Radiology

Medical Response to a Major Radiologic Emergency: A Primer for Medical and Public Health Practitioners[1]

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There are several types of serious nuclear or radiologic emergencies that would require a specialized medical response. Four scenarios of great public health, economic, and psychologic impact are the detonation of a nuclear weapon, the meltdown of a nuclear reactor, the explosion of a large radiologic dispersal device ("dirty bomb"), or the surreptitious placement of a radiation exposure device in a public area of high population density. With any of these, medical facilities that remain functional may have to deal with large numbers of ill, wounded, and probably contaminated people. Special care and/or handling will be needed for those with trauma, blast injuries, or thermal burns as well as significant radiation exposures or contamination. In addition, radiologists, nuclear medicine specialists, and radiation oncologists will be called on to perform a number of diverse and critically important tasks, including advising political and public health leaders, interfacing with the media, managing essential resources, and, of course, providing medical care. This article describes the medical responses needed following a radiologic or nuclear incident, including the symptoms of and specific treatments for acute radiation syndrome and other early health effects.

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Planners for emergency response to radiologic/nuclear (R/N) incidents focus on four events that could expose people to significant amounts of ionizing radiation and/or radioactive materials: the detonation of a nuclear weapon or improvised nuclear device (1), one probably comparable in impact to the Hiroshima and Nagasaki bombs; a crisis at a nuclear power plant, such as that at Chernobyl; the activation of a large explosive radiologic dispersal device, sometimes called a "dirty bomb"; or the placement of a hidden radiologic exposure device where it could expose many people to high doses. Since the physical, medical, economic, and psychologic consequences could range from the serious to the unimaginably catastrophic, should one of them take place, appropriate planning and preparations are absolutely essential (2,3). Physicians familiar with the biologic effects of radiation exposure from such events, and with the medical treatment of irradiated and/or contaminated individuals, will play vital roles in emergency response.

Some readers of this article may be emergency department (ED) physicians, medical center administrators, and other nonradiologists, and a number of them may have limited knowledge of ionizing radiation and radioactivity or of the management of local radiation injury, internal contamination with radionuclides, and acute radiation syndrome (ARS) (4,5). Several of the most important physical and radiobiologic terms and concepts are therefore explained in some detail in Appendixes E1–E5 (online). The issues of *absorbed dose*, *equivalent dose*, and *effective dose*, for example, the standard measures used to predict serious health effects, are presented in Table 1 and discussed in Appendix E1 (online). These three dose terms are conceptually quite different, but in much of the literature they are used rather loosely and interchangeably. So, too, are the associated International System dose units, the sievert (Sv) and the gray (Gy) (as are the older units, the rad and the rem). But in nearly all emergency situations, numerical values in sieverts and grays (or rad and rem) are the same, so this distinction matters little in practice. What is important to bear in mind, however, is the amount and parts of the body that are irradiated: An exposure of the whole body, or a significant portion of it, to 4 or 5 Sv (or Gy) is potentially lethal, while an extremity may be able to tolerate several times that dose.

Essentials

- Radiologists and other health professionals may be called on without warning to care for persons involved in a major radiologic or nuclear incident, such as the detonation of a nuclear weapon, the meltdown of a nuclear reactor, or the dispersal of radioactive contamination.
- Irradiation of an individual can occur either by means of the direct exposure pathway or through external or internal contamination. A patient may have also suffered acute injury, and once he or she is stabilized, attention can turn to decontamination and to the management of the effects of irradiation.
- Acute radiation syndrome (ARS) may manifest at relatively high exposures as three distinct clusters of symptoms; these indicate damage to the hematopoietic, gastrointestinal, and central nervous systems. Also, severe localized cutaneous injury may occur with heavy exposure, even in the absence of ARS.
- Specialized medical care can greatly enhance the likelihood of survival of those who receive whole-body doses of 3–7 Sv (300–700 rem).

Types of Radiogenic Health Effects

The types and severities of the various adverse radiogenic health effects caused by an R/N incident depend on several factors, including the radiation dose absorbed by different parts of the body, the rate at which it is delivered, the type of radiation (alpha, beta, gamma, neutrons), and the route(s) of exposure (6–8). At the subcellular level, effects result most importantly from radiogenic alteration of the information content of cellular DNA associated with unrepaired chromosomal strand breakage and disruption of base pairs, as discussed in Appendix E2 (online).

Health effects resulting from radiogenic DNA damage are of two general types, stochastic and deterministic. They differ fundamentally at both the molecular and the tissue levels.

The *stochastic* effect of primary concern is carcinogenesis, which may arise from certain radiation-induced transformations in the genetic material of one or more cells. For purposes of radiation protection, it is commonly assumed that such events occur randomly and independently, and that the probability of a health effect occurring is proportional to the dose; then even a small amount of exposure may (albeit with extremely low likelihood) give rise to an effect, typically long after the exposure.

Deterministic or *nonstochastic* effects in an organ, by contrast, arise from radiation-induced acceleration of the normal physiologic process of apoptosis (programmed cell death) and from the outright killing of so many essential cells that the tissue can no longer continue to function properly. Above a tissue-specific dose threshold, the severity of the damage increases with the number of cells disabled or killed, hence with the amount of radiation absorbed. Deterministic

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Abbreviations:
ALARA = as low as reasonably achievable
ARS = acute radiation syndrome
ED = emergency department
$LD_{50/60}$ = the dose at which 50% of a population will die within 60 days
NCRP = National Council on Radiation Protection and Measurements
R/N = radiologic/nuclear
REAC/TS = Radiation Emergency Assistance Center/Training Site

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Table 1

Quantities Used in Measurement of Ionizing Radiation, in Both International System and Traditional Units

Quantity	SI Unit	Traditional Unit	Relationship
Dose	gray (Gy) = J kg^{-1}	rad	1 Gy = 100 rad
Equivalent dose	sievert (Sv)	rem	1 Sv = 100 rem
Effective dose	sievert (Sv)	rem	1 Sv = 100 rem
Exposure	coulombs kg^{-1} in air	roentgen (R)	1 R ~1 rad in tissue
Activity	becquerel (Bq)	curie (Ci)	1 Ci = 3.7×10^{10} Bq

Note. —*SI* = International System; 1 mSv = 1 millisievert = 0.001 Sv.

effects that manifest after months or even years, such as cataract formation, are said to be *late* effects. Those that become apparent within hours, days, or weeks of an irradiation are known as *acute* or *early* effects. And a sufficiently high exposure over a short period of time will rapidly give rise to one or more forms of acute radiation syndrome (ARS), which can be life-threatening. (Older terms are *radiation sickness* and *radiation poisoning*. More recently it has also been called *multiple organ dysfunction syndrome*.)

Teratogenic effects that can arise from exposure in utero may share characteristics of both stochastic and deterministic responses.

Ordinarily, it is the possibility of late radiation-induced stochastic and teratogenic effects that are of primary importance to physicians and the public, and these are discussed in Appendix E3 (online). But following an R/N incident, of greatest immediate radiologic concern are the serious deterministic effects, such as acute local radiation injuries and ARS. It is on these effects that this article will focus.

Many of the recommendations that follow assume adequate time and resources to ensure a coherent emergency response. In the chaos of a real event, during which health care personnel may have to deal with overwhelming numbers of injured and contaminated victims, this guidance may represent somewhat idealized goals.

General Principles of Radiation Safety Apply Also during a Radiologic Emergency

It is the goal of a standard radiation safety program to protect patients, staff, and the public from routine but avoidable exposures (9,10). It is intended to prevent deterministic health effects from occurring altogether, and to limit stochastic hazards to "acceptable" levels (as determined by public health policymakers). Although it may not be possible to achieve either of these objectives during an emergency, many components of such a regular program may still provide useful guidelines even then.

The "golden rule" of any radiation protection program is that as staff carry out their responsibilities, they must keep everyone's exposure (including their own) as low as reasonably achievable (ALARA). There are four simple principles of ALARA to reduce the potential danger from *any* toxic source, including radioactive materials and ionizing radiation. These four commonsense, largely self-explanatory principles involve time, distance, shielding, and the removal or containment of contamination. To the extent possible and consistent with proper patient care (11), medical personnel should: *(a)* minimize the amount of time anyone is exposed to a source; *(b)* maximize the distance from it; *(c)* establish adequate shielding and barriers, whenever possible; and, if radioactive contamination is present on or within a patient or elsewhere, *(d)* remove it or contain it, to prevent both its further entry into the body and its spread to relatively clean areas.

Exposure to Ionizing Radiation versus Contamination with Radioactive Materials

Irradiation of an individual with *ionizing radiation* can occur either by means of the direct exposure pathway or through external or internal contamination with radioactive materials. Radiologists are well aware of the distinction between the two, but the staff they direct during a crisis and others may not be. The difference between the two must be made absolutely clear to health care workers.

Direct exposure takes place in nearby individuals during and immediately after the detonation of a nuclear weapon. The high-energy photons (gamma and x-rays), neutrons, and perhaps other particles produced can penetrate the body and cause damage. Similarly, contamination of the ground, buildings, etcetera, with radioactive materials by an R/N event can continue to expose people directly to gamma rays long after the event. But direct exposure does not render the body radioactive, and an exposed individual poses no threat to others. (Neutrons from the detonation of a nuclear weapon cause the body to become very slightly radioactive, but much less than what would create a health threat.) Contrary to common but erroneous belief, a person who has been exposed to ionizing radiation does not present a risk of harm to others, in particular to health care providers.

