

Internal Contamination – Early Rapid Assessments

Internal contamination occurs when unprotected personnel ingest, inhale, or are have wounds contaminated with radioactive material. Externally contaminated casualties who did not have respiratory protection should be evaluated for internal contamination. Internal contamination is more likely if significant contamination is found on the face, in/around the nostrils or mouth, or in/around open wounds.

Internal doses are assessed differently than external doses. The two primary differences are 1) Internal doses are calculated, not measured, and 2) The doses are committed doses. Internal doses are based on the intake – or the amount of radioactive material that initially enters the body. When a bioassay is performed one can ascertain the activity in the urine, for example, at that particular time. Calculations are then performed to determine how much activity initially entered the body to result in the concentration of radioactive material in the urine at the present time. The same for whole body counts, lung counts, or other methods for internal dose assessment.

The concept of committed dose accounts for the fact that internal doses are protracted. In other words, once the radioactive material deposits into the target organ it is there until it decays or the body removes it through normal biokinetic processes. Obviously, these two processes are both at work independently of each other. The committed dose is the dose received over a fifty year time period due to an internally deposited radionuclide. For regulatory purposes, once the fifty-years-worth of dose is calculated it is assigned for the year the intake occurred.

A quick way to estimate the potential dose due to inhalation is through the evaluation of nasal swabs. Samples should be collected by swabbing the anterior nares (separately, with separate swabs) with a cotton swab. They should be taken as soon after the suspected intake as possible, preferably within the first hour, or so. Delays in

obtaining nasal swabs will affect intake estimation since the nose clears fairly quickly. Each swab should be counted with a hand-held detector and the results summed.

It is important to count each swab individually since most people breathe fairly evenly across the nose. Therefore, a significant difference in the count rates may indicate cross contamination (a contaminated finger?). Once the summed count rate is converted to an activity (for β/γ emitters this is usually done by assuming a 10% counting efficiency – until otherwise verified – which means the count rate is divided by 10%, or 0.10) it is assumed to represent 10% of the initial intake. Since regulatory limits – called Annual Limits on Intake (ALIs) and found in EPA Federal Guidance Report No. 11 – are based on the intake, we have a benchmark to which to compare our estimated intake (Sugarman, et. al., *Health Physics* - June, 2010). Early magnitude estimation for medical decision making as described here is based on US ALIs. International recommendations for intake limitation can be used for benchmarking, if desired.

Example: Facial contamination is detected on an individual. Nasal swabs are quickly taken, the sum of which is 150,000 dpm. Therefore, the initial intake is estimated to be 150,000/0.10, or 1,500,000 disintegrations per minute (dpm) – or about 0.7 μCi (~ 26 kBq). Let's assume the contaminant is ^{137}Cs. The inhalation ALI for ^{137}Cs is 200 μCi (7.4 MBq). Our estimate is significantly below the US annual regulatory limit so this intake is not expected to be medically significant. Again, the ALI as used here is a US regulatory limit, not a medically derived limit. It does, however, make for a good comparison point.

In the event the radioisotope is unknown, if the emission (α, β, γ) can be determined one can make an assumption regarding the isotope of interest. For example, if an unknown alpha emitter is encountered, until the isotope can be identified assuming it is ^{241}Am is usually a safe bet for dose magnitude estimation purposes (see Table 4). It may not always be correct, but it ought to get the magnitude estimation in the right neighborhood. ALIs for common isotopes can be found below. Obviously, intake estimates should be verified by appropriate bioassay techniques.

Table 4 - US Inhalation ALIs for Assumed Radionuclides

Emission	Assumed Radionuclide	US ALI and solubility class	~ dpm
alpha	Am-241	0.006 μCi/0.2 kBq - W	1.3×10^4
beta	Sr-90	4 μCi/0.148 MBq- Y	8.9×10^6
gamma	Cs-137	200 μCi/7.4MBq - D	4.4×10^8

** Most restrictive ALI values from FGR-11 are listed.*

Table 5 - U.S. Inhalation ALIs for Specific Radionuclides

Nuclide	US ALI and Solubility Class	~ dpm
H-3	80,000 μCi/3 GBq (H_20 Vapor)	1.8×10^{11}
Co-60	30 μCi/1.1 MBq - Y	6.7×10^{7}
U-235, 238	0.04 μCi/1.48 kBq - Y	8.9×10^{4}
Pu-239	0.006 μCi/0.2 kBq - W	1.3×10^{4}
Cf-252	0.02 μCi/0.74 kBq - W	4.4×10^{4}

** Most restrictive ALI values from FGR-11 are listed.*

Open wounds present another route for radioactive contamination to enter the body. NCRP Report No. 156, Development of a Biokinetic Model for Radionuclide-Contaminated Wounds and Procedures for their Assessment, Dosimetry, and Treatment (2006) was consulted to calculate dose conversion factors for various radioisotopes and contaminant/wound types using the Activity and Internal Dose Estimates (AIDE, Bertelli) internal dosimetry software. Dividing the applicable regulatory dose limit by the corresponding dose conversion factor (DCF) results in what can be termed a derived reference level (DRL) – similar to an ALI, which is not defined for wounds (Toohey, et al., *Health Physics* - in press).

The DRL can be used as a reference point in much the same way as the ALI is used above. To apply this concept simply obtain an early wound count, convert the count rate to an activity (dpm), and compare it to the appropriate DRL below. Remember that just because the contamination levels are higher than the DRL does not necessarily mean there is a significant medical issue, but simply that the contamination levels may result in an internal dose close to the regulatory limit.

Please note that Table 6 is based upon US dose limits, but the dose conversion factors were based on effective dose (international guidance). This should not affect the use of this table for dose magnitude estimation. Remember that the point is to determine a point with which comparisons can be made. These comparisons can then be used to help guide medical decisions. International guidance will use different dose limits resulting in different DRLs (20 mSv – or 2 rem – divided by the appropriate DCF). Refer to NCRP No. 156 or contact REAC/TS for further guidance.

Table 6 - Selected DRLs for Defined Solubility Class (dpm)

Isotope	Based on*	Weak	Moderate	Strong	Avid
Co-60	ED	1.54E+08	1.54E+08	1.65E+08	2.01E+08
Sr-90	BS	2.20E+07	2.20E+07	2.25E+07	2.38E+07
Tc-99m	ED	2.00E+11	2.56E+11	9.33E+11	8.78E+11
I-131	Thy	7.06E+07	8.01E+07	1.26E+08	3.46E+08
Cs-137	ED	2.20E+08	2.20E+08	2.23E+08	2.34E+08
Ir-192	ED	4.49E+08	4.66E+08	6.21E+08	1.69E+09
U-235	BS	8.23E+05	8.23E+05	8.29E+05	8.46E+05
U-238	BS	8.55E+05	8.55E+05	8.63E+05	8.78E+05
Pu-239	BS	1.81E+03	1.81E+03	1.85E+03	1.92E+03
Am-241	BS	1.65E+03	1.65E+03	1.68E+03	1.74E+03
Cf-252	BS	5.14E+03	5.15E+03	5.75E+03	7.96E+03

** ED = Effective Dose, BS = Bone Surface, Thy = Thyroid*
ED reference point = 5 rem (committed)
Organ dose reference point = 50 rem (committed)

Approaches to Medical Management

Medical management is specific and isotope-dependent; consequently identifying the isotope is crucial. Both radioactive decay and biological elimination rid the body of radioactive materials. Combining both elimination rates provides the effective half-life, which is always shorter that either the radiological or biological half-life. Metabolism and elimination kinetics of the non-radioactive analog determine the metabolic pathway of the radionuclide. The major routes of intake are inhalation, ingestion, absorption through an open wound contamination, and transdermal absorption. Dissolution of uranium from embedded DU shrapnel has also been noted.

The medical management of internal contamination falls into several major categories:

- Reduction and/or inhibition of absorption of the isotope in the GI tract. Examples: gastric lavage, cathartics.
- Blocking uptake to the organ of interest. Example: Within 4 hours of exposure, administer potassium iodide (KI) to block uptake of radioactive iodine by the thyroid.
- Isotopic dilution. Example: Increase fluid hydration for internal tritium contamination.
- Altering the chemistry of the substance. Example: Prevent binding of uranyl ions with the renal tubules by use of sodium bicarbonate.
- Displacing the isotope from receptors. Example: Administer stable iodine to displace ^{99m}Tc

- Traditional chelation techniques. Example: Administer DTPA for internal deposition of plutonium.
- Early excision of radionuclides from wounds to minimize absorption.
- Bronchoalveolar lavage for severe cases of insoluble inhaled particles. This would be a technique rarely used and expected only in a case with a very large lung burden of an insoluble alpha emitter such as plutonium.

