APPENDIX A

PEER REVIEW

A peer review panel was assembled for radium. The panel consisted of the following members: Dr. Carmia Borek, Professor of Pathology, Columbia University; Dr. Douglas Crawford-Brown, Assistant Professor in the Department of Environmental Science, University of North Carolina; Dr. Haluk Ozkaynak, Lecturer, Harvard School of Public Health, Research Fellow, Energy and Environmental Policy Center, Kennedy School of Government, Harvard University; Dr. Ray Lloyd, Research Professor, Radiobiology Division, University of Utah. These experts collectively have knowledge of radium's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(i)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act, as amended.

A joint panel of scientists from ATSDR and EPA has reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply their approval of the profile's final content. The responsibility for the content of this profile lies with the Agency for Toxic Substances and Disease Registry.

APPENDIX B

OVERVIEW OF BASIC RADIATION PHYSICS, CHEMISTRY AND BIOLOGY

Understanding the basic concepts in radiation physics, chemistry, and biology is important to the evaluation and interpretation of radiation-induced adverse health effects and to the derivation of radiation protection principles. This appendix presents a brief overview of the areas of radiation physics, chemistry, and biology and is based to a large extent on the reviews of Mettler and Moseley (1985), Hobbs and McClellan (1986), Eichholz (1982), Hendee (1973), and Early et al. (1979).

B.l RADIONUCLIDES AND RADIOACTIVITY

The substances we call elements are composed of atoms. Atoms in turn are made up of neutrons, protons, and electrons; neutrons and protons in the nucleus and electrons in a cloud of orbits around the nucleus. Nuclide is the general term referring to any nucleus along with its orbital electrons. The nuclide is characterized by the composition of its nucleus and hence by the number of protons and neutrons in the nucleus. All atoms of an element have the same number of protons (this is given by the atomic number) but may have different numbers of neutrons (this is reflected by the atomic mass or atomic weight of the element). Atoms with different atomic mass but the same atomic numbers are referred to as isotopes of an element.

The numerical combination of protons and neutrons in most nuclides is such that the atom is said to be stable; however, if there are too few or too many neutrons, the nucleus of the atom is unstable. Unstable nuclides undergo a process referred to as radioactive transformation in which energy is emitted. These unstable atoms are called radionuclides; their emissions are called ionizing radiation; and the whole property is called radioactivity. Transformation or decay results in the formation of new nuclides some of which may themselves be radionuclides, while others are stable nuclides. This series of transformations is called the decay chain of the radionuclide. The first radionuclide in the chain is called the parent; the subsequent products of the transformation are called progeny, daughters, or decay products.

In general there are two classifications of radioactivity and radionuclides: natural and man-made. Naturally-occurring radionuclides exist in nature and no additional energy is necessary to place them in an unstable state. Natural radioactivity is the property of some naturally occurring, usually heavy elements, that are heavier than lead. Radionuclides, such as radium and uranium, primarily emit alpha particles. Some lighter elements such as carbon-14 and tritium (hydrogen-3) primarily emit beta particles as they transform to a more stable atom. Natural radioactive atoms heavier than lead cannot attain

a stable nucleus heavier than lead. Everyone is exposed to background radiation from naturally-occurring radionuclides throughout life. This background radiation is the major source of radiation exposure to man and arises from several sources. The natural background exposures are frequently used as a standard of comparison for exposures to various man-made sources of ionizing radiation.

Man-made radioactive atoms are produced either as a by-product of fission of uranium atoms in a nuclear reactor or by bombarding stable atoms with particles, such as neutrons, directed at the stable atoms with high velocity. These artificially produced radioactive elements usually decay by emission of particles, such as positive or negative beta particles and one or more high energy photons (gamma rays). Unstable (radioactive) atoms of any element can be produced.

Both naturally occurring and man-made radioisotopes find application in medicine, industrial products, and consumer products. Some specific radioisotopes, called fall-out, are still found in the environment as a result of nuclear weapons use or testing.

B.2 RADIOACTIVE DECAY

B.2.1 Principles of Radioactive Decay

The stability of an atom is the result of the balance of the forces of the various components of the nucleus. An atom that is unstable (radionuclide) will release energy (decay) in various ways and transform to stable atoms or to other radioactive species called daughters, often with the release of ionizing radiation. If there are either too many or too few neutrons for a given number of protons, the resulting nucleus may undergo transformation. For some elements, a chain of daughter decay products may be produced until stable atoms are formed. Radionuclides can be characterized by the type and energy of the radiation emitted, the rate of decay, and the mode of decay. The mode of decay indicates how a parent compound undergoes transformation. Radiations considered here are primarily of nuclear origin, i.e., they arise from nuclear excitation, usually caused by the capture of charged or uncharged nucleons by a nucleus, or by the radioactive decay or transformation of an unstable nuclide. The type of radiation may be categorized as charged or uncharged particles (electrons, neutrons, neutrinos, alpha particles, beta particles, protons, and fission products) or electromagnetic radiation (gamma rays and X-rays). Table B-l summarizes the basic characteristics of the more common types of radiation encountered.