On the other hand, people who spend time in an area or around objects or people *contaminated* with radioactive materials will continue to be exposed to ionizing radiation, and may themselves become contaminated, as well. Once such contamination has occurred, it will remain in place until it is properly removed (or, for a few radionuclides with short half-lives, until it decays away). High levels of such contamination could be hazardous, but health care providers who practice the principles of ALARA, wear appropriate personal protective clothing and equipment, and practice protective hygiene can minimize the potential for significant exposure or contamination.

Radioactive contamination consists almost always of radionuclides that emit high-energy alpha, beta, and/or photon (gamma and x-ray) radiation. (Appendix E1 discusses radioactivity and ionizing radiation.) The most important distinction among these three, with regard

to radiation safety, is that they have very different capabilities to penetrate shielding and/or tissues. Alpha rays are massive, slow-moving particles that deposit all of their kinetic energy so rapidly in ionizing the matter they traverse that they cannot even pass through the epidermis. They do not pose an external hazard, but they can cause harm if alpha-emitting radionuclides are internalized. If inhaled, for example, they can damage bronchial epithelium and lung tissue, or be transported to regional lymph nodes and eventually deposited in a critical organ like bone. Beta particles, by contrast, may be able to penetrate several centimeters into tissue. And high-energy gamma rays and x-rays are nonparticulate forms of radiation that can traverse the human body and can be shielded only by significant thicknesses of lead, concrete, etcetera. Beta- and gamma-emitters are therefore potentially both external and internal hazards.

Evading the harmful effects of these several forms of radiation requires different approaches to protection, as provided (along with a range of other radiation-related services) by a medical center's health physics or radiation safety personnel. Also, health physicists are available 24/7 at the U.S. Department of Energy's Radiation Emergency Assistance Center/Training Site (REAC/TS), (865) 576–1005, and at the Centers for Disease Control and Prevention, (770) 488-7100.

External Contamination and Decontamination

Contamination of people can be either external or internal.

External contamination is radioactive material (or the process of placing such material) on the surface of the body. Hospitals or clinics should designate an area or areas, separate from the main ED, that can be set up for decontamination. These preparations are meant to prevent the spread of radioactive materials to other areas, equipment, and people (12).

An appropriate way to eliminate contamination (13) is to treat it as if it were raw sewage. It is sometimes possible to remove 80%–90% or more of external contamination simply by disrobing the patient. If contamination is causing discomfort such as burning, it is the chemical (not the radiologic) nature of the contaminating substance that is responsible.

Ambulatory patients may assist with their own decontamination. Nonambulatory patients should be disrobed on a stretcher on a clean waterproof sheet. The patient's face should be protected, such as with the kind of splatter shield worn by ED personnel or a clean oxygen mask. If necessary, clothing should be cut off or removed carefully to prevent spread of radioactive materials through contact or airborne transmission. The clothing should be rolled away from the patient, folded into the first sheet on the stretcher and removed. Contaminated clothing and linens should be placed in plastic trash bags (marked as a radiohazard) for special waste disposal or, if the radioactive contaminant has not yet been identified, for further analysis; bags containing patient items should be labeled with the patient's name, unique identifier, date and time of collection, and the name of the collector.

Radiation detection equipment (the radiation-sensitive parts of which must be sealed in airtight, clear plastic bags to prevent permanent contamination) is used to survey the body and identify areas of radioactive contamination, relative to background levels. Localized areas of contamination should be outlined with a permanent marker and covered with clean gauze or other wrapping until decontamination begins, to prevent its spread. Surveys need to be carried out in this order of priority: open wounds first, then face and facial orifices (nose, mouth), then intact skin. Wound counts should be recorded for comparison with counts obtained after decontamination efforts. If there is facial contamination, swabs from the nose and mouth should be taken with a cotton-tipped applicator, one for each naris, and a 4 × 4 gauze for the mouth. If a sample is positive, the readings can be used by health physicists to estimate how much pulmonary or gastrointestinal contamination might have occurred. Negative counts on nasal or oral swabs may mean nothing, depending on the time since the incident occurred, but they still represent a pertinent "negative."

Contaminated wounds are a fast direct route for internalization of radioactive materials and then transportation to critical organs, so their decontamination is a high priority. This is accomplished in nearly the same manner as for other kinds of contamination; but aggressive scrubbing is to be avoided at first, in favor of more gentle irrigation and removal of radioactive foreign bodies, so as not to accelerate uptake. Then somewhat more vigorous scrubbing and debridement for biologic decontamination may be performed as usual. The area around a wound should be cleansed just as for infectious agents, but waterproof paper (rather than cloth surgical) drapes should be used. Contaminated irrigation fluid can be drained into a garbage can lined with a large plastic trash bag, after which the bag must be tagged as radioactive waste and placed in storage to await removal. To remove liquid materials while cleansing the wound, blot one time with 4 × 4 gauze pads and then discard. Once the wound has been cleaned, a repeat survey can confirm the removal of contamination, after which the wound should be managed per surgical protocols. Primary concerns include infection control, wound healing, and cosmetic effect, but not the presence of a small amount of contamination; wounds having only a small amount of contamination may be closed if surgically appropriate.

Contaminated areas of intact skin should be washed with regular soap and water. Standard or povidone-iodine surgical soap (eg, Betadine) may be used if there is a concern for microbial contamination. Total body showering is recommended only if there is widespread skin contamination, which will rarely be the case, but a mass casualty situation might require showering because of the lack of personnel to perform local decontamination. If hair or beard is contaminated, one can try shampooing with baby shampoo over a sink. Shaving is to be avoided, if possible, because

razors can cause microabrasions that potentially allow internal contamination; shaving eyebrows should be only a last resort, since they may not regrow.

The survey-wash-rinse sequence of a wound or intact skin is repeated until the readings on a survey meter have dropped to 2–3 times background levels, or until continued efforts lead to no further decreases in measured radiation levels. In general, no more than two or three cycles should be attempted. Too numerous or too vigorous attempts at decontamination can erode the outer keratinized layer of skin, induce hyperemia, or create skin abrasions, any of which could provide a pathway for internal contamination or infection through loss of an otherwise intact barrier.

Internal Contamination

There is little that can be, or needs to be, done immediately after a direct exposure, and external contamination is relatively easy to detect and remove quickly. The possibility of significant *internal contamination*, however, is a more difficult issue that requires a timely response with special expertise and equipment to prevent the rapid uptake of radionuclides by target organs.

Internal contamination can occur only through inhalation or ingestion (eg, of dust, soot, water, food), by way of percutaneous/transdermal absorption through intact skin, or via an open wound, abrasion, or burn. Some internalized chemical elements (and their radioisotopes) tend to remain within the body, often concentrating in a particular tissue (eg, iodine in the thyroid, or radium and the transuranics like plutonium or americium primarily in bone), while others may be eliminated in urine, feces, vomitus, tears, and perspiration, perhaps in conjunction with treatment (eg, the administration of nonradioactive potassium iodide). Those who are not injured but who are suspected of being internally contaminated should be referred as soon as possible for outpatient nonemergency management that includes collection of excreta (to be sent to a laboratory capable of performing radiobioassays) and/or lung or whole body gamma-ray counting.

The medical treatment of internal contamination is discussed below.

Table 2

Current NCRP and International Commission on Radiological Protection Recommendations for Limits on Normal Annual Exposure of Workers and Members of the General Public to Ionizing Radiation

Limit on Exposure	NCRP, 1993 (mSv y^{-1})*	ICRP, 2007 (mSv y^{-1})†
Occupational		
Stochastic (effective dose)	50 (5)	50 (5)‡
Deterministic (equivalent dose)		
To lens of eye	150 (15)	150 (15)
To skin, extremities	500 (50)	500 (50)
Embryo-fetus	0.5 (0.05) in a month	Approximately same as for member of public
General public		
Stochastic	1 (0.1)	1 (0.1)§
"Infrequent exposure"	5 (0.5)	
Deterministic		
To lens of eye	50 (5)	15 (1.5)
To skin	50 (5)	50 (5)
To extremities	50 (5)	
Negligible dose	0.01 (0.001)	

Note.—Data in parentheses are presented in rem y^{-1}. Limits are designed to prevent deterministic health effects from occurring altogether, and to restrict stochastic risks to levels deemed by public health authorities to be "acceptable." In the United States, such recommendations are commonly implemented as regulations, with the force of law, by the U.S. Nuclear Regulatory Commission (16) and other Federal agencies, and by the States. *ICRP* = International Commission on Radiological Protection.

* Source.—References 9, 14.

† Source.—References 10, 15.

‡ No more than 20 mSv (2 rem) averaged over 5 years.

§ Exceptionally, higher than 1 mSv y^{-1} (0.1 rem y^{-1}); but no more than 1 mSv y^{-1} averaged over 5 years.

Protection of Personnel

Personnel in the proximity of or in contact with a few individuals who are lightly contaminated externally will be exposed to ionizing radiation, although this generally (depending on the isotopes) involves very little risk. Personnel dealing with a multitude of more heavily contaminated patients, on the other hand, may accumulate a substantial dose over time. Unless they are careful and follow standard precautions against any hazardous materials, moreover, they can inadvertently transfer contamination to themselves, and from there to others.