There are over 8,000 isotopes, but only 10-15 are considered to be important in the military and in the civilian sector, and with regard to terrorism and to industrial accidents. Certain isotopes fall into general categories of interest as noted below:

"University Five" – ^{14}C, ^{32}P, ^{125}I, ^{131}I, ^{252}Cf: Used for isotopic labeling in biochemistry laboratories, and in medicine. Tritium is also common.
"Industrial Three" – ^{192}Ir, ^{137}Cs, ^{60}Co: ^{192}Ir is widely used in industrial radiography to photograph large objects such as oil pipes, airplane wings, etc. ^{137}Cs and ^{60}Co are used in industry because of their penetrating gamma rays and are considered to be prime agents for terrorism events.
"Military Five" – Tritium (^{3}H), ^{235}U, ^{238}U, ^{239}Pu, and ^{241}Am: Isotopes primarily used in the weapons complex, both in the DOE system and in the military.
Fission/Activation Products – encountered in response to a nuclear detonation – either an IND or a weapon – a reactor accident, or a waste transportation incident. Some are volatile and, depending on the activity, can pose a significant risk to the populace.

NCRP 65 (1980) is widely considered an important reference document for physicians who need to employ decorporation therapy in patients with internal deposition of radioactive materials. A new NCRP revision of this document (NCRP Report 161; 2010) provides significant additional new information and health physics guidelines for the management of internal contamination. It introduces a new dose/risk based term, Clinical Decision Guide (CDG), that can be used to help physicians decide when to treat, or not to treat. The data in Tables 7 and 8 are adapted from NCRP Report 161.

Therapy for Specific Radionuclides

This section provides (1) recommendations for decorporation therapy for specific radionuclides, and (2) drug information for treatment. Table 7 summarizes treatment recommendations for various radionuclides of concern in the medical management of internal contamination. Table 8 provides dose schedules for drug or treatment modalities. As stated in *Generic Procedures for Medical Response During a Nuclear or Radiological Emergency* (IAEA, 2005), when deciding on the treatment for internal contamination comparison is to be made between the benefit of removing the

radioactive contaminants using modalities associated with significant side effects and the short- and long-term health effects of the internalized radioactive materials without treatment.

Table 7 - Decorporation Therapy Recommendations in the USA for Radionuclides of Concern (NCRP Report 161, 2010).		
Radionuclides	**Treatment**	**Preferred Rx**
Actinium (Ac)	Consider DTPA	Consider DTPA
Americium (Am)	DTPA	DTPA
Antimony (Sb)	BAL, penicillamine	BAL
Arsenic (As)	BAL, DMSA	BAL
Barium (Ba)	Ba, Ca Therapy	See NCRP 161
Berkelium (Bk)	DTPA	DTPA
Bismuth (Bi)	BAL, Penicillamine, DMSA	DMSA
Cadmium (Cd)	DMSA, DTPA, EDTA	DMSA
Californium (Cf)	DTPA	DTPA
Calcium (Ca)	Ba, Ca Therapy	See NCRP 161
Carbon	No treatment available	N/A
Cerium (Ce)	DTPA	DTPA
Cesium (Cs)	Prussian blue	Prussian blue
Chromium (Cr)	DTPA, EDTA (antacids are contraindicated)	DTPA
Cobalt (Co)	DMSA, DTPA, EDTA, NAC	DTPA
Copper (Cu)	EDTA, penicillamine, trientine	Penicillamine
Curium (Cm)	DTPA	DTPA
Einsteinium (Es)	DTPA	DTPA
Europium (Eu)	DTPA	DTPA
Fission Products (Mixed)	Management depends on predominant isotopes present at time. Early: iodine; Late: strontium, cesium, and others	
Fluorine (F)	Aluminum hydroxide	Aluminum hydroxide
Gallium (Ga)	Consider penicillamine	Penicillamine
Gold (Au)	BAL, penicillamine	BAL
Indium (In)	DTPA	DTPA
Iodine (I)	Potassium iodide (KI), propylthiouracil, methamizole	KI
Iridium (Ir)	Consider DTPA, EDTA	Consider DTPA

Table 7 - Decorporation Therapy Recommendations in the USA for Radionuclides of Concern (NCRP Report 161, 2010).		
Radionuclides	**Treatment**	**Preferred Rx**
Iron (Fe)	Deferoxamine (DFOA), deferasirox, DTPA, DFOA and DTPA together	DFOA
Lanthanum (La)	DTPA	DTPA
Lead (Pb)	DMSA, EDTA, EDTA with BAL	DMSA
Manganese (Mn)	DFOA, DTPA, EDTA	DTPA
Magnesium (Mg)	Consider strontium therapy	Consider strontium therapy
Mercury (Hg)	BAL; EDTA; penicillamine; DMSA	BAL
Molybdenum (Mo)	Limited clinical experience	
Neptunium (Np)	Consider DFOA and/or DTPA	Consider DFOA and/or DTPA
Nickel (Ni)	BAL, EDTA	BAL
Niobium (Nb)	DTPA	DTPA
Palladium (Pd)	Penicillamine, DTPA	Penicillamine
Phosphorus (P)	Phosphorus Therapy	Phosphorus therapy
Plutonium (Pu)	DTPA, DFOA, EDTA, DTPA and DFOA together	DTPA
Polonium (Po)	BAL, DMSA, penicillamine	BAL
Potassium (K)	Diuretics	Diuretics
Promethium (Pm)	DTPA	DTPA
Radium (Ra)	Ra, Sr therapy	
Rubidium (Rb)	Prussian Blue	Prussian Blue
Ruthenium (Ru)	DTPA, EDTA	DTPA
Scandium (Sc)	DTPA	DTPA
Silver (Ag)	No specific therapy. Consider gastric lavage and purgatives.	
Sodium (Na)	Diuretic and isotopic dilution with 0.9 % NaCl	Diuretic and isotopic dilution with 0.9 % NaCl
Strontium (Sr)	Ra, Sr therapy	
Sulfur (S)	Consider sodium thiosulfate	Consider thiosulfate
Technetium	Potassium perchlorate	Potassium perchlorate
Thallium (Tl)	Prussian Blue	Prussian Blue

Table 7 - Decorporation Therapy Recommendations in the USA for Radionuclides of Concern (NCRP Report 161, 2010).		
Radionuclides	**Treatment**	**Preferred Rx**
Thorium (Th)	Consider DTPA	Consider DTPA
Tritium (^{3}H)	Force fluids	Water diuresis
Uranium (U)	Bicarbonate to alkalinize the urine. Consider dialysis	Bicarbonate
Yttrium	DTPA, EDTA	DTPA
Zinc (Zn)	DTPA, EDTA, Zinc sulfate as a diluting agent.	DTPA
Zirconium (Zr)	DTPA, EDTA.	DTPA

Table 8 - Dose Schedules for Drug or Treatment Modalities.	
Drug or Treatment Modality	**Dosage**
Acetylcysteine (NAC)	FDA does not specify age, IV 300 mg/kg in 5% dextrose in water over 24 hours for acetaminophen overdosage.
Deferoxamine (DFOA)	FDA does not specify age: Deferoxamine mesylate injectable (DFOA); IM is preferred. 1 g IM or IV (2 ampules) slowly (15 mg kg^{-1} h^{-1}); Repeat as indicated as 500 mg IM or IV q4h × 2 doses; then 500 mg IM or IV every 12 hours for 3 days.
Dimercaprol (BAL)	FDA does not specify age: IM: 300 mg per vial for deep IM use, 2.5 mg^{-1} kg (or less) every 4 hours for 2 days, then twice daily for 1 day then daily For days 5 – 10

Table 8 - Dose Schedules for Drug or Treatment Modalities.	
Drug or Treatment Modality	**Dosage**
Diethylenetriaminepentaacetate (DTPA, calcium or zinc)	Adults: IV: 1 g in 5 mL IV push over 3-4 minutes or IV infusion over 30 minutes diluted in 250 mL of 5 % dextrose in water, Ringers Lactate or Normal Saline (NS) Nebulized inhalation: 1g in 1:1 dilution with sterile water or NS Children under 12 years: 14 mg kg^{-1} IV as above, not to exceed 1.0 g IM: 1 g can be given with procaine to reduce pain (not FDA approved)
Edetate calcium disodium (EDTA)	FDA does not specify age: Ca-EDTA (edetate calcium disodium); 1,000 mg m^{-2} d^{-1} added to 500 mL D_5NS infused over 8 – 12 hours.
Penicillamine	FDA does not specify age: Oral: 250 mg daily between meals and at bedtime. May increase to 4 or 5 g daily in divided doses.
Phosphorus Therapy Potassium phosphate, dibasic	Oral: 250 mg phosphorus per tablet. Adults: 1 – 2 tabs oral four times daily with full glass of water each time, with meals and at bedtime. Children over 4 years: 1 tab oral four times daily.
Potassium iodide (KI)	Oral: tablets or liquid. Drug dose varies between 16 mg and 130 mg daily depending on age, thyroid exposure level, and whether or not pregnant or lactating.
Propylthiouracil (PTU)	Oral: 50 mg tabs, 2 tabs three times daily for eight days. FDA does not specify age.
Prussian Blue	Oral: Adults and Adolescents 3 g three times daily. Children 2 – 12 years: 1 g three times daily.
Sodium bicarbonate (for uranium only)	Oral or IV.

