Textbook of Military Medicine

Part I

Warfare, Weaponry, and the Casualty

Volume 2

MEDICAL CONSEQUENCES OF NUCLEAR WARFARE

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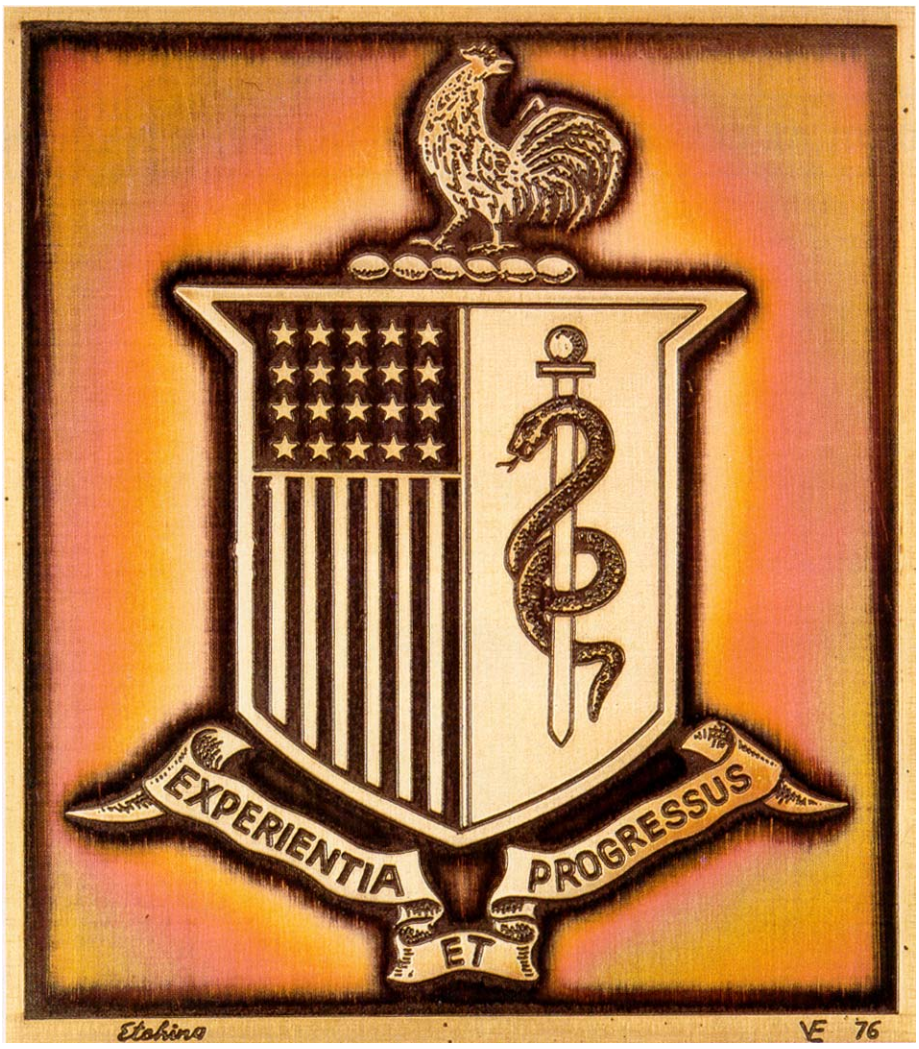

The Coat of Arms
1818
Medical Department of the Army

A 1976 etching by Vassil Ekimov of an
original color print that appeared in
The Military Surgeon, Vol. XLI, No. 2, 1917

The first line of medical defense in wartime is the combat medic. Although in ancient times medics carried the *caduceus* into battle to signify the neutral, humanitarian nature of their tasks, they have never been immune to the perils of war. They have made the highest sacrifices to save the lives of others, and their dedication to the wounded soldier is the foundation of military medical care.

Textbook of Military Medicine

SERIES ON COMBAT CASUALTY CARE

Published by the

Office of the Surgeon General
Department of the Army, United States of America

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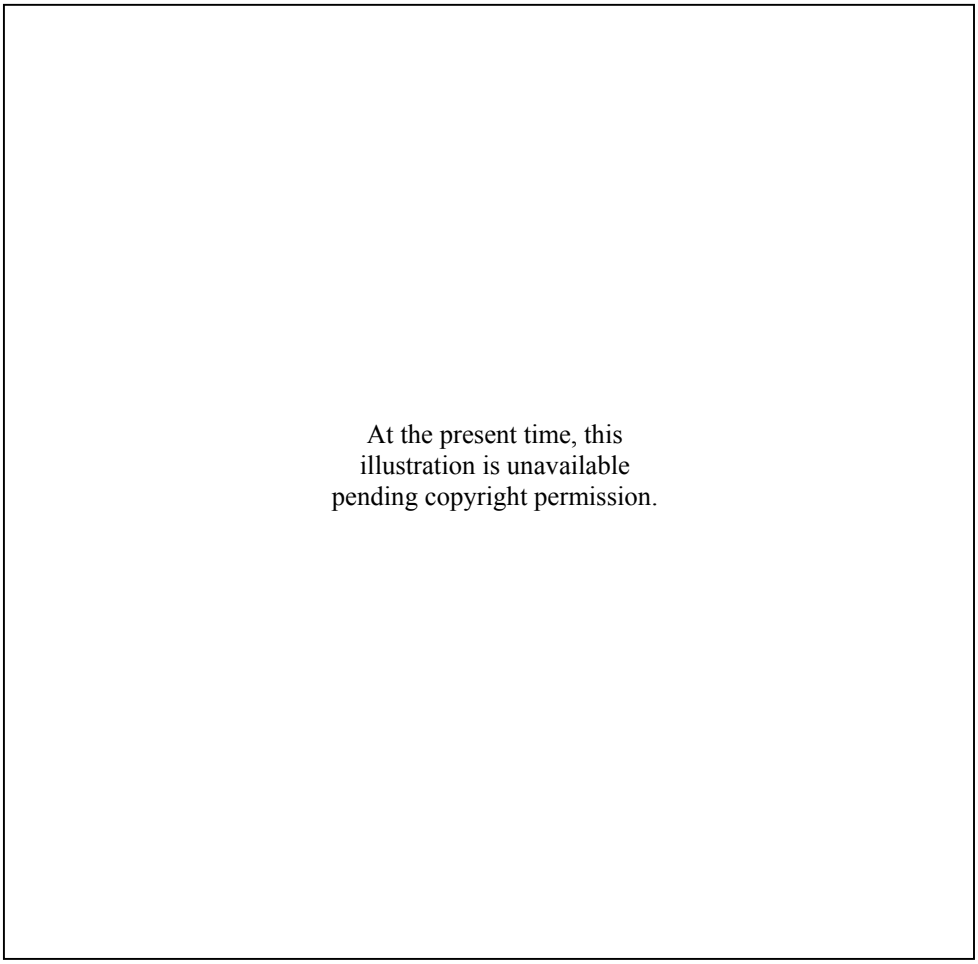

The artist, Ken Nakagawa, witnessed rescue operations performed by Japanese naval personnel along a riverbank in Hiroshima at 0840 on 6 August 1945. Approximately 280,000 deaths occurred as a consequence of this first atomic bombing. The reactions of other survivors are explored in Chapter 8.

Reprinted, by permission, from the Japanese Broadcasting Corporation (NHK). *Unforgettable fire: Pictures drawn by atomic bomb survivors*, 1st American ed., 90. New York: Pantheon Books, Random House, Inc.,

MEDICAL CONSEQUENCES OF NUCLEAR WARFARE

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5111 Leesburg Pike, Falls Church, Virginia 22041-3258

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Library of Congress Cataloging in Publication Data

Medical Consequences of Nuclear Warfare

Includes index.
1. Radiation-Physiological effect. 2. Nuclear weapons-
Physiological effect. (eds.) Zajtchuk, R.; Jenkins, D. P.; Bellamy, R. F.; Ingram, V. M.
I. Walker, Richard I. II. Cerveny, T. Jan

PRINTED IN THE UNITED STATES OF AMERICA

96 95 94 93 92 91 90 89 5 4 3 2 1

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Foreword

The dramatic technological, social, and economic progress of the twentieth century has yet to prevent the use of armed conflict to resolve political differences among nations. As those of us in military medicine prepare to support our forces into the next century, we must continually be ready for the many challenges presented by modern warfare.

The Army Medical Department has embarked on an ambitious readiness initiative. This new doctrine focuses on far-forward surgical care, increased intensive-care capabilities, a policy of returning soldiers to duty as far forward as possible, improved ground and air evacuation capabilities, new medical logistics systems that incorporate blood-distribution networks, and improved management of combat stress. Our goals are to maintain our momentum as we conserve fighting strength and to support our soldiers and their families both in peacetime and in time of war.

The military health-care system is the largest comprehensive health-care organization in the United States. Because the vast majority of our patients are not active duty military personnel, it may seem that our day-to-day activities are far removed from what we would be required to do during time of war. The ability to deploy a highly trained medical corps to any area of the world, however, is our highest priority. To be effective, we must not only maintain the highest standards of technical competence, but must also be prepared to use our skills creatively and courageously in situations that may be primitive, dangerous, or unknown. Major General James H. Rumbaugh, the late commander of Walter Reed Army Medical Center (who aptly described his organization as "the largest live-fire range in the Army"), understood that everything we do in our daily practice hones our expertise. Our readiness initiative will provide a clearer combat context in which to apply that expertise. Lessons of medical survival have been learned in previous conflicts at great cost. We cannot afford to forget them.

It is my hope that you will find the *Textbook of Military Medicine* series a useful addition to your readiness training programs, and that it will stimulate you to think about and plan for what will be required of each of us should the need arise to make a transition from peace to war.

Lieutenant General Frank F. Ledford, Jr.
The Surgeon General
U.S. Army

April 1989
Washington, D.C.

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TABLE 1-2
MEDICAL CONSEQUENCES OF NUCLEAR WEAPONS

Performance Decrement	Acute Effects	Delayed Effects
ETI*/Hypotension	Infection	Cancer
Motor	Bleeding	Life shortening
Cognitive	Dehydration	
Emesis/Diarrhea	Delayed wound healing	

*Early Transient Incapacitation

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Chapter 2

ACUTE RADIATION SYNDROME IN HUMANS

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INTRODUCTION

The importance of human sensitivity to ionizing radiation was recognized even before the detonation of the first nuclear weapon. However, the exact relationship of dose to human mortality is still not precisely known because clear human data are lacking, and analyses of human mortality have been based primarily on data from radiation accidents, radiation therapy patients, and atomic-bomb victims. These studies have been faulted because of the small numbers of subjects, imprecise dosimetry, or patients' preexisting health problems and treatments. Therefore, many studies with laboratory animals have been undertaken in an effort to define the relationship between radiation exposures and effects. Several comprehensive analyses of human data and animal data have been conducted in an effort to derive a dose-response for humans.

Information on humans and animals has made it possible to describe the symptomatology associated with the acute radiation syndrome (ARS). In humans, ARS is defined as the symptoms manifested after exposure to ionizing radiation, and is often called radiation sickness. From a physiological standpoint, ARS is a combination of subsyndromes. They appear in stages and are directly related to the level of radiation received (Figure 2-1). These subsyndromes begin to occur within hours after exposure and may last for several weeks.

PATHOPHYSIOLOGICAL SUBSYNDROMES

Radiation damage results from the sensitivity of cells to radiation, and those that replicate most rapidly are the most sensitive to radiation exposure. In descending order of sensitivity, these cell types are spermatogonia; lymphocytes; erythroblasts; other hematopoietic cells; cells of the small intestine, stomach, colon, epithelium, skin, CNS, muscle, and bone; and the protein collagen. Mature cells that are more highly differentiated appear to be the least affected by radiation. This difference in cell sensitivity is the basis for the distinction among the three subsyndromes of ARS.

In order of their occurrence with increasing doses of radiation, ARS is divided into hematopoietic, gastrointestinal, and neurovascular subsyndromes.

Each subsyndrome can be further divided into four stages: *prodromal, latent, manifest illness,* and *recovery.* Prodromal symptoms begin a few hours to 4 days after exposure. The severity, time of onset, and duration of symptoms relate directly to the exposure dose received. The latent period is a brief reprieve from symptoms, when the patient may appear to have recovered. This reprieve may last up to 4 weeks, depending on the dose, and then is likely to be followed by 2-3 weeks of manifest illness. The manifest illness stage is the most difficult to manage from a therapeutic standpoint, for this is the maximum state of immunoincompetence that the patient will suffer. If the patient survives the manifest illness stage, recovery is almost assured. Therefore, treatment during the first 6

weeks to 2 months after exposure is crucial to ensure recovery from a rapidly received, high dose (less than 5 Gy) of ionizing radiation.

Hematopoietic Subsyndrome

The target cells of the hematopoietic tissue are the stem cells. Their anatomical location in the bone marrow distributes them throughout the body. Dorsal exposure would maximize damage to the hematopoietic system, because the greatest percentage of active bone marrow lies in the spine and dorsal regions of the ribs and pelvis. Vertical exposure would be the least damaging per equivalent dose, due to absorption and consequent nonuniform dose distribution, thus sparing the dorsal marrow. A dose-dependent suppression of bone marrow may lead to marrow atrophy and pancytopenia. Prompt radiation doses of about 1-8 Gy cause significant damage to the bone marrow. Doses of approximately 3 Gy may result in death to 50% of exposed persons.[1] The biological response of bone-marrow stem and progenitor cells to radiation exposure is exponential in nature. For example, halving the dose received does not increase the survival of stem cells from 1% to 50%, but to only 10%. Therefore, shielding remains the best protection of bone marrow.

Prodromal symptoms may include nausea, vomiting, anorexia, and diarrhea. If severe diarrhea occurs during the first 2 days, the radiation dose may have been lethal. The hematopoietic prodrome may last up to 3 days. This is followed by about 3 weeks of latency, during which the patient will suffer from significant fatigue and weakness. The clinical symptoms of manifest illness appear 21-30 days after exposure, and may last up to 2 weeks. Severe hemorrhage from platelet loss and infection associated with pancytopenia from bone-marrow suppression are the lethal factors in the hematopoietic subsyndrome. Platelet counts of fewer than 20,000/mm^3 (hemocytometer counting chamber), decreased erythrocyte counts, and severely suppressed white cell counts (fewer than 1,000) may be seen. Clinical hematological studies (complete blood count with platelets) may follow a course similar to that shown in Figure 2-2. There is a progressive decrease in peripheral cellular elements with increasing radiation dose. Specifically, a 50% decrease of absolute lymphocytes within the first 24 hours, followed by a second drop within 48 hours, is pathognomonic of potentially lethal injury from penetrating ionizing radiation.

The nuclear accident in Chernobyl provided information indicating that the total hematological profile must be used in predicting the radiation dose.[2] As shown in Figure 2-2, the systemic granulocyte count will increase at varying times after exposure, and may result from increased chemotaxis due to cell damage after irradiation. This transient increase may provide a false low interpretation of dose, and therefore should not be used as the sole indicator of dose received. However, a lowered granulocyte count may indicate the beginning of an immunocompromised state, which will likely be followed by the onset of fever and possibly severe infection.

Overall, the systemic effects that can occur from the hematopoietic subsyndrome include immunodysfunction, increased infectious complications, hemorrhage, anemia, and impaired wound healing. Impaired wound healing may be due in part to endothelial damage, which significantly depresses the revascularization of injured tissue.[3]

Gastrointestinal Subsyndrome

The gastrointestinal subsyndrome overlaps the hematopoietic subsyndrome, but its consequences are more immediate. At radiation doses above 12 Gy, this subsyndrome supersedes the hematopoietic subsyndrome in lethality. Its prodromal stage includes severe nausea, vomiting, watery diarrhea, and cramps occurring within hours after irradiation, followed by a much shorter asymptomatic latent period of 5-7 days. Then the manifest illness begins, with vomiting and severe diarrhea accompanied by fever. At higher doses, bloody diarrhea, shock, and death may ensue.

The intestinal mucosa suffers severe pathological damage following radiation exposure. The turnover time of 3-5 days for intestinal mucosal epithelial cells explains the shortened latent period. Since severely damaged crypt stem cells do not divide, the aging mucosal lining is shed and not replaced. This results in loss of absorption and provides a portal for intestinal flora to enter the systemic circulation. Figure 2-3 depicts vascular coalescence, which also significantly decreases intestinal absorption abilities. Severe mucosal hemorrhage has been seen in experimental animal models (Figures 2-4 and 2-5). The overall intestinal pathology includes disturbance of absorption and secretion, glycocalyx disruption, mucosal ulceration, alteration of enteric flora, depletion of gut lymphoid tissue, and motility disturbances.[4]

Systemic effects of this subsyndrome may include malnutrition resulting from malabsorption; vomiting and abdominal distension from paralyticileus; dehydration, acute renal failure, and cardiovascular collapse from shifts in fluids and electrolytes; anemia from gastrointestinal bleeding; and sepsis from damaged intestinal lining.

Neurovascular Subsyndrome

This subsyndrome is difficult to define. The lethal dose is over 30 Gy, but there is little information on these doses for human exposure, and the causes of death are confusing.[1,3,5] Cardiovascular shock accompanies such high doses, resulting in a massive loss of serum and electrolytes through leakage into extravascular tissues. The ensuing circulatory problems of edema, increased intracranial pressure, and cerebral anoxia can bring death within 2 days.

The stages of the neurovascular subsyndrome are extremely compressed. The prodromal period may include a burning sensation that occurs within minutes,

nausea and vomiting that occur within 1 hour, and confusion, prostration, and loss of balance. During the latent period, apparent improvement for a few hours is likely to be followed by severe manifest illness. Within 5-6 hours, the overt clinical picture proceeds with the return of severe watery diarrhea, respiratory distress, and gross CNS signs. After receiving doses in this range, two victims of separate uranium or plutonium recovery accidents survived fewer than 48 hours, even though they received optimal life support in excellent care facilities.

The pathology of this subsyndrome may be due to massive damage of the microcirculation. This has been postulated as a causative mechanism in the damage of some organs. Preliminary experimental evidence indicates that the cause of initial hypotension may be an early, overwhelming surge of histamine released from degranulated mast cells.[5,6] In fact, animal models did not suffer this hypotension when pretreated with histamine (H_1) blockers.[7,8]

The radiation threshold for this dual subsyndrome is not as well defined as it is for the others. Experimental evidence indicates that 50 Gy will elicit the neurovascular subsyndromes. Whether the dose is 50 or 100 Gy is inconsequential; either is a supralethal dose resulting in severe performance decrement. Figure 2-6 shows the occurrence of radiation effects in relation to dose and time. Table 2-1 charts the pathophysiological events.

DETERMINANTS OF RADIATION EFFECTS ON HUMANS

Energy deposition, known as *linear energy transfer* (LET), can be correlated to the severity of damage to the tissue. Gamma and X rays, which are primarily responsible for ARS, pass through tissue almost unimpeded by the skin or protective clothing. Thick shielding (such as lead, concrete, or dirt) is required to protect a person from these radiations. These rays are called *low LET* because they do not leave a great deal of their energy behind. Exposure to gamma emitters (such as cobalt-60) results in an accumulation of the dose within the first few centimeters of tissue, followed by a gradual decline of the dose level to 50% at the radiation's exit from the body. In contrast, *high-LET* neutron exposure results in significant absorption of energy within the first few centimeters, with diminution of dose at increasing tissue depth. In these cases, unilateral radiation results in more uniform exposure with gamma than with neutron radiation. Bilateral or multilateral exposure increases the uniformity of dose in all cases.

Alpha and most beta particles have low energy levels and cannot pass through skin (high-energy beta excepted) or clothing. Therefore, internalization (ingestion, inhalation, or absorption through a wound) and systemic contamination with alpha or beta radionuclides must occur for these radioactive particles to cause problems. Once internalized, they are a significant threat, because almost all of their energy is deposited in a short path through tissue or even in a single cell.

Lethality Curve

The slope of a lethality curve is weighted heavily by data at each extreme of its distribution. In the majority of experimental cases, the ratio of the data points is less than 2, independent of species (Figure 2-7). The more inbred and homogenous the population, the steeper the slope. This fact underscores the importance of reliable dosimetry, not only in the experimental situation but also in accurately determining the human exposure doses after a nuclear accident. In a recent examination, this correlation of a steep dose-effect relationship (slope) was evaluated using available data from canine studies.[9] Purebred and inbred populations did not appear to be either more sensitive or more resistant than mongrels. Given the genetic heterogeneity of humans, this ratio has been useful in extrapolating from animal data to the human dose-response curve, and in defining a lethal dose of radiation that will kill 50% of the healthy, untreated, exposed personnel (the LD_{50}) within 30 to 60 days after exposure. In spite of the heterogeneity surrounding LD_{50} values, it "seems possible to conclude that the doses giving between 90%-95% mortality in most animal experiments are about twice those giving 5%-10% mortality."[10] In a recent review of animal data, a uniform dose normalized to the LD_{50} (D/LD_{50}) revealed that no deaths occurred when D/LD_{50} was less than 0.54.[11] When D/LD_{50} was greater than 1.3, mortality was 100%. Total survival in a population can apparently be changed to total mortality by increasing the dose by a factor of 2.4. Relationships between dose and lethality, drawn from a large number of animal studies, emphasize two important points on extrapolation to the human radiation response: *(a)* reliable dosimetry is extremely valuable, and *(b)* either therapy or trauma can significantly shift the dose-response relationship. An error in dosimetry of 0.5-1.0 Gy can result in large shifts along the dose-response curve, and effective therapy can increase the LD_{50} by approximately 1.0 Gy. The degree of trauma depends on the duration and intensity of the radiation exposure, and it can shift along the mortality curve.