Pregnant staff should be given the option of being exempted from direct care of large numbers of contaminated patients.

If available, calibrated personal dosimeters should be sealed in clear, airtight plastic bags and worn outside the clothing, to allow rapid access and the removal of any contamination. Workers and work areas should be surveyed with radiation detectors at appropriate intervals (as determined by prior readings).

Documentation should be available that contains guidance on what readings would suggest that an individual or environment is acceptably safe from radiation, taking into account the nature of the emergency. The National Council on Radiation Protection and Measurements (NCRP) (9,14) and the International Commission on Radiological Protection (10,15) have prepared recommendations for limits on effective doses to radiation workers under normal (nonemergency) conditions; more stringent recommendations on exposure limits exist for members of the public (Table 2). Some of these recommendations have been embedded into law, and may be found in the U.S. Code of Federal Regulations (16).

Table 3

NCRP Recommendations for Dose Levels of Concern for Emergency Workers

Short-term Whole-Body Dose	Acute Symptoms (%)	Acute Death, No Medical Care (%)	Acute Death, Medical Care (%)	Excess Risk, Fatal Cancer (%)
0.1 Sv (10 rem)	0	0	0	1
0.5 Sv	0	0	0	4
1 Sv (100 rem)	5–30	<5	0	8
1.5 Sv	40	<5	<5	12
2 Sv	60	5	<5	16
3 Sv	75	30–50	15–30	24
6 Sv	100	95–100	50	>40
10 Sv (1000 rem)	100	100	>90	

Note.—Of uninjured, healthy, adult emergency workers, percentages statistically expected to experience health effects at different whole-body dose levels; most "acute deaths" are likely to occur 30–180 days after exposure. Acute symptoms are nausea and vomiting beginning within 4 hours. The lifetime risk of fatal cancer refers to the excess above and beyond the 24% population likelihood that anyone will die of cancer without the additional radiation exposure. Reprinted, with permission, from reference 17.

Table 4

U.S. Department of Homeland Security Guidance for Dose Limits to Emergency Workers

Worker Activity	Dose Limit Guidance Projected (Sv)*
All	0.05 (5)
Protecting valuable property	0.10 (10)
Life saving or protection of large populations	0.25 (25)
Life saving or protection of large populations; voluntary and worker aware of risks	>0.25

Source.—Reference 18.

Note.—The U.S. Department of Homeland Security has provided guidance on dose limits for workers performing emergency services, where the societal benefit must clearly outweigh the individual risk. Data in parentheses are presented in rem.

While these recommendations and regulations are intended to apply during normal circumstances, they also provide a useful benchmark for crises.

Alternatively, dose levels of concern for emergency workers have been compiled in NCRP Commentary 19 (17), reproduced in Table 3. Table 4 presents similar guidance from the U.S. Department of Homeland Security on dose limits for workers performing emergency services, including medical personnel in the field (18). It is unlikely that staff at a treatment facility would experience such high doses unless the facility itself is in a heavily contaminated area.

Before the Crisis Hits: Medical Facility Planning and Training

The first step of radiologic emergency response is to plan ahead and prepare for possible crises (2,3,19–27).

Emergency response plans should be "scalable." That is, they should be designed to allow for a level of emergency response commensurate with the number of patients potentially involved, from a few to hundreds or more (28,29). Presented in a direct and user-friendly format, an emergency response plan should outline the respective roles and responsibilities of each participant and the various response steps to be taken. As the Joint Commission has emphasized, planning for a major emergency should be a community-wide exercise (30,31). Hospital planning and training should involve not only medical personnel, but also local public safety, public health, psychologic services, and emergency management officials, together with first responders from fire departments, emergency medical services, law enforcement, and other agencies. In addition, an ED's own planning process should involve radiation safety staff, the radiology and radiation oncology departments, security and communications, hospital administration, clinical affairs, and public relations. Communities with several hospitals or clinics should assure the capability for active collaboration among them (32).

Components of the plan should cover personnel and resource management, worker health and safety, and communication. An effective communications strategy, in particular, calls for the establishment and routine testing of redundant systems for emergency notification of essential response personnel by phone, public radio and television, two-way pagers, radios, cell phones, and computer-based messaging, some of which may be rendered nonfunctional in case of a nuclear blast. The strategy should cover agreed-on places where critical staff are to go if communications are disrupted; alternative routes and means of getting there, given that normal transportation may be cut off; and a readily accessible protocol that describes in detail how communications should be re-established.

Among key response personnel are senior hospital administrators, the hospital emergency response coordinator, the radiation safety officer, and chairs/directors of the emergency, diagnostic radiology, nuclear medicine, radiation oncology, surgery, and medicine departments. For those who may be called on to serve, there should be a clear understanding of the locations of agreed-on safe places where family members are to go, the possible ways of getting there, and multiple means of keeping in touch; belief that their own families are most likely safe will greatly enhance the effectiveness of medical responders.

Several organizations have produced planning templates to assist health care facilities in developing radiation event emergency response plans and to provide guidance for the medical management of casualties arising from such events (33–35).

Symptoms and Treatment of Acute Radiation Syndrome and Other Early Deterministic Health Effects

Radiation damage to tissues and organs can result in a variety of deterministic health effects, ranging from the barely noticeable to the catastrophic.

Figure 1

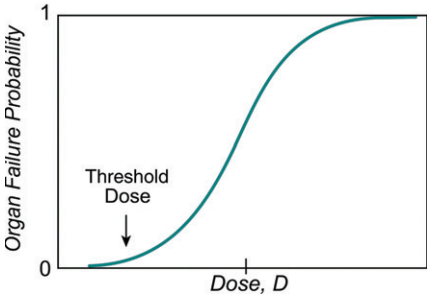


Figure 1: A dose-response relation for a deterministic effect in an organ or other tissue (as opposed to that for stochastic transformations in single cells) is usually sigmoidal in shape. At low doses, little if any damage occurs. Above an effective threshold—specific to the type of radiation, the tissue and biologic endpoint, and perhaps the individual—the damage increases with dose until the tissue is fully nonfunctional.

Table 5

Symptoms and Health Effects at Various Levels of Exposure

Exposure	Symptoms and Health Effects	Onset	End
0.15 Sv (15 rem)	Chromosome damage in circulating lymphocytes; sperm anomalies		
0.3–0.7 Sv	Mild nausea, mild headache;	6 hours	12 hours
	Mild lymphocyte depression	24 hours	
0.7–1.2 Sv	Vomiting in 5%–30%; delayed wound healing; drop in lymphocyte, platelet, granulocyte count; increased susceptibility to pathogens	3–5 hours	24 hours
1.2–3 Sv (120–300 rem)	Fatigue, weakness in 25%–60%; vomiting in 20%–70%; infection, fever; bleeding; wound/burn morbidity	2–3 hours	2 days
	LD_5–LD_{50} without special care		
2 Sv	Reversible skin effects (early erythema)		
3–6 Sv	Significant skin effects		
3–5 Sv	Fatigue, weakness in 80%–100%; transient, moderate vomiting in 50%–90%; diarrhea; loss of fluids; anorexia; ulceration; death of crypt cells, Peyer patch lymphoid tissue	hours–days	days–weeks
3.5–4 Sv	$LD_{50/60}$ without special care		
5–7 Sv	Moderate to severe vomiting in 50%–90%; fever, bloody diarrhea, gastrointestinal ulcerations, fluid/electrolyte shifts, infections, hemorrhage; marrow hypoplasia/aplasia; pancytopenia	1 hour	
7–8 Sv	Death highly probable		
>20 Sv (2000 rem)	cerebrovascular failure; loss of consciousness; death	minutes	days

Note.— Typical threshold doses for various radiobiologic effects that arise from an acute (rapid) whole-body exposure to x-or gamma rays. Doses that lead to death tend to be considerably higher than those that give rise to first symptoms. The numbers in this table are based largely upon those appearing in NCRP Report 138 (2) which, in turn, come from the Armed Forces Radiobiology Research Institute handbook (37) and other secondary and primary sources. They should be viewed as only rough guides, extracted from the very limited available data, on the doses that cause overlapping symptoms and different kinds of damage to several distinct biologic compartments. As discussed in the text and in Appendix E2 (online), the doses that give rise to deterministic effects depend on the type of radiation (ie, high vs low linear energy transfer), the tissue type, the biologic endpoint of concern, and the physiology of the individual (6).

Less than a decade after Roentgen discovered x-rays in the late 19th century, Bergonie and Tribondeau (1906) observed that radiosensitive cells tend to be less differentiated than radioresistant cells, and that they divide rapidly, displaying a high *mitotic index*. As has been verified numerous times in the years since, tissues with cells that undergo rapid proliferation or self-renewal are commonly more sensitive to radiation-induced cell killing and resultant deterministic effects. Also, cells with high metabolic activity, such as salivary gland cells, are very radiosensitive. (An exception is the peripheral circulating lymphocytes, which are highly differentiated and not mitotically active, but nonetheless highly radiosensitive; indeed, the monitoring of lymphocyte counts plays an important role in the management of patients with ARS, as will be discussed below.) Nonproliferating or slowly proliferating cells, such as those of the liver, kidneys, blood vessels, and connective tissues, are correspondingly less radiosensitive to cell killing, but not necessarily to the stochastic effect of cancer induction.