Table 8 - Dose Schedules for Drug or Treatment Modalities.	
Drug or Treatment Modality	**Dosage**
Radium and Strontium Therapy	Aluminum hydroxide: PO: 60 – 100 mL once. 10% Calcium Chloride Suspension. Adults: IV: 200 mg to 1 g every 1 – 3 d, slow IV, not to exceed 1 mL min–1 Calcium gluconate. PO: 10 g powder in a 30 cc vial, add water and drink
Succimer (DMSA) (Chemet®)	FDA approved pediatric dosing: Start dosage at 10 mg kg^{-1} or 350 mg m^{-2} oral every 8 hours for 5 days. Reduce frequency of administration to 10 mg kg^{-1} or 350 mg m^{-2} every 12 hours (two-thirds of initial daily dosage) for an additional 2 weeks of therapy. A course of treatment lasts 19 days.
Water diuresis	Oral: Fluids more than 3 – 4 L d^{-1}

KI Blockage of the Thyroid

Children are particularly susceptible to the potential for thyroid cancer following exposure to radioactive iodine. The uptake of radioactive iodine should be blocked by administering oral potassium iodide (KI) within 4 hours of exposure. Some people may be allergic to KI. There are alternatives to KI, but they should be discussed with the individual's personal physician.

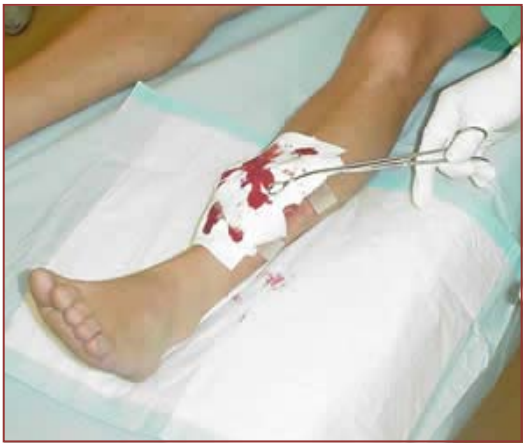
Table 9 - Potassium Iodide Recommended Doses	
Adults >40 y of age with thyroid exposure ≥ 5 Gy (500 rad)	130 mg d^{-1}
Adults 18 – 40 y of age with thyroid exposure ≥ 0.1 Gy (10 rad	130 mg d^{-1}
Pregnant or lactating women with thyroid exposure ≥ 0.05 Gy (5 rad)	130 mg d^{-1}
Children and adolescents 3 – 18 y of age with thyroid exposure ≥ 0.05 Gy (5 rad	65 mg d^{-1}
Infants 1 month – 3 y of age with thyroid exposure ≥ 0.05 Gy (5 rad)	32 mg d^{-1}
Neonates from birth – 1 month with thyroid exposure ≥ 0.05 Gy (5 rad)	16 mg d^{-1}

Section 6 – Decontamination Techniques

Safety of Health Care Personnel

Radiologically contaminated patients generally pose no danger to health care personnel. It is virtually impossible for a living patient to be so contaminated as to pose an acute threat to health care providers. The radiation exposure hazard from a radiologically contaminated casualty will very likely be negligible, so necessary medical or surgical treatment must not be delayed because of possible contamination.

Initial Management



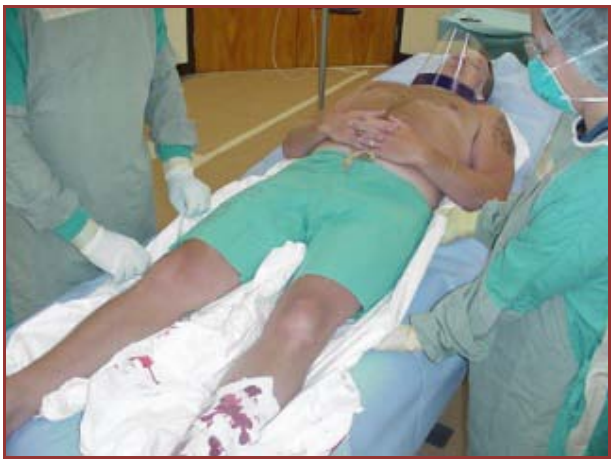
The initial management of a casualty contaminated by radioactive materials is to perform all immediate life/limbsaving actions without regard to contamination. Decontamination should never interfere with medical care and contaminated casualties should not be barred entry to a medical facility if entry is necessary for life-saving care. Casualties entering a medical unit after a radiological incident should be considered contaminated unless verified as non-contaminated. A quick head-to-toe survey should provide sufficient evidence of the presence or absence of gross contamination. This can usually be done as medical personnel are assessing the medical stability of the patient. Radiological decontamination, that is, the removal of radioactive materials from surfaces, often demands a significant contribution of resources and can take substantial time.

Decontamination Techniques

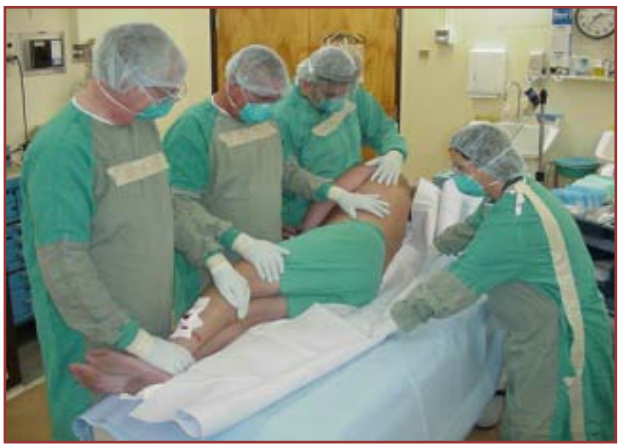
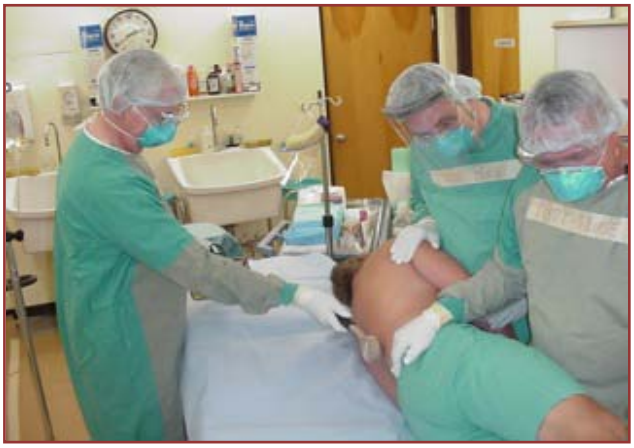
Gross radioactive contamination is typically fairly easily detected via a quick scan of the patient with appropriate instrumentation. Radiological decontamination is performed in a very similar manner to doctrinal chemical decontamination. The main difference is in timing. Chemical decontamination is often an emergency. Radiological decontamination is not. Decontamination should follow basic common sense. Unlike chemicals, radioactive materials cannot be "neutralized." They are only moved from one point to another. Radiological decontamination should be performed with that in mind. Therefore, the challenge is to remove the radioactive material from one area and transfer it to where you want it to be without spreading it to points in between.

The first priority is to ensure the patient is medically stable. Once the patient has been medically stabilized the first step is clothing removal. It stands to reason that clothing

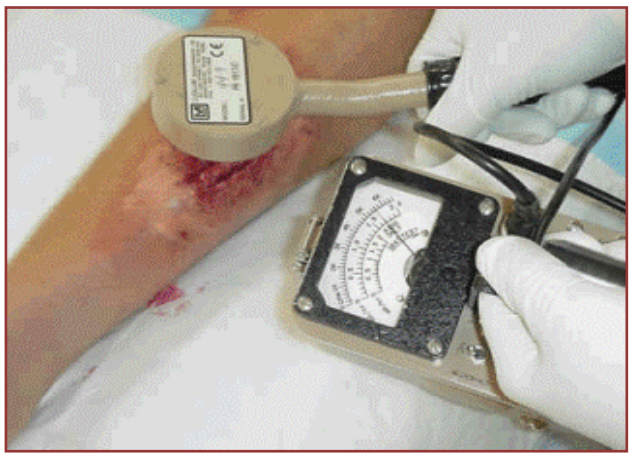
typically covers a large percentage of one's body, so properly removing the clothing will likely significantly decrease the amount of radioactive material with which the healthcare provider has to contend. This is done by cutting, not tearing, the clothing in a direction away from the patient's airway and rolling it outward away from the patient's skin, trapping the material in the clothing. If the patient is amenable, a splash shield may be applied.