Modification of Dose-Response Curve

Radiation lethality may be a consequence of changes in the cellular kinetics of renewal systems critical for survival.[12,13] If this is correct, then modification of the dose-response relationship is achievable by replacement of the mature functional cells or their essential factors, or by actual substitutions in the damaged cell-renewal system.

Factors that compromise or damage the hematopoietic system or the immune system will also negatively affect the dose-response curve. Severe trauma, poor nutritional status, and stress are in this category. Other factors that significantly modify the dose-effect curve are radiation quality, exposure geometry (such as partial-body exposure or nonuniform exposure), and dose rate.

Influence of Radiation Quality and Exposure Geometry on LD_{50}

Distribution of radiation dose (energy deposition) throughout the target tissue varies significantly with the energy and quality of radiation and with the geometry of the exposure. Figure 2-8 illustrates the effects of tissue depth on absorbed radiation dose from unilateral cobalt-60 and 1 MeV (million electron-volts) of mixed neutron-gamma radiations. To reconstruct the effects of an accidental exposure involving neutrons, we must consider the tissue depth of a large-animal model (such as the canine) and that of humans, relative to the absorption characteristics of these two different radiation types (gamma and neutron, 1 MeV).

Equivalent doses of different types of radiation, or of the same type at different energy levels, do not produce equivalent biological effects. However, the *relative biological effectiveness* (RBE) of two types of radiation can be compared. A significant number of studies establishes the LD_{50} for hematopoietic death in canines at approximately 2.60 Gy for 1,000 kVp (plate voltage in kiloelectron-volts) of cobalt-60 radiation, or 2,000 kVp of X radiation. For lower-energy X radiation (50-250 kVp), an average dose of 2.28 Gy would yield this LD_{50}.[14-21] These values suggest an RBE of approximately 0.87 for radiation higher than the standard 250 kVp of X ray energy. Canine exposure to mixed-fission neutron-gamma radiation yields an LD_{50} value of 1.48 Gy (compared to a derived value of 2.60 Gy for cobalt-60).[15] This results in an RBE of approximately 1.7. Using a neutron spectrum of similar energy, an LD_{50} of 2.03 Gy (compared to 2.80 Gy for 1 MVp of X radiation) was determined to have an RBE value of 1.38.[22] An RBE value of approximately 2.0 has been reported for rhesus monkeys exposed to fission neutrons of 1 MeV energy (the LD_{50} value was 2.60 Gy) and for X radiation of 300 kVp energy (the LD_{50} value was 5.25 Gy).[23] A significant RBE has been observed in the rhesus (LD_{50}) using gamma-neutron exposure, compared to the RBE for 250 kVp of X radiation.[24,25] Several studies used mice to establish RBE values for fission and high-energy neutrons pertaining to X radiation and cobalt-60 radiation.[25-28]

A radiation dose delivered to hematopoietic stem cells in bone marrow is the most damaging to the organism. Therefore, unilateral exposure with either gamma or neutron radiation will result in nonuniform dose distribution, whereas bilateral or rotational whole-body neutron exposure will have a greater RBE. Unilateral exposure usually occurs in accidents or warfare. Exposure to any type of unilateral radiation can result in lower doses to stem-cell populations that are distant from the source, with a consequent rise in the LD_{50} value (Table 2-2).

Influence of Trauma on LD_{50}

The combination of radiation exposure and trauma produces a set of circum-stances not encountered by most military and civilian physicians. In combined injury, two (or more) injuries that are sublethal or minimally lethal when

occurring alone will act synergistically, resulting in much greater mortality than the simple sum of both injuries would have produced. The mechanisms responsible for combined-injury sequelae are unknown, but they can significantly increase the consequences of radiation exposure across the entire dose-response curve. It must be emphasized that the survival of a patient following exposure in the hematopoietic dose range requires *(a)* a minimum critical number of surviving stem cells to regenerate a competent host defense system, *(b)* the functional competence of surviving cells composing the specific and nonspecific immune system, or *(c)* effective replacement or substitution therapy during the critical postexposure cytopenic phase. Trauma alone, depending on its intensity, may effectively depress host resistance to infection.[29-35] When imposed on a radiation-injured system, it can be lethal. In most instances, trauma symptoms will either mask or exacerbate the first reliable signs of radiation injury. This will cloud the situation if one is relying on biological dosimetry and prodromal symptoms for estimation of dose. In addition, the choice of treatment in these cases should include consideration of not only the patient's initial status but also the condition that will exist 7-21 days later when the radiation effects are seen.

Relatively few animal models of combined injury are available for determining effective therapy. The few reported studies demonstrate the synergistic effect of combined injuries. Sheep were exposed to 4 Gy of mixed neutron-gamma radiation and then 1 hour later subjected to an abrupt overpressure; this resulted in increased mortality from 25% for irradiated-only animals to 50% for the combined-injury animals.[36] A rat model showed a synergistic effect when a 250-kVp X-ray dose (LD_{50}) was followed in 7 days by a low-lethal (5%) level of air blast.[37] Mortality increased from approximately 46% for the irradiated-only animals to 76% for the combined-injury animals, and was related to radiation-induced thrombocytopenia, which compromised normal coagulation and maintenance of the capillary endothelium.

An open skin wound (combined injury) markedly increases the chances of infection. The immediate closure of wounds has been recommended.[38] Mortality in mice from exposure to 5.1 Gy of gamma radiation alone rose from 25% to 90% when combined with open dorsal skin wounds occurring 2 days after exposure. If wounds were immediately closed, mortality decreased to 18%. Closing of the skin wound obviously affected the mechanism of pathogenesis.

In combined injuries, burns produce the most significant synergistic increases in mortality. The dog, pig, rat, and guinea pig have been studied as animal models.[34,39-43] Table 2-3 summarizes this synergistic effect on the lethality of combined radiation and trauma. As little as 0.25 Gy, combined with a burn of 20% body surface area, increased mortality in dogs from 12% to 20%.[43]

In the early 1980s, investigators performed the most comprehensive analysis to date of the effect of combined injury (thermal and skin wound) on lethality and on the suppression of host resistance to subsequent bacterial challenge.[44,45] In

addition, they used cobalt-60 gamma versus mixed-fission neutron-gamma radiations in various ratios of LD_{50} on mice that had either thermal injuries or skin wounds. The addition of fission-energy neutrons to gamma radiation significantly lowered the LD_{50} in radiation-only experiments to give RBE values as high as 2.5. The addition of trauma to radiation exposures also significantly reduced the LD_{50}. The effect of combined injury on lethality was dominated by radiation. The RBE did not change with the addition of trauma.

Injuries to the abdomen may present significant problems to the irradiated subject. Blast overpressure, blunt trauma, and penetrating trauma are all significant causes of abdominal injury. The impact of laparotomy or splenectomy in mice that had received whole-body radiation has been evaluated.[38] Exposure to 5.1 Gy alone caused mortality of 27%, whereas laparotomy or splenectomy alone caused an approximate 5% mortality. Splenectomy at 2, 4, or 8 days after irradiation increased the mortality to 60%, 75%, and 85%, respectively. Laparotomy combined with radiation caused maximum mortality when surgery was performed on day 8. The role of the spleen in nonspecific resistance to bacterial infection has recently been demonstrated.[46]

The impact of combined injuries on the radiation dose-effect curve depends on the intensity and the time of injury relative to radiation exposure.[47,48] The biological consequences of these combined injuries will significantly affect the patient's abilities to survive and recover, and will markedly increase the casualty burden on medical personnel. Those patients in Hiroshima and Nagasaki who suffered conventional trauma along with radiation exposure developed significant complications 2-3 weeks later, corresponding to the time of hematopoietic depression. Until the 1986 reactor disaster in Chernobyl, the victims of Hiroshima and Nagasaki provided the only documentation on human radiation injuries and associated trauma. Hospitalized Chernobyl victims also experienced medical complications associated with bone-marrow damage and immunosuppression.

Effect of Clinical-Support Therapy on LD_{50} Dose-Effect Curve

Modification of survival throughout the LD_{50} dose range is achievable using a simple regimen of clinical support to replace or substitute the depleted functional cells after stem-cell destruction. In the cases of large-animal models (monkey, canine, and swine) and the human, therapy is directed at replacing the functions of the granulocytes and platelets. Experimental work performed more than 20 years ago showed the efficacy of supportive care centered on systemic antibiotics and transfusions of fresh platelets. Several canine studies indicated that antibiotics, singly or in combination, were successful in reducing mortality in the LD_{50} range.[18,49-51] Combination antibiotics, in conjunction with fresh whole-blood transfusions and parenteral fluids, have been effective in controlling dehydration and thereby reducing mortality. Reports that hemorrhage is easier to control than infection may be traced to the fact that several types of opportunistic pathogens are capable of overwhelming a compromised host.[18]

In an attempt to determine the lowest dose at which spontaneous regeneration would not occur, the dose range was extended in a later animal study from 4.0 to 5.5 Gy, well into 100% lethality (LD_{100}). The dose of 4.2 Gy resulted in an LD_{100}. Survival was significantly increased with good clinical support. This support consisted of *(a)* several antibiotics (penicillin G, dihydrostreptomycin, and tetracycline) administered at the onset of fever (8-13 days after exposure) and continued until fever subsided for 3-4 days and white cell count was greater than 1,000/mm^3; *(b)* the infusion of fresh platelet-rich plasma from 50 ml of blood, given when blood platelet levels were below 5,000/mm^3 (10-12 days after exposure); and *(c)* fluid therapy (isotonic saline or 5% dextrose) given during the period of anorexia. Soft food was usually given during this period to entice the animals to eat. The success with these regimens supports the hypothesis that infection and hemorrhage are the main contributors to lethal consequences of radiation exposure in the hematopoietic subsyndrome range. Controlling infection during the critical granulocytopenic and thrombocytopenic phase is the limiting factor in successful treatment.[49,51]

These studies have been extended over a dose range that is capable of determining the shift in LD_{50} that is due to treatment. Figure 2-9 shows the shift in the canine LD_{50} from 2.60 Gy to approximately 3.39 Gy measured as midline tissue dose. This results in a dose reduction factor of 1.3. The treatment regimen was essentially the same as above, with the addition of the newer antibiotics, gentamicin and claforan (cephotaxime-$S0_4$).[15] These collective data indicate that modest clinical care consisting of the infusion of fluids, antibiotics, and fresh platelets is capable of shifting the LD_{50} by a factor of 1.5. A more intensive regimen of support, including use of a sterile barrier and selective decontamination of intestinal bacteria, should allow an even greater shift in the LD_{50}. It must be emphasized that the practical application of these concepts requires that the damage to the stem-cell system be reversible; that is, the surviving fraction of hematopoietic stem cells must be capable of spontaneous regeneration.

Exposure Geometry: Heterogeneous Partial-Body and Nonuniform Exposure

Partial-body exposure can result in death through irradiation of specific target organs, such as the brain, lungs, and gastrointestinal structures. However, significant variations in the hematopoietic subsyndrome and related lethality can be seen when portions of the active marrow are either shielded physically from exposure or receive a smaller radiation dose due to nonuniform dose distribution through the body tissue. The earliest report of a shielding effect on the hematopoietic system was in 1963.[52] Exteriorized spleens of mice were shielded, which increased the LD_{50} from 550 to 975 R (roentgens). It was concluded that the shielded spleen contained competent and mobilizable hematopoietic stem cells that were capable of totally repopulating the depleted marrow space and significantly modifying the hematopoietic subsyndrome's dose-effect relationship. Many later experiments supported this finding by shielding either the hind limbs or tails of mice. A further

comparison in mice has been made of the therapeutic efficacy of this autorepopulation versus the efficacy of autologous and/or syngeneic bone-marrow transplantation.[26] In this study, one leg was shielded from lethal total-body exposure, allowing stem cells of the shielded leg to reseed the irradiated marrow space. Another set of mice received a similar exposure with the shielded leg later amputated. The marrow contents were harvested by a grinding technique and then auto-transplanted. (The grinding allowed greater efficiency in the stem-cell harvest.) Results indicated that autorepopulation of the marrow was more efficient than marrow transplant.

A series of experiments using canines further illustrated the protective effects of partial-body shielding.[53,54] Large-animal models can not only illustrate the relationships between tissue depth and dose, but can also approximate the nonuniform effects of exposure for more reliable extrapolation to the human radiation response. Shielding the lower body indicated an approximately sevenfold increase in LD_{50}.[54] One report emphasized that considerable hematopoietic tissue may be spared by nonuniform exposures to cobalt-60 gamma radiation.[55] Results indicated that the greater the dose gradient and the more nonuniform the exposure, the greater the survival of stem cells that are capable of repopulation.

These canine experiments illustrate the complexity of determining the dose received during an accidental exposure. Accidental whole-body irradiation will most likely not be strictly unilateral, due to backscatter and reflection of the radiation. It is also possible that some body regions may be shielded. These factors, as well as the anatomical position of the exposed subjects, can either increase or decrease the total dose received. Shielding and nonuniform dose distribution can therefore differ markedly in how much hematopoietic tissue they spare. The biological response of marrow stem and progenitor cells to radiation is exponential in nature.

Considerations on Establishing the Human LD_{50}

Similarly, it is difficult to calculate accurately the dose that a human has received after accidental radiation exposure. Radiation quality or type, dose rate, shielding, exposure geometry, and coincident trauma can significantly modify the relationship of dose and response.

Several comprehensive analyses of human and animal data have been conducted over the years in an effort to derive a dose-response curve for humans. Some reports serve as landmarks, but none has been completely successful. The quest for an LD_{50} for humans began in the late 1940s and continues today.[10,56,57] The most recent activity on this subject has shifted from the United States to the United Kingdom, where interest from the British Home Office produced comprehensive analyses.[10,58,59] The suggestion emerging from these analyses—that the LD_{50} might be as high as 6 Gy (body surface, free-in-air dose)—was controversial in

light of the long-held view that the value was 4.5 Gy or less. The 6-Gy free-in-air dose corresponds to an approximately 4.5-Gy bone-marrow dose, and the 4.5-Gy free-in-air dose corresponds to a 3.6-Gy bone-marrow dose. The 1986 LD_{50} value of 1.54 Gy to the bone marrow added to the controversy and sparked new interest in resolving these discrepancies.[59]

Available data on uncomplicated radiation exposures to the human within the hematopoietic-subsyndrome range are relatively limited. The evidence to date (excluding the 1986 nuclear disaster in Chernobyl and the 1987 radiation isotope incident in Goiânia, Brazil) is from three sources: *(a)* twenty cases of radiotherapy with whole-body, bilateral exposure to gamma radiation; *(b)* two nuclear criticality accidents involving mixed neutrongamma exposure of nine persons, one of whom died; and *(c)* the cases of thousands of persons exposed to the nuclear detonations over Hiroshima and Nagasaki in 1945. The following descriptions of the radiotherapy patients and nuclear criticality patients illustrate the type of information that, until recently, was used in determining the human LD_{50}.

Radiotherapy. Twenty adolescent patients (nineteen with Ewing's sarcoma and one misdiagnosed who actually had leukemia) were uniformly exposed to 3.0 Gy of whole-body cobalt-60 gamma radiation as a midline tissue dose at a dose rate of 0.2 Gy/minute.[60] All patients survived for at least 1 year. It appears that this experience would set the lower limit for the lethal dose at a dose greater than 3.0 Gy. However, several modifying factors must be considered. These patients were given excellent supportive clinical care during their hospital stay. They received fluids, electrolytes, and blood replacement (platelets for some) as necessary, and simple antibiotic treatment while under barrier nursing. It has been recently revealed that many of these patients received local radiation to the sites of the tumors before, and in some cases after, the whole-body exposure. These prior exposures complicate the picture because of possible abscopal effects on distant hematopoietic tissue. It is difficult to determine the effect of hospital-based care and support, but the Chernobyl experience and animal data point to a significant decrease in lethal consequences.

Radiation Accidents. Of many radiation accidents reviewed (Chernobyl excluded), two involved shielding, dose uniformity, and acute exposure (estimated as 2-10 Gy) that were comparable to LD_{50} values in humans. Both accidents were criticality accidents that involved fission neutrons, low-energy photons, and high-energy gamma rays. Four of the seven male workers exposed in the 1958 Y-12 Oak Ridge, Tennessee, accident and five of the workers exposed in the 1958 Vinca, Yugoslavia, accident are considered to have received relevant radiation doses.

Reconstruction of the Y-12 accident dose indicates a total marrow dose range of 3.25-4.40 Gy for upper limits to 1.9-2.6 Gy for lower limits, assuming lateral or anterior-posterior exposure.[10] These workers most likely were exposed to two

pulses separated by several seconds. The accident occurred during maintenance operations at a fuel-reprocessing plant. A uranyl nitrate solution was inadvertently allowed to collect, and a fission chain reaction began, followed by a second reaction and perhaps more. The first reaction probably gave the greatest part of the total dose to the workers. Seven persons received 1.0 Gy or more, and of them, four are considered to have received the higher homogeneous doses, which are more relevant.

Nausea and vomiting occurred in three workers within 2 hours after exposure, and one vomited on the second day. Diarrhea was not evident. Some complaints of soreness, fatigue, and weakness were registered. All showed hematological changes reflecting severe marrow damage. Hospital treatment was conservative, and the patients were discharged 39 days after exposure.

At Vinca, the exposure of five persons ranged from a lower limit of 1.8-2.3 Gy to an upper limit of 2.3-3.1 Gy,[10] occurring over several minutes when an unshielded research reactor temporarily ran out of control.[61,62] This led to the emission of a "softer" neutron spectrum than that which occurred in the accident at Y-12. Low-energy neutrons are not very penetrating, but do give rise to a measurable tissue gamma dose. Therefore, a calculation of marrow dose had to be estimated. Although the dose levels at both accidents were similar, the clinical responses of the victims differed significantly.

For the Vinca victims, severe nausea and vomiting occurred within the first hour. A larger dose to the superficial tissues was indicated by erythema, conjunctivitis, and loss of body hair. The most highly irradiated victim suffered severe diarrhea. Victims were nursed under sterile conditions, receiving fluids, electrolytes, blood-cell transfusions, and antibiotics. The hematological picture worsened through the 3 weeks after exposure, and five patients were injected with donor-matched bone-marrow cells at 4-5 weeks after exposure. The value of the marrow transplant is moot. It has been argued that the recipients were on their way to recovery and that the benefits of these transplants were temporary at best. One man, who received the highest dose of radiation, did not respond to treatment; he died of gastrointestinal complications on day 32.

PRESENT VIEW OF RADIATION EFFECTS ON HUMANS

Several new studies relate to the establishment of an LD_{50} for a low-LET radiation dose to the bone marrow of healthy young adults. These studies include several important observations that must be considered when estimating the radiation mortality response of humans. First, in selecting data groups for analysis, the influence of postirradiation clinical treatment must be taken into account. Carefully controlled experiments clearly indicate that treatment will elevate the estimate of the LD_{50} by as much as 30%.[63] The calculated LD_{50} of approximately 6 Gy for the Chernobyl patients treated for ARS also indicates a

benefit from intensive clinical support. This observation is reinforced by the fact that many of these patients had complicating burns, which have been shown to lower the LD_{50} in the Nagasaki victims and in studies of laboratory animals. These observations suggest that the British value of 4.5 Gy overestimates the bone-marrow LD_{50}, since this value is derived entirely from persons who received supportive therapy.[60] The data from the Ewing's sarcoma patients in this study seem particularly compromised, because these patients received not only antibiotics and platelets but also barrier nursing and possibly tumor pretreatment with X rays before receiving the 3 Gy of total-body radiation.[60] If this pretreatment with X rays can be confirmed, we must assume that the sensitivity of the patients to sub-sequent radiation therapy was reduced. These several factors suggest that anchoring the low end of a dose-response curve with these data is not justified.

