Ionizing Radiation

Introduction

Radiation that has sufficient energy to remove electrons from atoms is called "ionizing radiation." Ionization results in the production of negatively charged free electrons and positively charged ionized atoms. Ionizing radiation can be classified into two groups: photons (includes X-radiation and gamma radiation) and particles (includes alpha and beta particles and neutrons). The radioactive compound thorium dioxide, which decays by emission of alpha particles, was first listed in the *Second Annual Report on Carcinogens* (1981), and radon and its most common isotopic forms (radon-220 and radon-222), which also emit primarily alpha particles, were first listed in the *Seventh Annual Report on Carcinogens* (1994). Three types of ionizing radiation (X-radiation, gamma radiation, and neutrons) were first listed in the *Eleventh Report on Carcinogens* (2004). X-radiation and gamma radiation are included in one listing. The profiles for X-radiation and gamma radiation, neutrons, radon, and thorium dioxide, which are listed as *known to be human carcinogens*, follow this introduction.

X-Radiation and Gamma Radiation*

Known to be Human Carcinogens
First Listed in the *Eleventh Report on Carcinogens* (2004)

Carcinogenicity

X-radiation and gamma radiation are *known to be human carcinogens* based on sufficient evidence in humans. Epidemiological studies of radiation exposure provide a consistent body of evidence for the carcinogenicity of X-radiation and gamma radiation in humans. Exposure to X-radiation and gamma radiation is most strongly associated with leukemia and cancer of the thyroid, breast, and lung; associations have been reported at absorbed doses of less than 0.2 Gy (see "Properties," below, for explanation of radiation dose measurement). The risk of developing these cancers, however, depends to some extent on age at exposure. Childhood exposure is mainly responsible for increased leukemia and thyroid-cancer risks, and reproductive-age exposure for increased breast-cancer risk. In addition, some evidence suggests that lung-cancer risk may be most strongly related to exposure later in life. Associations between radiation exposure and cancer of the salivary glands, stomach, colon, bladder, ovary, central nervous system, and skin also have been reported, usually at higher doses of radiation (1 Gy) (Kleinerman *et al.* 1995, Ron 1998, Ron *et al.* 1999, Brenner *et al.* 2000, Garwicz *et al.* 2000, Lichter *et al.* 2000, Sont *et al.* 2001, Yeh *et al.* 2001, Bhatia *et al.* 2002).

The first large study of sarcomas (using the U.S. Surveillance, Epidemiology, and End Results cancer registry) (Yap *et al.* 2002) added angiosarcomas to the list of radiation-induced cancers occurring within the field of radiation at high therapeutic doses. Two studies, one of workers at a Russian nuclear bomb and fuel reprocessing plant (Gilbert *et al.* 2000) and another of Japanese atomic-bomb survivors (Cologne *et al.* 1999), suggested that radiation exposure could cause liver cancer at doses above 100 mSv (in the worker population especially with concurrent exposure to radionuclides). Among the atomic-bomb survivors, the liver-cancer risk increased linearly with increasing radiation dose. A study of children medically exposed to radiation (other than for cancer treatment) provided some evidence that radiation exposure during childhood may increase the incidence of lymphomas and melanomas. In addition, chronic lymphatic leukemia, Hodgkin's disease (malignant lymphoma), and cancer of the cervix, prostate, testis, and pancreas are generally considered not to be associated with radiation exposure.

X-radiation and gamma radiation are clearly carcinogenic in all species of experimental animals tested (mouse, rat, and monkey for X-radiation and mouse, rat, rabbit, and dog for gamma radiation). Among these species, radiation-induced tumors have been observed in about 17 tissues or organs, including those observed in humans (i.e., leukemia, thyroid gland, breast, and lung) (IARC 2000). Susceptibility to induction of benign and malignant tumors depends on tissue site, species, strain, age, and sex. Early prenatal exposure does not appear to cause cancer, but exposure at later stages of prenatal development has been reported do so. It has been suggested that radiation exposure of mice before mating increases the susceptibility of their offspring to cancer, but study results are conflicting.

Additional Information Relevant to Carcinogenicity

X-radiation and gamma radiation have been shown to induce a broad spectrum of genetic effects, including gene mutations, minisatellite mutations (changes in numbers of tandem repeats of DNA sequences), micronucleus formation (a sign of chromosome damage or loss), chromosomal aberrations (changes in chromosome structure or number), ploidy changes (changes in the number of sets of chromosomes), DNA strand breaks, and chromosomal instability. Genetic damage by X-radiation or gamma radiation has been observed in humans exposed accidentally, occupationally, or environmentally, in experimental animals exposed *in vivo*, and in cultured human and other mammalian cells. X-radiation and gamma radiation induce genetic damage in somatic cells and transmissible mutations in mammalian germ cells (sperm and egg cells and their precursors). The DNA molecule may be damaged directly, by interaction with ionizing radiation, or indirectly, by interaction with reactive products of the degradation of water by ionizing radiation (i.e., free electrons, hydrogen free radicals, or hydroxyl radicals) (IARC 2000, NTP 2003). The observed genetic damage is primarily the result of errors in DNA repair, but may also arise from errors in replication of damaged DNA. Epigenetic mechanisms (factors other than the primary DNA sequence) that alter the action of genes also may be involved in radiation-induced carcinogenesis. Proposed mechanisms for delayed or indirect radiation-induced genetic damage include genomic instability, induction of mutations by irradiation of the cytoplasm of the cell, and "bystander effects," in which genetic damage is induced in cells that were not directly exposed to ionizing radiation, apparently through cell signaling pathways.

Properties

As forms of electromagnetic radiation, X-rays and gamma rays are packets of energy (photons) having neither charge nor mass. They have essentially the same properties, but differ in origin. X-rays are emitted from processes outside the nucleus (e.g., bombardment of heavy atoms by fast-moving electrons), whereas gamma rays originate inside the nucleus (during the decay of radioactive atoms). The energy of ionizing radiation is expressed in electronvolts (eV), a unit equal to the energy acquired by an electron when it passes through a potential difference of 1 volt in a vacuum; 1 eV = 1.6×10^{-19} joules (J) (IARC 2000).