Deterministic (Nonstochastic) Health Effects

As noted above, a radiogenic deterministic effect is said to arise in a tissue or organ when ionizing radiation disables or kills so many of its essential or proliferative cells that it ceases to function properly. Such an effect will appear, with a reasonable degree of certainty, if a dose that exceeds an organ-specific *threshold dose* is delivered over a short period of time. Once beyond the threshold, the severity of the response in the tissue grows sigmoidally with dose (36) (Fig 1). Factors that determine the extent and severity of a health effect, and the parameters of the dose-response curve, include the total dose, the rate at which the dose is delivered, the kind of radiation, and the radiosensitivity and volume of tissue irradiated. Fibrosis of the lung, ulceration of bowel and esophagus, renal failure, destruction of a segment of the spinal cord and other consequences of high exposure to localized regions of the body have been studied extensively, particularly in connection with cancer radiation therapy. (One can easily destroy a tumor—it is the tolerance levels of the surrounding normal tissues that limit the aggressiveness, hence the likelihood of tumor eradication, of radiation therapy.)

A uniform whole-body dose of 0.3 Sv (30 rem) from an external exposure of penetrating radiation (ie, high-energy gamma rays, x-rays, or neutrons) delivered over a matter of minutes is likely to cause only mild symptoms, specifically nausea and perhaps vomiting (Table 5) (2,6,37). (Below that dose level, special testing may indicate subclinical lymphocyte depletions and damage to spermatogonia.) Around 2 Sv (200 rem),

significant lymphocyte depletion occurs within 24–48 hours. At 3 Sv, clear clinical symptoms of ARS may appear at about a week because of damage to the bone marrow. As the dose increases above this level, damage to the cells of other organ systems will begin to accumulate. $LD_{50/60}$ (the dose at which 50% of a population will die within 60 days) is commonly held to be on the order of 3.5–4 Sv (350–400 rem) (although estimates vary) for patients not receiving medical treatment. With aggressive and skilled supportive care, victims may survive doses of 5–6 Sv, and occasionally even as high as 7–8 Sv.

As with the human response to many other hazards, the young and the very old are more susceptible to radiogenic injuries and illnesses.

ARS Is the Issue of Early Concern in a Radiation Disaster

The disaster at Chernobyl and the bombing of Hiroshima and Nagasaki serve as reminders that high doses of radiation give rise to severe deterministic health effects, including death. A number of individuals were far enough from the epicenters of these events to survive the blast and thermal injuries, yet suffered varying levels of ARS; this was caused by damage to the most radiosensitive organ systems, namely bone marrow, the lining of the small bowel, the skin, and, at high doses, the microvasculature that supports the nervous system (and all other organ systems).

The severity of signs and symptoms of ARS and the rapidity of their onset increase with the dose above the tissue-specific threshold levels. In some situations it is possible for a health or medical physicist to calculate an estimate of dose to an individual. Generally, though, health care providers must make a presumptive diagnosis based on knowledge of the exposure scenario (38) or on the appearance of clinical signs and symptoms. This issue is discussed below and in the literature (37,39–42).

The NCRP has provided a good, succinct definition of ARS (2): "The acute radiation syndrome is a broad term used to describe a range of signs and symptoms that reflect severe damage to specific organ systems and that can lead to death within hours or up to several months after exposure." Three distinct clusters of symptoms, associated with damage to three separate biologic compartments, point to the onset of ARS. These are known as the hematopoietic or bone marrow syndrome, the gastrointestinal syndrome, and the central nervous system or cardiovascular syndrome, and they occur with increasing whole-body dose in this respective order. A fourth cluster, the cutaneous syndrome, may accompany the others if there is significant widespread or local irradiation of the skin. Above a few sieverts, there may be some damage to more than one compartment, and symptoms will overlap.

For each of the ARS syndromes, the disease progression over time has classically been divided into the same four stages: prodromal, latent, manifest illness, and recovery or death. These stages are distinct, more or less, and the timing and severity of health effects characteristic of each is strongly dependent on the dose received and on the efficacy of available medical treatment.

After a significant total or partial body exposure, symptoms of ARS (2,6,7, 37,43) (which are themselves life-threatening in some situations) usually are exhibited early on as the *prodromal* stage, also called the "N-V-D" stage, with nausea and vomiting, and for higher doses, diarrhea. These initial signs are much the same for all the ARS syndromes, but their severity and speed of onset depends on the dose received. Other prodromal stage symptoms include easy fatigability, headache, anorexia, parotitis, erythema, and fever.

Fever is usually low grade except at extremely high, life-threatening doses. Any person known to have received at least some radiation exposure and presenting with a markedly elevated temperature may possibly have received a high radiation dose. This suspicion should be corroborated by the presence of other findings consistent with a life-threatening radiation exposure or confirmed by means of laboratory findings. In most cases, however, the presence of high-grade fever should trigger a search for another cause, such as infection, rather than one specific to ionizing radiation.

Extreme supralethal irradiation can also cause profound hypotension, confusion, ataxia, loss of consciousness, and seizures; here, too, if there is no good antecedent history of such high-level exposure, another cause should be sought.

In the subsequent symptom-free *latent* stage, the patient may appear and feel relatively well. Its duration is inversely proportional to the dose, and lasts for 1 or a number of weeks for survivable exposures. Absence of a latent phase—that is, a progressive worsening from prodromal signs and symptoms directly into the manifest illness—provides a clinical indication that the dose received may not be survivable.

During the *manifest illness* stage, symptoms of ARS may appear within a manner of days with relatively high doses or develop over months if caused by a lesser exposure. These symptoms are somewhat characteristic of whichever of the three syndromes is dominant.

Finally, recovery time for a survivor is a complex function of the whole-body exposure (or, if exposure is nonuniform, the amounts and tissues of the body that receive high levels of radiation), age and prior state of health, and the degree and timing of the medical care available. Recuperation can take from weeks to years. For those who do not recover, death may occur within days, weeks, or months; again, dose will be a principal determinant of how rapidly a victim succumbs.

The Manifest Illness Stage: Symptoms Characteristic of the Three ARS Syndromes

The first cluster of adverse health effects to appear in the manifest illness stage is the *hematopoietic*. Blood-forming tissues renew their cell populations at a rate greater than 1% per day, and they tend to be highly radiosensitive. The cells that are lost earliest and most readily from an irradiation are the peripheral circulating lymphocytes; the rapidity with which the lymphocyte count drops, moreover, and the level to

Table 6

The Three Syndromes of ARS and Their Health Effects at Each Stage of Disease Progression

Syndrome	Onset Dose	Prodromal	Latent	Manifest Illness	Recovery
Hematopoietic/ bone marrow	0.7 Sv (mild symptoms may occur as low as 0.3 Sv)	Symptoms are anorexia, nausea, and vomiting; onset occurs 1 hour to 2 days after exposure; stage lasts for minutes to days	Some stem cells in bone marrow are dying, although patient may appear and feel well; stage lasts 1–6 weeks	Anorexia, fever, and malaise; drop in all blood cell counts occurs for several weeks; primary cause of death is infection and hemorrhage; survival decreases with increasing dose; most deaths occur within a few months of exposure	In most cases, bone marrow cells will begin to repopulate the marrow; for <3 Sv, may be full recovery for a large percentage of individuals, from a few weeks up to 2 years after exposure. $LD_{50/60}$ is about 3.5–4 Sv, but death may occur in some at 1.2 Sv (120 rem)
Gastrointestinal	10 Sv (symptoms may occur at 6 Sv)	Anorexia, severe nausea, vomiting, cramps, and diarrhea; onset occurs within a few hours; stage lasts about 2 days	Some stem cells in bone marrow and cells lining gastrointestinal tract are dying, although patient may appear and feel well; stage lasts less than 1 week	Malaise, anorexia, severe diarrhea, fever, dehydration, and electrolyte imbalance; death is due to infection, dehydration, and electrolyte imbalance, and occurs within 2 weeks of exposure	LD_{100} is about 8 Sv
Cardiovascular/ central nervous system	50 Sv (symptoms may occur at 20 Sv)	Extreme nervousness and confusion; severe nausea, vomiting, and watery diarrhea; loss of consciousness; and burning sensations of the skin; onset may occur within minutes of exposure; stage lasts for minutes to hours	Patient will not return to partial functionality for >50 Sv; stage may last for hours, but often is less	Watery diarrhea, convulsions, and coma; onset occurs within hours for >50 Sv, and death within days	No recovery

Note.—The symptoms of ARS arise first from depletion of the supply of leukocytes (bone marrow/hematopoietic syndrome), then from destruction of the mucosal lining of the gastrointestinal tract (gastrointestinal syndrome) and, at highest doses, from damage to the microvasculature that supplies the central nervous system (central nervous system syndrome). This table is based largely on the Centers for Disease Control and Prevention's "Acute Radiation Syndrome: A Fact Sheet for Physicians" (43).

which it falls in the first 12–48 hours following an R/N incident, depends on dose. Damage to the bone marrow and depletion of peripheral circulating lymphocytes, and the onset of the hematopoietic syndrome, begins typically with an acute whole-body exposure on the order of 0.7 Sv (70 rem) or more (Tables 5 and 6). Above a level of 2.5–5 Sv of acute whole-body irradiation, significant hematopoietic or bone marrow damage occurs, worsening as the dose increases. Over days or weeks, the numbers of white blood cells and platelets decrease at rates that depend on the absorbed dose. The hematopoietic syndrome results from the loss both of peripheral circulating lymphocytes and of hematopoietic stem/progenitor cells in the bone marrow. Hematopoietic "stem" cells (not to be confused with embryonic stem cells capable of developing into any cell line in the human body) have the capacity to differentiate only into mature blood cell lines. As the dose increases, with progressive marrow hypoplasia and then aplasia occurring at 5–6 Sv (500–600 rem), adverse health outcomes may include pancytopenia, infections, and hemorrhage.