The second observation to emerge from these new studies is the dependence of LD_{50} on dose rate, particularly at rates of 0.6 Gy/ hour or less, as seen in data from human experience and studies with laboratory animals.[11,64] This dependence is particularly important when attempting to use low-dose-rate studies as estimates of prompt LD_{50}. Table 2-4 shows a model for the relationship between dose rate and LD_{50}.[11]

The third observation is that the LD_{50} for the human cannot be modeled on a 70-kg animal. This is true even if the analysis is based on all animal studies to date, if the model is carefully controlled for body weight, and if the dose rate is below 0.5 Gy/minute. The LD_{50} may be more species-independent at prompt dose rates, where data from several large mammals, including humans, appear to converge.[65]

A fourth observation is that although the LD_{50} for the human may not be exactly like that of another 70-kg mammal, the slope derived from the animal model is much more credible than the unacceptably shallow slope observed in the Hiroshima and Nagasaki analyses. These differences in slope may be due to differences in *(a)* the accuracy of dose determination, *(b)* the homogeneity of the sample populations for humans and animals, or *(c)* the postirradiation treatment. With no acceptable slope that can be empirically derived directly from human data, the recommendation is to use the slope obtained from the Oak Ridge National Laboratory animal model (Figure 2-10). The LD_{90} and LD_{10} should be taken as the values for the limits of the dose-response curve because the extrapolations are totally unreliable beyond that range. The slope should be expressed as the ratio of the LD_{90} to the LD_{10}. This expression maintains linearity over the entire curve and has a value of 1.9, which is in good agreement with other such values.[64,65]

The final observation is the degree of agreement that is emerging among the values for the LD_{50}, especially from the Hiroshima and Nagasaki data. Recently, a value of 1.54 Gy for the midlethal bone-marrow dose for Hiroshima was pub-

lished.[59] This value was derived from survey data relating the mortality of persons in wooden houses to their distance from the hypocenter of the bomb. Using preliminary calculations of dose versus ground range, the Hiroshima LD_{50} was determined to be 1.54 Gy.[59] However, if one uses the latest calculations, the value becomes 2.3 Gy to the bone marrow. This value is in general agreement with the reported value of 2.24-2.50 Gy, based on doses and essentially the same model.[66] Both of these values were skewed by the inclusion of data from deaths due to burns and blast effects. If one increases these values by 17.5% (the difference in LD_{50} for radiation only, and radiation combined with blast injuries and burns), the values increase to 2.75-3.0 Gy. Another recent analysis of the data from Hiroshima estimates the LD_{50} to be 2.72 Gy by correlating white blood-cell counts to the percentage of mortality. Considering the diversity of these analyses and the approaches by which they were derived, their agreement is remarkable. Even more remarkable is the fact that these values agree with the human values obtained 20 years ago for patients, when adjusted for bone-marrow dose and prompt dose rates.

There is good agreement among the data (particularly the recent data from Hiroshima and Nagasaki) that the NATO human LD_{50} should not be raised for healthy untreated persons. Based on the range of values discussed, the recommended value for the LD_{50} is 3.0 Gy to bone marrow (4.3 Gy free in air).

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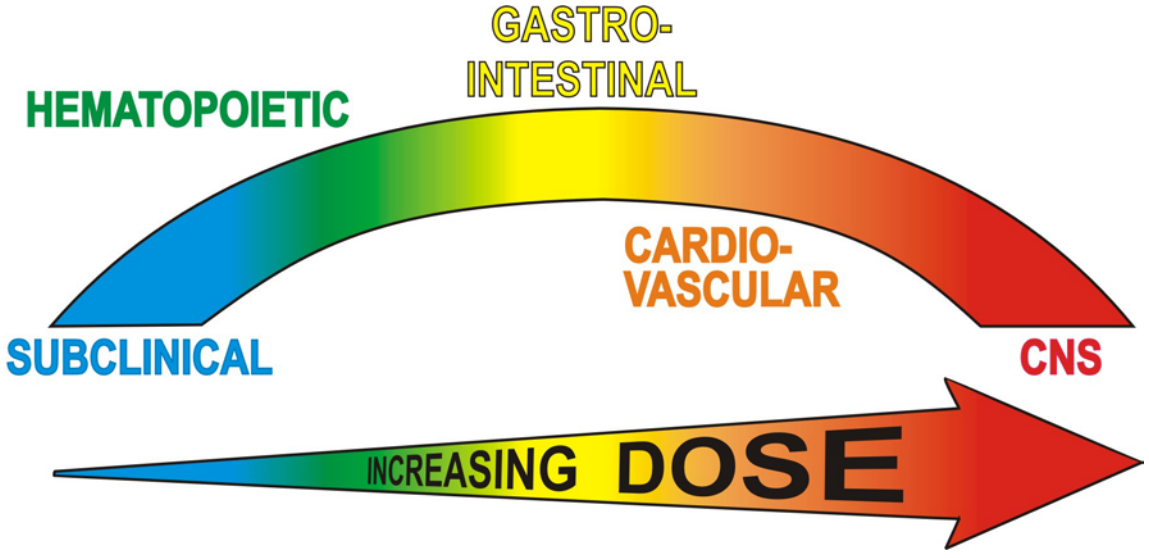

Figure 2-1. Increasing severity of radiation effects with increasing dose. (Label for each radiation effect is color-coded to dose range [on arc] producing that effect.)

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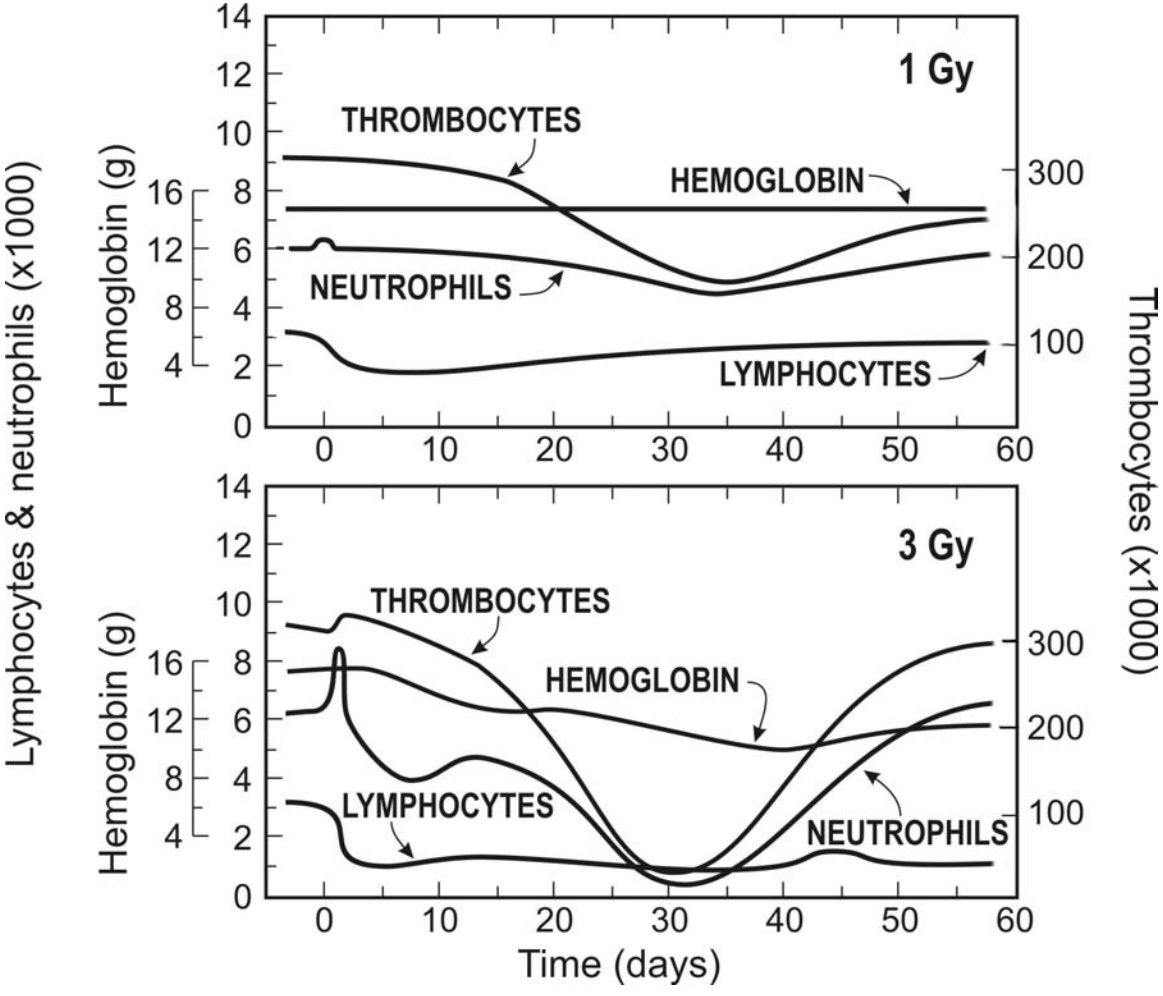

Figure 2-2. Hematological response to whole-body exposure. Comparison of 1-Gy and 3-Gy gamma-radiation effects on hematopoietic system.

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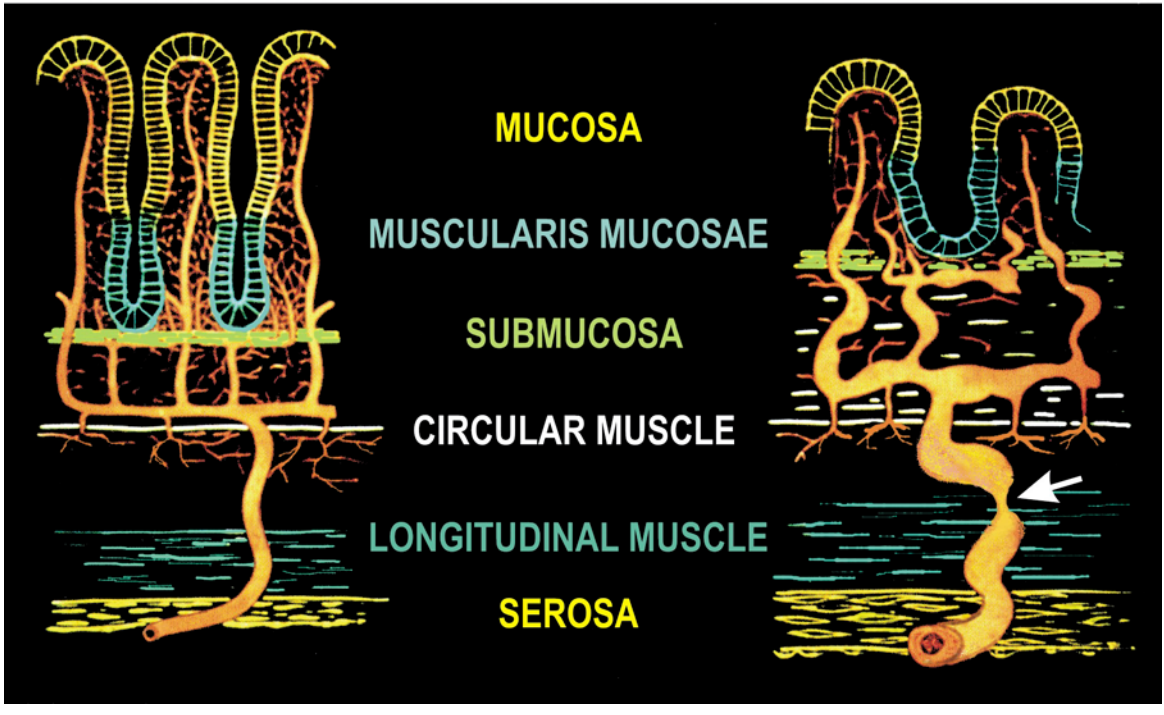

Figure 2-3. Normal intestinal tissue (left) and irradiated intestinal tissue (right). Dramatic changes are manifested by loss of mucosal lining, damage to crypt cells, and coalescence of capillary networks into large cisternae. (Label for each layer of tissue is color-coded to its portion of each illustration.)

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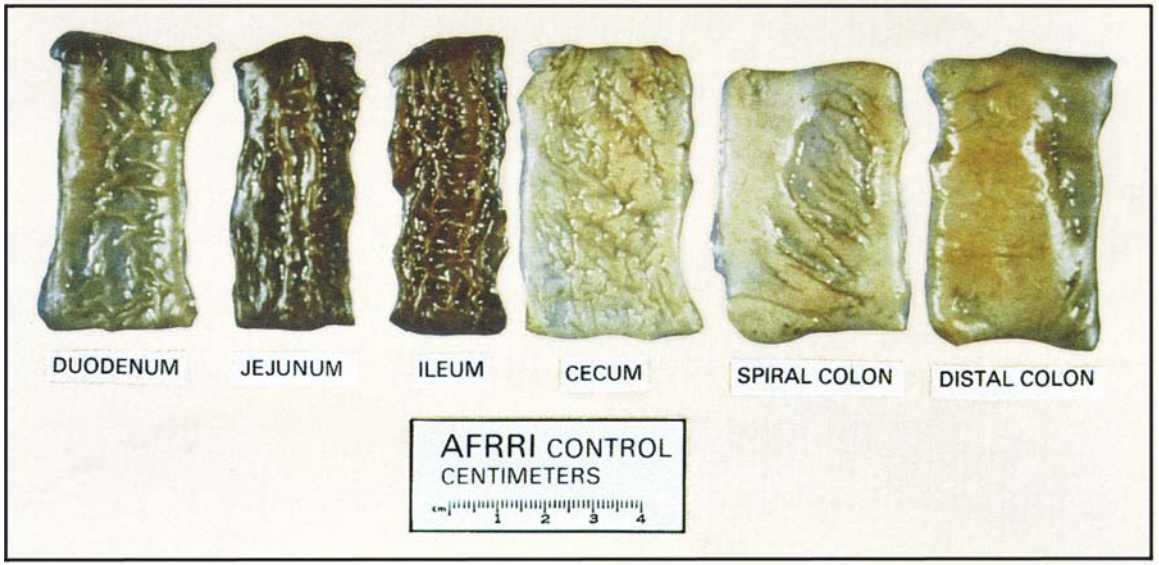

Figure 2-4. Porcine intestinal segments from normal animals. Normal tissue appears pink to gray.

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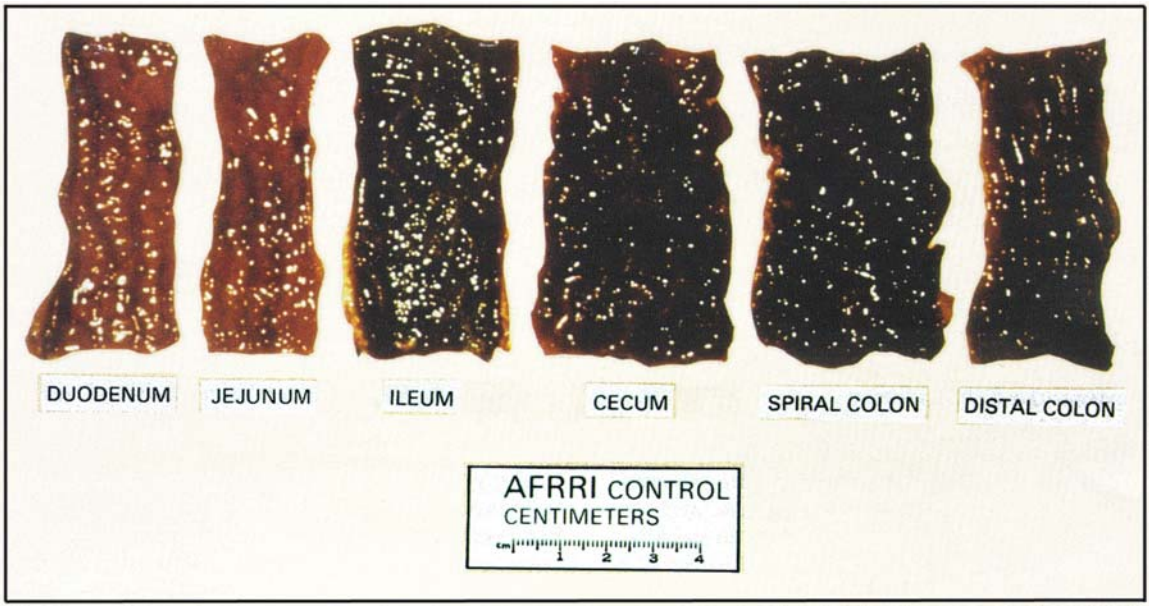

Figure 2-5. Porcine intestinal segments from 4-Gy-irradiated animals. Irradiated tissues from all segments show signs of severe hemorrhage and ulceration.

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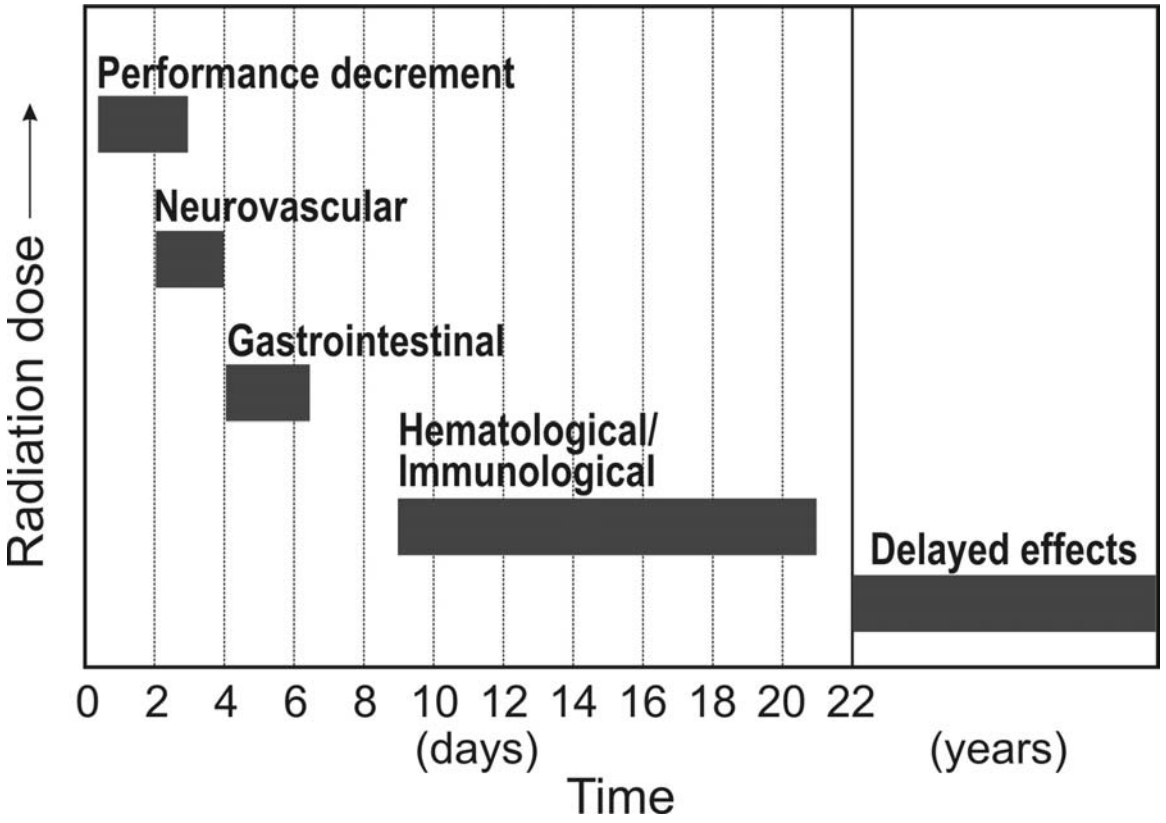

Figure 2-6. Occurrence of radiation effects in relation to dose and time. As radiation dose increases, time to mainifestation of effect decreases.

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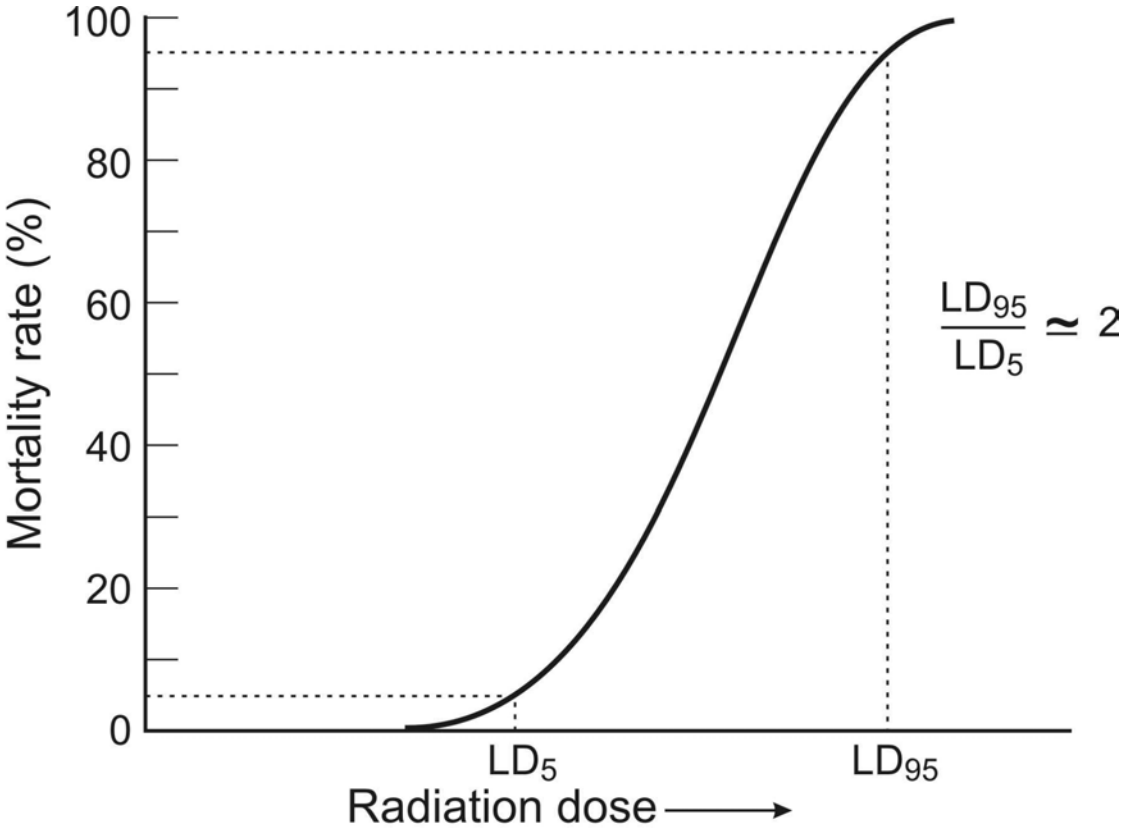

Figure 2-7. Standard dose-response curve.