The energy of X-rays typically ranges from 5 to 100 keV. Lower in energy than gamma rays, X-rays are less penetrating; a few millimeters of lead can stop medical X-rays. The energy distribution of X-radiation is continuous, with a maximum at an energy about one third that of the most energetic electron. The energy of gamma rays resulting from radioactive decay typically ranges from 10 keV to 3 MeV. Gamma rays often accompany the emission of alpha or beta particles from a nucleus. Because of scattering and absorption within the radioactive source and the encapsulating material, the emitted photons have a relatively narrow energy spectrum (i.e., are monoenergetic). Gamma rays are very penetrating; they can easily pass through the human body, but they also can be absorbed by tissue.

Several feet of concrete or a few inches of lead are required to stop the more energetic gamma rays (BEIR V 1990).

As photons interact with matter, their energy distribution is altered in a complex manner as a result of energy transfer. The amount of energy deposited by ionizing radiation per unit of path length in irradiated material is called the "linear energy transfer" (LET), expressed in units of energy per unit length (e.g., kiloelectronvolts per micrometer). X-rays and gamma rays are considered low-LET radiation. In tissue, they transfer their energy primarily to electrons. Compared with high-LET radiation (such as neutrons and alpha particles), low-LET radiation tends to follow more tortuous paths in matter, with more widely dispersed energy deposition.

Use

X-rays, gamma rays, and materials and processes that emit X-rays and gamma rays are used in medicine, the nuclear power industry, the military, scientific research, industry, and various consumer products.

Medical use of ionizing radiation in both diagnosis and therapy has been widespread since the discovery of X-rays by Wilhelm Conrad Roentgen in 1895, and radioactive sources have been used in radiotherapy since 1898. Advances in the latter half of the 20th century increased the use of medical radiation, and some newer techniques, particularly radiotherapy, computed tomography, positron emission tomography, and interventional radiation involving fluoroscopy, use higher radiation doses than do standard diagnostic X-rays. Radiation therapy may involve use of external beams of radiation, typically high-energy X-rays (4 to 50 MeV) and cobalt-60 gamma rays (UNSCEAR 2000).

Military uses of materials and processes that emit X-radiation and gamma radiation include the production of materials for nuclear weapons and the testing and use of nuclear weapons. In 1945, atomic bombs were detonated over Hiroshima and Nagasaki, Japan. Between 1945 and 1980, nuclear weapons were tested in the atmosphere of the northern hemisphere; during the most intense period of testing, between 1952 and 1962, approximately 520 tests were carried out (IARC 2000).

Several industrial processes use ionizing radiation. Industrial radiography uses gamma radiation to examine welded joints in structures. In the oil industry, gamma radiation or neutron sources are used to determine the geological structures in a bore hole (a process called "well logging") (NCRP 1989). Ionizing radiation also is used to sterilize products and irradiate foods (to kill bacteria and parasites) (IARC 2000).

Ionization-type smoke detectors contain americium-241 (^{241}Am), which emits gamma radiation and alpha particles. In the past, detectors with up to 3.7 megabecquerels (MBq) of ^{241}Am were used in commercial and industrial facilities, but current smoke detectors contain less than 40 kBq (IARC 2000). Television sets emit low-energy X-rays through a process by which electrons are accelerated and bombard the screen (ATSDR 1999). Other products containing sources of ionizing radiation (of unspecified types) include radioluminescent clocks and watches, gaseous tritium light devices (e.g., self-luminous signs), thoriated gas lamp and lantern mantles, radioactive attachments to lightning conductors, static elimination devices, fluorescent lamp starters, porcelain teeth, gemstones activated by neutrons, and thoriated tungsten welding rods. All of these products have restrictions as to the maximum radioactivity allowable in the product and contribute little to the overall population exposure to ionizing radiation (IARC 2000).

Sources

The most important sources of X-radiation and gamma radiation include natural sources, medical uses, atmospheric nuclear weapons tests, nuclear accidents, and nuclear power generation. Ionizing radiation is present naturally in the environment from cosmic and terrestrial sources. Cosmic radiation is a minor source of exposure to X-radiation and gamma radiation; most natural exposure is from terrestrial sources. Soil contains radioactivity derived from the rock from which it originated. However, the majority of radioactive elements are chemically bound in the earth's crust and are not a source of radiation exposure unless released through natural forces (e.g., earthquake or volcanic activity) or human activities (e.g., mining or construction). Generally, only the upper 25 cm of the earth's crust is considered a significant source of gamma radiation. Indoor sources of gamma radiation may be more important than outdoor sources if earth materials (stone, masonry) were used in construction (IARC 2000).

Exposure

Biological damage due to ionizing radiation is related to dose and dose rate, which may affect the probability that cancer will occur (IARC 2000). Radiation dose is a measure of the amount of energy deposited per unit mass of tissue and may be expressed as the absorbed dose, equivalent dose, or effective dose. The standard unit for absorbed dose is the gray (Gy), which is equal to 1 J/kg of deposited energy. The absorbed dose formerly was expressed in rads (1 Gy = 100 rads). The biological effect of high-LET radiation is greater than that of low-LET radiation at the same absorbed dose; therefore, a dose measurement independent of radiation type was derived to reflect the biological effectiveness of radiation in causing tissue damage. The "equivalent dose" (also known as the "dose equivalent") is obtained by multiplying the absorbed dose by a radiation weighting factor (WR; formerly called the "quality factor"). Radiation weighting factors are assigned to radiation of different types and energies by the International Commission on Radiological Protection based on their biological effects relative to those of a reference radiation, typically X-rays or gamma rays; WR ranges from 1 (for low-LET radiation) to 20 (for high-LET radiation). The standard unit for the equivalent dose is the sievert (Sv). The equivalent dose formerly was expressed in rems (1 Sv = 100 rem). Because WR = 1 for both X-rays and gamma rays, the absorbed and equivalent doses are the same (ICRP 1991). Another measurement, the "effective dose," takes into account the fact that the same equivalent dose of radiation causes more significant biological damage to some organs and tissues than to others. Tissue weighting factors (WT) are assigned to different organs and tissue types, and the effective dose is calculated as the sum of the tissue-weighted equivalent doses in all exposed tissues and organs in an individual. The effective dose is expressed in sieverts. The collective radiation dose received by a given population may be expressed as the "collective equivalent dose" (also known as the "collective dose equivalent"), which is the sum of the equivalent doses received by all members of the population, or as the "collective effective dose," which is the sum of the effective doses received by all members of the population. Both the collective equivalent dose and the collective effective dose are expressed in person-sieverts.