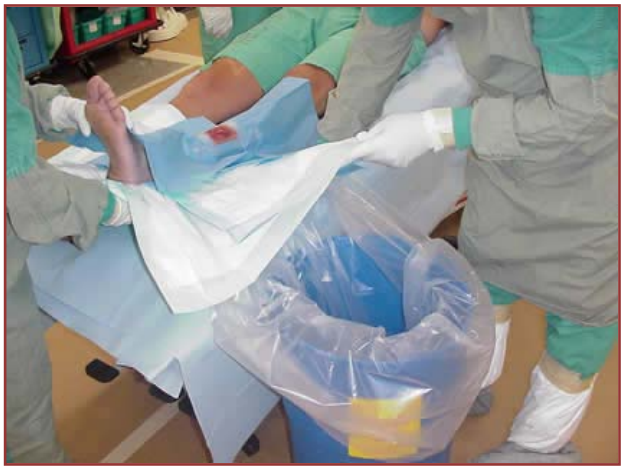
Once the clothing has been cut, a log roll procedure can be used to remove the clothing. Notice in the picture below, multiple sheets have been placed on the bed. The top sheet is folded over the clothing creating a clean surface onto which the patient can be rolled. The patient is then rolled to the other side where the sheet is folded over the clothing and then removed from the bed by rolling it toward the feet. Once the sheet is removed a quick survey can be performed of the back looking for any obvious areas of contamination. At this point the overall contamination levels should be significantly reduced. Be sure to bag the clothing/top sheet and send it out for sampling. This is an excellent representation of the types of radioactive materials that may have to be dealt with when evaluating internal contamination.

In this case the patient was found to have a contaminated wound on the lower left leg that needs attention. Decon priorities are 1) wounds, 2) body orifices around the face, and 3) intact skin. In order to address the contaminated wound one should prepare the area for decontamination. The wound dressing should be removed and saved for further evaluation. The intact skin immediately adjacent to the wound should be quickly decontaminated using a baby-wipe (wipe away from the wound). This is done to minimize any contamination that may get transferred back into the wound and to ensure that contamination in this area is not confused with the actual counts in the wound.



Finally, drapes should be applied to the area to prevent the spread of contamination to uncontaminated areas. After the draping is properly applied wound decon can begin. Gently irrigate the wound using sterile saline or something similar. The purpose of the initial irrigation is to attempt to remove the bulk of the contamination, so do not be too aggressive in order to prevent splashing and potentially spreading contamination. The runoff should be directed into a receptacle – a lined garbage can



usually works well. It may also be a good idea to attempt to collect the runoff at the wound site via the use of absorbent pads. All waste generated should be kept in a pre-arranged location for later collection and disposal.

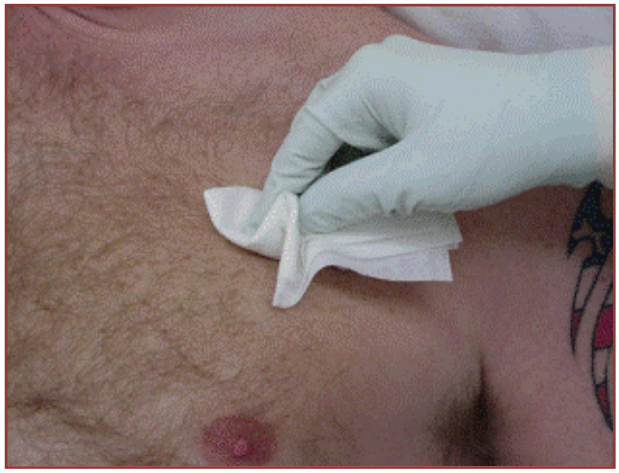
Once it is felt that decon efforts have likely significantly reduced the wound contamination levels the wound should be covered, the drapes removed, a clean pad be placed under the area, and the wound should be resurveyed.

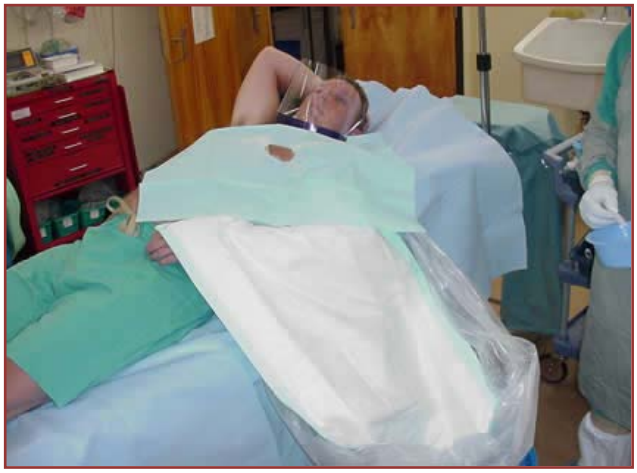

If the wound is still contaminated the process should be repeated until no further progress is made. Should the contamination levels continue to be elevated and decontamination progress is overly slow or nonexistent, the wound should be explored for foreign bodies by the treating physician. Minor debridement may be necessary. Keep in mind that wounds will still need to be scrubbed before closure for infection control purposes. This may remove the remaining contamination. In general, small amounts of contamination in a wound do not override the concerns for proper infection control and cosmetic effect.

Decontamination of body orifices in and around the face poses a challenge in that easily applied methods are limited. Many times the nares can be decontaminated simply by having the patient blow his/her nose. If the patient is able to cooperate, irrigation is an option as long as care is taken not to force more contamination into the body – placing the patient in a dependent position (preferably sitting up), putting the nozzle just past the area of contamination, and allowing the solution to flow back out through the nostrils is a possibility. Routine methods used to irrigate the eyes are acceptable, but care should be taken to ensure the run-off is directed away from the nose/mouth and to prevent it from entering the ears.

When decontaminating the skin care should be taken to avoid visible irritation. Abrading the skin may allow an entry point for radioactive materials deposited on its surface. When performing skin decontamination it's always better to start with the

simplest method available. One good option that generates very little waste is the use of baby wipes, which are – afterall – designed with decontamination in mind. If baby wipes do not work more aggressive steps may be taken, taking care to maintain the integrity of the skin. Gently scrubbing with a soft cloth and tepid water and soap is another option.





The cleaning motion should go from the outside in, much like cleaning up a paint spill. The goal is to minimize the area of contamination, not to spread it outwardly. It may be helpful to drape the area and set up a collection basin, much like is done when decontaminating a wound, if large amounts of fluids are going to be used for irrigation.

Should hair become contaminated it can be washed, taking care not to allow the wash/rinse water to run to the face. On areas such as hairy chests it's best not to shave the area since this may lead to skin abrasions. Clipping the hair is a better idea, but only if necessary. Keep in mind that the patient may be averse to having his/her hair cut. Do not shave or clip eyebrows.

Decontamination of Partial-Thickness Burns

Partial-thickness burns should be thoroughly irrigated and cleaned with mild solutions to minimize irritation of the burned skin. Blisters should be left closed; open blisters should be irrigated and treated in accordance with appropriate burn protocols. In full-thickness burns, radioactive contaminants will slough in the eschar. As there is no circulation in the burned tissue, contaminants will remain in the layers of dead tissue.

Bare skin and hair should be thoroughly washed, and if practical, the effluent should be sequestered and disposed of appropriately. Excision of wounds is appropriate when surgically reasonable. Radioactive contaminants in the wound surfaces will be removed with the tissue.

Section 7 – Biodosimetry

Biodosimetry is the use of a biological response as an indicator of radiation dose. Cytogenetic biodosimetry is considered the gold standard for determination of patient whole-body radiation dose. For inquiries regarding biodosimetry call REAC/TS at (865)576-3131.

Early-Response Multi-Parameter Biodosimetry

No single assay is sufficiently robust to address all potential radiation scenarios, including management of mass casualties and diagnosis for early medical treatment. Recommendations for use by first responders and first receivers involve a prioritized multiple-assay biodosimetric-based strategy. NCRP Commentary No. 19 (NCRP, 2005) recommends multi-parameter triage (*i.e.*, time to vomiting, lymphocyte kinetics, and other biodosimetry and biochemical indicators) as the current best early biodosimetric assessment of a victim's absorbed dose. Biodosimetry is not intended to replace, but to augment other methods of dose assessment such as early health physics dose estimation and formal dose reconstruction.