Signs and symptoms of the hematopoietic syndrome include a wide variety of infections up to and including general overwhelming infection or sepsis. A concomitant loss of megakaryocytes and resultant decrease in functional platelets increase the threat of uncontrolled hemorrhage. Appropriate care includes fluid and electrolyte management, administration of blood products, infection control, and nutritional support.

With intensive and dedicated nursing and supportive care, patients may be able to survive exposures ranging as high as 5–8 Sv. Patients are unlikely to survive without this type of support, however, particularly as the effects of radiation on other organ systems become predominant.

The full-blown *gastrointestinal* syndrome occurs for a whole-body dose of 10 Sv, which is not survivable, but there may be symptoms at 6 Sv. It results from damage to the epithelial lining of the small intestine, the loss of epithelial stem cells in crypts of the microvilli, and the loss of the microvasculature that supports the lining of the gastrointestinal tract. Radiation-induced damage to the gastrointestinal mucosa can cause electrolyte shifts, profound fluid losses, diarrhea, and bloody diarrhea that leads to frank bleeding. Severe diarrhea following destruction of the mucosal layer of the gastrointestinal tract can be fatal due to loss of fluids, protein, and electrolytes. Also, bacteria and other infectious agents traversing the denuded

bowel epithelium may cause lethal septicemia, a phenomenon further aggravated by the coincident depletion of lymphocytes and neutrophils. High fever at this point is characteristic. At doses higher yet, loss of epithelial stem cells may lead to death within weeks. Malabsorption and ileus may lead to malnutrition and other sequelae. Volume depletion results in hypotension, cardiovascular collapse, and renal failure. With acute doses greater than 10 Sv (1000 rem) to the whole body, or to a significant portion of it (apart from the limbs), loss of life is virtually certain.

The hematopoietic and gastrointestinal syndromes may be accompanied by *cutaneous radiation injury*. Damage to the skin can also occur in the absence of ARS, since nonpenetrating beta particles and low-energy photons may deposit excess dose only to the integument (44). Such an injury may become apparent within hours or may not be seen for weeks, depending on the dose. At low doses, itching, tingling, and edema may occur. The threshold dose for temporary epilation is on the order of 3–5 Sv, and that for erythema is 5–6 Sv. Above 10 Sv localized to the skin, the injury progressively worsens with increasing dose, advancing from dry desquamation, wet desquamation, and bullae (blister) formation to ulceration and necrosis. Chronic, possibly severe, skin infections and recurrent ulceration may complicate the process.

A localized injury resulting from depopulation of the basal layer of skin, sometimes called an *acute local radiation injury* or a *radiation burn*, may be debilitatingly painful and life-threatening because of concomitant infections. Radiation skin damage differs from that caused by extreme heat or by chemicals in that it appears as a delayed effect, whereas thermal and chemical burns show themselves nearly immediately following exposure. The capacity of skin to heal is diminished if the area also underwent trauma, and there may be recurrent breakdown even if a scar forms.

The *central nervous system* syndrome, also called the *cerebrovascular* or *neurovascular* syndrome, occurs at much higher doses than the others, above 50 Sv (5000 rem) (although there may be symptoms at 20 Sv), and it is likely to cause death even before other findings of radiation sickness appear. It comes about because of failure and collapse of the neurologic and cardiovascular systems. While the fundamental cause of the hematopoietic and gastrointestinal syndromes is clear—the depletion of critical populations of stem cells essential for the replenishment of the circulating blood cells or of the epithelial lining of the gastrointestinal tract, respectively—the exact cause of death from the central nervous system syndrome is not yet understood as well (6); it is probably related to damage from increased pressure within the cranial vault caused by edema, vasculitis, and meningitis (43). Symptoms include severe vomiting, confusion, disorientation, ataxia, even seizures, and coma sets in quickly, perhaps within hours. Death will result within days. At 50–100 Sv, there is usually no latency period, and the prodromal and manifest illness stages may be indistinguishable from one another. Aside from neurogenic vomiting, the other neurologic findings noted above are not characteristic of lower doses—so, in the absence of a credible history of exposure to 20 Sv or more, other causes should be sought.

Treatment of ARS and of Internal Contamination

Triage

In mass casualty situations, triage decisions must be made rapidly and with limited clinical information. Astute and experienced clinicians may recognize early, transient, subtle signs of radiation injury or illness, which should be noted and recorded. But the detrimental physiologic effects of even moderate radiation exposures may be far from obvious in some patients, not becoming apparent for days or weeks. It complicates matters considerably that the reaction of an individual to an exposure depends on a number of independent variables, including the dose, the dose rate, the nature and energy of the radiation, the type and volume of tissue irradiated, the victim's age and state of health, and the quality of medical care available (45–48).

Table 7

REAC/TS Emergency Department Checklist for Ionizing Radiation Injuries and Illnesses

Checklist for Ionizing Radiation Injuries/Illness
Activate the radiologic emergency reception team
First priority: stabilize life- or limb-threatening conditions
Exposure to radiation vs contamination with radioactivity
Addressing external contamination
Addressing internal contamination
Early indications of ARS
Early management of potential ARS
Forensics

Note.—This checklist is to be inserted into standing orders. See Appendix E4 (online) for details.

Various schemas have been designed to assist clinicians in the triage and prioritization of patients for further treatment. Figure 2 and Table 7, for example, outline the process prepared by REAC/TS (currently developing a Web site that will include a revised chart and table) (39). An alternative approach is provided by the Radiation Event Medical Management Web site (available at *www.remm.nlm.gov*) (49). And the METREPOL ("medical treatment protocols") group at the University of Ulm (Germany) has developed a method for grading the severity of ARS in radiation mass-casualty events (50). Any of these can provide guidance to admitting physicians on the routing of patients into the appropriate one of three disjoint categories: *(a)* those who have experienced only a mild exposure; *(b)* those who have undergone a more severe (potentially life-threatening) exposure; and *(c)* those who have received an exposure that is highly likely to be fatal, even with medical attention. In general, persons who appear to have had mild exposures should be managed with watchful waiting. People with severe exposures should receive immediate active intervention to the extent that it exists. And those with clearly lethal exposures should receive palliative care. Triage of patients will

Figure 2

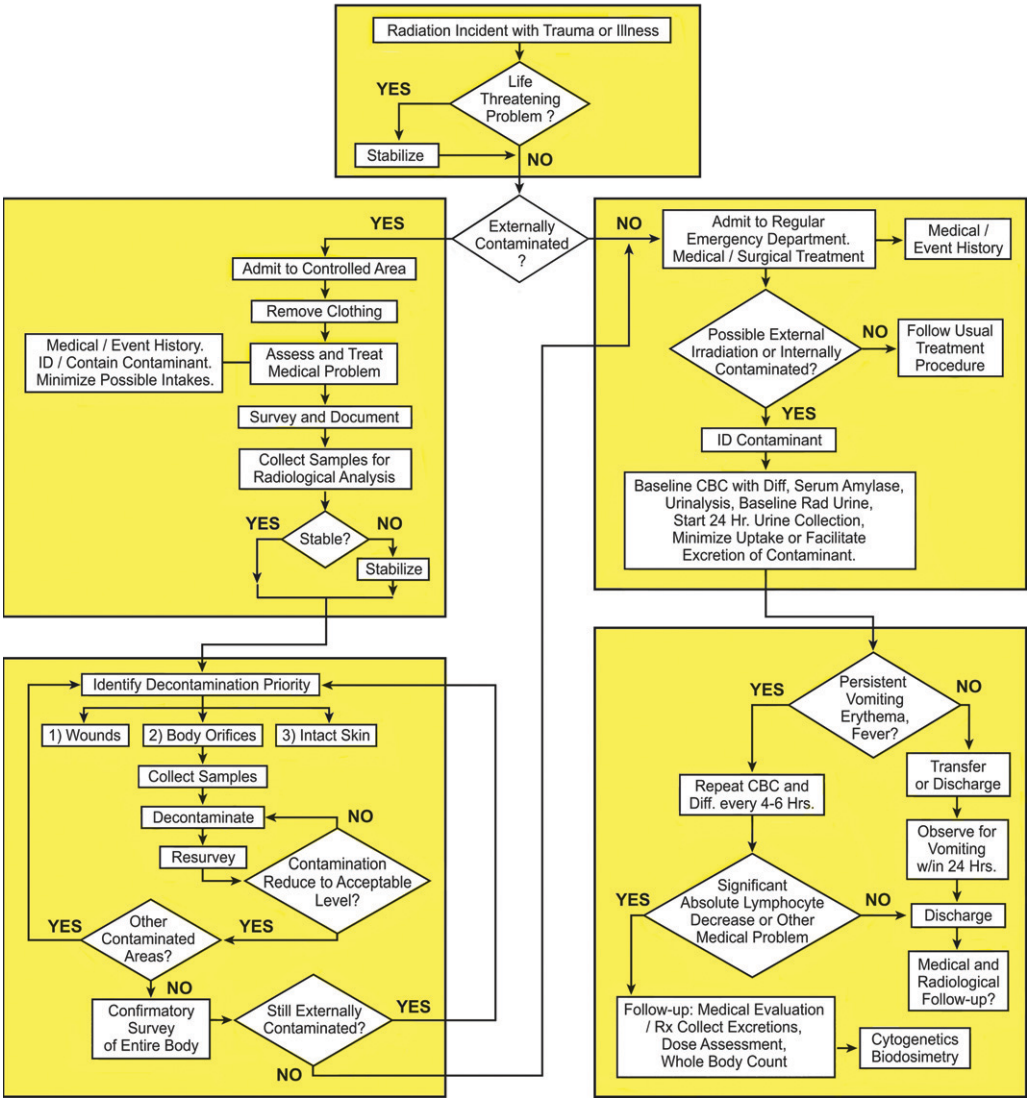


Figure 2: Medical treatment prioritization flow diagram for those exposed to ionizing radiation and/or contaminated with radioactivity. (Diagram courtesy of REAC/TS, Oak Ridge, Tenn.)

need to be modified depending on available personnel, laboratory capacity, hospital beds, and other infrastructure.