All individuals are exposed to ionizing radiation from a variety of natural and anthropogenic sources. Of the general population's exposure to all types of ionizing radiation (not just X-radiation and gamma radiation), natural sources contribute over 80%; radon gas and its decay products account for about two thirds of natural exposure, and the other third is from cosmic radiation, terrestrial radiation, and internally deposited radionuclides. The remaining exposure to ionizing radiation is from anthropogenic sources, such as medical procedures (15%), consumer products (3%), and other sources (totaling less than 1%), which include occupational exposures, nuclear fallout, and the nuclear fuel cycle (BEIR V 1990). In 2000, the worldwide estimated average annual per-capita effective doses of ionizing radiation (of any type) were 2.4 mSv (with a range of 1 to 20 mSv) for natural background exposure and 0.4 mSv (with a range of 0.04 to 1 mSv) for medical diagnostic exposure. Average annual effective doses from past atmospheric nuclear testing, the nuclear power plant accident in Chernobyl, Ukraine, and nuclear power production were only 0.005 mSv, 0.002 mSv, and 0.0002 mSv, respectively (UNSCEAR 2000). Of the estimated worldwide

exposure to X-radiation and gamma radiation, about 43% is from natural sources and about 55% from medical diagnosis and treatment; all other sources contribute less than 2% (UNSCEAR 1993, IARC 2000).

Radiation exposure from medical uses is much more variable than that from natural background radiation (even though the latter varies considerably among locations) because of marked differences in the quality of medical care among cultures. In the more developed nations, higher percentages of the population receive regular medical care, and thus exposures from diagnostic radiology and radiotherapy tend to be higher than in developing nations. Exposure to diagnostic X-rays varies but generally is low; plain film examinations of the chest and extremities involve relatively low effective doses (0.05 to 0.4 mSv), whereas examinations of the abdomen and lumbar spine or pelvis may result in higher effective doses (1 to 3 mSv). Radiation therapy uses much larger doses of radiation than do diagnostic procedures. For example, treatment for leukemia usually involves irradiation of the total bone marrow, with absorbed doses of about 10 to 20 Gy delivered in several fractions (UNSCEAR 2000).

Excluding uranium miners and other workers whose radiation exposure is individually monitored, approximately 5 million people (worldwide) are occupationally exposed to natural sources of ionizing radiation (of any type) at levels above the natural background. About 75% are coal miners (whose estimated average annual effective dose is 1 to 2 mSv), about 13% are other underground miners (whose estimated average annual dose is 1 to 10 mSv), and about 5% are airline crews (who receive an estimated average annual dose of up to 3 mSv). Miners are exposed mainly through inhalation of radon; thus, they are exposed primarily to alpha particles, but also to gamma radiation. Airline crews are exposed primarily to gamma radiation, but also to neutrons (UNSCEAR 1993, IARC 2000).

Medical workers may be exposed to many different types of radionuclides and radiation. In the early 20th century before radiation hazards were recognized, radiologists were exposed to high doses of X-radiation (IARC 2000). The first dose limit established for radiologists in 1902 allowed exposure of approximately 30 Gy per year (Mabuchi 2002), but doses are now much lower (< 1 mSv) (Mostafa *et al.* 2002). From 1985 to 1989, the average annual effective dose of ionizing radiation to medical workers was about 0.5 mSv (UNSCEAR 1993). Other settings with potential for occupational exposure to ionizing radiation include the nuclear industry, military activities, research laboratories, and various industries where radioactive materials or radiography are used (IARC 2000).

Regulations

DOT

Rules have been set governing the marking, labeling, packaging, handling, and transportation of radioactive materials

EPA

Clean Air Act:

Emissions of radionuclides, other than radon, to the air shall not exceed those amounts that would cause any member of the public to receive in a year an effective dose equal to or greater than 10 mrem

Comprehensive Environmental Response, Compensation, and Liability Act:

Reportable Quantity (RQ) = 0.001-1,000 curies (range for 758 radionuclides)*

Marine Protection, Research, and Sanctuaries Act:

Ocean disposal of high level nuclear waste is prohibited and any request for ocean disposal of low level waste requires a permit that must be approved by both houses of Congress

Nuclear Waste Policy Act:

Numerous requirements have been set that will limit the total amount of radiation entering the environment from the Yucca Mountain site for over 10,000 years

Disposal systems for waste shall be designed to provide a reasonable expectation that for 10,000 years after disposal any member of the general population in the general environment shall not receive a combined annual dose of radiation greater than 15 mrem

Regulations have been developed to limit radiation releases from disposal systems for spent nuclear fuel of high-level or transuranic nuclear waste

Resource Conservation and Recovery Act:

Radioactive waste mixed with various specified RCRA hazardous wastes are prohibited from land disposal

Safe Drinking Water Act:

Maximum Contaminant Level (MCL) = 4 mrem (beta particle and photon activity)

The EPA also has authority under the Atomic Energy Act, the Low-Level Radioactive Waste Policy Act, the Waste Isolation Pilot Plant Land Withdrawal Act, the Clean Water Act, and the Public Health Service Act to regulate radioactive contaminants in the environment.