B.2.2 Half-Life and Activity

For any given radionuclide, the rate of decay is a first-order process that depends on the number of radioactive atoms present and is

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TABLE B-1. Characteristics of Nuclear Radiations

Radiation	Rest Mass	Charge	Typical Energy Range	Path Length (Order of Magnitude) Air	Path Length (Order of Magnitude) Solid	General Comments
α	4.00 amu	2+	4-10 MeV	5-10 cm	25-40 μm	Identical to ionized He nucleus
ß (negatron)	5.48×10^{-4} amu 0.51 MeV	-	0-4 MeV	0-1 m	0-1 cm	Identical to electron
Positron (ß positive)	5.48×10^{-4} amu 0.51 MeV	+	-	0-1 m	0-1 cm	Identical to electron except for charge
Proton	938.26 MeV 1.0073 amu	+	-	-	-	-
Neutron	1.0086 amu 939.55 MeV	0	0-15 MeV	0-100 m	0-100 cm	Free half life: 16 min
X (e.m. photon)	-	0	eV-100 keV	0.1-10 m[a]	0-1 m[a]	Photons from electron transitions
γ (e.m. photon)	-	0	10 KeV-3 MeV	0.1-10 m[a]	1 mm-1 m	Photons from nuclear transitions

[a]Exponential attenuation in the case of electromagnetic radiation.

α = alpha
ß = beta
X = X-ray
γ= gamma
amu = atomic mass unit
MeV = Mega electron volts
KeV = Kiloelectron volts
cm = centimeter
m = meter
μm = micrometer
mm = millimeter
e.m. = electromagnetic

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characteristic for each radionuclide. The process of decay is a series of random events; temperature, pressure, or chemical combinations do not effect the rate of decay. While it may not be possible to predict exactly which atom is going to undergo transformation at any given time, it is possible to predict, on the average, how many atoms will transform during any interval of time.

The source strength is a measure of the rate of emission of radiation. For these radioactive materials it is customary to describe the source strength in terms of the source activity, which is defined as the number of disintegrations (transformations) per unit time occurring in a given quantity of this material. The unit of activity is the curie (Ci) which was originally related to the activity of one gram of radium, but is now defined as:

1 curie (Ci) = 3.7×10^{10} disintegrations (transformations)/second (dps) or

2.22×10^{12} disintegrations (transformations)/minute (dpm).

The SI unit of activity is the becquerel (Bq); 1 Bq = 1 transformation/second.

Since activity is proportional to the number of atoms of the radioactive material, the quantity of any radioactive material is usually expressed in curies, regardless of its purity or concentration. The transformation of radioactive nuclei is a random process, and the rate of transformation is directly proportional to the number of radioactive atoms present. For any pure radioactive substance, the rate of decay is usually described by its radiological half-life, T_R, i.e., the time it takes for a specified source material to decay to half its initial activity.

The activity of a radionuclide at time t may be calculated by:

$$A = A_o e^{-0.693t/T_{rad}}$$

where A is the activity in dps, A_o is the activity at time zero, t is the time at which measured, and T_{rad} is the radiological half-life of the radionuclide. It is apparent that activity exponentially decays with time. The time when the activity of a sample of radioactivity becomes one-half its original value is the radioactive half-life and is expressed in any suitable unit of time.

The specific activity is the radioactivity per unit weight of material. This activity is usually expressed in curies per gram and may be calculated by

$$\text{curies/gram} = 1.3 \times 10^{8}/(T_{rad})(\text{atomic weight})$$

where T_{rad} is the radiological half-life in days.

In the case of radioactive materials contained in living organisms, an additional consideration is made for the reduction in observed activity due to regular processes of elimination of the respective chemical or biochemical substance from the organism. This introduces a rate constant called the

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biological half-life (T_{biol}) which is the time required for biological processes to eliminate one-half of the activity. This time is virtually the same for both stable and radioactive isotopes of any given element.