The probability of survival depends largely on dose. In broadest terms, $LD_{50/60}$ for individuals without pre-existing, underlying comorbidity but who receive no specialized medical attention is on the order of 3.5–4 Sv, as mentioned above. Some clinical evidence and laboratory studies suggest that with excellent supportive care, victims may recover following acute whole-body exposures of 5–6 Sv, and a few of as much as 7–8 Sv. There are no substantiated reports of anyone surviving a 10-Sv whole-body dose.

For a radiation event in which there has been an explosion, patients may present with blast injuries, blunt and penetrating trauma (including lacerations and open wounds), and hemorrhage, as well as thermal and chemical burns. As with any other serious medical condition, the first priority involves the stabilization of medical and surgical conditions according to routine emergency medicine standards of care or, for the severely injured, advanced trauma life-support protocols. Each of these conditions requires definitive medical and surgical care before addressing the effects on the patient of irradiation or contamination. At the same time, if numbers of incoming patients are highly contaminated, it is critical that health care workers wear appropriate personal protective clothing and equipment and practice the principles of ALARA and protective hygiene, as discussed above.

In the face of significant acute whole-body doses, surgeries need to be performed within the first 24–36 hours

Figure 3

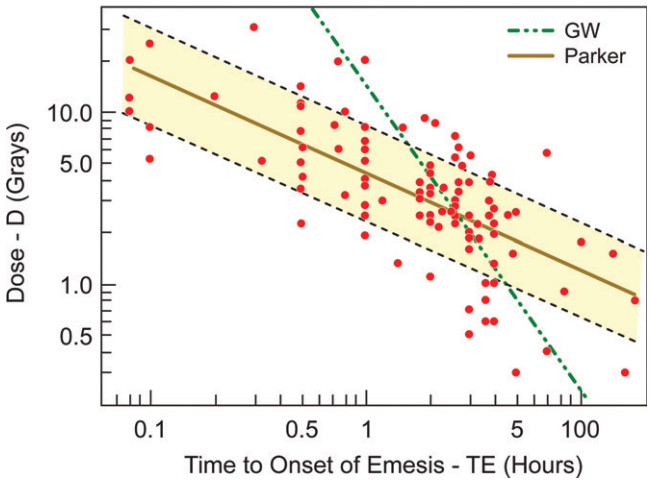


Figure 3: An early clinical indicator of the degree of exposure to ionizing radiation is the time to onset of emesis. The more vertical single regression line was fitted by Goans and Waselenko (53) to 108 data points contained in the REAC/TS database. A reanalysis by Parker and Parker (54) of the same data includes a new best fit line: ln $D = 1.50–0.57$ ln TE, where dose, D, is in grays, and time to emesis, TE, in hours. Also shown are a pair of $\pm 1\sigma$ confidence limit lines, where the standard error (σ) in ln D is 0.65.

Table 8

Percentage of the Population Who Experience Emesis Following Various Levels of Whole-Body Exposure, and Average Time Until It Occurs

Dose (Sv)	Percentage of Population	Time to Emesis (h)
0		
1	20	
2	35	4.6
3	55	2.6
4	70	1.7
5	85	1.3
6	95	1.0
7	98	0.8
8	99	0.7
9	100	0.6
10	100	0.5

Note.—Used, with permission, from the REAC/TS Accident Registry.

because patients with acute hematopoietic syndrome typically exhibit poor wound healing and are immunologically incompetent; they are at a heightened risk for infection when procedures are delayed. This approach is reasonable because persons with a good chance of long-term survival will not die within the first few days solely because of their radiation exposures. Nonetheless, anyone suspected of having received several sieverts should receive no further radiation exposure (ie, for diagnostic purposes) unless absolutely necessary.

Early radiation-treatment decisions, conversely, are based on signs and symptoms evident during the first 24–48 hours and on the results of laboratory tests performed during that time. The addition of traumatic injury, burns, or some pre-existing conditions (eg, diabetes mellitus) to significant radiation exposure results in a so-called *combined injury*. Victims with combined injury are more likely to exhibit severe health effects at lower doses, and have a significantly reduced probability of recovery from high exposures. That is, morbidity and mortality from radiation injuries and illnesses increase dramatically in the face of trauma and/or burns.

If heavy internal contamination is suspected, significant intervention may be required early on to prevent incorporation of radionuclides into critical organs, which might otherwise give rise to severe health effects, as will be discussed below.

Psychologic issues will also be important (51). Many individuals who arrive at the ED will be physically intact but emotionally traumatized, those sometimes called the "worried well." Following a radiologic accident in Goiânia, Brazil, in 1987, for example, more than 110 000 people were concerned enough to request a radiologic survey (52). In such an event, people cleared of physical trauma and radiation exposure can be reassured and released from the hospital and referred to counseling if there are indications of need for it.

Finally, in a chaotic situation with many people highly agitated and in confused states of mind, a simple but effective way to track the contamination status, diagnosis, and treatment of patients over time is to attach a hard copy of the medical record package, or at least a brief note, either to clothing or to a cord hung around the neck.

Determining Dose and Dose Rate

Some readily obtainable patient information can help clinicians make estimates of exposure, which assist in guiding management. This information includes the incident and medical histories, the time to the onset of vomiting, and the results of several simple blood tests, such as the complete blood count with white blood cell differential and serum amylase.

A person's location relative to a radiation source and to any shielding can be an important metric for establishing dose. Victims should be asked where they were at the time of the event and whether they were screened by any protective barriers. Public health departments may be able to provide estimates of dose at various locations soon after an event, based on environmental monitoring and modeling and on information provided by the U.S. Department of Energy, the U.S. Department of Homeland Security, state agencies, and others.

With an acute whole-body dose greater than 1 Sv, typical symptoms of nausea, vomiting, weakness, and fatigue may present within hours. A widely accepted approach to estimating exposure, especially in conjunction with decrements in the absolute lymphocyte count, is based on an empirical relationship between dose received and the average time to emesis (53,54) (Fig 3 and Table 8). If robust laboratory capacity is absent, tracking the onset of nausea and vomiting may be among the only tools clinicians have to diagnose ARS. These early effects are fairly nonspecific, however, and may not be readily distinguishable from the prodromes of more commonly

encountered illnesses. It has recently been argued, moreover, that time to onset of emesis should be used with caution as an estimator of dose, because it is "imprecise and may lead to a very high false-positive rate" (55). Clinicians should look for other adverse health effects in their patients, as well, to rule in or rule out alternative diagnoses.

If laboratory capacity remains intact, tracking the rate and magnitude of decline in absolute lymphocyte counts over a period of hours to days, a technique sometimes called *lymphocyte depletion kinetics*, serves as the single best estimator of radiation exposure and clinical outcome (Fig 4a). A decrease in absolute lymphocyte levels may be observed at whole-body doses as low as 100 mSv (10 rem) (56–58), but clinically significant decrements may not be seen below 1–2 Sv. Depending on the absorbed dose, such changes can begin within hours of exposure, so current recommendations are to perform a complete blood count with differential as a baseline right away, and then every 6–12 hours thereafter for 2–3 days. The complete blood count is relatively inexpensive and can be performed quickly. Dose-response curves have been developed for lymphocyte depletion allowing physicians to determine the possibility of impending significant ARS (Table 9). The kinetics of various peripheral hematopoietic component cell populations over longer periods of time (Fig 4b), and their dependence on dose, in particular, will be discussed below.

An elevated serum amylase provides a supplementary piece of information that may also be an early sign of serious radiation exposure involving the head and neck. The results of this test are nonspecific, however, and may also reflect alcohol intake, a stress response, trauma to the face or abdomen, or other factors.