Table 10 – Multiple Parameter Biodosimetry

Dose, Gy	% emesis	Median onset of emesis (hours)	Absolute Lymphocyte count; % of normal in first 24 h	Relative increase in serum amylase day 1	Number of dicentrics per 50 metaphases
0	-	-	100	1	0.05-0.1
1	19	-	88	2	4
2	35	4.6	78	4	12
3	54	2.6	69	6	22
4	72	1.7	60	10	35
5	86	1.3	53	13	51
>6	90-100	1.0	< 47	>15	-

From Table 10, it is evident that emesis within 1-2 h is particularly serious while a drop in lymphocyte count to 1/2 or 1/3 of baseline values within 24 hours signals a potentially lethal situation. After 24 h, increases in serum amylase are also potentially confirmative. As noted below, early, rapid deployment, high-throughput cytogenetic dosimetry utilizing the internet is expected to be very valuable in triage of large numbers of people. Conversely, from the time-to-emesis data, if a patient has not vomited in 8-10 h, then any dose is very likely less than 1 Gy and he/she can be moved to outpatient facilities.

Consensus biodosimetric guidelines currently include measurement of:

- Signs and symptoms
- Radioactivity assessment
- Hematology
- Personal and area dosimetry
- Cytogenetics
- EPR-based dose assessment
- Serum amylase activity, C-Reactive Protein, FLT-3 ligand, citrulline, blood protein assays, etc.)

Cytogenetic Biodosimetry

Cytogenetic biodosimetry has been used for decades to estimate dose on the basis of radiation-induced chromosome aberrations in circulating lymphocytes. It is mainly applicable to recent whole-body acute radiation exposures. Due to the low background level of dicentric chromosomes in lymphocytes the assay's sensitivity is comparatively high, with a threshold whole-body dose of 0.1 to 0.2 Gy (based on analysis of 1,000 cells), and it shows a strong dose dependence up to 5 Gy for acute photon exposures. The reproducibility, relative specificity of dicentric aberrations to radiation, and its sensitivity to doses below acute medical significance have allowed the assay to become the gold standard in radiation biodosimetry. One drawback is that the standard method of scoring 500-1000 metaphase spreads requires about 4 to 5 days, including timely transport to the laboratory, processing and scoring the sample, and providing a dose estimate. Most scorers will therefore be able to evaluate no more than ~ 300 metaphase cells per day. However, studies at REACTS have demonstrated that "remote" scorers in differing locations can utilize the internet to share the work load, overcome the "bottleneck" inherent in scoring cells, and thereby reduce the time to generate dose estimates.

Many laboratories have automated metaphase finders in routine use which speeds up the process by quickly locating scoreable cells. In addition, triage testing has demonstrated that scoring as few as 50 cells per sample can produce dose estimates within +/- 0.5 Gy of the true dose 9 out of 10 times. This level of accuracy is generally considered sufficient to guide the initial clinical treatment decisions.

Other methods currently used in cytogenetic dosimetry include the cytokinesis-block micronucleus, the chromosome translocation, and premature chromosome condensation assays. The micronucleus test requires less skill in scoring but also has a more variable background frequency which is known to be dependent on the age and gender of lymphocyte donor. Like dicentrics, micronuclei are unstable aberrations that disappear over time. In addition, many chemicals can induce micronuclei. For this

reason it is often used as a general toxicology screening test. The micronucleus assay is therefore not considered radiation-specific.

The translocation assay is used primarily to estimate dose from historical exposures. Unlike dicentrics and micronuclei, which are eliminated from the peripheral blood over a relatively short time, translocations have been shown to persist for decades. Translocations are detectable by use of a molecular cytogenetic method referred to as chromosome "painting" or fluorescence in situ hybridization (FISH). In numerous studies the frequency of translocations has been shown to be strongly influenced by the age of the lymphocyte donor.

Premature chromosome condensation (PCC) occurs when cells at the interphase stage of the cell cycle are treated to induce the chromosomes to condense prematurely into the familiar shapes of metaphase chromosomes. After the cells are fixed and stained, the chromosomes are examined for fragments which are indicative of chromosome breaks. The PCC assay enables direct observation of radiation-induced damage earlier than is possible when cells must be stimulated to reach mitosis before preparation of the chromosomes. As shown in Table 11 the PCC assay can detect higher doses than possible with the dicentric assay but the method still requires further validation. Guidance for useful multi-parameter biodosimetric techniques is provided in Table 11.

Table 11. Guidance on Choice of Biodosimetry Methods

Dose Range (Gy)	Recommended Dosimetry Method	Clinical Symptoms
0.1 - 1	Dicentric assay	None to slight decrease in blood count
1.0 - 3.5	Lymphocyte depletion kinetics/dicentrics	Mild to severe bone marrow damage
3.5 - 7.5	Lymphocyte depletion kinetics/PCC	Pancytopenia, mild to moderate GI damage
7.5 - 10.0	Lymphocyte depletion kinetics/PCC	Bone marrow and GI damage
> 10.0	PCC	GI, neurological, and cardiovascular damage

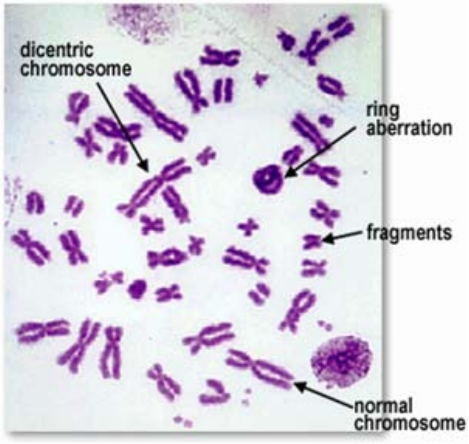
Dicentric Analysis

Dicentric chromosomes are formed when broken segments of two irradiated chromosomes are misrepaired forming a chromosome with two centromeres. The number of dicentric chromosomes correlates well with the absorbed dose. In the dicentric assay, stimulated lymphocytes are arrested, fixed, and dropped onto glass

slides during the metaphase stage of mitosis where the chromosomes are condensed and become visible under the microscope. The images can then be captured electronically and shared over the internet allowing multiple "readers" to analyze the metaphase spreads for the presence of dicentric chromosomes.

Based on calibration curves produced from *in vitro* exposures, a dose estimate can be made according to the number of dicentrics detected per cell. This assay is generally accepted as the most specific and sensitive method (0.2 Gy) for determining doses from recent exposures to ionizing radiation (*i.e.* within days to ~6 months). Additionally, statistical techniques are available that can determine if the body received a homogeneous dose distribution or if the dose was delivered in a non-homogeneous manner. The usefulness of this assay is greatly reduced for measuring doses received more than 6 months before the assay because of the half-life (i.e. turnover) of lymphocytes resulting in the instability, and thus loss, of dicentric chromosomes.

Radiation-induced dicentric chromosomes are mechanically unstable during mitosis and are therefore eliminated as the lymphocyte pool is regenerated. In contrast, chromosome translocations are stable during cell division and can be measured using FISH. In this molecular cytogenetic method, fluorochrome-labeled DNA probes that are specific for typically three pairs of chromosomes can be used to detect exchanges by means of fluorescence microscopy. The stability of chromosome translocations has been shown to remain elevated for decades. This method has been used for dosimetry reanalysis of WWII atomic bomb survivors and in civilian radiation accidents that happened decades ago.



Cytokinesis-Block Micronucleus Assay

The cytokinesis-block micronucleus assay is another method useful in biological dosimetry. In contrast to the direct examination of chromosomes, the micronucleus test is an indirect method to assess chromosome damage and is performed on cells at the interphase stage in the cell cycle. Micronuclei are characterized as small, round-to-oval structures located within the cytoplasm of a cell but physically distinct and separated from the main nucleus. Because they resemble the main nucleus in shape, texture and staining properties, and contain DNA, micronuclei are easily detected as markers of damaged (i.e. broken) chromosomes. The analysis of micronuclei requires less skill, proceeds rapidly, especially with automated slide scanning equipment and typically includes samples of 1,000 cells or more. The test has been improved significantly

through the introduction of the cytokinesis-block method and has been shown to be sensitive to doses as low as 0.1 Gy. On the downside, unlike the dicentric assay, age and gender are factors known to affect the background frequency. In vitro studies have demonstrated that a dose of 1 Gy can be estimated with an uncertainty of 0.2 Gy. In vivo studies have shown the lower detection level is about 0.3 Gy.

Premature Chromosome Condensation

One limitation of assays requiring lymphocyte stimulation is that cells receiving higher radiation doses also experience cell cycle delay and may not reach mitosis. This can result in a large underestimation of the absorbed dose. Chromosomes, however, can be forced to condense prematurely by fusing human lymphocytes with Chinese hamster ovary (CHO) mitotic cells in the presence of polyethylene glycol (PEG).