FDA

Rules have been set that govern ionizing radiation for the treatment of foods for human consumption and the production and processing of animal feed and pet food

Performance standards have been set for ionizing radiation-emitting, light-emitting, and sonic and ultrasonic products

Rules have been established for use of radioactive drugs in research

Rules have been set for radiology and diagnostic therapeutic devices including mammography

NRC

Standards for Protection Against Radiation: Occupational radiation dose limits for adults = 5 rem/yr (total effective dose) or 50 rems (sum of the deep-dose equivalent to any individual organ or tissue other than the lens of the eye); 15 rems (eye-lens dose equivalent); 50 rems (shallow-dose equivalent to the skin or any other extremity). Additional limits have been established for minors and fetuses/embryos

Requirements have been set for the medical use of radioactive material and the issuance of licenses authorizing use of the material

Requirements have been set for the packaging, preparing for shipping, and transporting of licensed radioactive material

Rules have been established governing the receiving and storing of radioactive materials in geological repositories

OSHA

Comprehensive regulations have been set for workers exposed to ionizing radiation (including both X- and gamma-radiation) which include monitoring requirements, restricting areas with radiation, established exposure limits, and various precautionary procedures

Guidelines

ACGIH

Effective Dose = 50 mSv (single year); 20 mSv (averaged over 5 years)

Annual Equivalent Dose = 150 mSv (lens of eye); 500 mSv (skin); 500 mSv (hands and feet)

Embryo-fetus exposures once the pregnancy is known = 0.5 mSv (monthly equivalent dose); 2 mSv (dose to surface of women's abdomen for remainder of pregnancy); 1/20 of Annual Limit on Intake (ALI) for radionuclides

See Introduction for information on where to obtain additional detail on regulations and guidelines.

*No separate CAS registry number assigned to X-radiation and gamma radiation.

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Neutrons*

Known to be a human carcinogen
First Listed in the *Eleventh Report on Carcinogens* (2004)

Carcinogenicity

Neutrons are *known to be human carcinogens* based on studies of their mechanisms of carcinogenesis, which demonstrated that neutrons cause genetic damage in humans similar to that caused by X-radiation and gamma radiation, induce chromosomal aberrations in humans, and produce gamma radiation when they interact with biological materials. In addition, there is sufficient evidence that neutrons are carcinogenic in experimental animals.

Neutrons induce similar genetic effects as X-radiation and gamma radiation. They induce a broad spectrum of genetic damage, including gene mutations, micronucleus formation, sister chromatid exchange, chromosomal aberrations, DNA strand breaks, and chromosomal instability. Genetic damage by neutron radiation has been observed in humans exposed occupationally or medically, in experimental animals exposed *in vivo*, and in cultured human and other mammalian cells. Studies of humans exposed to neutron radiation showed that induced chromosomal aberrations persisted for decades, and some cell-culture studies showed genomic instability in the progeny of irradiated human cells (IARC 2000, Littlefield *et al.* 2000). Many cell-culture studies have consistently demonstrated that neutron radiation induces chromosomal aberrations in human peripheral lymphocytes (circulating white blood cells) more effectively than gamma radiation (IARC 2000). Reciprocal translocations (exchanges of DNA between chromosomes) in male germ cells were observed in rhesus monkeys.

Although the genetic damage caused by neutron radiation is qualitatively similar to that caused by X-radiation and gamma radiation, it differs quantitatively. In general, neutron radiation induces chromosomal aberrations, mutations, and DNA damage more efficiently than does low-LET radiation; DNA lesions caused by neutron radiation are more severe and are repaired less efficiently; and neutron radiation induces higher proportions of complex chromosomal aberrations (Pogozelski *et al.* 1999, Boei *et al.* 2001, Brenner *et al.* 2001).

Neutrons are clearly carcinogenic in all species of experimental animals tested, including mouse, rat, rabbit, dog, and monkey. Among these species, radiation-induced tumors have been observed in at least 20 tissues or organs, including those observed in humans (i.e., leukemia, thyroid gland, breast, and lung) (IARC 2000). Susceptibility to induction of benign and malignant tumors depends on tissue site, species, strain, age, and sex.

There are no adequate epidemiological data available to evaluate the carcinogenicity of neutron radiation in humans.

Additional Information Relevant to Carcinogenicity

Low-energy neutrons, such as fission neutrons (those resulting from the splitting of atomic nuclei), are a significantly more potent animal carcinogen than is low-LET radiation (such as X-rays or gamma rays). Types of ionizing radiation with differing LET differ in their effects on biological tissue; however, the observed differences are not sufficient to indicate that the biological effects of high- (i.e. neutron) and low-LET radiation differ qualitatively. There is no conclusive evidence of a signature alteration that might distinguish tumors induced by high-LET radiation from those induced by low-LET radiation.

Properties

Neutrons are electrically neutral particles found in the nuclei of atoms and are similar in mass to protons, which also are present in the nucleus. Because neutrons have no electrical charge, they do not interact with atomic electrons, but they do interact with atomic nuclei. The nuclear force, which holds particles together in the nucleus and leads to these interactions, has a very short range, which means that a neutron must pass close to a nucleus for an interaction to take place. These atomic interactions generate protons, alpha particles, and other nuclear fragments, along with gamma radiation. Because of the small size of the nucleus in relation to the atom as a whole, neutrons have a low probability of interaction and thus are very penetrating. Depending on their energy, they can travel up to several tens of centimeters through tissue (IARC 2000). Water (in nuclear reactors) and thick concrete (in particle accelerators) typically are used as shielding, because interactions with hydrogen nuclei (single protons, which are similar in mass to neutrons) are most effective at reducing neutron energy.

Neutrons induce ionizing events in tissue through elastic collisions with the nuclei of atoms composing tissue molecules. In collisions of neutrons with the hydrogen nuclei of water (the major component of the human body), the recoiling hydrogen nuclei (charged protons) are the source of ionizing events. Elastic collisions of high-energy neutrons (over 50 MeV) with larger nuclei, such as those of carbon, oxygen, nitrogen, and calcium atoms, result in violent interactions that produce many low-energy charged particles. Because the masses of protons and the other recoiling nuclei are much greater than the mass of an electron, neutron radiation generates a dense ion path, causing more damage to tissue than a similar dose of X-rays or gamma rays. Neutrons therefore are considered high-LET radiation. With each collision, about half of the neutron's energy is given to the proton. As the neutron loses energy, it slows down until it is absorbed into the nucleus of an atom, which often makes the absorbing atom radioactive (IARC 2000, Busby 2001a).