At the same time that an initial blood sample is taken, it is advantageous also to collect 10 mL of blood in a lithium-heparin vacuum hematology tube (eg, green-top Vacutainer) to send for radiation *cytogenetic biodosimetry* by way of chromosome aberration analysis, if indicated (a sodium-heparin tube is acceptable but not preferred; keep the tube at room temperature—do not refrigerate). A cell will attempt to repair some radiogenic chromosomal damage (59), but occasionally the repair is carried out incorrectly. Among the most visible of resulting errors

Figure 4

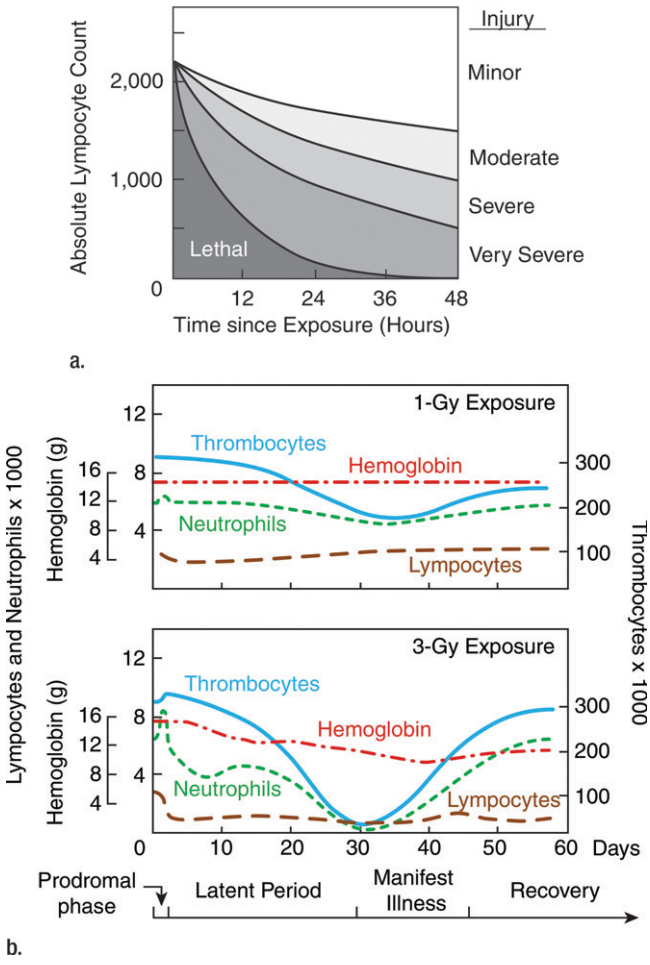


Figure 4: Early laboratory indications of exposure to ionizing radiation. **(a)** Top image shows time-dependent lymphocyte depletion kinetics following either severe or moderate radiation exposures. As early as 6–12 hours following exposure, there may some indication of the severity of the exposure (56–58). **(b)** Bottom two images show a stylized time-dependent response model of the various peripheral hematopoietic components to an acute 1-Sv (100-rem) or 3-Sv whole-body dose. The concentration of neutrophils, in particular, passes through a potentially lethal nadir about a month after exposure. The timing of the processes indicated here depends strongly on the dose and on the physiology of the individual.

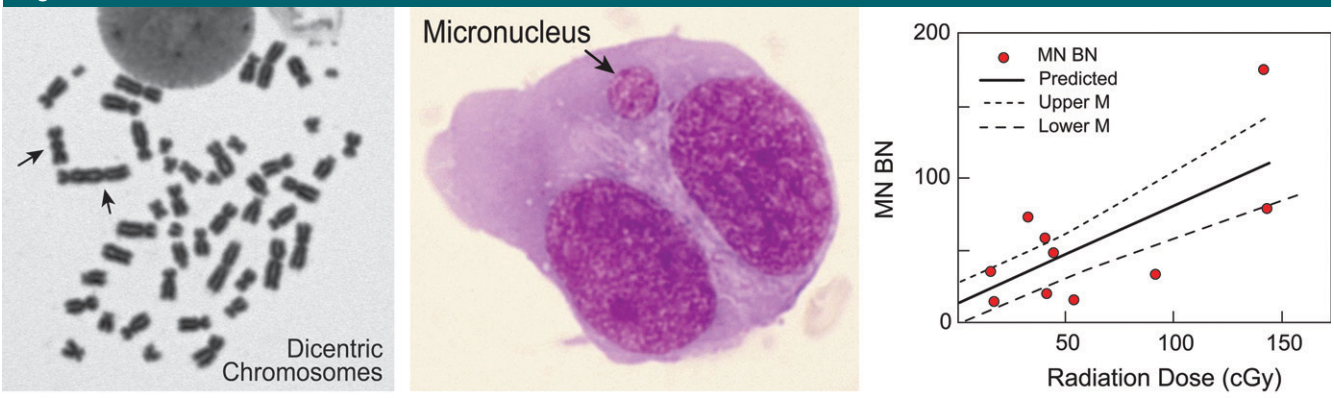
Table 9

Lymphocyte Depletion Kinetics for Acute Whole-Body Irradiations

	Lymphocyte Count by Day ($\times 10^9$/L)					
Dose (Sv)	0.5	1	2	4	6	8
0	2.45	2.45	2.45	2.45	2.45	2.45
1	2.30	2.16	1.90	1.48	1.15	0.89
2	2.16	1.90	1.48	0.89	0.54	0.33
3	2.03	1.68	1.15	0.54	0.25	0.12
4	1.90	1.48	0.89	0.33	0.12	0.044
5	1.79	1.31	0.69	0.20	0.06	0.020
6	1.69	1.15	0.54	0.12	0.03	0.006
8	1.48	0.89	0.33	0.044	0.006	<0.001

Note.—Baseline mean absolute lymphocyte count is assumed to be 2.50×10^9/L. Data used, with permission, from the REAC/TS Accident Registry.

Figure 5



a. b. c.

Figure 5: Biologic effects resulting from radiation-induced damage to DNA molecules. **(a)** Metaphase spread of cultured lymphocytes, with radiation-induced dicentric chromosome aberrations indicated by arrows. **(b)** Binucleated lymphocyte from a cell culture, in which the micronucleus resulted from damage that prevented the cell from dividing normally at mitosis. **(c)** When such structures are quantified and compared with a standardized dose-response curve, the radiation dose to the patient can be estimated. This "in vivo" micronuclei dose-response curve, generated from patients undergoing fractionated radiation therapy, demonstrates the estimation of an equivalent whole-body radiation dose to the patient. Clinical studies such as this are few, but important, since they lend increased clinical credibility to this radiation biodosimetry assay for the individual patient. The usual "in vitro" tissue culture assays cannot and do not compensate for the internal biochemistry existing in the patient at the time of the radiation exposures. A similar type of biodosimetry analysis involves quantifying dicentric chromosomes in the lymphocytes. *MN BN* = micronuclei in binuclear T-lymphocytes, *M* = 95% confidence bounds for the mean. Figure 5a and 5b courtesy of Dr Gordon Livingston, REAC/TS Cytogenetic Biodosimetry Laboratory, Oak Ridge, Tenn. Figure 5c reprinted, with permission, from reference 60.)

Table 10

Chromosomal Aberration Analysis of Dicentric/Acentric Forms That Are Pathognomic for Acute Whole-Body Irradiation

Dose (Sv)	Per 50 Cells	Per 1000 Cells
0	0.05–0.1	1–2
1	4	88
2	12	234
3	22	439
4	35	703
5	51	1024

Note.—Two different samplings were made of the same set of cells irradiated to each dose level. The results indicate that in a crisis, a 50-cell count may be about as reliable as the much more time-consuming (2 days) standard 1000-cell study, since the two exhibit nearly the same dose-response relationship. Used, with permission, from the REAC/TS Accident Registry.

are *dicentric chromosomes*, with two centromeres (Fig 5a). Dose-response curves for the numbers of dicentrics in cultured peripheral circulating lymphocytes have been developed (Table 10), but their interpretation should involve trained biodosimetrists. Dose-response curves have been developed for various radiations against which numbers of chromosome aberrations and other cellular irregularities in a patient can be compared (Fig 5b and 5c) (60).

Unfortunately, culturing lymphocytes takes 48 hours, and performing the dicentric assay itself is time consuming. Moreover, there are only two laboratories in the United States capable of conducting dicentric chromosomal analysis, at REAC/TS and at the Armed Forces Radiobiology Research Institute (Bethesda, Md); obtaining assay results may take up to a week after small incidents and much longer following mass casualty events.

Immediate General Medical Care and Monitoring of the Heavily Exposed but Potentially Salvageable Patient

The standard medical management of an individual with an acute but potentially survivable radiation exposure (61–64) starts with good medical, surgical, and supportive care. Within hours of an R/N incident, acutely life- and limb-threatening medical and surgical conditions are the first priority, while a medical history and the history of the event are being collected. Once the patient is stabilized, the clinician may then pay attention to the management of direct exposure and of external and internal contamination, bearing in mind that the signs and symptoms of radiation injury and/or illness might not appear for hours to days and sometimes weeks.

Exposures as low as 1–1.5 Sv (100–150 rem) can require the use of antiemetics and close attention to fluid and electrolyte balance. Loss of fluids and electrolytes can be particularly problematic in infants, children, and the elderly.

As the dose increases to greater than about 2 Sv, vomiting may be severe, albeit short-lived, on the order of 1–2 days. Antiemetics such as the phenothiazines, like prochlorperazine (eg, Compazine) or chlorpromazine (eg, Phenergan), are not very effective for radiation-induced vomiting. 5-Hydroxytryptamine$_3$ ($5HT_3$ or serotonin) receptor inhibitors like ondansetron (Zofran) or granisetron (Kytril) may be called for. These will certainly be required should doses be high enough to cause the gastrointestinal syndrome. Pain control should be provided as necessary with oral, intravenous, or intramuscular medications.