Under such conditions the time required for a radioactive element to be halved as a result of the combined action of radioactive decay and biological elimination is the effective half-life:

$$T_{eff} = (T_{biol} \times T_{rad})/(T_{biol} + T_{rad}).$$

Table B-2 presents representative effective half-lives of particular interest.

B.2.3 Interaction of Radiation with Matter

Both ionizing and nonionizing radiation will interact with materials, that is, it will lose kinetic energy to any solid, liquid or gas through which it passes by a variety of mechanisms. The transfer of energy to a medium by either electromagnetic or particulate radiation may be sufficient to cause formation of ions. This process is called ionization. Compared to other types of radiation that may be absorbed, such as ultraviolet radiation, ionizing radiation deposits a relatively large amount of energy into a small volume.

The method by which incident radiation interacts with the medium to cause ionization may be direct or indirect. Electromagnetic radiations (X-rays and gamma photons) are indirectly ionizing; that is, they give up their energy in various interactions with cellular molecules, and the energy is then utilized to produce a fast-moving charged particle such as an electron. It is the electron that then secondarily may react with a target molecule. Charged particles, in contrast, strike the tissue or medium and directly react with target molecules, such as oxygen or water. These particulate radiations are directly ionizing radiations. Examples of directly ionizing particles include alpha and beta particles. Indirectly ionizing radiations are always more penetrating than directly ionizing particulate radiations.

Mass, charge, and velocity of a particle all affect the rate at which ionization occurs. The higher the charge of the particle and the lower the velocity, the greater the propensity to cause ionization. Heavy, highly charged particles, such as alpha particles, lose energy rapidly with distance and, therefore, do not penetrate deeply. The result of these interaction processes is a gradual slowing down of any incident particle until it is brought to rest or "stopped" at the end of its range.

B-2.4 Characteristics of Emitted Radiation

B.2.4.1 Alpha Emission. In alpha emission, an alpha particle consisting of two protons and two neutrons is emitted with a resulting decrease in the

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TABLE B-2. Half-Lives of Some Radionuclides in Adult Body Organs

Radionuclide	Critical Organ	Half-Life[a]		
		Physical	Biological	Effective
Hydrogen-3[b] (Tritium)	Whole body	12.3 y	12 d	11.97d
Iodine-131	Thyroid	8 d	138 d	7.6 d
Strontium-90	Bone	28 y	50 y	18 y
Plutonium-239	Bone	24,400 y	200 y	198 y
	Lung	24,400 y	500 d	500 d
Cobalt-60	Whole body	5.3 y	99.5 d	9.5 d
Iron-55	Spleen	2.7 y	600 d	388 d
Iron-59	Spleen	45.1 d	600 d	41.9 d
Manganese-54	Liver	303 d	25 d	23 d
Cesium-137	Whole body	30 y	70 d	70 d

[a]d = days, y = years.
[b]Mixed in body water as tritiated water.

atomic mass number by four and reduction of the atomic number by two, thereby changing the parent to a different element. The alpha particle is identical to a helium nucleus consisting of two neutrons and two protons. It results from the radioactive decay of some heavy elements such as uranium, plutonium, radium, thorium, and radon. Alpha particles have a large mass as compared to electrons. Decay of alpha-emitting radionuclides may result in the emission of several different alpha particles. A radionuclide has an alpha emission with a discrete alpha energy and characteristic pattern of alpha energy emitted.

The alpha particle has an electrical charge of +2. Because of this double positive charge, alpha particles have great ionizing power, but their large size results in very little penetrating power. In fact, an alpha particle cannot penetrate a sheet of paper. The range of an alpha particle, that is, the distance the charged particle travels from the point of origin to its resting point, is about 4 cm in air, which decreases considerably to a few micrometers in tissue. These properties cause alpha emitters to be hazardous only if there is internal contamination (i.e., if the radionuclide is ingested, inhaled, or otherwise absorbed).

B.2.4.2. Beta Emission. Nuclei which are excessively neutron rich decay by B-decay. A beta particle (ß) is a high-velocity electron ejected from a disintegrating nucleus. The particle may be either a negatively charged electron, termed a negatron (ß-) or a positively charged electron, termed a positron (R+). Although the precise definition of "beta emission" refers to both fi- and D+, common usage of the term generally applies only to the negative particle, as distinguished from the positron emission, which refers to the 13+ particle.

B.2.4.2.1 Beta Negative Emission. Beta particle (ß-) emission is another process by which a radionuclide, usually those with a neutron excess, achieves stability. Beta particle emission decreases the number of neutrons by one and increases the number of protons by one, while the atomic mass remains unchanged. This transformation results in the formation of a different element. The energy spectrum of beta particle emission ranges from a certain maximum down to zero with the mean energy of the spectrum being about one-third of the maximum. The range in tissue is much less. Beta negative emitting radionuclides can cause injury to the skin and superficial body tissues but mostly present an internal contamination hazard.