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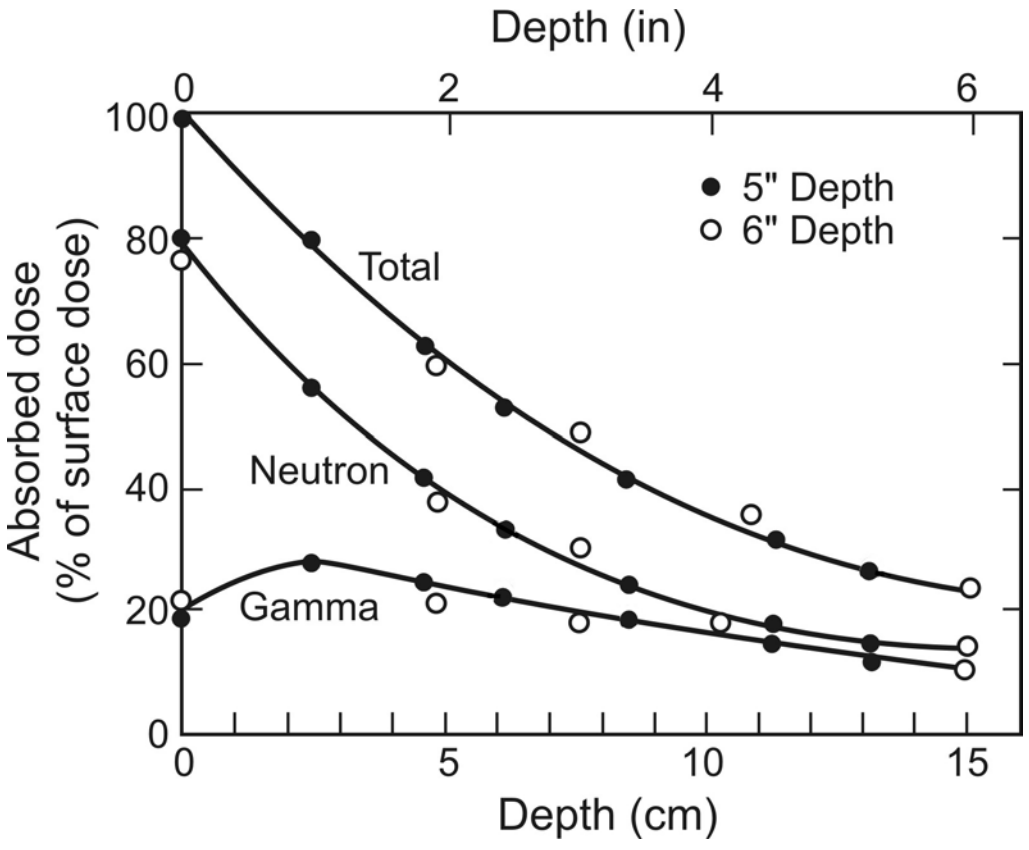

Figure 2-8. Depth-dose relationship in phantoms. Effect of tissue depth on absorbed radiation dose from unilateral mixed-fission gamma and 1-MeV neutron radiations. Low-LET, high-energy gamma radiation produces a more uniform exposure than does fission neutron radiation.

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Preface

Medical Consequences of Nuclear Warfare is the second volume of Part 1, *Warfare, Weaponry, and the Casualty.* It addresses the increasingly important medical challenges of the consequences and management of radiation injuries.

The presence of vast nuclear arsenals has had a paradoxical effect on our collective human consciousness: because we are unavoidably aware of the potential destruction stored in those warheads, we are less likely to use them in a global thermonuclear war. However, maintaining this deterrent carries its own high price. The likelihood of accidental detonations, small-yield nuclear attacks in regional conflicts, and radiation injuries in reactors and weapons plants increases as familiarity with this powerful force spreads. Arms limitations agreements among superpowers are important, but third world nations now too have access to the materials and technology necessary to enter the nuclear arena. The volatility of world politics may be moving beyond the ability of any policy- or lawmaking group to control. Given the devastating medical consequences that would follow a nuclear detonation or accident, the training of the medical corps in treating radiation syndromes will be a crucial factor in the effective management of casualties.

The rapidly expanding science of medical radiobiology has greatly affected the prospective readiness of the military medical corps to deal with these injuries. The Armed Forces Radiobiology Research Institute has been a leader in the establishment of the base of scientific and clinical knowledge from which the current concepts of medical management have evolved. In addition to research, the institute is involved in continuing medical education and in our nation's emergency response system. It is in a unique position to understand the importance of converting vast amounts of laboratory data into practical, efficient medical techniques and treatments. The authors have written their chapters from a combined academic and military perspective in order to specifically help the military physician.

Captain Richard I. Walker, MC, U.S. Navy, and Major T. Jan Cerveny, MC, U.S. Air Force, provided the expertise in the organization of this textbook. The first chapter is an overview of nuclear events and their consequences. The following chapters examine the effects of radiation exposure on humans and the ways they will affect triage, diagnosis, and treatment protocols as well as military logistics. A discussion of the latest prospects for radioprotection concludes the text.

It is possible that no amount of knowledge or training will help any medical unit to deal with the mass casualties that a large-scale radiation incident or accident would incur. However, data from accidental and therapeutic radiation exposures, together with ongoing clinical research results, are all useful in determining the treatment of individual victims of smaller incidents who are in a position to be saved.

The *Textbook of Military Medicine* series is a reality because of the vision and support of the late Major General James H. Rumbaugh; Lieutenant General Frank F. Ledford, Jr., the Surgeon General of the Army; Lieutenant General (ret.) Quinn H. Becker, our former Surgeon General; and Major General Robert H. Buker, Deputy Surgeon General of the Army.

The editors gratefully acknowledge the assistance in the preparation of this volume of Junith Van Deusen, Modeste E. Greenville, Sonia Jones, and Carolyn B. Wooden of the Publications Division of the Armed Forces Radiobiology Research Institute.

Colonel Russ Zajtchuk
U.S. Army

April 1989

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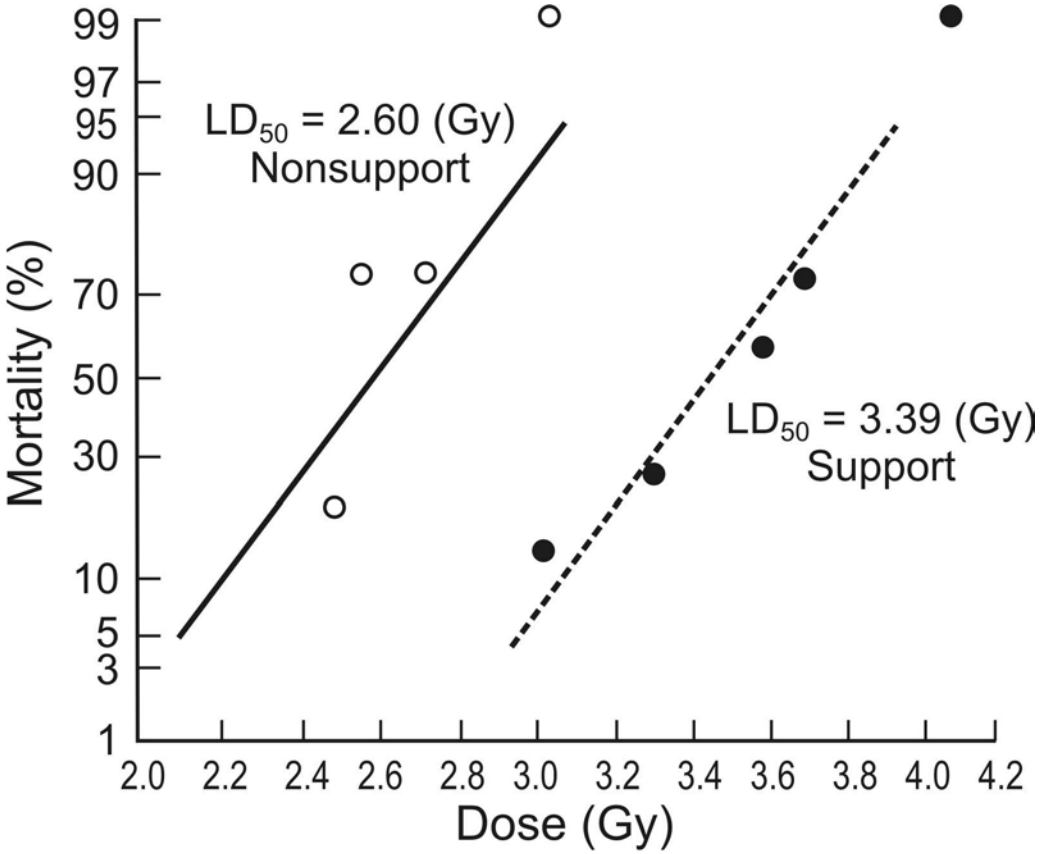

Figure 2-9. Effect of clinical support therapy on LD_{50}. Parenteral fluids, platelets, and antibiotics to control infection during critical nadirs in granulocyte and platelet counts provide the basis for successful treatment.

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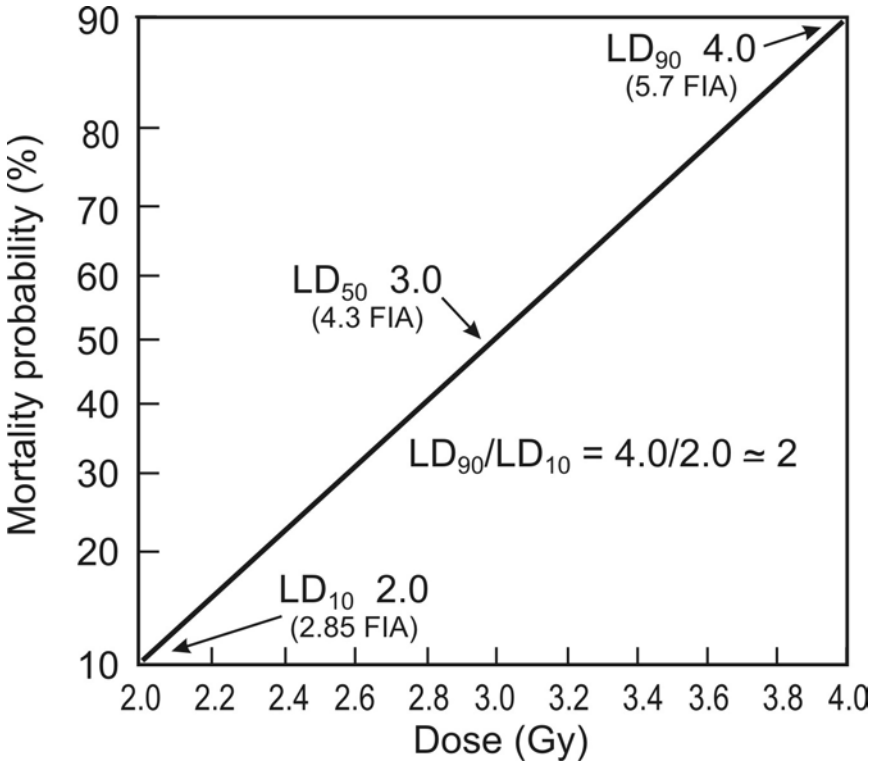

Figure 2-10. Human mortality for high-dose-rate, low-LET radiation doses to bone marrow. Doses beyond LD_{90} or below LD_{10} cannot be reliably extrapolated. Slope, calculated from this animal model, is expressed as ratio of LD_{90} to LD_{10}.

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Chapter 3

TRIAGE AND TREATMENT OF RADIATION-INJURED MASS CASUALTIES

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INTRODUCTION

The effective medical sorting of mass casualties (triage) and their subsequent treatment after a nuclear event have been considered extremely difficult or even impossible.[1] In the case of a major exchange of strategic nuclear weapons (500-5,000 MT), the triage of casualties using the remaining resources would certainly be futile and frustrating. Without transportation and tertiary medical-care facilities, the only benefit would be to identify persons who are capable of combat. Even the minimally injured casualty may receive little (if any) meaningful attention in such a situation.

However, if a nuclear event occurs, it is more likely to take place on a limited scale rather than as a strategic weapons exchange.[1] After a smaller-scale tactical detonation (0.1-2.0 kt) or a nuclear detonation by terrorists, hundreds or a few thousand casualties are more probable than millions[2] or billions.[3] Considerable medical resources may be intact and available for treating many of them. This chapter presents plans for the management of large numbers of casualties suffering either radiation injury alone or conventional trauma combined with radiation injury.

PRINCIPLES OF TRIAGE

In conventional triage, patients are assigned to one of the following priority categories, depending on the nature and extent of their injuries: *(a)* The *immediate treatment* group includes patients who have a high chance of survival if they are given immediate life-saving treatment or surgery that is relatively quick and uncomplicated. *(b)* The *delayed treatment* group includes patients who may need major surgery, but who can be sustained on supportive treatments until surgery is possible. *(c)* The *minimal treatment* group includes patients with relatively minor injuries who can care for themselves or who can be helped by untrained personnel. *(d)* The *expectant* category includes patients with serious or multiple injuries requiring extensive treatment, as well as patients with a poor chance of survival. This group should receive supportive treatments that are compatible with resources, including large doses of analgesics.

The speed of assessing and categorizing the status of patients is the key to effective triage. Any method is useful that gives the triage officer a quick, accurate idea of the extent of injury. When making the assessment rapidly based on anatomical findings, the probability of injury is related to the degree of estimated force on the body part. For example, a patient close enough to a nuclear explosion to be caught in the blast wind is assumed to have internal and possibly occult traumatic injury. Such a patient will most likely be in the expectant category (Table 3-1). A slower but more accurate method of assessment is to expose the injured area directly and perform an abdominal examination. Even

with a relatively small number of casualties, this exam might be prohibitively time consuming in the critical moments shortly after a nuclear event.

Rapid assessment based on physiological status will permit the gathering of useful information on respiratory rate and systolic blood pressure in a large number of patients. In contrast, a determination of the Glasgow coma scale score[4] (although fairly rapid in experienced hands) is less useful than a brief neurological evaluation of the patient's degree of alertness, responsiveness to verbal and painful stimuli, and state of consciousness. Attention to other relatively obvious factors, such as extremes of age (under 5 years or over 55 years) and preexisting or recently induced cardiovascular or respiratory illness, will aid in establishing a patient's status as expectant.

Operational Considerations for Triage

Regardless of the findings from an anatomical or physiological assessment of the patient, the first priority of the military triage officer is to conserve the fighting force. Combatants in the expectant category, however, should no receive aid or resources that might be of greater benefit to less severely injured noncombatants, even if these resources seem to be in adequate supply. In rare circumstances, a terminally injured unit commander might receive resources to permit continued functioning in a crucial command role.

This chapter pertains primarily to the management of acutely irradiated casualties following the detonation of a nuclear weapon. The military physician should recognize two essential facts in dealing with mass casualties during military triage in a declared war: *(a)* all medical resources fall under the jurisdiction of the military, and *(b)* peacetime triage practices are of limited use. However, in more limited events (such as a major nuclear reactor accident), the military may be asked to assist with the management of mass casualties under the constraints of peacetime disaster triage.

Peacetime Triage. In peacetime, a two-tiered system of care for the critically ill is assumed. Based on the triage decision, the patient goes either to the emergency room of the nearest community hospital or to the regional trauma center. This system depends on rapid, reliable transportation in which trained attendants monitor the patient with radio guidance from trauma staff at the hospital or center.[5]

In this scheme, the sorting of patients is based on a physiological trauma score in which the less-injured patient, with a score of 15-16, is in the delayed category, a third priority. Patients with a trauma score of 3 or less are considered expectant (the fourth, or last, priority). Third- and fourth-priority patients would probably be sent to the local hospital emergency room. All patients with trauma scores of 4-10 (first priority) and some with scores of 11-12 (second priority) would go to the trauma center.[5]

Military Triage. Military triage contrasts starkly with that used in peacetime, but the two do have some elements in common. For example, military triage decisions would most likely be made at the level of the batallion aid or clearing station. The local community hospital might be equivalent to the second-echelon radiation decontamination center and field hospital. Only fixed medical-care facilities or existing tertiary-care facilities that are able to perform surgery would suffice as trauma centers for handling combined-injury casualties.

In wartime, it cannot be assumed that rapid and reliable transportation of wounded persons is possible, as it is in peacetime or might be in smaller, low-yield nuclear events. In the confusion of armed conflict, casualties with a wide variety of injuries might be expected to arrive at the nearest medical-care facility regardless of its capability. Extra effort will be needed to keep the patient moving forward in the system to an appropriate level of care. The greatest number of lives will be saved only by ensuring that time and materials are not allocated to hopeless cases or to those whose injuries are so minor or uncomplicated that definitive care can be postponed.

In a nuclear disaster, triage decisions cannot be made on the evidence or probability of conventional injury alone. When significant radiation exposure is combined with conventional injuries, there may be a dramatic shift of patients to the expectant category (Table 3-1). In order to make an appropriate decision, the triage officer must recognize the symptoms of ARS and understand the difficulties in estimating radiation exposure from clinical findings.

Signs and Symptoms of Radiation Injury

It will be difficult to assess the radiation doses of persons who have been injured in a mass-casualty disaster. Thus, a system has been devised to identify radiation exposure based on the symptoms of "unlikely," "probable," or "severe" radiation injury (Table 3-2).[6] These symptoms are nonspecific, and permit only the cursory screening of a large number of cases.

Cutaneous Phenomena. Information about the cutaneous changes after ionizing radiation exposure comes mainly from accidental or therapeutic high-dose local radiation exposures and, to a lesser extent, from studies of the victims of the 1986 nuclear reactor accident in Chernobyl, USSR, and the 1987 cesium-137 accident in Goiânia, Brazil. Skin injury in those events resulted from very intense local irradiation or direct contact of the skin with radioactive material. Burns among casualties at Hiroshima and Nagasaki in 1945 were caused by heat rather than radiation exposure.[3]

When extremely high doses of whole-body radiation (100 Gy) are delivered acutely, skin may have the sensation of tingling or being on fire even though no lesion immediately appears. Within the first 24 hours, there is the appearance of a characteristic transient erythema secondary to capillary dilation and the release of

histamine-like substances. The initial erythema usually peaks within 24 hours, and then disappears for 1-3 weeks. Thereafter, it may reappear with pain and edema. Severe pain may occur if more radio-resistant nerve tissue is surrounded by necrotizing tissues. Melanotic pigmentation (Figure 3-1) or ulceration may develop.[7] Pain from nerve compression may occur as healing and atrophy take place. Hair loss over the affected area occurs at the end of the second or third week. In contrast to erythema induced by high-dose beta radiation, skin injury from gamma radiation occurs only at doses that damage the bone marrow. Thus, if sufficient marrow is exposed, thrombocytopenia with cutaneous petechiae, purpura, and hemorrhage can be expected. In granulocytopenic patients, otherwise-noninvasive surface bacteria may colonize areas of wet desquamation and lead to suppurative lesions.

The threshold dose for gamma-radiation-induced erythema is about 3-5 Gy; for desquamation, it is about 10 Gy. Ulceration develops at doses of 20 Gy. At doses of more than 40 Gy, gangrenous radionecrosis can be confidently predicted, if the dose is well documented and can be confirmed on review of the evidence.[8] Different body areas may have different radiation sensitivities; a gradient from greater to lower resistance is observed for scalp, face and neck, trunk, ears, groin, and extremities. Exposure of the skin to temperatures greater than 42°C may enhance cutaneous radiosensitivity and increase the probability of a more severe injury.[7]

Beta-emitting isotopes from smoke and fallout can cause desquamation from high-dose local radiation delivered to exposed skin surfaces, but only if these isotopes are in contact with the skin for longer than 1 hour. Since beta radiation is not as penetrating as gamma radiation, dry desquamating skin lesions secondary to beta burns may not be as serious as wet desquamating lesions, which occur as the result of high-dose exposure and suggest that underlying structures are involved. The wet lesions may be complicated by secondary infection, and usually indicate a poor prognosis.

Gastrointestinal Phenomena. A sense of fatigue and malaise associated with nausea and loss of appetite is characteristic even of relatively low-dose radiation exposure (1-2 Gy). The abrupt onset of nausea and vomiting occurs with acute high-dose radiation in the range of 5-10 Gy. These initial symptoms may be followed by a short latent period of 1-2 days. The severity of initial symptoms, including diarrhea, serves as a useful index of probable outcome, as does the rapidity of onset or a delay in the appearance of symptoms. Following the latent period, an increase in vomiting, diarrhea, and anorexia, as well as dehydration and signs of infection, can be expected.[9]

An abrupt onset of bloody diarrhea after acute high-dose radiation indicates lethal exposure. If less-acute doses are received, diarrhea may not appear for several days or a week after exposure. The onset of diarrhea within a week of exposure is usually associated with death. However, patients have survived when the onset of

radiation-related diarrhea was delayed for more than 1 week after protracted radiation exposure.[10] Nausea and vomiting occur after exposure to doses greater than 2.5 Gy. Identification of the onset of these symptoms may be useful in the initial triage of a radiation-only casualty. However, in combined chemical-nuclear warfare environments, chemical agents may account for much of the nausea and vomiting.