The PCC assay can also be chemically induced by incubating lymphocytes with a protein phosphatase inhibitor (e.g. okadaic acid), adenosine triphosphate, and a mitosis-promoting factor which avoids the need to maintain cultures of CHO cells. The PCC assay enables direct observation of chromosome damage and earlier than is possible when cells must be stimulated to mitosis. The assay's lower limit of detection is not as low as that of dicentric chromosome assay. It is sensitive to doses higher than detectable with the dicentric chromosome aberration assay.

Electron Paramagnetic Resonance (EPR)

Exposure of humans to ionizing radiation results in radiation-induced changes that can be measured and, depending on the absorbed dose, quantified. The use of EPR for biodosimetry is based on the capability of the technique to provide specific and sensitive measurement of unpaired electrons in solid tissue which are created in proportion to the absorbed dose. The lifetimes of these electrons are very short (nanoseconds) in aqueous systems such as most biological tissues but can be extremely stable in non-aqueous media, including teeth, bone, fingernails, and hair. EPR has been used for *in vitro* analyses of exfoliated teeth to measure doses in populations from Japan and the former Soviet Union. The effectiveness of EPR has been well demonstrated.

Molecular Markers in Body Fluids and Tissues

Molecular markers (biomarkers) represent underlying changes in physiology arising from physical damage (e.g., cell lysis and the release of intracellular proteins into the circulation, oxidation by-products or DNA breakage), underlying changes in biochemistry (e.g., the presence of new metabolites or changes in levels of key gene

products), and/or changes in cellular composition of tissues. These markers include molecules as diverse as proteins and small molecule metabolites.

Within minutes to hours after exposure to ionizing radiation, proteins are modified and activated, and large-scale changes occur in the gene expression profiles involving a broad variety of cell-process pathways. There are presently approximately 90 known proteins that show changes in expression or undergo post-translational modifications after exposure to ionizing radiation. Some of these change in a dose-dependent fashion. Use of biochemical markers in a multi-parameter assay represents an exciting new development in radiation dosimetry.

Section 8 – Delayed Effects

Delayed effects of radiation include radiation-induced carcinogenesis, genetic issues in offspring, late organ effects (typically vascular changes, fibroatrophy and thyroid dysfunction), cataracts, and infertility.

Lung Complications

Radiation injury to the lung is an important, medically difficult aspect of high-dose radiation incidents that may occur several months post-exposure. The most radiosensitive subunit of the lung is the alveolar/capillary complex, and early radiation-induced lung injury is often described as diffuse alveolar damage. These complications may arise due to acute doses to the lungs in excess of 800 to 1,000 rads (8-10 Gy). Reactive oxygen species generated by radiation damage are directly toxic to lung cells and initiate a cascade of molecular events that alter the cytokine milieu of the microenvironment, creating a self-sustaining cycle of inflammation and chronic oxidative stress. A variety of cytokines have been implicated as indicators/mediators of lung injury.

Replacement of normal lung parenchyma by fibrosis is generally the culminating event. Depending on the dose/dose rate and volume of lung irradiated, acute radiation pneumonitis may develop, characterized by dry cough and dyspnea. Fibrosis of the lung, which causes further dyspnea, is a possible late complication.

Studies on Long-Term Effects of Radiation

The Biological Effects of Ionizing Radiation (BEIR) Committee 7 of the National Academy of Sciences, in its recent report (BEIR VII, 2006), extensively considered the mathematical risk-dose models currently in use. The BEIR VII committee concluded that the best model for the risk of delayed effects is still the linear non-

threshold model (LNT). The LNT model implies that the risk of a given delayed effect goes through zero at zero dose and increases linearly with increasing dose.

The Dosimetry System 2002 (DS02) is the latest dose reconstruction from the Hiroshima and Nagasaki weapon events. A large cohort of radiation survivors have been followed since 1945. Statistically significant evidence is noted for radiation-induced leukemia of all varieties except CLL. In addition, radiation-induced carcinoma has been reported for the breast, thyroid, colon, stomach, lung, and ovary. Borderline or inconsistent results are noted for radiation-induced carcinoma of the esophagus, liver, skin, bladder, CNS system, multiple myeloma and lymphoma.

Cancer Risk

Medical personnel at all levels of care need to be knowledgeable about the worry and psychological distress that patients experience regarding delayed effects of radiation exposure. Using the current statistics available from the American Cancer Society (US Mortality, 2006 http://www.cancer.org/docroot/stt/stt_0.asp?from=fast, 2009 presentation), we can estimate the number of cancer deaths in a population. The Society says that in 2006 cancer was the cause of 23.1% of all deaths.

Let's assume a population of ten million people. Using the numbers above, 2.31 million people would be expected to die due to cancer. According to NCRP Report No. 115 (1993) the lifetime excess risk of fatal cancer is 4% per Sv (0.04% per rem) for a worker population and 5% per Sv (0.05% per rem) for the general population. In other words, if this same population received an excess total dose of 10 rem (0.1 Sv) over their life spans there would be (10,000,000 people)(0.0005 deaths per person per rem)(10 rem) = about 50,000 excess deaths, or about 0.5% at 10 rem (or 5% at 100 rem/1Sv).

The American Cancer Society says that one out of every two men will be diagnosed with cancer; one out of three women will be. This equates to about 42% of the population being diagnosed with cancer within their lifetimes. BEIR VII estimates that that 43 out of every 100 people in the US will be diagnosed with cancer in their lifetimes. It additionally estimates that approximately one cancer per 100 people (~1%) could result from a single exposure to 10 rem (0.1 Sv) above background, implying that the radiation-induced cancer rate is about 10% per Sv.
The reader should note that risk estimates among various Federal agencies, advisory groups, and international committees vary a bit (BEIR V and VII, IAEA, NCRP, EPA, UNSCEAR, etc.), but all are generally in the above range.

Resources that may be helpful in medical consultation with irradiated patients include:

- The Health Physics Society website: *Ask the Experts* (http://hps.org/publicinformation/asktheexperts.cfm)
- BEIR V, VII and UNSCEAR 1988, 2000 reports
- Various reports of the NCRP and ICRP such as NCRP 115 and ICRP 60 and 103
- The American Cancer Society website (http://www.cancer.org/docroot/home/index.asp)

Non-Cancer Effects

Radiation also causes late effects other than cancer. These include cataracts (particularly of the posterior pole of the lens), hyperparathyroidism, and a decrease in both T-cell mediated immunity and in the B-cell humoral response. Survivors of in-utero exposure have also experienced infant microcephaly, mental retardation, growth and development delay, and lower IQ and poor school performance.

Radiation-induced cataracts are well documented, most notably seen in the posterior pole of the lens. Neutrons are particularly effective in cataract formation. The threshold dose for cataract formation is approximately 2 Gy (greater with fractionated doses). At 40 Gy dose to the eye, approximately 100% will form cataracts. The latency period ranges from 2 months to 35 years. In general, with increased dose to the eye, the latency period decreases.

Radiation and Pregnancy

Pregnant women are almost always worried about possible fetal effects from radiation exposure. The gestational age of a fetus is calculated from the beginning of the last menstrual (LMP) and averages 280 days, divided into three trimesters. During the first two weeks following ovulation, successive biological events include fertilization, formation of the free blastocyst, transit down the fallopian tube and implantation. No statistically significant effects have been noted for medically significant irradiation before conception.

If irradiation occurs during transit of the blastocyst down the fallopian tube, an "all or none" effect is generally noted. If implantation is successful, the pregnancy generally has a successful outcome. During the first trimester period of organogenesis, the embryo is sensitive to growth-retarding effects because of the criticality of cellular activities and the high proportion of radiosensitive cells.
For uterine doses > 0.5 Gy, growth retardation, gross congenital malformations, and microcephaly have been the predominant effects. Interestingly, there has been no report of external irradiation inducing morphologic malformation in a fetus unless it also exhibits growth retardation or a CNS anomaly.

The highest risk of mental retardation is irradiation of the fetus during the period of major neuronal migration (8-15 weeks) and the incidence is dose dependent. At 1 Gy fetal dose, approximately 75% will experience mental retardation. Conversely, at 16-25 weeks gestation, the fetus shows no increase in mental retardation at fetal doses < 0.5 Gy.

Exposure to high levels of radiation is clearly a risk factor for childhood leukemia. Japanese adult atomic bomb survivors had a 20-fold increased risk of developing acute leukemia (except CLL) usually within 6 to 8 years after exposure. Studies on in-utero exposure and childhood exposure to low levels of radiation show mixed results.

Section 9 – Psychological Support and Risk

The importance of early recognition of signs of stress or other psychological issues cannot be overstressed, therefore early involvement of mental health professionals, clergy, etc., should be considered. Since risk is such a personal concept it may be difficult to deal with the anxieties in a population associated with a real or imagined radiological event. One has to keep in mind that many sources misrepresent the hazards associated with radiation.