B-2.4.2.2 Positron Emission. In cases in which there are too many protons in the nucleus, positron emission may occur. In this case a proton may be thought of as being converted into a neutron, and a positron (ß+) is emitted, accompanied by a neutrino (see glossary). This increases the number of neutrons by one, decreases the number of protons by one, and again leaves the atomic mass unchanged. The gamma radiation resulting from the annihilation (see glossary) of the positron makes all positron emitting isotopes more of an external radiation hazard than pure 13 emitters of equal energy.

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B.2.4.2.3 Gamma Emission. Radioactive decay by alpha, beta, positron emission or electron capture often leaves some of the energy resulting from these changes in the nucleus. As a result, the nucleus is raised to an excited level. None of these excited nuclei can remain in this high-energy state. Nuclei release this energy returning to ground state or to the lowest possible stable energy level. The energy released is in the form of gamma radiation (high energy photons) and has an energy equal to the change in the energy state of the nucleus. Gamma and X-rays behave similarly but differ in their origin; gamma emissions originate in the nucleus while X-rays originate in the orbital electron structure.

B.3 ESTIMATION OF ENERGY DEPOSITION IN HUMAN TISSUES

Two forms of potential radiation exposures can result -- internal and external. The term exposure denotes physical interaction of the radiation emitted from the radioactive material with cells and tissues of the human body. An exposure can be "acute" or "chronic" depending on how long an individual or organ is exposed to the radiation. Internal exposures occur when radionuclides, which have entered the body (e.g., through the inhalation, ingestion, or dermal pathways), undergo radioactive decay resulting in the deposition of energy to internal organs. External exposures occur when radiation enters the body directly from sources located outside the body, such as radiation emitters from radionuclides on ground surfaces, dissolved in water, or dispersed in the air. In general, external exposures are from material emitting gamma radiation, which readily penetrate the skin and internal organs. Beta and alpha radiation from external sources are far less penetrating and deposit their energy primarily on the skin's outer layer. Consequently, their contribution to the absorbed dose of the total body dose, compared to that deposited by gamma rays, may be negligible.

Characterizing the radiation dose to persons as a result of exposure to radiation is a complex issue. It is difficult to: (1) measure internally the amount of energy actually transferred to an organic material and to correlate any observed effects with this energy deposition; and (2) account for and predict secondary processes, such as collision effects or biologically triggered effects, that are an indirect consequence of the primary interaction event.

B.3.1 Dose Units

B.3.1.1 Roentgen. The roentgen (R) is a unit of exposure related to the amount of ionization caused in air by gamma or x-radiation. One roentgen equals 2.58×10^{-4} Coulomb per kilogram of air. In the case of gamma radiation, over the commonly encountered range of photon energy, the energy deposition in tissue for a dose of 1 R is about 0.0096 joules(J)/kg of tissue.

B.3.1.2 Absorbed Dose and Absorbed Dose Rate. Since different types of radiation interact differently with any material through which they pass, any

attempt to assess their effect on humans or animals should take into account these differences. The absorbed dose is defined as the energy imparted by the incident radiation to a unit mass of the tissue or organ. The unit of absorbed dose is the rad; 1 rad = 100 erg/gram = 0.01 J/kg in any medium. The SI unit is the gray which is equivalent to 100 rad or 1 J/kg. Internal and external exposures from radiation sources are not usually instantaneous but are distributed over extended periods of time. The resulting rate of change of the absorbed dose to a small volume of mass is referred to as the absorbed dose rate in units of rad/unit time.

B.3.1.3 Working Levels and Working Level Months. Working levels are units that have been used to describe the radon decay-product activities in air in terms of potential alpha energy. It is defined as any combination of short-lived radon daughters (through polonium-214) per liter of air that will result in the emission of 1.3×10^5 MeV of alpha energy. An activity concentration of 100 pCi radon-222/L of air, in equilibrium with its daughters, corresponds approximately to a potential alpha-energy concentration of 1 WL. The WL unit can also be used for thoron daughters. In this case, 1.3×10^5 MeV of alpha energy (1 WL) is released by the thoron daughters in equilibrium with 7.5 pCi thoron/L. The potential alpha energy exposure of miners is commonly expressed in the unit Working Level Month (WIN). One WLM corresponds to exposure to a concentration of 1 WL for the reference period of 170 hours.