Cardiovascular, Respiratory, Metabolic, and Neurological Phenomena. If a casualty has no conventional injuries or psychosomatic complaints, then cardiovascular, respiratory, metabolic, and neurological symptoms usually indicate terminal high-dose radiation exposure. Radiation-related hypotension, radiation pneumonitis, or ETI identify persons who may be expected to die within 2-3 days. This prognosis is certain, despite a variable period of transient improvement that occurs shortly after the event.

Initial symptoms of high-dose exposure may not be distinct from those of lower-dose exposures. Nausea and vomiting may occur even without direct exposure to the gut in patients who received high-dose local radiation to the head or chest.

Metabolic abnormalities can be expected after radiation of moderate to high doses, and include the consistent finding of non-bacteria-mediated hyperthermia with marked fever and shaking chills. A 25% drop in plasma glucose may occur within the first day, but a neuroglycopenic state of confusion has not been observed. Hemorrhagic coagulopathies, associated with disseminated intra-vascular coagulation and a reduction in noncellular clotting factors, are possible. Liver injury probably accounts for hypoglycemia and the coagulation factor deficiencies.[11,12] Cardiac arrhythmias associated with electrolyte imbalance (hyper- or hypokalemia) may occur.

In the later stages after lung exposure, the loud crepitus of radiation pneumonitis, which has been likened to the "thundering of a rain storm on an iron roof,"[10] is associated with tachypnea and severe hypoxemia.

ETI in primates (and its locomotor equivalent in rodents) is characterized by the complete but temporary cessation of motor function, and does not occur unless high-dose radiation is delivered acutely.[13] Transient loss of consciousness is not typical of ETI. Unconsciousness is more suggestive of conventional head injury.

Hematological Phenomena. The most useful and rapid method of assessing the degree of radiation exposure is to obtain serial total lymphocyte counts. Optimally, this should be done every 6 hours during the first 48 hours, or at least once every 24 hours after exposure. This estimate and its interpretation need to be standardized for the available laboratory methodology. To that end, a chart of blood cell morphology (Figure 3-2) and a nomogram of the acute radiation-induced change in lymphocytes/mm^3 (Figure 3-3) may be useful. A laminated copy of this nomogram should be included in the field kit of every medical

officer. Changes in peripheral blood granulocytes do not give as clear a picture of the severity of radiation injury because their numbers are affected by stress and infection, fall more slowly, and vary widely.

Sophisticated methodology has become available that permits the rapid and quantitative determination of the total and differential leukocyte counts at DEPMEDS (Deployable Medical Systems) field hospitals. Using the QBC II assay methodology,[14] a total lymphocyte count requires only a fingerstick blood sample (rather than a phlebotomy) and can be performed by relatively inexperienced personnel. Effective suppression of electrical power surges and adequate supplies of special sample tubes would be needed to permit this option on the nuclear battlefield at a field hospital.

A drawback of this method is that monocytes cannot be differentiated from lymphocytes unless a separate Wright-stained slide is prepared and interpreted. Such a determination done by hand would become prohibitively time consuming and labor intensive in a mass-casualty situation. However, with the QBC II methodology, the determination of the total granulocyte percentage and the mononuclear cell percentage is automated (although it still requires data transcription by hand).

Triage of the Combined-Injury Patient

Priorities in handling patients of conventional trauma are modified in cases of concurrent radiation injury. Triage priority is based on the conventional injury as well as the degree of radiation suffered by the combined-injury victim (Table 3-1).

All patients exposed to more than 4.5 Gy are in the expectant category, as are those with exposure of 1.5-4.5 Gy who cannot be given care immediately. If exposure was less than 1.5 Gy, the nature of the conventional injury will dictate the treatment priority. Casualties who receive radiation exposure alone over a wide range of doses will need little if any treatment initially.[15]

Since an estimate of the exposure dose in the early phases of radiation-casualty triage will be almost impossible, a more practical triage scheme, based on symptoms of unlikely, probable, or severe radiation exposure, will be useful (Table 3-2). In the event of combined injuries, symptoms of probable or severe exposure may be confused with symptoms associated with conventional injury. In giving the benefit of the doubt to such patients, those with injuries treatable on an immediate basis should receive prompt attention. However, if radiation exposure does account for the observed symptoms, the patient in the conventional categories of immediate (Table 3-3) or delayed (Table 3-1) may actually be expectant. Even with severe symptoms of radiation exposure, patients with minimal traumatic injury may be capable of survival if evacuated for observation and advanced medical management. However, if transportation resources are

limited, disposition of the minimally injured but heavily exposed patient should coincide with that of the casualty in the expectant category. Patients in the delayed category with probable radiation symptoms are expectant, unless adequate tertiary-care facilities are readily available. Regardless of the triage scheme used, it is probable that a number of combined-injury patients in the expectant category will receive treatment for more immediate and delayed conventional injuries.

Conventional injuries that are particularly relevant following a nuclear detonation include burn, blast, and eye trauma.

Burn Injury. The extent of a thermal burn may be rapidly estimated according to the "rule of nines."[4] Conventional thermal burns are predicted to be among the most frequent injuries to troops on the nuclear battlefield.[15] A more severe hematopoietic subsyndrome is likely if partial-thickness burns involve more than 10% of the body surface.[10]

Blast Injury. Dynamic overpressure from the explosion of a nuclear weapon will induce overt crush injuries and occult internal bleeding.[16] The triage officer should suspect occult traumatic injuries, which will likely place the irradiated patient in the expectant category.

Eye Injury. Eye injuries from a thermonuclear flash may be as minor as transient blind-ness (for a few seconds to minutes) or a permanent retinal scar in which peripheral vision is spared.[3,16] These are minimal injuries. However, permanent foveal damage with 20/200 visual acuity may occur if the victim focuses directly on the nuclear fireball. A variety of eye injuries resulting primarily from protracted high-dose radiation exposure was observed among firefighters at the Chernobyl reactor accident. These injuries will most likely lead to permanently impaired vision.[10] Clearly, if the corrected visual acuity of a patient is 20/200 or less after more than 1 hour from time of injury, the usefulness of that person as a combatant will be limited, and assignment to a category of delayed treatment is appropriate. Gross eye injuries, most likely from flying objects after a nuclear blast, may have a dramatic appearance, but they are frequently minimal and should not divert attention from more significant injuries.

MEDICAL MANAGEMENT OF THE COMBINED-INJURY CASUALTY

Patient management will focus on three issues. First, basic life-support concerns need to be quickly addressed for casualties in the immediate category; an airway, adequate ventilation, and circulatory function should be assured for patients whose injuries will permit them to survive. Concerns about internal or external contamination with radioactivity should be second priority. Finally, an effort should be made to retrieve data from any dosimeters carried by the military com-

bat unit. Currently, radiation dosimeters cannot be relied on to accurately estimate the severity of an individual's radiation injury. Dosimeters do not account for partial shielding and do not reflect the delivery rate of a radiation dose, and so make only a small contribution to the diagnostic picture. Any data from physical dosimeters must be interpreted by the medical attendant in light of the observed physiological changes.

Because most of the radiation exposure likely to be encountered on the battlefield has no immediate life-threatening consequences, the medical attendant should first focus on conventional injuries. Needless risks, such as prolonged contact with contaminated clothing or wash water, must be avoided, but in emergency medical treatment, direct contact with a contaminated patient is usually not hazardous. No conclusive evidence exists that any attendant has ever been adversely affected by brief contact with a radiation casualty. On the other hand, in a nuclear attack that is combined with chemical or biological weapons (which may be more likely than a nuclear attack alone), the attendant will need to wear protective gloves, as well as a mask outfitted with an entire chemical ensemble, to manage these casualties safely.

Wearing this chemical ensemble will pose special problems in primary medical management. Even if the mask is equipped with a voice emitter, verbal communication over more than a few yards will be hampered. In the early phases of identification and triage, familiarity with a brief dictionary of sign language will be useful. The signs for “radiation casualty” and “chemical casualty” are illustrated in Figure 3-4.

Concerns in the Treatment of the Combined-Injury Patient

Once an airway, proper ventilation, and circulatory stability have been established, definitive care should be planned for the casualty who can survive. Treatment planning is based on the competent handling of conventional injury and the anticipation of predictable sequelae of radiation injury. In the following discussion, early placement of a peripheral intravenous catheter for infusion of adequate quantities of fluids and blood components is assumed. The use of central venous lines in protected sites for long-term infusions is also discussed.

The decision to apply any of these measures to the combined-injury patient will be a difficult one, and will have to be based on the availability of resources and the projected number of casualties. The prognosis for combined injury is markedly worse than for either traumatic or radiation injury alone. Patients with moderate or severe conventional injuries who arrive at tertiary centers that are capable of handling combined injuries will probably receive the maximum available care, unless they have received obviously massive doses of radiation (over 8 or 9 Gy). It will be hard to justify the decision to continue therapeutic interventions in a trauma patient whose dose of radiation is eventually determined to exceed 4 Gy. Continuing advanced life-support measures will not be in the best

interests of a patient who will most likely suffer a protracted, terminal illness. Nor will less-injured patients benefit if their access to hospital resources is limited because of the excessive allocation to hopeless cases. On the other hand, the military organization should attempt to assure that the psychological support of casualties in the expectant category are augmented as much as possible by nonmedical personnel.

Specific Treatment Concerns

Surgery. Since exposure to doses of less than 5 Gy is of no immediate threat to health, conventional injury that is surgically remediable deserves priority treatment. Ideally, surgery should be initiated as soon as possible, or within 36 hours of radiation exposure,[3] and be completed before 48 hours.[17] Surgery after this time is contraindicated for at least 6 weeks, or until there is evidence that immunocompetence has returned and that incised tissue is able to revascularize. Clearly, the best candidate for surgery is the patient who requires only one procedure with no surgical revision. Patients who have been exposed to more than 1.5 Gy, who have extensive injuries, and who need multiple procedures and reconstructive surgery are classified as expectant. However, patients who have suffered severe conventional injury, who have had successful wound closure, and who then received radiation may actually be more radioresistant and better able to survive.[17] Decontamination of the radiation casualty should include prompt surgical debridement, if needed, and washing of the surgical area with mild antiseptic soaps. The skin should be cleansed before surgery to adequately reduce any radioactivity in the area of the incision. An important secondary concern is to cleanse crevice areas (nails, ears, and skinfolds) and orifices (particularly mouth and anogenital regions). To avoid abrading the skin, washing should be done gently with mild soaps and hair should be clipper-cut instead of shaved. These procedures will eliminate at least 95% of a patient's surface contamination with isotopes.

Anesthesia and Pain Control. In controlled trials with animals, the induction and recovery from anesthesia for irradiated subjects do not differ from those for nonirradiated subjects.[18] However, anecdotal experience in humans has suggested that the times of induction and recovery from anesthesia may be prolonged.[19] In irradiated animals and humans, there is a clear resistance to the effects of analgesics. However, care should be exercised to avoid overtreatment with sedative narcotics and anesthetics.[9]

In a local high-dose radiation injury (over 40 Gy) to an extremity, prompt amputation gives the patient the greatest pain relief and makes the most efficient use of resources. The use of nonsteroidal anti-inflammatory drugs and thrombolytic agents, as well as topical corticosteroids, has been claimed to delay the appearance of dermal necrosis and to lessen the pain of local skin damage.[20] However, topical corticosteroids are contraindicated in thermal burn injuries.

Control of Infections. A variety of measures has been advocated to reduce infections in the irradiated patient. These measures include meticulous hygiene of skin and orifices, aseptic skin punctures, reverse isolation, and prophylactic administration of immunoglobulin G. Difficulties associated with the strict maintenance of reverse isolation procedures are obvious. Laminar airflow rooms are in limited supply, constant surveillance is required for nosocomial infectious agents in plumbing fixtures and ice machines, and food must be free of gram-negative bacteria (no raw fruit, vegetables, or salad). The best result that might be achieved by these methods is a reduction in the appearance of new infections. Meanwhile, endogenous reinfection would be little affected unless antibiotics to eliminate opportunistic pathogens from the gut are effectively used. Although measures to control infection are prudent, their efficacy has not been clearly shown. Life- threatening infections remain a complication in the management of radiation casualties.

Maximum doses of two or three antibiotics of different classes should be infused empirically when specific signs of bacterial infection occur. These signs include the appearance of a sudden fever spike, usually in the presence of a depressed leukocyte count (that is, granulocytes fewer than 500/mm^3). Prophylactic antibiotic treatment has given good results when used perioperatively in patients who have penetrating abdominal wounds.[21] The use of poorly absorbed oral antibiotics that selectively decontaminate the gut may be indicated as a preventive measure in patients known to have been exposed to moderate or high radiation doses. Even commonly used and widely available antibiotics (penicillins, streptomycins, and sulfas) may be useful with mass casualties, because sensitive and otherwise-noninvasive organisms usually become prominent pathogens in immunosuppressed radiation casualties.[10] Antifungal and antiviral agents are indicated when specific signs of these infections occur.

Antibiotics may rapidly become scarce in a mass-casualty radiation disaster and should be allocated to the victims most likely to survive. Such patients include *(a)* those with minimal injuries and evidence of localized infection, *(b)* those who require only one surgical procedure, and *(c)* those with contaminated wounds who have received lower doses of radiation.

Antiemetics and Antidiarrheals. The phenothiazine class of antiemetics, when used in the high doses needed to relieve a radiation victim's nausea and vomiting, has an unacceptably high incidence of extrapyramidal neurological side effects. Since the currently available antiemetic agents are of limited use, intense research efforts have been directed to finding new agents. Promising results have been obtained with the use of serotonin (5-HT3) blocking agents. This class of drugs significantly reduces radiation-induced emesis in the ferret, nonhuman primate, and human. However, some of the drugs may result in nausea.[22] Results of clinical trials of these relatively nontoxic agents are pending, as is their approval as agents potentially useful in the field by NATO forces. The goal in the use of any effective antiemetic is threefold: *(a)* to enhance patient comfort without

drug side effects, *(b)* to reduce the risk of aspiration pneumonia, and *(c)* to conserve body fluid and electrolytes. It may be possible to prevent emesis by administering serotonin antagonists prophylactically or immediately after exposure. Diarrhea from radiation damage to the gut may be controlled in part by a restricted-fiber diet and in part by medication. Drugs such as diphenoxylate HCI, codeine, or atropine have been advocated. If these are ineffective and the damage is localized to the large bowel, hydrocortisone enemas may help. The late complication of bowel stricture from local radiation damage is managed surgically.[23]

Fluids and Electrolytes. While adequate supplies of intravenous fluids are not likely to be available in a situation involving mass radiation casualties, the survival of patients with milder cases of fluid and electrolyte loss may be enhanced by replacement therapy. Careful measurement of the volume of losses will serve two purposes: *(a)* patients with severe degrees of fluid loss can be categorized as expectant, and *(b)* the proper volume of replacement can be given to patients who are capable of surviving. Measurement of the relative volumes of vomitus and diarrhea will help guide the fluid replacement. Those with more vomiting than diarrhea will suffer the greater loss of chlorides and may develop alkalosis, while those with secretory, cholera-like diarrhea may develop hypokalemia and hyponatremia with total-body salt depletion. The collection and measurement of excretions, including urine, serve another purpose: with the proper collection of serial specimens and access to radioanalysis equipment, estimates of internal radionuclide contamination can be made by measuring the radioactivity of the samples. In the event of combined-burn injury involving more than 10% of the body surface, crystalloid infusions are just as satisfactory as colloid, but a higher volume of infusate may be necessary.[24]

Placement of central venous catheters made of silicone elastomer (such as the Hickman or Broviac type)[25] should be considered a minor surgical procedure and be accomplished within the first 36 hours, if needed. Vascular obstructions and exotic infections increasingly complicate the use of these lines in immunocompromised patients,[26-28] and so they should be limited to the critically injured patients who need them most. However, a long-term illness following serious radiation injury will dictate that long-term venous access be maintained. The probability of wound-healing disturbances and the chronicity of phlebotoxic intravenous therapy involved in the care and treatment of any critically ill patient make central venous access preferable to peripheral intravenous access.

Using peripheral lines in the radiation casualty has further disadvantages: *(a)* placement is difficult if hemostasis is compromised and local hemorrhage develops, *(b)* placement is restricted to percutaneous insertion after 36 hours, even if a venous cutdown is otherwise desirable, *(c)* the lines are unsuitable for infusion of hyperosmolar solutions, and *(d)* the lines are at greater risk of becoming infected at the catheter tip if used longer than 72 hours. Long-term use of the percutaneous subclavian cannula made of polyethylene or polyvinyl chloride is

contraindicated because of the high rates of infection, vascular occlusion, and thrombogenicity associated with these materials.

Blood Component Therapy. Impaired hemostasis after radiation injury is best related to the decline in platelet numbers that occurs several weeks after exposure. After protracted lower-dose irradiation, the decline in platelets may take more than 2 weeks. In the interim, autologous platelets can be harvested, cryopreserved, and stored for later reinfusion. This procedure was used successfully to aid the victims of the Chernobyl reactor accident. If bleeding develops, patients with reduced numbers of platelets secondary to marrow suppression benefit from platelet transfusion even if the count is greater than 20,000/mm^3. However, prophylactic platelet transfusions are indicated on a regular basis if the count falls below 20,000/mm^3, even in the absence of bleeding.

Platelets can be collected either by harvesting the platelet-enriched plasma obtained by centrifugation of fresh units of whole blood, or by using plateletpheresis. Although pheresis technology is complicated and expensive, each pheresis platelet concentrate provides the equivalent of platelets from five to eight whole-blood donations. Thus, a single pheresis unit is the usual transfusion dose and can be obtained in a single cost-effective procedure.[29]

Anemia develops rapidly in the critically injured radiation casualty. Maintenance of perfusion pressure and oxygen delivery to injured areas, better wound healing, and an enhanced sense of well-being will depend on preventing anemia through red-cell transfusions. As with patients suffering thermal burns alone, patients with radiation skin burns and those with combined injuries require more red-cell transfusions.[10] A recall system is essential for the large number of healthy blood donors needed to keep up with the demand for red cells for mass casualties.

Erythrocytes may be stored for up to 10 years using modern cryopreservation techniques. Critical government and military leaders should stockpile autologous blood for use in case of wartime emergency.

In the fight against infections, fresh heterologous granulocyte infusions, bone-marrow transplants, and even the use of recombinant leukocyte stimulatory factors, such as granulocytemacrophage colony-stimulating factor (GM-CSF), have been advocated. Adequately controlled clinical investigations are needed to demonstrate the effectiveness and safety of these three therapies. Unfortunately, such a study was not performed during the clinical use of GM-CSF in the 1987 radiation disaster in Brazi1.[30,31] Further research is needed if the preservation of granulocytes for autologous transfusion is to be made practical. A protocol has yet to be developed for the rational and balanced use of the many humoral hematopoietic stimulatory factors and the timing of their administration. The disappointing results from attempts to use conventional bone-marrow transplants in radiation victims have obviated the use of this procedure in the treatment of mass radiation casualties.[10]

Chelation Therapy. Chelator treatment of internal contamination is most effective when initiated within the first 2 hours, before the radionuclide leaves the vascular space and enters the cell. Currently available chelating agents are not lipophilic and will not cross the cell membrane. Ethylenediaminetetraacetic acid (EDTA) is widely available, but it is toxic regardless of the route of administration. The calcium disodium salt of EDTA is used to avoid hypocalcemic tetany. To avoid nephrotoxicity, the maximal total dose of intravenous EDTA should not exceed 550 mg/kg given as a dilute solution in divided doses over at least 4 days. Intramuscular EDTA (75 mg/kg three times daily) is very painful and should only be given with a local anesthetic. EDTA is contraindicated in renal and hepatic disease. EDTA is used to chelate lead, zinc, copper, cadmium, chromium, manganese, and nickel; none of these metals is related to nuclear weapons or reactor accidents. Its use in radiation accidents is largely confined to the treatment of contamination with the transuranic elements, plutonium and americium.

Diethylenetriaminepentaacetic acid (DTPA) is more effective than EDTA for the treatment of transuranic element contamination. This agent is particularly useful for plutonium, curium, californium, berkelium, and americium, which are commonly involved in nuclear weapons accidents. DTPA is administered intravenously or by external lavage as a dilute solution of the calcium or zinc trisodium salt in physiological saline or glucose. The recommended intravenous dose is 1,000 mg/day infused over 1 hour in 250 ml of solution for 4-5 days. Used as a solution for the irrigation of radionuclide-contaminated wounds, it will cause pain unless a local anesthetic (such as 2% lidocaine) is added.[32]

Nutritional Support. In combined-injury patients and in nonirradiated critically ill patients, heightened catabolic stress and impaired nutritional status may play pivotal roles in morbidity and mortality. The incidence of wound infections and sepsis has been reduced by correcting the indices of malnutrition in postoperative patients.[33] Malnutrition may also contribute to impaired wound healing, depressed immune response, prolonged postoperative ileus, bowel atrophy, increased respiratory infections and insufficiency, impaired ventilatory responses to hypoxia and hypercarbia, delayed weaning time for patients on ventilators, and prolonged hospitalization. Since many of the above phenomena or characteristics can be linked to radiation exposure alone, their accentuation in the malnourished radiation victim is highly probable.