Use

Neutron radiation is used less than other types of radiation in industry, medicine, and research. Neutron radiation has not been used widely for medical purposes because it has not shown clear therapeutic benefits, compared with conventional radiotherapy. However, there has been renewed interest in fast-neutron therapy for some cancers (Britten *et al.* 2001, Forman *et al.* 2002). Current medical uses of neutrons include external beam therapy, boron neutron capture therapy, and to make radioisotopes used in medical diagnosis and cancer therapy. Neutron sources are used in oil-well logging and to induce chain reactions in nuclear reactors. Other uses include neutron activation analysis and radiography (for determination of the elemental composition and moisture content of various materials), sterilization of materials, radiometric dating of rocks, and scientific and engineering research (ATSDR 1999, IARC 2000, Lowy *et al.* 2001, Busby 2001b).

Sources

The atomic nucleus is the source of all neutron radiation, but neutrons can be released in several ways. Because the nuclear constituents are tightly bound, several million electronvolts are required to free a neutron from most nuclei (IARC 2000). Sources of neutron radiation include the following: the interaction of high-energy cosmic rays with the earth's atmosphere, nuclear fusion or fission of atomic nuclei in nuclear reactors or atomic explosions, collision of charged particles with a lithium or beryllium target, and spontaneous fission of californium-252 (ATSDR 1999, IARC 2000).

Exposure

The worldwide population is exposed to neutron radiation from natural sources. Populations with additional exposure include cancer patients receiving radiation therapy, nuclear-industry workers, survivors of atomic bomb blasts, and airline crews and passengers. In almost all cases, individuals are exposed to mixed radiation fields in which neutrons are a minor component. Exceptions are patients receiving neutron radiotherapy and airline crews and passengers, who may receive up to 60% of their equivalent dose from neutron radiation.

The general population is exposed to neutrons primarily from cosmic radiation originating from outer space; however, only the most energetic particles produce effects at ground level (IARC 2000). A small portion of cosmic radiation originates from the sun. The amount increases during periods of increased sunspot and solar flare activity, which run in approximately 11-year cycles; the largest event to date occurred in February 1956, during which neutron counts at ground level rose 3,600% above normal background levels (ATSDR 1999, IARC 2000). The average dose of neutron radiation from cosmic radiation increases at higher altitudes; the dose in Denver, Colorado, at an altitude of 1,600 meters is approximately twice that received at sea level (IARC 2000). The estimated annual effective dose from neutron radiation at sea level and a 50° latitude is 80 mSv (UNSCEAR 2000).

Airline crews and passengers are exposed to varying doses of neutron radiation, depending on flight route, aircraft type, and number of hours in flight. Annual average equivalent doses for airline crews have been estimated to range from 0.6 to 3.6 mSv. Collective equivalent doses of neutron radiation received by passengers have been estimated based on air travel rates. For example, in 1985, total time in flight was estimated as 3×10^9 passenger hours; based on an estimated average equivalent dose rate of 1.6 mSv per hour, the annual collective equivalent dose was 5,040 person-Sv. By 1997, time in flight had grown to 4.3×10^9 passenger hours, resulting in an annual collective equivalent dose of 7,200 person-Sv (IARC 2000).

Occupational exposure to neutron radiation occurs to a limited extent in the nuclear industry; however, these workers are exposed primarily to gamma radiation. A study using data from 1977 to 1984 estimated the average annual effective dose of neutron radiation among U.S. radiation workers employed by Department of Energy (DOE) contractors, nuclear power stations, and the U.S. Navy to be 1.8 mSv, and the collective effective dose to be 67.5 person-Sv (IARC 2000). In another U.S. study, the average equivalent dose of neutron radiation to nuclear power plant workers was 5.6 mSv, and the collective equivalent dose was 0.038 person-Sv (NCRP 1989). Overall, less than 3% of the total annual effective radiation dose to nuclear industry workers in the United Kingdom from 1946 to 1988 was due to neutrons (Carpenter *et al.* 1994). Oil-field workers may be exposed to low doses of neutron radiation during well logging; the average annual equivalent dose was estimated as 1 to 2 mSv (Fujimoto *et al.* 1985).

The atomic bombs exploded over Hiroshima and Nagasaki, Japan, in 1945 released low levels of neutron radiation to the environment (an estimated 1% to 2% of the total dose of ionizing radiation from the bombs was from neutrons). Workers involved in the production of nuclear weapons may be exposed to low levels of neutron radiation (IARC 2000). In 1979, 24,787 U.S. workers in DOE facilities (80% of whom performed defense-related work) were monitored for exposure to neutron radiation; only 326 (1.4%) received annual equivalent doses higher than 5 mSv (IARC 2000).

Regulations

FDA

Rules have been established to limit unnecessary exposures from radiology and diagnostic or therapeutic devices

Rules governing ionizing radiation for the treatment of foods have been established

NRC

Occupational dose limits for adults for radioactivity = 5 rem/yr (total effective dose) or 50 rems (sum of the deep-dose equivalent to any individual organ or tissue other than the lens of the eye); 15 rems (eye-lens dose equivalent); 50 rems (shallow-dose equivalent to the skin or any other extremity). Additional limits have been established for minors and embryos/fetuses

Requirements have been established for the medical use of radioactive material and the issuance of licenses authorizing use of the material

OSHA

Comprehensive regulations have been set for workers exposed to ionizing radiation (including neutrons) which include monitoring requirements, restricting areas with radiation, established exposure limits, and various precautionary procedures

Guidelines

ACGIH

Effective Dose = 50 mSv (single year); 20 mSv (averaged over 5 years)

Annual Equivalent Dose = 150 mSv (lens of eye); 500 mSv (skin); 500 mSv (hands and feet)

Embryo-fetus exposures once the pregnancy is known = 0.5 mSv (monthly equivalent dose); 2 mSv (dose to surface of women's abdomen for remainder of pregnancy)

*No separate CAS registry number is assigned to neutrons.