B.3.2 Dosimetry Models

Dosimetry models are used to estimate the internally deposited dose from exposure to radioactive substances. The models for internal dosimetry consider the quantity of radionuclides entering the body, the factors affecting their movement or transport through the body, distribution and retention of radionuclides in the body, and the energy deposited in organs and tissues from the radiation that is emitted during spontaneous decay processes. The models for external dosimetry consider only the photon doses to organs of individuals who are immersed in air or are exposed to a contaminated ground surface. The dose pattern for radioactive materials in the body may be strongly influenced by the route of entry of the material. For industrial workers, inhalation of radioactive particles with pulmonary deposition and puncture wounds with subcutaneous deposition have been the most frequent. The general population has been exposed via ingestion and inhalation of low levels of naturally occurring radionuclides as well as man-produced radionuclides from nuclear weapons testing.

B.3.2.1 Ingestion. Ingestion of radioactive materials is most likely to occur from contaminated foodstuffs or water or eventual ingestion of inhaled compounds initially deposited in the lung. Ingestion of radioactive material may result in toxic effects as a result of either absorption of the radionuclide or irradiation of the gastrointestinal tract during passage through the tract, or a combination of both. The fraction of a radioactive

material absorbed from the gastrointestinal tract is variable, depending on the specific element, the physical and chemical form of the material ingested, and the diet, as well as some other metabolic and physiological factors. The absorption of some elements is influenced by age usually with higher absorption in the very young.

B.3.2.2 Inhalation. The inhalation route of exposure has long been recognized as being of major importance for both nonradioactive and radioactive materials. The deposition of particles within the lung is largely dependent upon the size of the particles being inhaled. After the particle is deposited, the retention will depend upon the physical and chemical properties of the dust and the physiological status of the lung. The retention of the particle in the lung depends on the location of deposition, in addition to the physical and chemical properties of the particles. The converse of pulmonary retention is pulmonary clearance. There are three distinct mechanisms of clearance which operate simultaneously. Giliary clearance acts only in the upper respiratory tract. The second and third mechanisms act mainly in the deep respiratory tract. These are phagocytosis and absorption. Phagocytosis is the engulfing of foreign bodies by alveolar macrophages and their subsequent removal either up the ciliary "escalator" or by entrance into the lymphatic system. Some inhaled soluble particulates are absorbed into the blood and translocated to other organs and tissues. Dosimetric lung models are reviewed by James (1987) and James and Roy (1987).

B.3.3 Internal Emitters

The absorbed dose from internally deposited radioisotopes is the energy absorbed by the surrounding tissue. For a radioisotope distributed uniformly throughout an infinitely large medium, the concentration of absorbed energy must be equal to the concentration of energy emitted by the isotope. An infinitely large medium may be approximated by a tissue mass whose dimensions exceed the range of the particle. All alpha and most beta radiation will be absorbed in the organ (or tissue) of reference. Gamma-emitting isotope emissions are penetrating radiation and a substantial fraction may travel great distances within tissue, leaving the tissue without interacting. The dose to an organ or tissue is a function of the effective retention half-time, the energy released in the tissue, the amount of radioactivity initially introduced, and the mass of the organ or tissue.

B.4 BIOLOGICAL EFFECTS OF RADIATION

When biological material is exposed to ionizing radiation, a chain of cellular events occurs as the ionizing particle passes through the biological material. A number of theories have been proposed to describe the interaction of radiation with biologically important molecules in cells and to explain the resulting damage to biological systems from those interactions. Many factors may modify the response of a living organism to a given dose of radiation. Factors related to the exposure include the dose rate, the energy of the

radiation, and the temporal pattern of the exposure. Biological considerations include factors such as species, age, sex, and the portion of the body exposed. Several excellent reviews of the biological effects of radiation have been published, and the reader is referred to these for a more in-depth discussion (Hobbs and McClellan 1986; ICRP 1984; Mettler and Moseley 1985; Rubin and Casarett 1968).

B.4.1 Radiation Effects at the Cellular Level

According to Mettler and Moseley (1985), at acute doses up to 10 rad (100 mGy), single strand breaks in DNA may be produced. These single strand breaks may be repaired rapidly. With doses in the range of 50 to 500 rad (0.5 to 5 Gy) , irreparable double-stranded DNA breaks are likely, resulting in cellular reproductive death after one or more divisions of the irradiated parent cell. At large doses of radiation, usually greater than 500 rad (5 Gy), direct cell death before division (interphase death) may occur from the direct interaction of free-radicals with essentially cellular macromolecules. Morphological changes at the cellular level, the severity of which are dose-dependent, may also be observed.