Simple and reliable methods of nutritional assessment are not available, particularly in the irradiated patient, whose lymphocytes will be affected independent of nutritional status. However, parameters that can be used to assess nutritional status in critically ill patients are serum albumin, transferrin, body weight, allergic skin reactions, thickness of triceps skin fold, and direct assay or clinical evidence of micronutrient deficiencies.

In selecting the route of administration of nutrients in the radiation victim, the following considerations are important. The oral route is the safest, most econom-

ical, and most natural way to provide nutrients. However, some patients will be unable to consume sufficient quantities of nutrients because anorexia occurs over a wide range of radiation doses. If the alimentary tract has not been injured by radiation, and if inanition supervenes and persists, then nutrients can be infused by nasogastric, gastric, or intestinal feeding tubes. Fluid loss associated with the cholera-like diarrhea of the gastrointestinal subsyndrome may require that nutrients and fluids be administered by both the enteral and parenteral routes. With appropriate placement of an enteral feeding tube, the use of intravenous fluids can be reduced, and transition to enteral therapy alone will be facilitated.

The catabolic critically ill radiation casualty will require no less than 2,500-2,800 kcal/day. This requirement can be met by the infusion of a balanced mixture of glucose, amino acids or protein, and lipids. Based on ideal body weight, total protein or amino acid infusion should approach (but not exceed) 2 g/kg/day. Simple carbohydrates (3.5-6.0 g/kg/day) adequately supply most of the 30-40 kcal/kg of nonprotein nutrients needed. Usually, a maximum of 30% of the total caloric requirement can be supplied as lipids. However, short-term peripheral infusion of up to 80% of total calories as lipids is acceptable if central venous access is unavailable.

The infusion of micronutrients, including vitamins, minerals, and trace elements, may need to be adjusted with long-term parenteral therapy. The usual daily replacement dosages of essential water-and fat-soluble vitamins, with the exception of vitamin K, are commercially supplied in a single vial. In thermal-burn-injury patients, the requirements for B-complex vitamins and vitamin C are increased. Vitamin K is given as a 10-mg intramuscular injection once a week. If renal impairment supervenes, the normal requirement for potassium (60-100 meq/day), magnesium (8-12 meq/day), and phosphorus (30-60 meq/day) may need to be reduced. Since sodium depletion may occur with diarrhea in the gastrointestinal subsyndrome, sodium infusion of over 150 meq/day may be needed. If chelation therapy with EDTA is undertaken, supplements of zinc (>4 mg/day), copper (>1.5 mg/day), chromium (>15 μg/day), manganese (>0.8 mg/day), and iron (>2 mg/day) may be needed. The patient who receives multiple blood transfusions will not need iron supplements until after the blood count has stabilized. Trace element supplements, including iodine and selenium, should be considered if prolonged parenteral feeding becomes necessary.

SUMMARY

Triage

The degree of injury of a radiation casualty can be categorized by the symptoms of exposure. Casualties can be rapidly sorted on the basis of unlikely, probable, or severe radiation symptoms. This rapid sorting of victims allows the conventional traumatic injuries to receive appropriate attention. Lymphocyte counts are the

most necessary laboratory procedure in the first hours and days after exposure. Information from currently available physical dosimeters is of limited value and cannot be relied on entirely in making triage decisions.

Triage is greatly complicated if the patient has suffered combined injuries. A shift in priority to the expectant category is likely for a radiation casualty who requires more than one surgical procedure or who has received a surface burn of more than 10%.

Medical Management

In the first hours after radiation injury, the priority will be to treat the injuries that require immediate attention. Candidates for surgery must be carefully chosen. Only radiation victims who can be attended to within 36 hours and whose condition does not call for multiple procedures should go to surgery.

Decontamination of surface radionuclides is nearly always a second priority after the initial resuscitative support, and can be effectively done with lavage before surgery. Chelation therapy for internal radionuclide contamination can be safely accomplished with the experimental agent DTPA, but the effectiveness of this therapy with mass casualties remains uncertain.

The use of antiemetics and antidiarrheals may contribute significantly to patient comfort. Unfortunately, in effective doses, the currently available agents have major side effects that impair the patient's performance.

The prevention of infection and the appropriate use of antibiotics are important in the first few weeks after exposure. Within the first 7-10 days, selective gut decontamination should be used before leukopenia and sepsis occur. Two to 3 weeks later, if infection is indicated by fever and leukopenia, parenteral antibiotics should be initiated. To help prevent infection with new organisms, environmental control measures should be instituted as soon as possible.

Supportive therapy with blood components has been shown to be extremely effective in combating hemorrhage and anemia following combined injury. However, granulocyte transfusions and bone-marrow transplants as currently used appear to be of little help. A combination of simple supportive measures, including fluids, electrolytes, antibiotics, adequate nutrition, and platelet transfusions, can significantly reduce mortality, as shown by studies of animal research models.

Effective triage will permit the use of limited resources to improve the greatest number of radiation casualties. Survival after either radiation injury alone or combined injury can be greatly enhanced by the application of currently available treatments. Research into new and experimental therapeutic agents for the

treatment of radiation injury may be expected not only to benefit the civilian population, but also to enhance the survival of the fighting force.

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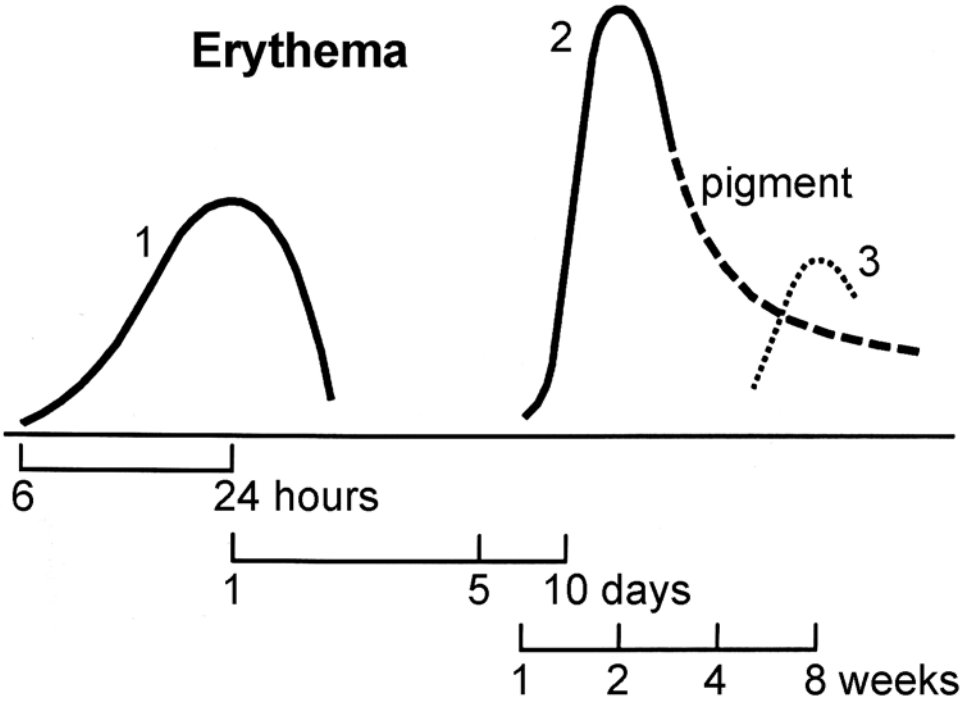

Figure 3-1. Appearance of waves of erythema after irradiation of human skin. Dotted lines indicate pigmented lesions. Source: Redrawn from reference 6.

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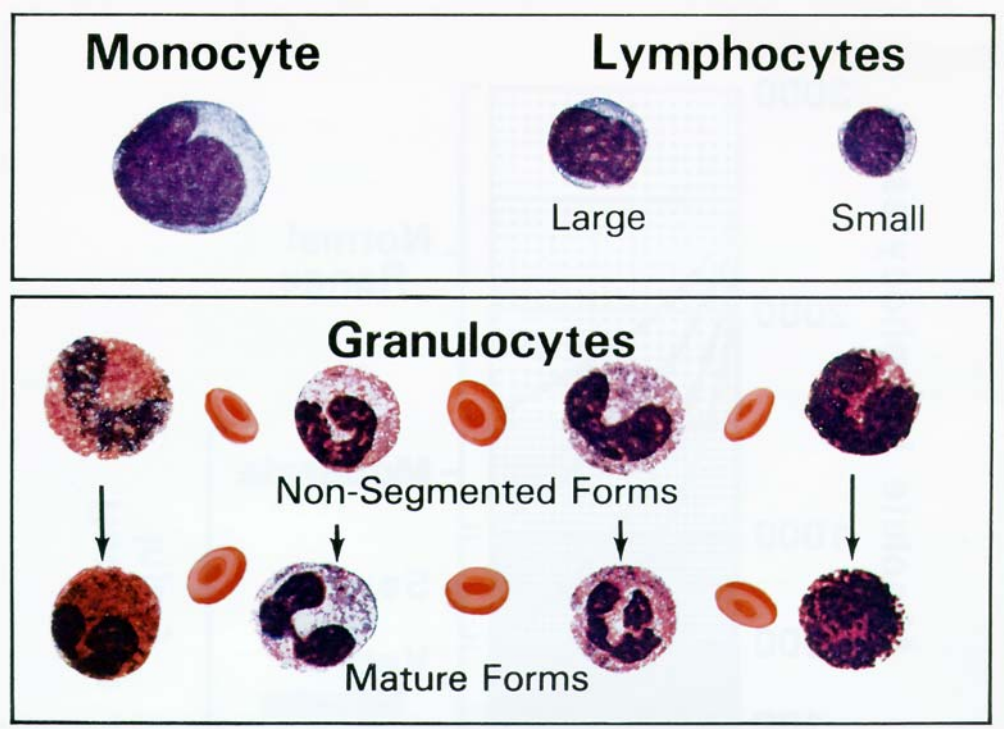

Figure 3-2. Appearance of human mononuclear cells (lymphocytes and monocytes) compared to human granulocytic cells (eosinophils, neutrophils, and basophils) in their nonsegmented and segmented (mature) forms. Erythrocytes are shown for contrast in size.

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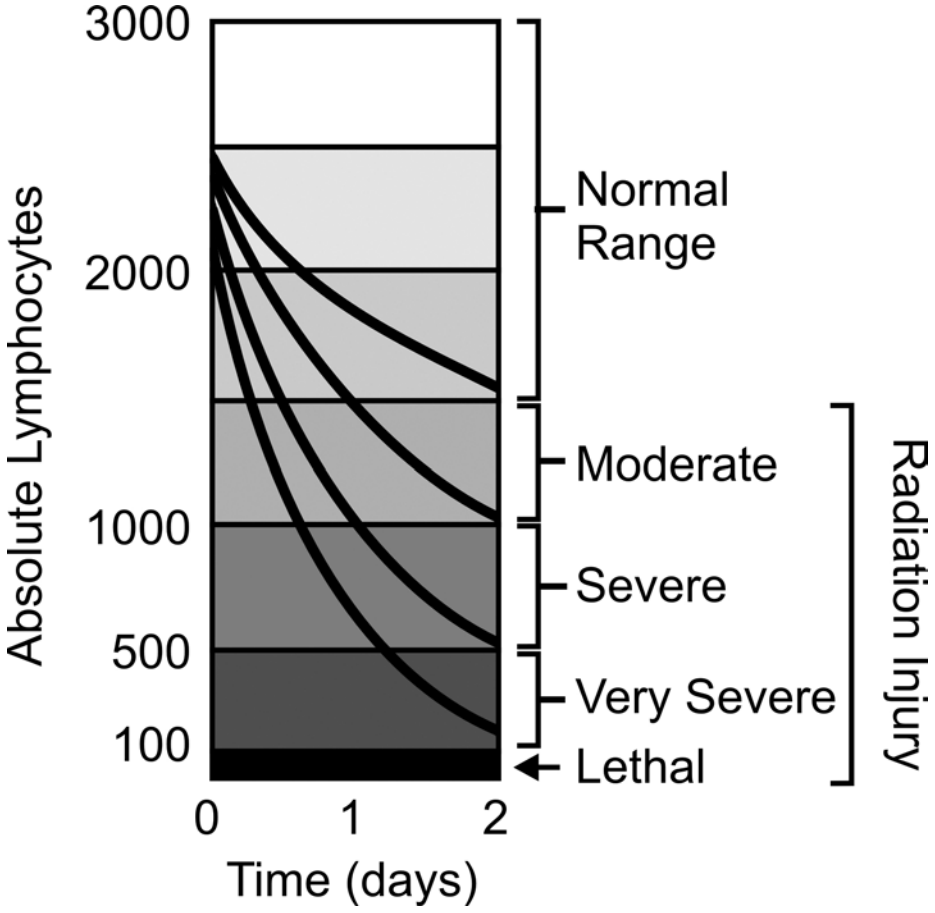

Figure 3-3 To use a lymphocyte nomogram: *(a)* determine total lymphocytes/mm^3 every 6 hours; *(b)* because the absolute number of lymphocytes (Y axis) depends on technique, use standardized laboratory methodology; *(c)* because the ordinal scale (X axis) depends on acuteness of radiation exposure, do not use scale shown if exposure is protracted.

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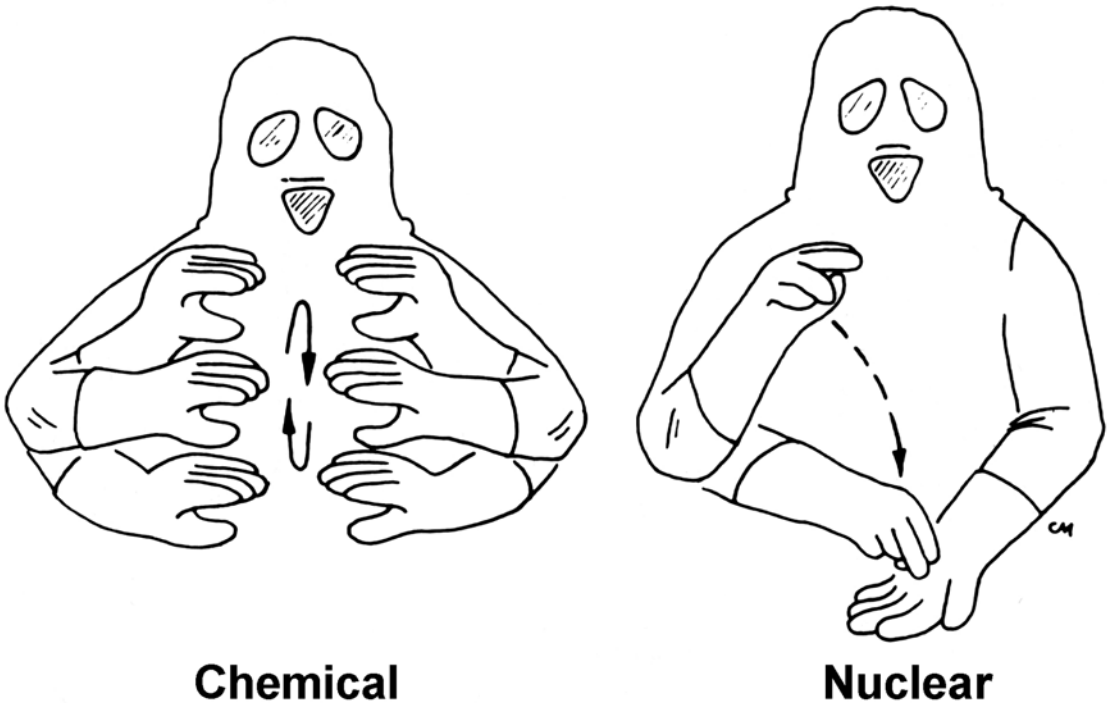

Figure 3-4. To sign for “chemical,” make a “C” with hands and move them in a circle away from lower thorax and toward shoulders. To sign for “nuclear,” thrust second and third fingers toward open palm of opposite hand.

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TABLE 3-1
PRIORITIES IN COMBINED-INJURY TRIAGE WHEN RADIATION DOSES ARE KNOW*

Conventional Triage Categories if Injuries Are Only Trauma**	**Changes in Expected Triage Category Following Whole-Body Radiation Dose (GY)**		
No radiation exists	<1.5	1.5-4.5	>4.5
T1	T1	T1	T4
T2	T2	T4	T4
T3	T3	T4	T4
T4	T4	T4	T4

*Decision based on whole-body radiation dose, assuming all casualties are wearing personal dosimeters.

**Conventional Triage Categories:

T1: Immediate treatment, high survival group
T2: delayed treatment, patient can be sustained
T3: Minimal treatment, minor injury group
T4: Expectant, seriously injured–poor survival

Source: Adaptation from data in NATO Handbook on the Concept of Medical Support in NBC Environments (reference 15).

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TABLE 3-2
ESTIMATION OF POSSIBLE RADIATION INJURY BASED ON SYMPTONS

Symptoms	Unlikely	Probable	Severe
Nausea	(–)	(++)	(+++)
Vomiting	(–)	(+)	(+++)
Diarrhea	(–)	(±)	(± to +++)
Hyperthermia	(–)	(±)	(+ to +++)
Erythema	(–)	(–)	(– to ++)
Hypotension	(–)	(–)	(+ to ++)
CNS dysfunction	(–)	(–)	(– to ++)

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TABLE 3-3
PRIORITIES IN COMBINED-INJURY TRIAGE WHEN RADIATION INJURY IS POSSIBLE

Conventional Triage Categories if Injuries Are Only Trauma*	Changes in Expected Triage Category Following Possibility of Radiation Injury				
	Unlikely	Probable	Confirmed		
No radiation exists			Minimum**	Moderate	Severe
T3	T3	T3	T3	T3	T3
T2	T2	T2/T4	T3	T4	T4
T1	T1	T3/T4	T3	T4	T4
T4	T4	T4	T4	T4	T4

*Conventional Triage Categories:
T1: Immediate treatment, high survival group
T2: Delayed treatment, patient can be sustained
T3: Minimal treatment, minor injury group
T4: Expectant, seriously injured–poor survival
**Acute radiation dose of approximately 0.5 Gy

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Chapter 1

NUCLEAR EVENTS AND THEIR CONSEQUENCES

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INTRODUCTION

Radiation damage to human cells was first recognized just 4 months after the reported discovery of X rays by Wilhelm Conrad Roentgen. In 1896, Dr. J. Daniels found that the irradiation of his colleague's skull resulted in loss of hair. Since then, many other biomedical effects of radiation have been described.

The understanding of atomic physics increased rapidly in the early twentieth century and culminated in the Manhattan Project, which harnessed the power of the atom in a bomb. Thus began the nuclear era in international relations and warfare, bringing new challenges to the military physician.

Today, more and more countries are developing nuclear weapons, with those in the United States and the Soviet Union achieving the greatest capabilities. One modern American or Soviet submarine carries nuclear weapons that can release energy equivalent to 500 bombs of the size used at Hiroshima in 1945. This vast power is greater than the energy released from all weapons in all previous wars combined. Of course, the extensive use of these nuclear weapons in a confrontation would nullify an effective medical response. Rational minds must continue to recognize this potentially devastating nuclear power and maintain a general peace, as they have for over 40 years.

The deterrent effect of nuclear weapons does not mean that military physicians can ignore the possibility of their use. The most likely situations requiring a medical response are the use of weapons against a deployed naval force, a remote city, or a remote facility; a third-world conflict; a terrorist act; or an accident involving a nuclear weapon.

Military medical preparedness can focus beyond nuclear weapon events. Today, nuclear material is used in medicine, industry, and power generation, bringing increased risk of occupational and accidental exposures. New radiation hazards in space will have to be overcome if successful peacetime and military uses of that frontier are to be realized. Military physicians trained to respond to weapons-related injuries can bring expertise to these situations.

NUCLEAR AND PHYSICAL PROCESSES IN WEAPONS

Weapons-related injuries can be best understood after examining the destructive forces—*blast*, *thermal*, and *radiation*–that produce them. In comparison with a conventional explosive weapon, a nuclear weapon's effectiveness is due to its unequalled capacity to liberate a tremendous quantity of energy in a very small space in an extremely short time. This section presents a simple description of the physical processes taking place within the first few thousandths of a second after a nuclear weapon detonation.

Nuclear Energy

Energy may be broadly classified as potential or kinetic. Potential energy is energy of configuration or position, or the capacity to perform work. For example, the relatively unstable chemical bonds among the atoms that comprise trinitrotoluene (TNT) possess chemical potential energy. Potential energy can, under suitable conditions, be transformed into kinetic energy, which is energy of motion. When a conventional explosive such as TNT is detonated, the relatively unstable chemical bonds are converted into bonds that are more stable, producing kinetic energy in the form of blast and thermal energies. This process of transforming a chemical system's bonds from lesser to greater stability is exothermic (there is a net production of energy). Likewise, a nuclear detonation derives its energy from transformations of the powerful nuclear bonds that hold the neutrons and protons together within the nucleus. The conversion of relatively less stable nuclear bonds into bonds with greater stability leads not only to the liberation of vast quantities of kinetic energy in blast and thermal forms, but also to the generation of ionizing radiations.