According to *The Medical Basis for Radiation-Accident Preparedness III, The Psychological Perspective* (Ricks, et.al., 1990) simply conveying information is not enough. Successful communication regarding radiation incidents is multi-faceted, and some of the issues have not necessarily been well addressed. For instance:

- The media is oftentimes seen as covering viewpoints, not truth
- To a scientist objectivity means adhering to evidence in the search for the truth, to a journalist it may simply mean balance
- Politics seems to be more newsworthy than science
- Claims of risk seem to get more press than claims of safety.

And it is not always the news media providing the images that shape our opinions. We have all read our share of comic books and seen many television shows that link radiation exposure and contamination with radioactive materials to "glowing in the dark," immediate and severe "radiation sickness" after exposure to radiation, mutations, genetic effects, etc. It's important to realize the significance of these images regardless of how misleading they may be.

Immediate Psychological Response

Sandman says in *Explaining Environmental Risk* (1986) that it is necessary to "alert people when they ought to be alerted and reassure them when they ought to be

reassured." Radiation elicits fear. Public anxiety associated with radiation emergencies appears to be out of proportion to the radiation induced health effects (IAEA, 2005). Often this fear is considerably out of proportion to the true medical significance of the radiation-related event. Radiation illness symptoms in just a few people can produce devastating psychological effects on an entire community or group of responders/care providers that is uninformed about the physical hazards of radiation. This acute anxiety has the potential to become the significant source of emotional stress.

Care should be taken to ensure unnecessary stressors are not added. The IAEA recommends that, if possible, it may be beneficial to provide educational materials/counselors at receiving centers, take care to factor in religious/cultural/social customs when surveying or decontaminating patients, try not to separate parents from children, etc.

It has been the experience at REAC/TS that many people express some of the preliminary symptoms of ARS – particularly nausea – due to their anxiety. It is important that responders and medical care providers are able to recognize the difference between real victims and those who are simply afraid.

Long-Term Psychological Effects

Long-term psychological effects of radiation exposure can manifest years after the causative exposure. Those who have been exposed – or think they might have been exposed - may experience feelings of vulnerability, post-traumatic stress, chronic anxiety, and loss of control. The patient may also experience fear for the safety of future generations.

Affected individuals appear to fall into one of three groups:

- Those who are distressed
- Those who may exhibit behavioral changes
- Those with high risk to develop psychiatric illness.

Common reactions may manifest as sadness, anger, fear, difficulty sleeping, impaired ability to concentrate, and disbelief, or as nonspecific somatic complaints. This condition is often referred to as "MIPS", Multiple Idiopathic Physical Symptoms.

Outcomes vary widely. Most individuals improve over time, but for a few individuals, the course is less benign. Physicians and psychologists must remember that people with no prior history are vulnerable to psychiatric illness after a radiation exposure. This could also include crucial emergency response and field medical staff.

Treatment

Following a radiation event, those who suspect they were involved will likely turn to trusted healthcare providers or mentors for information and guidance. Healthcare providers will therefore play a key role in determining the long-term care and medical surveillance of people's response to a radiological event. General health care providers should be able to care for these patients with proper information about the potential long-term effects of radiation injury and with liberal referral to psychiatric or psychological services.

A well-organized and sustained, effective medical response will instill hope and confidence, reduce fear and anxiety, and support the continuity of basic functions. Casualties should be treated with the primary psychology maxims of proximity, immediacy, and expectancy in order to minimize long-term consequences. In other words, treat close to home, as early as possible, and communicate to the patients that expectations are that they will return to normalcy.

While initial radiation dose estimations may be available fairly quickly, it is common for some time to elapse before final results are available. During this time period ensuring consensus among experts, and thus a common message, can help to allay patient fear and anger.

Impacts on Health Care Providers and Responders

On September 30, 1987, in Goiânia, Brazil a large scale radiological incident occurred as a result of individuals removing a ^{137}Cs radiotherapy device from an abandoned clinic and breaching the source capsule. The individuals were unaware of the radiation/contamination hazards. It was about 2.5 weeks before the radiological implications of the incident were discovered and it resulted in the deaths of four people. This incident acts as a nice case study not only for the medical management of irradiated/contaminated patients, but for gaining insight into the psychological aspects of radiation accidents. More information can be found in the IAEA report *The Radiological Accident in Goiânia* (www-pub.iaea.org/MTCD/publications/PDF/Pub815_web.pdf).

It seems obvious that the victims and their families experienced psychological issues that needed addressed, as well as members of the community where this incident occurred. It is, however, interesting to note the psychological impact of the incident on responders in Goiânia. The impacts varied widely depending on multiple factors such as individual personality traits, the ability to cope with stress, the accident phase in which the responder was involved, and the job the individual performed. The greatest impact was to those who first uncovered the facts and had to deal with the victims' early health effects. A variety of specialists who responded to the accident were surveyed about the psychological impact of the incident on them. 100% of the

specialists surveyed who were involved with the response from time zero to two months (October and November) reported feeling a psychological impact compared to 50% of those who worked in January and February. Feelings of the incident responders included guilt, pity, and helplessness.

The working conditions of the early responders had a large impact on the psychological toll. They worked 12-15 hours per day in unfamiliar and uncomfortable conditions (radioactive contamination, necessary protective clothing, etc.). Temperatures were as high as 100^{O} F. The population's apprehension, and outright fear, sometimes resulted in unexpected confrontations. And, as can be expected, the chaotic nature of the early phases of a large scale emergency response exacerbated the problems (Ricks, et. al., 1990).

Many of the responders reported they noticed behavioral changes in their coworkers such as increased alcohol use and aggressive behavior. Other signs of stress may also be seen. Clearly, it is important to provide support to responding personnel, be they in the field or in the hospitals and/or clinics. Some suggestions for consideration include:

- Encourage the workers to talk about their stress (decompression). It may be eased through catharsis
- Pay attention to behavior changes and try to understand the underlying reasons
- Provide assistance to team leaders when they are making decisions regarding work assignments to help ensure the person assigned is right for the job and that the work (and radiation dose) is being equally and fairly distributed
- Consider providing pre-assignment personality and psychological evaluation

Admittedly, the Goiânia accident is not typical of the type of response in which most health care providers will participate. However, it does provide some insight into the way that people may respond under stress and/or when working in radiological situations where they may not feel comfortable, or even at risk. Team members need to watch out for each other; this is true for hospital and field response.