The sensitivity of various cell types varies. According to the Bergonig-Tribondeau law, the sensitivity of cell lines is directly proportional to their mitotic rate and inversely proportional to the degree of differentiation (Mettler and Moseley 1985). Rubin and Casarett (1968) devised a classification system that categorized cells according to type, function, and mitotic activity. The categories range from the most sensitive type, "vegetative intermitotic cells," found in the stem cells of the bone marrow and the gastrointestinal tract, to the least sensitive cell type, "fixed postmitotic cells," found in striated muscles or long-lived neural tissues.

Cellular changes may result in cell death, which if extensive, may produce irreversible damage to an organ or tissue or may result in the death of the individual. If the cell recovers, altered metabolism and function may still occur, which may be repaired or may result in the manifestation of clinical symptoms. These changes may also be expressed at a later time as tumors or mutations.

B.4.2 Radiation Effects at the Organ Level

In most organs and tissues the injury and the underlying mechanism for that injury are complex and may involve a combination of events. The extent and severity of this tissue injury are dependent upon the radiosensitivity of the various cell types in that organ system. Rubin and Casarett (1968) describe and schematically display the events following radiation in several organ system types. These include: a rapid renewal system, such as the gastrointestinal mucosa; a slow renewal system, such as the pulmonary epithelium; and a nonrenewal system, such as neural or muscle tissue. In the rapid renewal system, organ injury results from the direct destruction of highly radiosensitive cells, such as the stem cells in the bone marrow.

Injury may also result from constriction of the microcirculation and from edema and inflammation of the basement membrane (designated as the histohematic barrier - HHB), which may progress to fibrosis. In slow renewal and nonrenewal systems, the radiation may have little effect on the parenchymal cells, but ultimate parenchymal atrophy and death over several months result from HHB fibrosis and occlusion of the microcirculation.

B.4.3 Acute and Chronic Somatic Effects

B.4.3.1 Acute Effects. The result of acute exposure to radiation is commonly referred to as acute radiation syndrome. This effect is seen only after exposures to relatively high doses (>50 rad), which would only be expected to occur in the event of a serious nuclear accident. The four stages of acute radiation syndrome are prodrome, latent stage, manifest illness stage, recovery or death. The initial phase is characterized by nausea, vomiting, malaise and fatigue, increased temperature, and blood changes. The latent stage is similar to an incubation period. Subjective symptoms may subside, but changes may be taking place within the blood-forming organs and elsewhere which will subsequently give rise to the next stage. The manifest illness stage gives rise to symptoms specifically associated with the radiation injury. Among these symptoms are hair loss, fever, infection, hemorrhage, severe diarrhea, prostration, disorientation, and cardiovascular collapse. The symptoms and their severity depend upon the radiation dose received.

B.4.3.2 Delayed Effects. The level of exposure to radioactive pollutants that may be encountered in the environment is expected to be too low to result in the acute effects described above. When one is exposed to radiation in the environment, the amount of radiation absorbed is more likely to produce long-term effects, which manifest themselves years after the original exposure, and may be due to a single large over-exposure or continuing low-level exposure.

Sufficient evidence exists in both human populations and laboratory animals to establish that radiation can cause cancer and that the incidence of cancer increases with increasing radiation dose. Human data are extensive and include epidemiological studies of atomic bomb survivors, many types of radiation-treated patients, underground miners, and radium dial painters. Reports on the survivors of the atomic bomb explosions at Hiroshima and Nagasaki, Japan (with whole-body external radiation doses of 0 to more than 200 rad) indicate that cancer mortality has increased (Kato and Schull 1982). Use of X-rays (at doses of approximately 100 rad) in medical treatment for ankylosing spondylitis or other benign conditions or diagnostic purposes, such as breast conditions, has resulted in excess cancers in irradiated organs (BEIR 1980, 1990; UNSCEAR 1977, 1988). Cancers, such as leukemia, have been observed in children exposed in utero to doses of 0.2 to 20 rad (BEIR, 1980, 1990; UNSCEAR 1977, 1988). Medical use of Thorotrast (colloidal thorium dioxide) resulted in increases in the incidence of cancers of the liver, bone,

and lung (ATSDR 1990a; BEIR 1980, 1990; UNSCEAR 1977, 1988). Occupational exposure to radiation provides further evidence of the ability of radiation to cause cancer. Numerous studies of underground miners exposed to radon and radon daughters, which are alpha emitters, in uranium and other hard rock mines have demonstrated increases in lung cancer in exposed workers (ATSDR 1990b). Workers who ingested radium-226 while painting watch dials had an increased incidence of leukemia and bone cancer (ATSDR 199Oc). These studies indicate that depending on radiation dose and the exposure schedule, ionizing radiation can induce cancer in nearly any tissue or organ in the body. Radiation-induced cancers in humans are found to occur in the hemopoietic system, the lung, the thyroid, the liver, the bone, the skin, and other tissues.