To discover where these energies come from, consider the nucleus of the helium atom, which is composed of two neutrons and two protons bound tightly together by the *strong* (or specifically nuclear) *force.* If we compare the bound neutrons and protons to those in the unbound state, we find that the total mass of the separate neutrons and protons is greater than their mass when they bind together to form the helium nucleus. The mass that has been lost in the process of forming the nuclear bonds is called the *mass defect.* Einstein's famous equation, E = mc2 (energy equals mass multiplied by the speed of light squared), quantifies the conversion of this missing mass into the binding energy that holds together the helium nucleus**.** This is the potential energy stored in the bonds of the strong force. A small amount of mass, when multiplied by the speed of light squared (an extremely large number), has a large amount of binding energy. If the total binding energy for each element is calculated and divided by its total number of nucleons (that is, neutrons plus protons; for helium, two neutrons plus two protons equals four nucleons), a measure is obtained of how tightly the average nucleon is bound for that particular atom. A plot of this "average binding energy per nucleon" for each element gives the curve in Figure 1-1.

It is significant that this curve has a broad maximum. This means that there is a range of elements for which the neutrons and protons are most tightly bound and, thus, have the most stable nuclear bonds. If nuclei having less stable nuclear bonds can be converted into nuclei having more stable bonds, the system will pass from a state of lesser to greater stability, and energy will be released. This is the energy source of nuclear weapons. The process can occur in two ways: *fission* or *fusion.* Fission is the process of breaking less stable larger elements (such as uranium and plutonium) into two of the more stable midrange elements. Fusion is the process of combining lighter nuclei (such as those of deuterium and tritium, which are

isotopes of hydrogen) into heavier elements lying farther up the curve of binding energy per nucleon.

Energy Release in Nuclear Weapons

A fission nuclear device is practical for only three elements: uranium-233, uranium-235, and plutonium-239. In order to construct an efficient weapon, instability is induced in one of these nuclei by striking it with a neutron. The unstable nuclear bonds are broken, the nucleus splits apart, and relatively more stable nuclear bonds are reformed by each of the two midrange fission fragments. This is accompanied by the release of a large quantity of energy and the prompt emission of gamma rays and neutrons *(initial nuclear radiation).* It is important to note that approximately 82% of the fission energy is released as kinetic energy of the two large fission fragments. These fragments, being massive and highly charged particles, interact readily with matter. They transfer their energy quickly to the surrounding weapon materials, which rapidly become heated. The fission fragments consist of over 300 different isotopes of thirty-eight separate chemical elements. Most of the fragments are highly unstable radioactively and will later contribute to the radiologically and chemically complex fallout field.

One fission event alone does not make a weapon, which requires a self-perpetuating, exponentially escalating chain reaction of fissions. This is achieved by the suitable physical arrangement of certain nuclear materials. Also, since the weapon must not reach the proper, or *critical,* configuration until the desired time of detonation, some way must be found to make the transition on demand from a safe, or *subcritical,* condition to the critical state. In a functioning fission device, this is done by altering the mass, shape, or density of the nuclear materials.

The two basic classes of fission weapons are the *gun-assembled device* and the *implosion device.* The gun-assembled weapon is a mechanically simple design that uses a “gun tube” arrangement to blow together two small masses of uranium-235 to form a supercritical mass. The 15-kiloton-yield weapon used at Hiroshima was a gun-assembled device (1 kiloton, or kt, equals the energy released by detonation of 1,000 tons of TNT, and 1 megaton, or MT, equals 1,000,000 tons of TNT). The implosion weapon uses an extremely complex system of precisely formed, conventional chemical-explosive lenses to crush a mass of plutonium-239 to supercritical density. The first tested nuclear weapon (the Trinity device) and the 21-kt-yield weapon used at Nagasaki were implosion devices. From the viewpoint of a weapon's accessibility, it is fortunate that the much more easily constructed gun-assembled weapon cannot effectively use the more readily producible pluto-nium-239. Instead, it must be fueled with uranium-235, which is more difficult to obtain.

The limit on a fission weapon's yield, from an engineering viewpoint, is several hundred kilotons. Therefore, the multi-megaton weapons in the American and Soviet inventories are fusion weapons, deriving much of their power from the

combination of light isotopes of hydrogen (deuterium and tritium) into heavier nuclei lying farther up the curve of binding energy per nucleon. Due to the presence of powerful forces of electrostatic repulsion, initiation of the fusion of deuterium and tritium requires extremely high temperatures, about 50,000,000°C. The only practical way to achieve those temperatures in a weapon on earth is to detonate a fission device inside the fusion materials. The deuterium and tritium then fuse and release energy, partly in the form of highly energetic and penetrating fusion neutrons, which have energies about ten times the typical energies of fission-generated neutrons. The fusion weapon then uses these high-energy fusion neutrons to cause secondary fissions. Thus, a fusion weapon actually generates power from both fission and fusion processes, usually in roughly equal proportions.

An *enhanced radiation weapon,* or neutron bomb, might be produced by altering the design of a standard small-yield fusion weapon to permit the high-energy fusion neutrons to better escape the device. This modification increases the initial production of neutron radiation, reduces the proportion of the weapon's energy expressed in blast and thermal effects, and reduces the amount of residual fallout radiation. Thus, a given total yield produces more biologically damaging neutron radiation, less destruction of materiel from blast and thermal effects, and less residual radiation fallout.

Production of Blast and Thermal Effects

The blast and thermal effects of detonation produce by far the greatest number of immediate human casualties in nuclear warfare. The nuclear reactions within the weapon have died out after the first one-millionth of a second, and the fission and fusion events have produced a vast quantity of energy, which has been rapidly and locally transferred to the bomb materials in the form of heat. The weapon's materials (bomb casing, electronics, chemical explosive residues, and 80% of the original nuclear fuels, which even in a relatively efficient device remain unreacted) now exist as a highly energetic plasma of positive ions and free electrons at high temperature and high pressure. Through a process of electron-ion interaction known as *bremsstrahlung,* the plasma becomes an intense source of X rays. These X rays leave the vicinity of the bomb materials at the speed of light, heat the first several meters of air surrounding the weapon, and generate a fireball with an initial temperature of 1,000,000°C. The intensely hot fireball reradiates thermal energy in the form of electromagnetic radiation at infrared, visible, and ultraviolet frequencies.

At about the same time, the weapon's materials have started to expand supersonically outward, dramatically compressing and heating the surrounding air. This phenomenon, called *case shock,* is the source of the destructive blast wave and further thermal radiations. A unique interaction between the X-ray-heated air and the case-shock-heated air is responsible for the nuclear weapon's characteristic double pulse of thermal output. Added to these blast and thermal effects is the

initial nuclear radiation (primarily neutrons and gamma rays) which is produced promptly by the fission and fusion processes, and the *residual radiation* (primarily gamma rays and high-energy electrons) which are produced later by decay of the radioactive fission fragments composing the fallout field. Figure 1-2 depicts the typical energy partition for a standard fission or fusion device and the energy partition expected from a typical enhanced-radiation weapon (neutron bomb).

The range of the blast, thermal, and radiation effects produced by the detonation of a nuclear weapon depends on many factors, perhaps the most significant of which, for the battlefield soldier, is total weapon yield. Figure 1-3 shows the range over which the various effects are lethal, as a function of yield. It is noteworthy that initial radiation is the dominant threat for only very small tactical devices, and thermal effects are dominant for large-yield strategic weapons.

BLAST, THERMAL, AND RADIATION EFFECTS

The destructive blast, thermal, and radiation effects of a fission or fusion weapon all stem from the device's capacity to transform the very strong nuclear bonds of uranium, plutonium, deuterium, and tritium from a relatively unstable state to a more stable one. The quantitative difference between the effects of a nuclear weapon and the effects of a conventional explosive is the result of the dramatically greater strength of the nuclear bonds. A qualitative difference arises from the production of *(a)* initial nuclear radiations from the fission and fusion processes themselves and *(b)* delayed radioactivity from decay of the unstable fission fragment byproducts.

Blast Effects

During the detonation of a standard fission or fusion nuclear device, the rapidly expanding plasma gives rise to a shock or blast that is responsible for dissipating about 50% of the total energy of the weapon. This represents a tremendous amount of energy, even in small, tactical-sized weapons of a few kilotons. As the blast wave travels outward from the site of the explosion, it is composed of static and dynamic components that are capable of producing medical injuries and structural damage. The static component of the blast wave is a wall of compressed air that exerts a crushing effect on objects in its path. The dynamic component is the movement of air caused by and proportional to the difference between the static overpressure and the ambient pressure. In this discussion, the static and dynamic components will be called the *blast wave* and *blast wind,* respectively.

In discussing the structural damage to buildings after a nuclear detonation, it is difficult to separate the effects of the static component from those of the dynamic component. For example, the 5-psi (pounds per square inch) blast wave and 160-mph blast winds associated with the blast wave's passage would destroy a two-story brick house.

However, the medical problems resulting from exposure to the shock wave can be divided into those that result from the static component and those that result from the dynamic component. Injuries resulting from the blast waves will be caused by exposure to high pressures with very short rise times, and will consist primarily of internal injuries. For example, the threshold level for rupture of the eardrum is about 5 psi. Although this injury is very painful, it would not limit the accomplishment of a critical military mission. The 160-mph winds that accompany the passage of a 5-psi blast wave would be sufficiently strong to cause displacement and possible injuries. At the other end of the spectrum, a pressure level of 15 psi will produce serious intrathoracic injuries, including alveolar and pulmonary vascular rupture, interstitial hemorrhage, edema, and air emboli. If the air emboli make their way into the arterial circulation, cerebral and myocardial infarctions may ensue. The initial outward signs of such pulmonary damage are frothy bleeding through the nostrils, dyspnea, and coughing. Victims may be in shock without any visible wounds. In addition, serious abdominal injuries, including hepatic and splenic rupture, may result from a rapid and violent compression of the abdomen.

The blast winds that accompany the blast wave can also produce injuries. Debris carried by the wind may cause missile injuries ranging from lacerations and contusions to fractures and blunt trauma, depending on the projectile's size, shape, and mass. Wind velocity of 100 mph will displace a person, resulting in lacerations, contusions, and fractures from tumbling across the terrain or from being thrown against stationary structures. Winds capable of causing displacement injuries or missile injuries would be produced by a blast wave with an overpressure of less than 5 psi. At this pressure level, the blast winds are more significant in producing injury than is the static component of the blast wave. At high pressure levels, both the static and dynamic components are capable of producing serious injuries.

Although the LD_{50} (lethal dose, or fatal injury, for 50% of cases) from tumbling occurs at about 50 mph, the LD_{50} from impact occurs at about 20-25 mph. The LD_{50} from blast is estimated to occur at 6 psi, due primarily to the force of blast winds. For a small tactical weapon or terrorist device with a yield of 0.5 kt, the range for this level of overpressure would extend to slightly less than 0.5 km. For larger tactical or strategic weapons with yields of 50 and 500 kt, the range for LD_{50} at 6 psi would expand to just under 2 km and just under 4 km, respectively.

Protection from the effects of the blast wave is difficult to achieve because it is an engulfing phenomenon. The best protection can be found in a blast-resistant shelter. However, protection from the effects of the blast winds can be achieved in any location offering shielding from the wind. If adequate shelter is not found, the best defense against blast effects is to lie face down on the ground with feet pointed toward ground zero. This reduces the body's surface area that is exposed to wind-borne debris and offers less resistance to the force of the blast wind.

Thermal Effects

Following the detonation of a standard fission or fusion device, approximately 35% of the weapon's energy is dissipated as thermal energy. The general types of injuries resulting from this energy are burns, including *flash burns* and *flame burns,* and certain eye injuries, including *flash blindness* and *retinal burns.*

The thermal output after a nuclear detonation occurs in two distinct pulses, as a result of the interaction of the shock wave with the leading edge of the fireball. The first pulse contains only about 1% of the total thermal energy output and is composed primarily of energy in the ultraviolet range. Because the first pulse is of very short duration and the ultraviolet energy is rapidly absorbed by the atmosphere, it does not contribute significantly to producing casualties. The second pulse is composed primarily of energy in the infrared and visible portions of the electromagnetic spectrum, contains about 99% of the thermal energy liberated by the nuclear detonation, and is responsible for subsequent burns and vision problems.

Burn Injury. The two types of burn injury, flash burn and flame burn, are caused by different events and have different prognoses. Flash burn results from the skin's exposure to a large quantity of thermal energy in a very brief time. This often leaves the affected area of the skin with a charred appearance. However, since the heat pulse occurs rapidly and the thermal conductivity of the skin is low, the burn is often superficial, killing only the outer dermal layers and leaving the germinal layer essentially undamaged. In contrast, flame burn results from contact with a conventional fire, such as clothing or the remains of a building ignited by the fireball's thermal pulse. In most cases, the healing of a flame burn is abnormal because the germinal layer has been damaged.

Since the heat pulse travels at the speed of light, protection from burns is not possible unless warning is given in time to find cover. The electromagnetic energy of the thermal pulse travels in a straight line, so any barrier placed in its path will offer some protection. Even clothing will provide some protection from the deposition of thermal energy onto the skin. Since light colors tend to reflect rather than absorb thermal energy, light-colored clothing will offer more protection than dark-colored clothing.

Figure 1-3 shows the range of LD_{50} for burn injury from weapons of different yields. Notice that for weapons of very low yield, the range for burn injury LD_{50} is about equal to the range for the LD_{50} from blast and radiation. As the weapon yield increases, the range for burn injury increases much more rapidly than the range for blast injury or radiation injury. This means that burns will always be present after the detonation of a nuclear device, and for weapons with a yield above 10 kt, burns will be the predominant injury. Because of the large number of burn casualties and the time- and labor-intensive treatment that they require, burn

injury is the most difficult problem to be faced by the military medical community in a nuclear conflict.

Eye Injury. Thermal energy may also cause eye injury. The two types of eye injury that would occur would not burden a medical facility. Flash blindness is a temporary condition that results from a depletion of photopigment from the retinal receptors. This happens when a person indirectly observes the brilliant flash of intense light energy from a fireball. The duration of flash blindness can be as short as several seconds during the day, followed by a darkened afterimage for several minutes. At night, flash blindness can last three times longer, with a loss of dark adaptation for up to 30 minutes. This could seriously compromise military operations.

Another eye injury is retinal burn, which results from looking directly at the fireball and focusing its image on the retina. This intense light energy is strong enough to kill the retinal receptors and create a permanent blind spot. It is surprising that retinal burn is no more detrimental to mission accomplishment than is flash blindness.

To protect against injury, the eyes can be closed and shielded after the individual receives warning of a detonation. Using one of the lead-lanthanum-zirconium-titanium goggles that have been developed may provide further protection.

Effects of Initial and Residual Radiations

A detonating fission or fusion weapon produces a variety of nuclear radiations. Initial radiation occurs at the time of the nuclear reactions, and residual radiation occurs long after the immediate blast and thermal effects have ended. The nuclear radiations include neutrons, gamma rays, alpha particles, and beta particles, which are biologically damaging and may significantly affect human health and performance. Initial radiation consists of neutrons and gamma rays produced within the first minute after detonation. Mechanisms for producing initial radiation are *(a)* the generation of neutrons and gamma rays directly from the fission and fusion processes, *(b)* the production of gamma rays through inelastic scatter reactions with elements in the atmosphere surrounding the weapon, and *(c)* the isomeric-decay and neutron-capture gamma rays. Residual radiation primarily includes gamma rays, beta particles, and alpha particles generated beyond the first minute after detonation. Most of these radiations are produced by the decay of the fission fragments generated by weapon fission processes, but some are activated bomb components and surface materials made radioactive by exposure to the intense neutron flux generated by fission and fusion events.

The broad classes of initial radiation and residual radiation come from an analysis of a 20-kt ground burst. The hot fireball produced by this weapon, laden with highly radioactive fission fragments, rises upward through the atmosphere so quickly that, after about 60 seconds, it reaches a height from which the initial

radiations no longer strike the ground. A person on the ground would therefore be safe from the initial radiations after 1 minute. As the yield of the weapon is increased, the fireball rises more quickly, but the 60-second point remains approximately the same. The main hazard from initial radiation is acute external whole-body irradiation by neutrons and gamma rays. Figure 1-3 shows that it is only for very small tactical weapons that the initial radiation is potentially fatal at distances where the blast and thermal effects are survivable. Therefore, significant initial radiation hazards are restricted to the first minute after detonation and to several hundred meters surrounding a small-yield tactical weapon. Conversely, residual fallout covers a wide geographic area and remains a significant biological hazard long after detonation.

Fallout. Our consideration of the origin of radioactive debris begins with a review of the basic nuclear and physical processes that occur as the device detonates. As the fissile material splits, the massive and highly charged fragments carry away 82% of the fission energy, and release it as heat within the bomb components. This transforms the components into an extremely hot plasma. Bremsstrahlung interactions between the electrons and positive ions within this plasma generate an intense source of low-energy X rays, which leave the plasma and interact with the first several meters of air surrounding the weapon. The X rays heat this air to an extremely high temperature and initiate the development of the fireball that is characteristic of nuclear explosions. The rapid outward expansion of weapon material dramatically compresses and heats the air around the weapon (case shock), further contributing to the generation of the fireball. This hot bubble of gas, containing highly radioactive fission fragments and activated weapon material, is the origin of the fallout radiation.

Sources of fallout include *(a)* highly unstable fragments produced by the fissioning of plutonium or uranium, *(b)* roughly 80% of the nuclear fuels that remain unreacted after the weapon has blown itself apart (uranium or plutonium for all weapons, as well as tritium for fusion devices), and *(c)* activation products (weapon components and ground elements made radioactive by exposure to the weapon's intense neutron flux). Another contributor to fallout is *salting*, the inclusion of materials in a weapon that will activate when exposed to the initial neutron flux, thus increasing the amount of residual radioactive isotopes. Because of operational limitations in using a salted weapon, it is expected that this technique will be rarely used. Since the fission fragments produced by the fissioning of uranium or plutonium account for most of the activity in the fallout field, the fusion process is relatively "clean" regarding the production of residual radiation.

Early fallout is radioactive material deposited within the first day after detonation. This fallout is the most significant for the military because it is highly radioactive, geo-graphically concentrated, and local. It tends to consist of larger particles (approximately 0.01-1.0 cm in diameter) usually deposited within a few hundred miles of ground zero. Because the material has had little time to decay, it is

radiologically very active. The biological hazards from early fallout are external whole-body gamma-ray irradiation from gamma emitters deposited on the ground; external beta-particle irradiation from beta emitters deposited on the skin; and internal beta-particle irradiation from beta- emitting isotopes that are ingested, injected, or inhaled.

Delayed fallout generally consists of the smaller particles deposited after the first 24 hours. This material is less significant as an immediate hazard to the military because it has a longer time to decay and it is deposited over a wider area. Under certain circumstances, delayed fallout may be distributed worldwide, presenting a long-term health hazard, primarily through internalized exposure.

The ultimate deposition of nuclear fallout on the ground is influenced by the physical interactions of the rising fireball with the atmosphere. For a ground or near-surface burst, the interaction of the fireball with ground debris also affects the fallout deposition. As the hot gas bubble quickly rises through the atmosphere, it creates and is followed by a strong vacuum directly from below. This generates winds that rush radially inward toward ground zero and upward toward the ascending fireball. For a near-surface burst, these winds can pick up large quantities of dirt and debris from the ground and inject them into the fireball (a process called *stem formation).* This material, along with any other ground material directly vaporized by a surface burst, then provides condensation centers within the fireball. The gaseous fission fragments condense more quickly on these relatively larger debris particles than they would have otherwise, greatly increasing early local fallout. This fallout is deposited quickly in a concentrated area relatively near ground zero. Thus, a ground or near-surface detonation is the most significant fallout hazard to the military. The activation of surface materials through irradiation of ground elements by the direct neutron flux of a near-surface burst may also increase the local fallout hazard to troops traveling through that area soon after detonation.

In the case of a pure airburst detonation with no secondary ground materials injected into the fireball, the cloud rises and cools, and the fission fragment vapors begin to cool and condense at certain temperatures (characteristic of their particular elements). Therefore, because the time for airburst fission-product condensation is delayed and because fission products do not condense on large particles of ground debris, the proportion of fallout activity expressed as early local fallout is greatly reduced.

Characteristics of Fallout and the Prediction of Hazards. The factors that determine the extent of anticipated fallout hazard are:

- The total fission yield (fission fragments are the largest contributor to fallout activity)

- The ratio of energy produced in a fusion weapon, by fission process versus fusion process (the higher the fission fraction, the more fission products and consequently the greater the radiological hazard)

- The specific design of the weapon (for example, an enhanced radiation weapon will produce proportionately less fallout than an equivalent-yield standard nuclear weapon)

- The altitude of burst (a ground or near-surface detonation produces the greatest early local hazard)

- The composition of surface elements near ground zero in a near-surface burst (accounting for the neutron flux-induced activation potential of surface materials)

- The meteorological conditions (winds and precipitation introduce by far the greatest uncertainties in predicting where and when the fallout will be deposited)

- The time after detonation (the more time allowed for radiological decay, the less the activity of the fallout field)

In terms of absolute quantity of energy from fallout, approximately 10% of the quoted energy yield of a typical fission weapon will be decay radiation; for fusion weapons, it will be approximately 5%.

The elemental distribution of fission fragments is almost independent of whether the fissile material is plutonium or uranium. In each case, approximately 38 different chemical elements are produced, consisting of about 300 separate radionuclides. Thus, the chemical and radiological characteristics of the fallout field are extremely complex and, in practice, are amenable only to empirical analysis. The fission fragments are highly unstable and decay primarily by emitting gamma rays and beta particles. Activated weapon materials and ground elements, as well as unspent tritium from a fusion weapon, will decay by the same means. The unspent uranium and plutonium from fission processes decay by emitting alpha particles, which are a hazard primarily if they are inhaled. The immediate detection of fallout radiation is not possible with the physical senses, so appropriate instruments must be used. However, the heavy early, local fallout material is usually visible as a dust-like deposit that may look like a film on shiny surfaces. These visible particles are the most hazardous component of fallout.