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Radon
CAS No. 10043-92-2

Known to be a human carcinogen
First Listed in the *Seventh Annual Report on Carcinogens* (1994)

Rn

Carcinogenicity

Radon and its isotopic forms radon-222 and radon-220 are *known to be human carcinogens* based on sufficient evidence of carcinogenicity in humans. Increased incidences of lung cancer have been reported in numerous epidemiological studies of groups occupationally exposed to radon at high doses (IARC 1988, ATSDR 1990). Evidence supporting this listing was based principally on earlier mortality studies of underground mine workers. In one of the largest prospective studies, two cohorts totaling 3,400 white and 780 Native American uranium miners and millers in Colorado were followed from 1950 to 1977 (IARC 1988). Among white males, the risk of lung cancer was significantly increased 4- to 6-fold, depending on the comparison population used; the risk of cancer at other tissue sites was not increased. The risk of lung cancer increased significantly with increasing cumulative exposure, supporting a causal relationship. Other prospective and retrospective cohort and case-control studies of uranium miners, together with studies of iron-ore (hematite), other metal, and fluorite miners, conducted between the 1960s and 1980s consistently found that lung-cancer risk increased with increasing cumulative exposure (despite some methodological limitations in exposure estimation, particularly in retrospective studies) (IARC 1988). In some cohorts, radon exposure also was associated with increased risks of tracheal and bronchial cancer. Smaller case-control studies also suggested an association between lung-cancer risk and indoor residential exposure to radon, mainly from ground sources.

The findings in humans are supported by findings of sufficient evidence of carcinogenicity from studies in experimental animals. Inhalation studies have been conducted in male rats, male hamsters, and dogs of both sexes. Radon significantly increased the incidence of respiratory-tract tumors in male rats and dogs, but not in hamsters, compared with unexposed animals. In male rats, radon caused lung cancer (adenoma, adenocarcinoma, alveolar/bronchiolar carcinoma, and squamous-cell carcinoma), and incidences of respiratory-tract tumors were increased further by exposure to both radon and cigarette smoke or cerium hydroxide particles. In dogs of both sexes, exposure to a combination of radon, radon decay products, and uranium ore dust caused nasal carcinoma and lung cancer (epidermoid carcinoma, alveolar/bronchiolar carcinoma, and fibrosarcoma). One review of studies with rats exposed to radon by inhalation also reported increased incidences of tumors of the upper lip and urinary tract. Only three hamsters developed features of squamous carcinoma after 16 to 17 months exposure to radon decay products or radon decay products and uranium ore dust. IARC (1988, 2001) also has concluded that there is sufficient evidence for the carcinogenicity of radon and its decay products in experimental animals.

Properties

Radon is a naturally occurring element and is the heaviest of the noble (chemically inert) gases, with a density of 9.73 g/L at 0°C. Of radon's 20 known isotopes, only three occur naturally, all of which are radioactive. Radon-222, produced by the decay of radium-226, is the most common and most stable, with a half-life of 3.82 days. Radon-220, or thoron, is produced in the decay series of thorium-232 and has a half-life of 55 seconds. Radon-219, or actinon, is produced in the decay series of uranium-235 and has a half-life of 4 seconds (CEE 2003).

Radon is colorless, tasteless, and odorless, with a melting point of –71°C, a boiling point of –61.8°C, and a vapor pressure of 395.2 mm Hg at –71°C. It is fairly soluble in water and organic solvents. Radon spontaneously decays into a series of short-lived radioisotopes of heavy metals (polonium, lead, and bismuth) commonly referred to as "radon daughters" or "radon progeny." Decay of radon and of its decay products results in the release of alpha particles and gamma radiation. When radon is released into air, its solid decay products readily attach to airborne dust (IARC 1988, ATSDR 1990).

Use

Radon is used primarily for research; it has no significant industrial uses. It is used to initiate and influence chemical reactions, as a surface label in the study of surface reactions, in combination with beryllium or other light materials as a source of neutrons, in petroleum and uranium exploration, and in earthquake prediction (ATSDR 1990, HSDB 2003). In U.S. locations with naturally high levels of radon in water or air, exposure to radon has been used since the early 1900s to purportedly treat a wide variety of diseases, such as skin disorders, hardening of the arteries, ulcers, allergies, arthritis, and high blood pressure (ATSDR 1990). Radon also was used to treat malignant tumors; it was encapsulated in gold "seeds," which were implanted at the tumor site (ATSDR 1990).

Production

Radon is produced in nature by radioactive decay of radium. Radon-222 is produced by decay of radium-226, a long-lived product of the uranium-238 decay series. Radon-220 is produced by decay of radium-224 in the thorium-232 decay series, and radon-219 by decay of radium-223 in the uranium-235 decay series. It is estimated that every square mile of soil to a depth of 6 inches contains about 1 g of radon. Radon is released from soil into air and groundwater, and thus occurs at low concentrations throughout the environment. Radon concentrations are highest in areas with uranium and thorium ore deposits and granite formations (ATSDR 1990). Radon-222 makes by far the largest contribution to environmental radon concentrations and is the isotope on which exposure estimates have been based (IARC 2001).

Radon was produced commercially for use in radiation therapy, but for the most part has been replaced by other radionuclides. Some radon is produced in research laboratories and universities for use in experimental studies. Radon is not imported or exported (ATSDR 1990, HSDB 2003).