Laboratory animal data indicate that ionizing radiation is carcinogenic and mutagenic at relatively high doses usually delivered at high dose rates. However, due to the uncertainty regarding the shape of the dose-response curve, especially at low doses, the commonly held conservative position is that the cancer may occur at dose rates that extend down to doses that could be received from environmental exposures. Estimates of cancer risk are based on the absorbed dose of radiation in an organ or tissue. The cancer risk at a particular dose is the same regardless of the source of the radiation. A comprehensive discussion of radiation-induced cancer is found in BEIR IV (1988), BEIR V (1990), and UNSCEAR (1982, 1988).

B.4.4 Genetic Effects

Radiation can induce genetic damage, such as gene mutations or chromosomal aberrations, by causing changes in the structure, number, or genetic content of chromosomes in the nucleus. The evidence for the mutagenicity of radiation is derived from studies in laboratory animals, mostly mice (BEIR 1980, 1988, 1990; UNSCEAR 1982, 1986, 1988). Evidence for genetic effects in humans is derived from tissue cultures of human lymphocytes from persons exposed to ingested or inhaled radionuclides (ATSDR 199Oc, 1990d). Evidence for mutagenesis in human germ cells (cells of the ovaries or testis) is not conclusive (BEIR 1980, 1988, 1990; UNSCEAR 1977, 1986, 1988). Chromosome aberrations following radiation exposure have been demonstrated in man andn in experimental animals (BEIR 1980, 1988, 1990; UNSCEAR 1982, 1986, 1988).

B.4.5 Teratogenic Effects

There is evidence that radiation produces teratogenicity in animals. It appears that the developing fetus is more sensitive to radiation than the mother and is most sensitive to radiation-induced damage during the early stages of organ development. The type of malformation depends on the stage of development and the cells that are undergoing the most rapid differentiation at the time. Studies of mental retardation in children exposed in utero to radiation from the atomic bomb provide evidence that radiation may produce

teratogenic effects in human fetuses (Otake and Schull 1984). The damage to the child was found to be related to the dose that the fetus received.

B.5 UNITS IN RADIATION PROTECTION AND REGULATION

B.5.1 Dose Equivalent and Dose Equivalent Rate. Dose equivalent or rem is a special radiation protection quantity that is used to express the absorbed dose in a manner which considers the difference in biological effectiveness of various kinds of ionizing radiation. The ICRU has defined the dose equivalent, H, as the product of the absorbed dose, D, the quality factor, Q, and all other modifying factors, N, at the point of interest in biological tissue. This relationship is expressed as follows:

$$H = D \times Q \times N.$$

The quality factor is a dimensionless quantity that depends in part on the stopping power for charged particles, and it accounts for the differences in biological effectiveness found among the types of radiation. By definition it is independent of tissue and biological end point and, therefore, of little use in risk assessment now. Originally Relative Biolotical Effectiveness (RBE) was used rather than Q to define the quantity, rem, which was of use in risk assessment. The generally accepted values for quality factors for various radiation types are provided in Table B-3. The dose equivalent rate is the time rate of change of the dose equivalent to organs and tissues and is expressed as rem/unit time or sievert/unit time.

B.5.2 Relative Biological Effectiveness. The term relative biologic effectiveness (RBE) is used to denote the experimentally determined ratio of the absorbed dose from one radiation type to the absorbed dose of a reference radiation required to produce an identical biologic effect under the same conditions. Gamma rays from cobalt-60 and 200 to 250 KeV X-rays have been used as reference standards. The term RBE has been widely used in experimental radiobiology, and the term quality factor used in calculations of dose equivalents for radiation protection purposes (ICRP 1977; NCRP 1971; UNSCEAR 1982). The generally accepted values for RBE are provided in Table B-4.

B.5.3 Effective Dose Equivalent and Effective Dose Equivalent Rate. The absorbed dose is usually defined as the mean absorbed dose within an organ or tissue. This represents a simplification of the actual problem. Normally when an individual ingests or inhales a radionuclide or is exposed to external radiation that enters the body (gamma), the dose is not uniform throughout the whole body. The simplifying assumption is that the detriment will be the same whether the body is uniformly or nonuniformly irradiated. In an attempt to compare detriment from absorbed dose of a limited portion of the body with the detriment from total body dose, the ICRP (1977) has derived a concept of effective dose equivalent.