MEDICAL CONSEQUENCES OF NUCLEAR WEAPONS

Military planners are concerned with the effect of nuclear weapons on the human component of operational systems. It is futile to harden machinery to large

amounts of radiation if the human operator is incapacitated by relatively small doses. Radiobiology research can help reduce the logistical drain on medical resources caused by large numbers of severely injured casualties. Targeting and contingency planning depend on knowing radiation effects on military personnel.

The Chernobyl Accident

Unlike controlled radiotherapy, radiation associated with weapon detonations or accidents can result in uncontrolled and usually unpredictable exposures, which make radioprotective measures difficult. As seen in the 1986 accident in Chernobyl, USSR, *dosimetry* (measurement of radiation dose) is also difficult. Physical dosimeters, if available, may be lost during a nuclear event or may record cumulative doses with no information on dose rate. Furthermore, dosimeters provide point data rather than whole-body data. Biological dosimetry is also imperfect, and the time-consuming tests of lymphocyte depletion and cytogenetic damage (such as those used for Chernobyl victims) give different results. Dosimetry with uncontrolled exposures is complicated by two other factors with which military physicians may have to cope.

One is the uneven distribution of exposures on a victim due to shielding. Thus, pockets of critical cells that are necessary to regenerate affected tissues may survive, even if some parts of the body receive very high doses of radiation. Bone-marrow transplants were generally unsuccessful in Chernobyl victims, partially because of the survival of some host stem cells in the bone marrow; as surviving marrow was regenerated, it rejected the transplanted marrow cells.

Another complication of dosimetry in accidents or warfare is that other injuries, such as burns or mechanical trauma, can be superimposed on radiation injuries. The prognosis for these combined injuries is much graver than for radiation injuries alone, so combined injuries must be carefully considered during *triage* (sorting of casualties). It is estimated that 65%-70% of weapon-related injuries will be combined injuries, with burns and radiation being the most common combination (Table 1-1).

Burns and radiation effects were the most common injuries seen in seriously injured victims of the Chernobyl disaster. Thousands of medical and paramedical personnel were available for the relatively small number of patients at Chernobyl, but this will not be the case in military situations. If a nuclear weapon is detonated, physicians will have to adapt to mass-casualty management techniques, which require simplified and standardized care.

Today, scientists are exploiting the tremendous advances in biotechnology—the new knowledge and techniques in gene regulation, immunology, neurobiology, and related sciences—and will soon develop significant protection for the human body from the consequences of radiation exposure and associated injuries.

Nature of Radiation Injuries

Almost every major organ system can be affected by radiation exposure, and management in a nuclear accident or warfare will require the coordinated efforts of physicians, allied health professionals, and health-physics personnel.

A nuclear device detonated over a major city will cause tremendous numbers of casualties. The day after the detonation, 45,000 dead and 90,000 injured were counted in Hiroshima. Modern weapons would result in a much larger number of casualties. As the number of persons killed immediately due to blast and thermal injuries increases, so does the number of individuals at some distance from the epicenter who have serious but potentially survivable injuries. Therefore, an understanding of these injuries is extremely important to preserve human life and ensure the success of military operations.

Damage to the human body by ionizing radiation is caused by the deposition of energy. This is true for both electromagnetic radiation (such as X rays and gamma rays) and particulate radiation (such as beta particles, which are high-speed electrons, or neutrons). This energy deposition results in reactive chemical products, including free radicals (such as the hydroxide radical). These free radicals can further combine with body chemicals, primarily water, to form reactive species (such as hydrogen peroxide). These elements then combine with cellular components to cause damage. The primary targets of damage within the cell are deoxyribonucleic acid (which can be attacked not only by reactive chemical products but also by direct effects of the radiation itself), cellular and nuclear membranes, and enzymes.

The amount of damage sustained is a function of the radiation's quality, dose, and dose rate, and of the individual cell's sensitivity. The higher the dose, or the greater the deposition of radiation energy, the greater the damage expected. *Quality* refers to particular types of radiation (such as gamma radiation or neutron radiation) and their relative abilities to damage humans. Neutrons seem to be more effective in producing organism death, and gamma rays appear to be more effective in inducing performance decrement. In general, the more quickly a dose of radiation is delivered to the body, the more severe the consequences. The most sensitive cells are those that tend to divide rapidly, such as the bone-marrow cells and the cells lining the crypts of the gastrointestinal tract. Less sensitivity is exhibited by cells that divide more slowly or not at all, such as cells in the central nervous system (CNS).

The irradiation of cells has both acute and delayed effects (Table 1-2). Acute effects involve cell death, cell injury, and the release of disruptive mediators within the cell, which can lead to performance decrements. Other acute effects are infection and uncontrolled bleeding due to destruction of the bone marrow, dehydration and electrolyte imbalance due to denudation of the epithelial lining of the intestine, and slow healing of wounds. Delayed effects include cancer and

nonspecific life shortening. Eventually, either the organism dies, or regeneration and recovery occur.

Military attention is focused primarily on acute effects because they are of the most immediate concern to the tactical military commander. Performance decrement occurs within minutes or hours after relatively low exposures to radiation. It includes a phenomenon called *early transient incapacitation* (ETI), a temporary inability to perform physically or cognitively demanding tasks. This inability can be accompanied by hypotension, emesis, or diarrhea. A pilot or a soldier in a nuclear/biological/chemical protective suit could be critically affected by a symptom like emesis. Performance decrement may be due to lesions other than those associated with the lethal consequences of radiation injury to cells. This hypothesis might be significant in the development of practical radioprotectants.

Acute Radiation Syndrome and Associated Subsyndromes

With increasing doses of radiation, changes take place in body tissues or organs, some of which are life threatening. The symptoms that appear soon after radiation exposure are called the *acute radiation syndrome* (ARS). This large category may be broken down into the *hematopoietic, gastrointestinal,* and *neurovascular subsyndromes* (Figure 1-4).

The hematopoietic subsyndrome is seen within two weeks after biologically significant radiation doses of 1.0-2.5 grays (Gy). This damage to the body's blood-forming organs, specifically to the bone marrow, can lead to suppressed production of white blood cells and platelets, which in turn leads to increased susceptibility to infection and uncontrolled bleeding. Treatment consists of administering platelets and preventing infection during the time required for bone-marrow repair. Much research is directed toward finding means to enhance the repair or replacement of this tissue.

The gastrointestinal subsyndrome appears within a week or two after exposure to higher doses, which are sometimes survivable. After this exposure, crypt cells in the epithelial lining of the intestine are destroyed. This leads to excessive fluid loss and imbalance of electrolytes within the body, which may result in loss of the intestinal wall. Treatment focuses on preventing fluid loss and on balancing electrolytes during the time required for gastrointestinal repair.

The neurovascular subsyndrome appears within a few days after much higher doses of radiation, and consists of irreversible damage to the CNS. There is no treatment, other than making the patient as comfortable as possible.

Combined Injury

ARS and its medical effects are significantly complicated when radiation injury is combined with conventional blast trauma or thermal burn injuries. The following

data show that the insult to the body from combined radiation and conventional injuries is much more severe than it would be from a single injury.

In Figure 1-5, the percent of mortality in rats that received an LD_{50} burn is compared to the percent of mortality when this insult was combined with sublethal to minimally lethal doses of radiation. Rats receiving 1.0 or 2.5 Gy of radiation alone had no mortality, while those receiving 5.0 Gy alone had about 20% mortality. Animals that received an LD_{50} burn and 1.0 Gy of radiation (which by itself was not lethal) had increased mortality up to 70%. Animals that received 2.5 Gy of radiation in combination with an LD_{50} burn had mortality approaching 95%. Those that received an LD_{50} burn and an LD_{20} irradiation with 5.0 Gy showed 100% mortality. Thus, radiation combines synergistically with either burn or blast injuries to increase lethality.[1]

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PIN 902241-000

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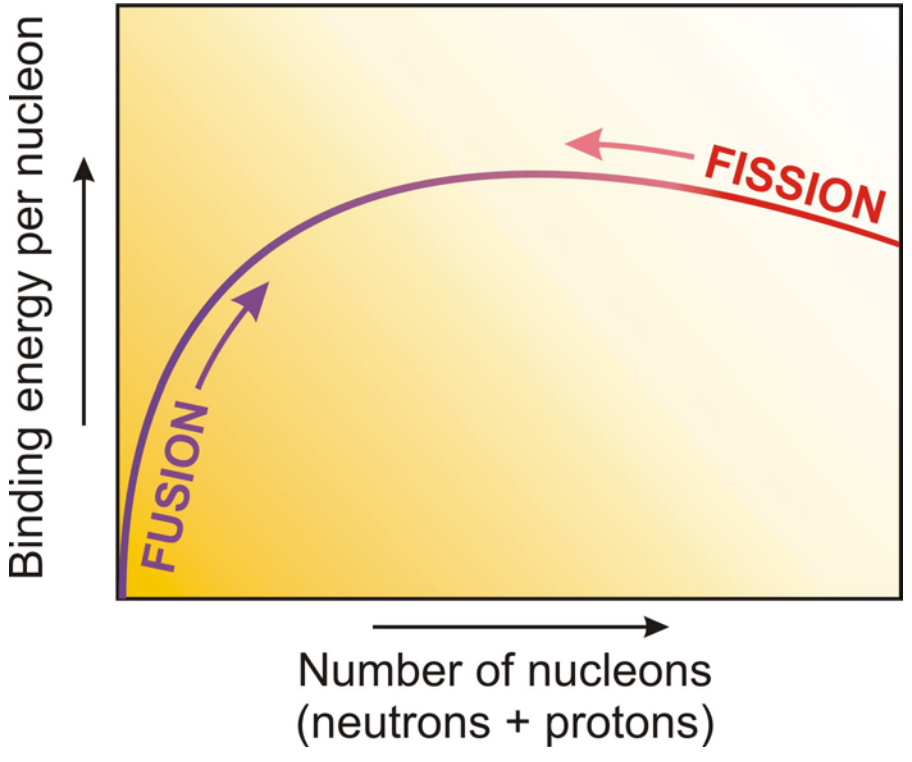

Figure 1-1. Curve of binding energy per nucleon.

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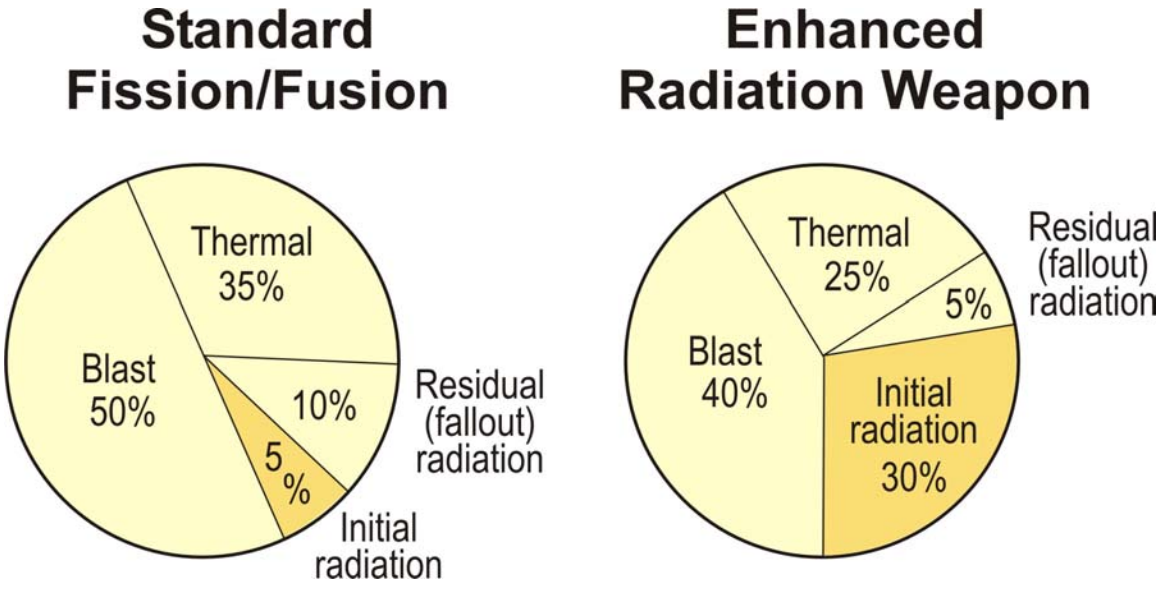

Figure 1-2. Energy partition of a nuclear weapon.

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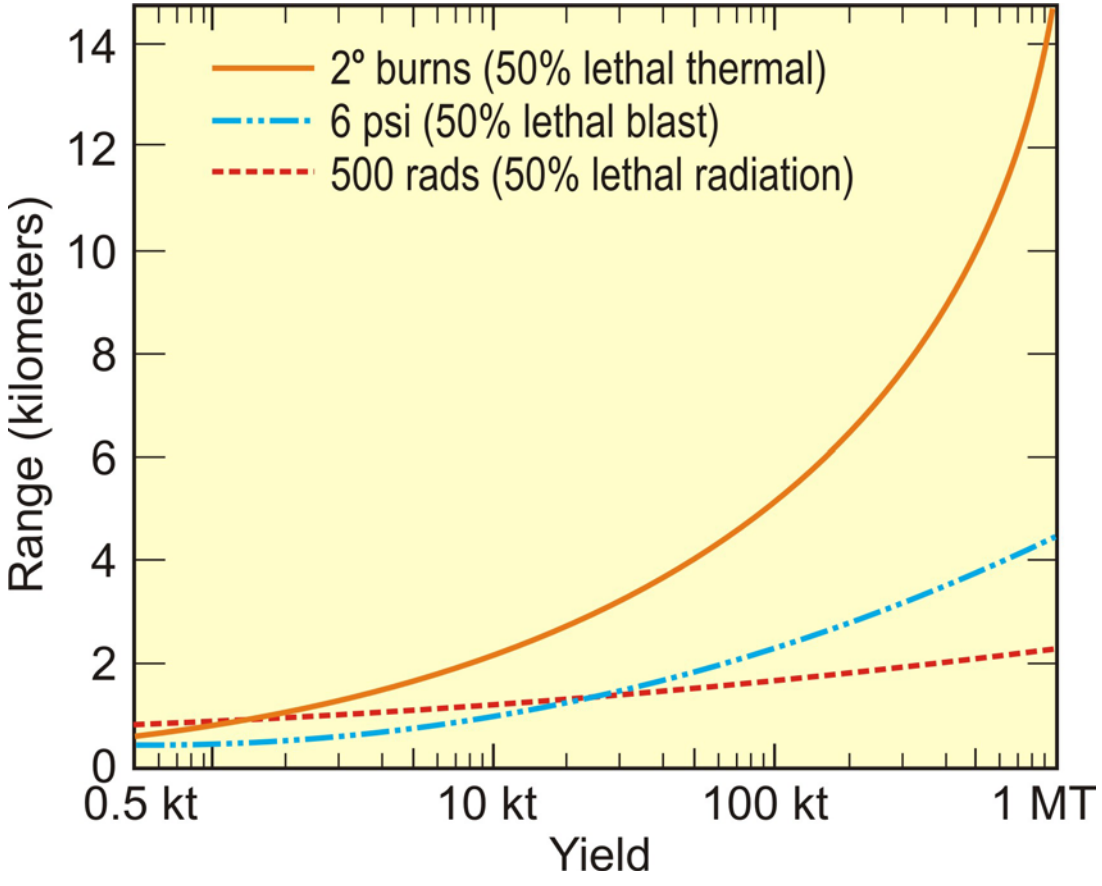

Figure 1-3. Range of effects of a nuclear weapon.

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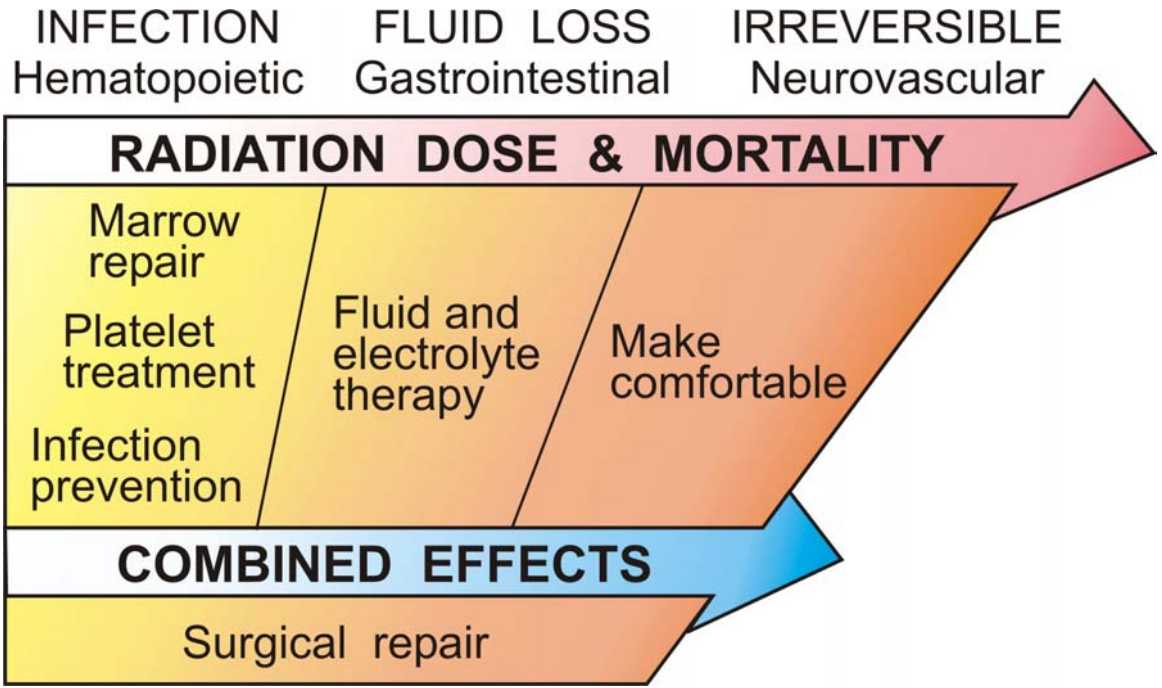

Figure 1-4. Major acute radiation subsyndromes after injury to bone marrow, intestine, or neurovascular system

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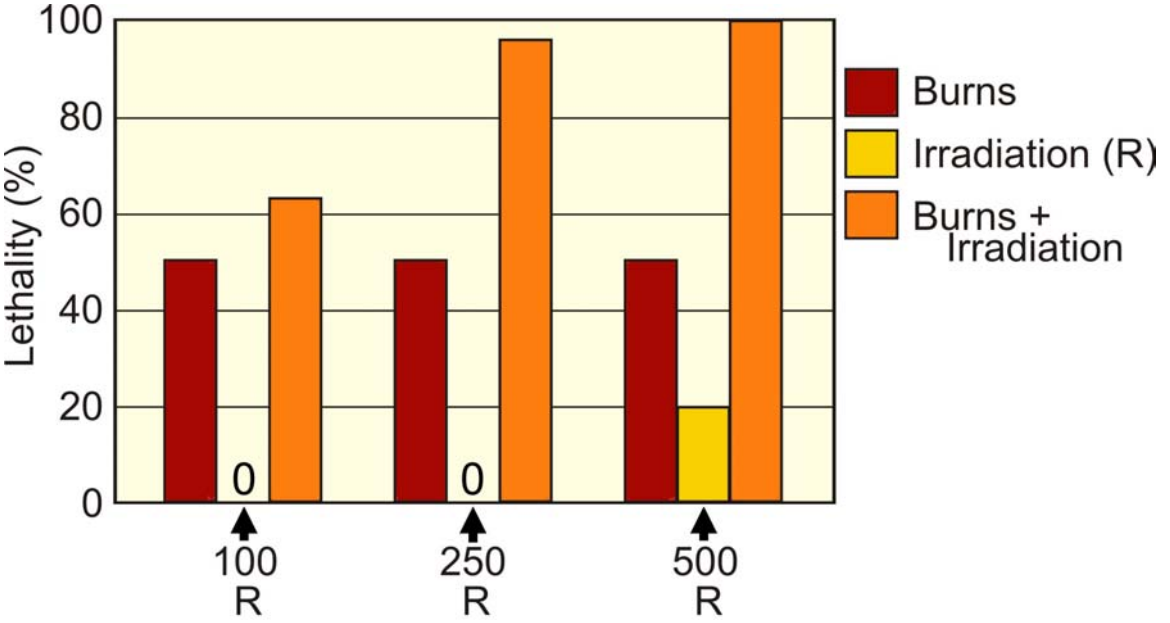

Figure 1-5. Combined effects of simultaneous burns and whole-body irradiation on rats

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TABLE 1-1
PERCENT DISTRIBUTION OF INJURIES SUSTAINED IN A NUCLEAR WAR

Type of Injury	Percent Distribution
Single Injuries (30%-40%)	
Irradiation*	15-20
Burns	15-20
Wounds	≤ 5
Combined Injuries (65%-70%)	
Burns + Irradiation	40
Burns + Wounds + Irradiation	20
Wounds + Irradiation	5
Wounds + Burns	5

*Including fallout

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