Appendix A – Supplemental Information

REAC/TS Patient Treatment Algorithm

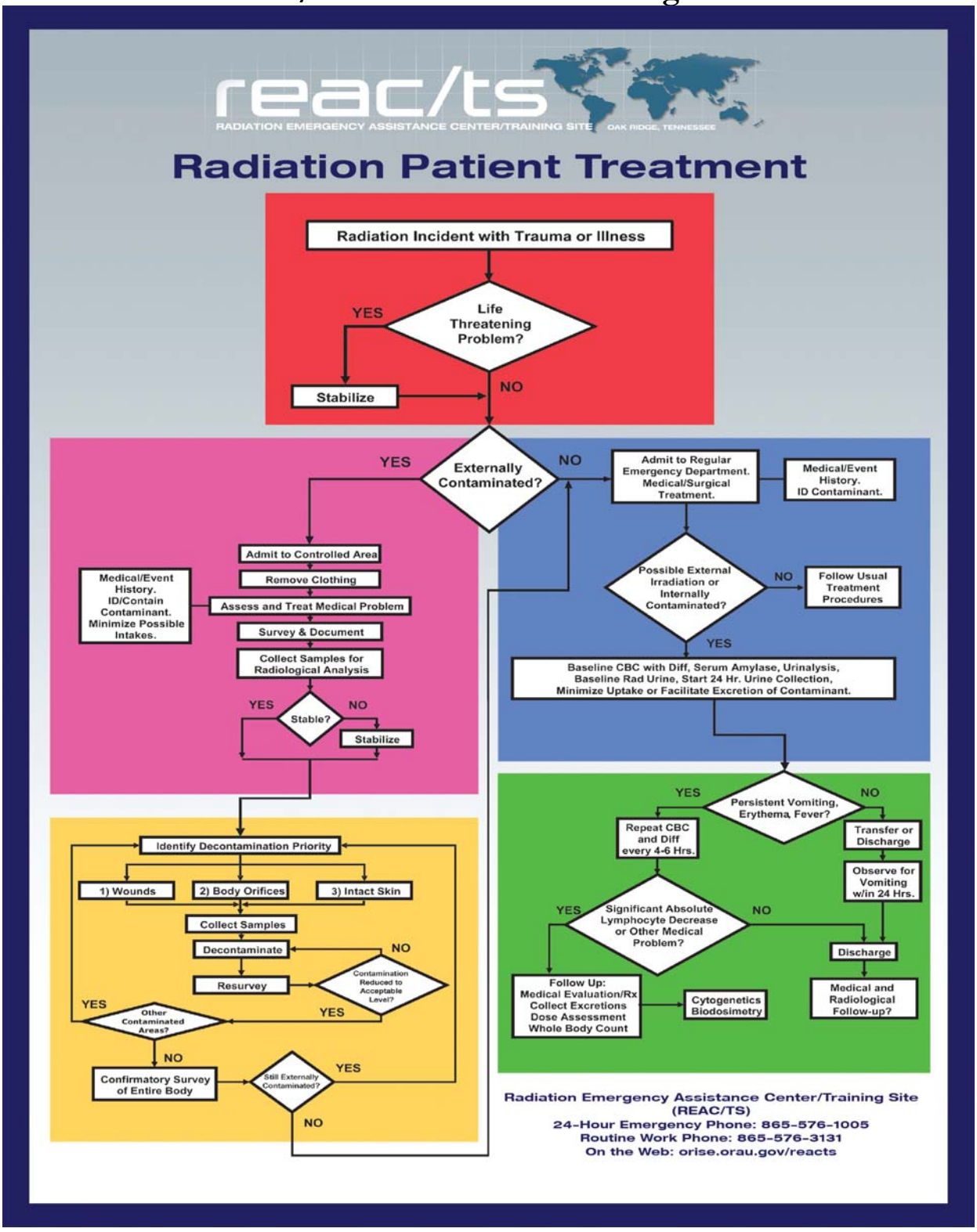


Table 12 – Approximate Skin Injury Thresholds vs. Acute Doses

Approx. Dose	Predicted Effect	Time Post Exposure*
300 rads (3 Gy)	Epilation	14-21 days
600 rads (6 Gy)	Erythema	Early, then 14-21 days later
1000-1500 rads (10-15 Gy)	Dry Desquamation	2-3 Weeks
1500-2500 rads (15-25 Gy)	Wet Desquamation	2-3 Weeks
> 2500 rads (> 25 Gy)	Deep Ulceration/Necrosis	Dependent upon dose

* At higher doses the time to onset of signs/symptoms may be compressed.

Table 13 – Approximate Thresholds for Acute Radiation Syndromes

Dose	Syndrome	Signs/Symptoms*
0-100 rads (0-1 Gy)	NA	Generally asymptomatic, potential slight drop in lymphocytes later (near 1 Gy)
> 100 rads (> 1 Gy)	Hematopoietic	Anorexia, nausea, vomiting, initial granulocytosis and lymphocytopenia.
> 6-800 rads (> 6-8 Gy)	Gastrointestinal	Early severe nausea, vomiting, watery diarrhea, pancytopenia
> 2000 rads (> 20 Gy)	Cardiovascular/ CNS	Nausea/vomiting within first hour, prostration, ataxia, confusion

* At higher doses the time to onset of signs/symptoms may be compressed.

Table 14 – Activity Conversions

1 terabecquerel	1 TBq	27 curies
1 gigabecquerel	1 GBq	27 millicuries
1 megabecquerel	1 MBq	27 microcuries
1 kilobecquerel	1 kBq	27 nanocuries
1 becquerel	1 Bq	27 picocuries
1 kilocurie	1 kCi	37 terabecquerels
1 curie	1 Ci	37 gigabecquerels
1 millicurie	1 mCi	37 megabecquerels
1 microcurie	1 μCi	37 kilobecquerels
1 nanocurie	1 nCi	37 becquerels

Table 15 – Dose Equivalent/Equivalent Dose Conversions

1 sievert	1 Sv	100 rem
1 millisievert	1 mSv	100 millirem
1 microsievert	1 μSv	100 microrem
1 rem	1 rem	10 millisieverts
1 millirem	1 mrem	10 microsieverts
1 microrem	1 μrem	10 nanosieverts

Table 16 – Absorbed Dose Conversions

1 gray	1 Gy	100 rads
1 milligray	1 mGy	100 millirad
1 microgray	1 μGy	100 microrad
1 rad	1 rad	10 milligrays
1 millirad	1 mrad	10 micrograys
1 microrad	1 μrad	10 nanograys

Table 17 – Standard Prefixes for Units of Measurements

Multiple	Prefix	Symbol
10^{18}	exa	E
10^{15}	peta	P
10^{12}	tera	T
10^{9}	giga	G
10^{6}	mega	M
10^{3}	kilo	k
10^{2}	hecto	h
10^{1}	deka	da
10^{-1}	deci	d
10^{-2}	centi	c
10^{-3}	milli	m
10^{-6}	micro	μ
10^{-9}	nano	n
10^{-12}	pico	p
10^{-15}	femto	f
10^{-18}	atto	a

Table 18 – Acronyms

ALC	absolute lymphocyte count
ALI	annual limit on intake
ANC	absolute neutrophil count
ARS	acute radiation syndrome
BAT	Biodosimetry Assessment Tool
BEIR	Biological Effects of Ionizing Radiation
Bq	becquerel
CBC	complete blood count
Ci	curie
CLL	chronic lymphocytic leukemia
CPM	counts per minute
CRP	C-reactive protein
CSF	colony-stimulating factor
DPM	disintegrations per minute
DRD	direct read-out dosimeter
DTPA	diethylenetriaminepentaacetic acid
DU	depleted uranium
EDTA	ethylenediaminetetraacetate
FDA	Food and Drug Administration
FISH	fluorescent in-situ hybridization
G-CSF	granulocyte colony-stimulating factor
GI	gastrointestinal
G-M	Geiger-Mueller
GM-CSF	granulocyte-macrophage colony-stimulating factor
Gy	gray
ICRP	International Commission on Radiation Protection
IND	Improvised nuclear device
KI	potassium iodide
LD	lethal dose
MOPP	mission-oriented protective posture
NCRP	National Council on Radiation Protection and Measurements
PCC	premature chromosome condensation
QD	every day
QF	quality factor
RDD	radiation dispersal device
REAC/TS	Radiation Emergency Assistance Center/Training Site
RES	radiation exposure status
s.c.	subcutaneous
Sv	sievert

UNSCEAR	United Nations Scientific Committee on the Effects of Atomic Radiation
WBC	white blood count (sometimes whole body count)

Appendix B - Additional Response Resources

DOE – National Nuclear Security Administration – NNSA – http://nnsa.energy.gov/emergency_ops/index.htm: The National Nuclear Security Administration (NNSA) ensures that capabilities are in place to respond to any NNSA or Department of Energy (DOE) facility emergency. It is also the nation's premier responder to any nuclear or radiological incident within the United States or abroad and provides operational planning and training to counter both domestic and international nuclear terrorism.

Armed Forces Radiobiology Research Institute – AFRRI – www.afrri.usuhs.mil/: The AFRRI mission is to preserve the health and performance of U.S. military personnel and to protect humankind through research that advances the understanding of the effects of ionizing radiation. To these ends, the institute collaborates with other government facilities, academic institutions, and civilian laboratories in the United States and other countries to research the biological effects of ionizing radiation. In addition, it provides medical training and emergency response to manage incidents related to radiation exposure. A similar pocket guide (*Medical Management of Radiological Casualties, 3rd Edition, 2009*) was produced by AFRRI to help guide military medical operations.

USG DHHS Radiation Event Medical Management – REMM – http://www.remm.nlm.gov/**:** Part of the U.S. Department of Health & Human Services, REMM provides guidance on radiation-event diagnosis and treatment for health-care providers. The primary functions: (1) Provide guidance for health care providers, *primarily physicians*, about clinical diagnosis and treatment during mass casualty radiological/nuclear (rad/nuc) events, (2) Provide just-in-time, evidence-based, usable information with sufficient background and context to make complex issues understandable to those *without* formal radiation medicine expertise, and (3) Provide web-based information that is also downloadable in advance, so that it would be available during an event if the internet is not accessible

International Atomic Energy Agency (IAEA) – IAEA's Response System – http://www-ns.iaea.org/tech-areas/emergency/iaea-response-system.htm: The prime objectives of the IAEA's Response System is to facilitate the (1) exchange of official real-time information among States/relevant international organizations; (2)

provision of assistance/advice to States/relevant international organizations upon request; and (3) provision of relevant, timely, truthful, consistent and appropriate public information. REAC/TS is a member of the IAEA Response Assistance Network (RANET).

World Health Organization (WHO) – Radiation Emergency Medical Preparedness and Assistance Network (REMPAN): The network is designated to provide emergency medical and public health assistance to people over-exposed to radiation. It also facilitates a long-term care and follow-up of radiation accident victims and conducts research in radiation emergency medicine, radiotherapeutics, bio-dosimetry and radiation epidemiology. REAC/TS is a WHO/REMPAN collaboration center.

Center for Disease Control and Prevention (CDC), Emergency Preparedness and Response – http://www.bt.cdc.gov/radiation**:** A government website intended to increase the nation's ability to prepare for and respond to public health emergencies, including radiological events.