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TABLE B-3. Quality Factors (QF)

1. X-rays, electrons, and positrons of any specific ionization

   QF = 1.

2. Heavy ionizing particles

Average LET in Water (MeV/cm)	QF
35 or less	1
35 to 70	1 to 2
70 to 230	2 to 5
230 to 530	5 to 10
530 to 1750	10 to 20

For practical purposes, a QF of 10 is often used for alpha particles[a] and fast neutrons and protons up to 10 MeV. A QF of 20 is used for heavy recoil nuclei.

[a]The ICRP (1977) recommended a quality factor of 20 for alpha particles.

LET = Linear energy transfer
MeV/cm = Megaelectron volts per centimeter
MeV = Megaelectron volts

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TABLE B-4. Representative LET and RBE Values*

Radiation	Energy (MeV)	Av. LET (keV/μ)	RBE	Quality Factor
X-rays, 200 kVp	0.01-0.2	3.0	1.00	1
Gamma rays	1.25	0.3	0.7	1
	4	0.3	0.6	1
Electrons (ß)	0.1	0.42	1.0	1
	0.6	0.3	1.3	1
	1.0	0.25	1.4	--
Protons	0.1	90.0	--	6
	2.0	16.0	2	10
	5.0	8.0	2	10
Alpha particle	0.1	260.0	--	--
	5.0	95.0	10-20	10
Heavy ions	10-30	~150.0	~25	20
Neutrons	thermal		4-5	3
	1.0	20.0	2-10	10

*These values are general and approximate. RBE and QF values vary widely with different measures of biological injury.

MeV = Megaelectron volts
KeV/μ = Kiloelectron volts per micron
RBE = Relative biological effectiveness
kVp = Kilovolt potential
LET = Linear energy transfer

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The effective dose equivalent, H_E is

$$H_E = (\text{the sum of}) \, W_t H_t$$

where H_t is the dose equivalent in the tissue, W_t is the weighting factor, which represents the estimated proportion of the stochastic risk resulting from tissue, T, to the stochastic risk when the whole body is uniformly irradiated for occupational exposures under certain conditions (ICRP 1977). Weighting factors for selected tissues are listed in Table B-5.
The ICRU (1980), ICRP (1984), and NCRP (1985) now recommend that the rad, roentgen, curie and rem be replaced by the SI units: gray (GY), Coulomb per kilogram (C/kg), becquerel (Bq), and sievert (Sv), respectively. The relationship between the customary units and the international system of units (SI) for radiological quantities is shown in Table B-6.

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TABLE B-5. Weighting Factors for Calculating Effective Dose Equivalent for Selected Tissues

Tissue	Weighting Factor
Gonads	0.25
Breast	0.15
Red bone marrow	0.12
Lung	0.12
Thyroid	0.03
Bone surface	0.03
Remainder	0.30

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TABLE B-6. Comparison of Common and SI Units for Radiation Quantities

Quantity	Customary Units	Definition	SI Units	Definition
Activity (A)	Curie (Ci)	3.7×10^{10} transformations s^{-1}	becquerel (Bq)	s^{-1}
Absorbed Dose (D)		rad (rad)	$10^{-2} Jkg^{-1}$	gray (Gy) Jkg^{-1}
Absorbed Dose Rate (D)	rad per second (rad s^{-1})	$10^{-2} Jkg^{-1}s^{-1}$	gray per second (Gy s^{-1})	$Jkg^{-1}s^{-1}$
Dose Equivalent (H)	rem (rem)	$10^{-2} Jkg^{-1}$	sievert (Sv)	Jkg^{-1}
Dose Equivalent Rate (H)	rem per second (rem s^{-1})	$10^{-2} Jkg^{-1}s^{-1}$	sievert per second (Sv s^{-1})	$Jkg^{-1}s^{-1}$
Linear Energy Transfer (L_∞)	kiloelectron volts per micrometer ($keV\mu M^{-1}$)	$1.602 \times 10^{-10} Jm^{-1}$	kiloelectron volts per micrometer ($keV\mu m^{-1}$)	$1.602 \times 10^{-10} Jm^{-1}$

S^{-1} = per second
Jkg^{-1} = Joules per kilogram
$Jkg^{-1}s^{-1}$ = Joules per kilogram per second
Jm^{-1} = Joules per meter

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