Antimicrobials will not be needed immediately following an R/N incident because radiation-related infections will not appear for days. Even those who appear to make it safely through the early stage of their illness, however, do face a serious

danger of potentially fatal sepsis when the neutrophil count passes through its nadir (Fig 4b). The greater the dose, the faster the nadir is reached. Following radiation doses high enough to cause significant ARS, prophylactic and infection-directed antibacterial, antiviral, antifungal, and occasionally anthelminthic agents will be required, along with infectious disease specialty consultation.

If an acute whole-body dose of over 2 Sv is suspected, cytokines or colony-stimulating factors may be appropriate, along with hematology specialty consultation. Cytokines stimulate the production, differentiation, and replenishment of various kinds of white blood cells and have been shown in controlled animal trials to significantly increase the likelihood of surviving high whole-body doses. Some examples are: granulocyte colony-stimulating factor (G-CSF) (filgrastim, Neupogen); pegylated G-CSF (pegfilgrastim, Neulasta); granulocyte macrophage–colony-stimulating factor (sargramostim, Leukine). The Strategic National Stockpile of the Centers for Disease Control and Prevention has been provisioning Neupogen for use in increasing the neutrophil line in humans following a high radiation exposure (65).

Bone marrow stem cell transplants are usually reserved for victims of 6–10-Sv doses without comorbid conditions. But the experience with transplants in accidental radiation exposures has not been promising. Such patients will have a much better chance of survival if transferred to a facility that specializes in management of critically ill pancytopenic individuals. The Radiation Injury Treatment Network of the National Marrow Donor Program (66) is developing a network of specialty treatment facilities and scenarios for management of patients with significant cytopenias.

Diagnosis and Medical Management of Internal Contamination

As suggested above, the routes by which contaminants gain entry into the body are limited: inhalation into the respiratory tract, ingestion into the gastrointestinal tract, percutaneously by transdermal absorption through normal skin, or through open wounds, abrasions, or burns.

The nature of the subsequent radiation exposure is strongly influenced by the physico-chemical form of the contaminants and their radioactive decay characteristics. The form of a radionuclide dictates its level of solubility (and a given isotope may exist in both soluble and insoluble forms), hence its potential for passage across membranes into circulation. A soluble radionuclide will be more readily absorbed, and it is then distributed within the body according to biokinetic principles. Insoluble particles, by contrast, tend not to cross membranes well, and their ultimate disposition and biologic effect will be controlled by factors such as their size—which determines where they may become lodged (eg, at bifurcations of the bronchial tree.) The effect of insoluble isotopes may thus be more localized than that of more soluble forms of the same chemical. Finally, the eventual spatial distribution of the contaminants and their radioactive decay characteristics together determine the deposition of radiation dose.

Contamination around the mouth or nose, or persistently high readings of gamma radiation from a survey meter after repeated external decontamination efforts, may indicate internal contamination. Suggestion of internal contamination by positive nasal or oral swabs should be confirmed through bioassay monitoring of feces and urine and possibly of blood. While difficult (and perhaps impractical) to carry out during a crisis, it is advantageous to estimate the amount of intake of radioactive material by bioassay or by whole body counting, as soon as possible. The Centers for Disease Control and Prevention is currently developing protocols to convert thyroid scanners, gamma cameras, and other radiation detection equipment commonly found in hospitals for use as whole-body counters (67).

The ability to detect internal contamination depends strongly on the types of radiation released by the offending isotope(s). Gamma-emitting isotopes, for example, can normally be detected and identified quite readily by equipment such as Geiger-Muller (GM) probes. Holding a GM probe to the sternum or between the clavicles can provide an effective screen for the presence of internal contamination in a patient not contaminated externally. Also, scintillation detectors routinely available in nuclear medicine departments and in medical and health physics laboratories may be able to detect gamma emitters, including those excreted in bodily fluids. High-energy beta radiation may also be detected by the use of GM probes and scintillation detectors. Alpha and low-energy beta radiations, by contrast, are much harder to sense, particularly in the mass casualty environment. Identifying plutonium, for example, requires use of special detectors or alpha spectroscopy.

Once inside the body, nearly all radioisotopes behave chemically exactly like stable isotopes of the same element. The management of internal contamination is thus much the same as the treatment of poisoning, and it is carried out best by emergency physicians and medical toxicologists. It may be possible to reduce uptake and/or hasten clearance of radioisotopes with standard decontamination and detoxification techniques such as with antacids or a cathartic such as castor oil or magnesium sulfate.

In some cases, when there is reasonable suspicion of significant internal contamination and the radionuclides have been identified, specific medical countermeasures exist (68,69). These should be used as soon as possible, since delays in administration may render them less effective or useless. Following a large release of radioactive iodine, which is unlikely with a radiologic dispersal device but probable with a nuclear weapon or power plant incident, public health officials may recommend administration of potassium iodide (KI), especially to children and pregnant women (70). Radioiodines are known from Chernobyl data (71) to cause thyroid injury and to be carcinogenic, especially to the fetus and to children under 18 years of age. If taken within 4–6 hours of contamination, stable iodine in the form of nonradioactive KI saturates iodine binding sites within the thyroid and inhibits incorporation of radioiodines into the gland. If the individual remains in a contaminated area,

KI should be readministered daily. A contraindication to KI administration is a known allergy to iodine.

Chelating agents such as diethylenetriamine-pentaacetic acid (DTPA) as the zinc or calcium salts (Zn- and Ca-DTPA) can expedite the removal of radioisotopes of the rare earths and of actinides such as californium, plutonium, and americium (72). Sodium bicarbonate is used to treat renal chemical toxicity of uranium (which is generally a far greater hazard than its radiologic toxicity.) Oral administration of insoluble Prussian blue (ferric III hexacyano-ferrate II) is the countermeasure of choice for cesium-137 (found in high concentrations for miles around Chernobyl following the accident), and for isotopes of thallium (73).

The decision to treat or not to treat for internal contamination is based on risk/benefit considerations of the dose and the age and condition of the individual patient. Likewise, the judgment on when to stop treatment is at times a complex issue, requiring assessment of the effectiveness of treatment by sequential bioassays and consideration of the risks versus the benefits of continuing the therapy. Several readily available reports provide medical guidance for such therapies (34,74).

Children

Children have special medical needs during a radiologic emergency (75), because they are at least as likely as adults to suffer deterministic health effects. Also, some of their tissues are inherently more radiosensitive to stochastic effects, and they breathe more rapidly, thereby inhaling radioactive dust and depositing it in their lungs at a greater rate; for both reasons, they are at greater jeopardy of eventually developing cancer. They tend to be emotionally less resilient as well, and may incur long-term psychologic harm during a disaster. The American Academy of Pediatrics (76) has prepared a set of guidelines and recommendations for children in a radiologic emergency, and the JumpSTART Web site provides an approach to pediatric triage during crises (77).

Long-term Concerns

The primary subject of this article has been the emergency medical management of immediate health threats in persons involved in radiologic incidents, but it is recognized that stochastic and some delayed deterministic effects may arise over the long term. Anyone suspected of having received a whole-body dose of 100 mSv (10 rem) or more, even if there is no evidence of deterministic effects, might be advised to undergo periodic health examinations.

Conclusion

Physicians and other health personnel may be called on without warning to care for persons involved in a major radiologic incident associated with the detonation of a nuclear weapon or improvised nuclear device, the meltdown of a nuclear reactor, or the dispersal of radioactive contamination, such as by a radiologic dispersal device. Radiologists, radiation oncologists, nuclear medicine specialists, and medical and health physicists, in particular, will be looked to for leadership and expertise because of their knowledge of radiation and its biologic effects.

There is considerable technical and management guidance available to assist in guiding the health care response to an emergency situation that otherwise can easily degenerate into panic and chaos, and much of this is condensed and provided or referred to in this article.

The first rule in effective management is to be prepared. Preparation requires becoming knowledgeable about various emergency scenarios and thinking through appropriate responses to them before they occur. That is why it is essential for radiologists, radiation oncologists, nuclear medicine specialists, medical physicists, and emergency physicians to make a serious effort to be prepared to confront and manage the health care response to any nuclear or radiologic emergency that might occur.

Additional Radiologic Emergency Response Information and Resources

Along with the references indicated above, a range of information may be found in Appendix E5 (online). In urgent situations, three national centers and a Web site that can provide immediate and valuable guidance and assistance are as follows:

Armed Forces Radiobiology Research Institute (AFRRI) (Bethesda, Md), Medical Radiobiology Advisory Team (MRAT), U.S. Department of Defense. Web site: www.afrri.usuhs.mil. Phone: (301) 295–0316.

Centers for Centers for Disease Control and Prevention (CDC) (Atlanta, Ga), Emergency Preparedness and Response. Web site: www.bt.cdc.gov. E-mail: cdcinfo@cdc.gov. Phone: (800) CDC-INFO.

Radiation Emergency Assistance Center/Training Site (REAC/TS) (Oak Ridge, Tenn), U.S. Department of Energy. Web site: www.orise.orau.gov/reacts, Phone: (865) 576–1005.

Radiation Event Medical Management (REMM), U.S. Department of Health and Human Services. Web site: www.remm.nlm.gov.

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