Exposure

Among the general population, radon accounts for about half of the worldwide average annual background effective dose of radiation, which is 2.4 mSv (IARC 2001). Elevated radon levels have been discovered at locations in virtually every U.S. state, but levels vary considerably, even within a given location. The U.S. Environmental Protection Agency (EPA) developed a generalized map of U.S. radon zones by county, based on predicted average indoor radon screening levels: Zone 1 includes counties with predicted levels above 4 pCi/L (148 Bq/m^3), Zone 2 includes counties with predicted levels between 2 and 4 pCi/L, and Zone 3 includes counties with predicted levels below 2 pCi/L (74 Bq/m^3) (EPA 2003a). In general, Zone 1 areas are concentrated in the northern half of the United States and the Appalachian mountains, and Zone 3 areas are concentrated in the piedmont and coast of the Southeast, Louisiana, Arkansas, Oklahoma, and Texas, and on the Northwest coast. The U.S. EPA estimates that 1 in 15 homes have elevated radon levels (4 pCi/L or higher). As of 2003, radon exposure in U.S. single-family homes was thought to be a causal factor in as many as 15,000 to 22,000 lung cancer deaths per year (EPA 2003b).

The primary routes of environmental exposure to radon are inhalation and ingestion. Radon in the groundwater, soil, or building materials enters working and living spaces and decays, emitting ionizing radiation. Environmental radon concentrations vary with

geographical location and other factors. Average radon concentrations in U.S. groundwater are about 8.8 Bq/L in large aquifers and 28.9 Bq/L in small aquifers and wells. In the continental United States, concentrations in outdoor air range from about 4.1 to 15.2 Bq/m^3, with a mean of about 8.9 Bq/m^3. However, concentrations of up to 30 Bq/m^3 were measured on the Colorado Plateau. Average radon levels are higher in indoor than outdoor air; indoor levels reportedly range from 55 to 157 Bq/m^3 (ATSDR 1990). Emanation of radon from rock, soil, and groundwater can cause significant radon concentrations in tunnels, power stations, caves, public baths, and spas (IARC 1988).

Workers employed in uranium, hard-rock, and phosphate mining potentially are exposed to radon at high concentrations. Uranium miners generally are believed to have the highest exposures. However, the number of operating U.S. underground uranium mines decreased from 300 in 1980 to only 16 in 1984, and the number of underground uranium mine workers from 9,000 in 1979 to 448 in 1986. Concentrations of radon decay products in the air of underground mines vary. Annual geometric mean concentrations of radon decay products in U.S. uranium mines from 1976 to 1985 ranged from 800 to 2,664 Bq/m^3, while concentrations in phosphate mines ranged from 888 to 8,880 Bq/m^3. Radon exposure in underground mines has been greatly reduced through engineering controls. In New Mexico mines, implementation of control measures reduced radon exposure by an order of magnitude from 1967 to 1980 (ATSDR 1990).

Regulations

EPA

Clean Air Act

- Emissions of radon-222 from an underground uranium mine shall not exceed the amount that would cause a member of the public to receive an effective dose greater than 10 mrem/yr
- No source at a Department of Energy facility shall emit into the air more than 20 pCi/m^2 per sec of radon-222 as an average for the entire source

Comprehensive Environmental Response, Compensation, and Liability Act

- Reportable Quantity (RQ) = 0.1 curies (Radon-220 and Radon-222)

Indoor Radon Abatement Act

- Sets a long-term goal that indoor air be as free from radon as the ambient air outside buildings and authorizes funds for radon-reduction activities

Uranium Mill Tailings Radiation Control Act

- Inactive uranium processing sites shall not release radon-220 or radon-222 to the air at concentrations exceeding 20 pCi/m^2 per sec

Guidelines

ACGIH

Recommended Dose Limit to Radon Daughters = 4 Working Level Months per year (WLM/yr)

Recommended intake of radionuclides for embryo-fetus exposures once the pregnancy is known = 1/20 of Annual Limit on Intake (ALI)

NIOSH

Recommended Exposure Limit (REL) to radon progeny = 1 Working Level Month (WLM)

A comprehensive set of recommended standards for occupational exposure to radon progeny has been developed

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Thorium Dioxide
CAS No. 1314-20-1

Known to be a human carcinogen
First Listed in the *Second Annual Report on Carcinogens* (1981)

ThO_2

Carcinogenicity

Thorium dioxide is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity in humans. Evidence for the carcinogenicity of thorium dioxide comes from follow-up studies of patients who were injected (intravascularly) with Thorotrast (thorium dioxide used as a contrast agent in medical radiology, see "Use" section). A large excess of liver tumors (primarily cholangiocellular and hemangiosarcoma) was observed in the Thorotrast-treated patients. Excesses of other cancers, including leukemia and bone cancer, were reported in other studies (van Kaick *et al.* 1978, da Motta *et al.* 1979, Faber 1979, Mori *et al.* 1979). Since thorium dioxide was first listed in the *Second Annual Report on Carcinogens*, additional follow-ups of the Thorotrast cohorts have been reported. These cohort studies were reviewed by the International Agency for Research on Cancer (IARC 2001) as part of their evaluation of "Some Internally Deposited Radionuclides." IARC reported the results of five major cohort studies (Germany, Denmark, Japan, Portugal, and Sweden), which followed over 10,000 patients injected with Thorotrast between the 1930s and the 1950s. These studies confirm the findings of the earlier studies and reported relative risks for mortality or incidence for liver cancer ranging from 36 to 129. Risks were correlated with the volume of injected Thorotrast. Hemangiosarcoma, typically a very rare tumor, accounted for approximately one-third of the tumors. The risk of leukemia, excluding chronic lymphoid leukemia, was increased 11 to 20 fold in Thorotrast-treated patients. Findings regarding extrahepatic bile duct, gallbladder, and pancreatic cancers and mesothelioma were inconsistent across studies (IARC 2001).

The findings in humans are supported by findings of sufficient evidence of carcinogenicity of thorium dioxide in experimental animals. When administered by intravenous injection, thorium dioxide induced hemangioendotheliosarcomas or reticuloendotheliosarcomas of the liver, spleen, and lung in rabbits, cholangiocellular carcinomas in hamsters, and liver cell adenomas in rats. Subcutaneous injection of thorium dioxide induced local fibrosarcomas in rats and mice; intraperitoneal injection induced sarcomas in rats, mice, hamsters, rabbits, and guinea pigs (Wegener 1979, CHIP 1981, IARC 2001).

Properties

Thorium dioxide is the oxide of the radioactive metallic element thorium, the second member of the actinide series of elements. Thorium-232 is the most common of the naturally occurring isotopes of thorium; it decays by emission of alpha particles and has a half-life of 1.4×10^{10} years (Hedrick 2000). The other two long-lived isotopes that decay by emission of alpha particles are thorium-230 (half-life of 77,000 years) and thorium-229 (half-life of 7,300 years). Decay products include radium-228, radium-224, and radon-220 (IARC 2001). Thorium dioxide has a molecular weight of 264 and occurs as a heavy, white crystalline powder that has a melting point of 3,390°C (the highest of any metal oxide) and a boiling point of 4,400°C. It is insoluble in water and alkalies and slightly soluble in acids and biological fluids. Thorium dioxide is incandescent when heated. It is available in the United States in stocks of different particle sizes with purities ranging from 99.5% to 99.99%. The X-ray contrast medium,

Thorotrast, is a 25% colloidal thorium dioxide suspension in aqueous dextrin (Kirk-Othmer 1997, IARC 2001, HSDB 2003).

Use

Thorium was discovered in 1828, and its radioactivity was discovered in 1898. In the early 1900s, the only commercial use for thorium was in gas lamp mantles. Although demand for gas mantles declined with the advent of electric lights, mantle manufacturing still accounted for 92% of thorium's nonfuel use as late as 1950 (Hedrick 2000). The use of thorium in the United States has decreased substantially because of concerns over its naturally occurring radioactivity (Hedrick 2002). Principal uses for thorium dioxide are in high temperature ceramics, gas mantles, nuclear fuel, flame spraying, crucibles, medicines, nonsilica optical glass, and thoriated tungsten filaments, and as a catalyst. It also has been used as a diagnostic aid (radiopaque medium) in feline medication (HSDB 2003).

Thorotrast was used as a contrast agent in medical radiology. It was used extensively as an intravascular contrast agent for cerebral and limb angiography in Europe, the United States and Japan. It also was injected directly into the nasal cavity, paranasal sinus, spleen, brain, and other sites. Thorotrast treatment lead to deposition of thorium and its decay products in body tissues and organs, especially the reticuloendothelial tissue and the bone, which resulted in continuous alpha-particle irradiation throughout life (BEIR IV 1988). Use of Thorotrast was discontinued in the 1950s when harmful latent effects were observed (Grampa 1971, IARC 2001).

Production

Thorium occurs in several minerals, including monazite, thorite, huttonite, and thorogummite. Most thorium production occurs from mining monazite as a by-product from heavy-mineral sands mined for titanium and zirconium minerals. Between 1987 and 1994 only one U.S. company produced monazite, with all of the monazite exported. Thorium-bearing monazite production ended in the United States in 1994, and since then all U.S. production of thorium-containing products have relied on imports and existing industry and government stocks. About eight domestic companies continue to process or fabricate various forms of thorium for non-energy uses such as described above (Hedrick 2002). Twelve current U.S. suppliers of thorium dioxide were identified in 2003 (ChemSources 2003).

Imports of thorium dioxide equivalents ranged from approximately 43,000 lb/yr (19,500 kg/yr) to more than 150,000 lb/yr (68,000 kg/yr) between 1983 and 1987 (ATSDR 1990). Between 1998 and 2002 annual imports of thorium compounds, expressed as thorium dioxide equivalents, ranged from a low of 1,400 lb (600 kg) in 2002 to a high of 24,000 lb (10,900 kg) in 2000. Imports of thorium compounds have been declining over the years due to limited uses for the compounds (Hedrick 2002).

Exports of thorium dioxide equivalents ranged from approximately 2,200 lb (1,000 kg) to 45,000 lb (20,400 kg) between 1983 and 1987 (ATSDR 1990). Between 1990 and 1994, exports fluctuated between a low of 15 lb (7 kg) in 1994 and a high of 5,800 lb (2,600 kg) in 1991 (Hedrick 2000). No current exports were identified.

Exposure

The primary routes of potential human exposure to thorium dioxide are inhalation, intravenous injection, ingestion, and dermal contact. Although thorium is widespread in the environment from both natural and anthropogenic sources, concentrations in air, soil, drinking water, and foods are very low. Very few studies have investigated daily intakes of thorium in the general population; however, estimated total daily intakes of thorium-230 and thorium-232 in air, food, and water ranged from approximately 0.02 to 0.17 pCi. Higher exposures could occur for people living near hazardous waste sites or mining areas that contain thorium (ATSDR 1990).

EPA's Toxics Release Inventory (TRI) reported industrial releases of thorium dioxide from 1988 to the present. Between 1988 and 1993, industrial releases ranged from 42,000 lb (19,100 kg) (1993) to 679,129 lb (308,053 kg) (1988). After 1993, one pound (0.45 kg) of thorium dioxide was released in 1995 and 1996, and no releases were reported from 1997 to 2001 (TRI01 2003).

Occupational exposures may occur in the mining, milling, and processing of uranium, tin, rare-earth metals, and phosphate and in gas mantle manufacturing and other thorium-processing industries (ATSDR 1990, IARC 2001). Potential exposure also may have occurred during the formulation, packaging, preparation, or administration of the compound as a pharmaceutical. Based on the amount of Thorotrast produced, more than 2.5 million people worldwide were exposed to thorium dioxide between 1930 and 1950 (IARC 2001). The injection dosages ranged from 2 to 70 mL of Thorotrast solution, depending on the area to be X-rayed (Saragoca *et al.* 1972). Once injected, Thorotrast is not cleared from the body and results in life-long exposure (BEIR IV 1988).

Regulations

EPA

Emergency Planning and Community Right-To-Know Act (EPCRA)

Toxics Release Inventory: Listed substance subject to reporting requirements

FDA

Thorium dioxide is not currently approved for marketing

Guidelines

ACGIH

Recommended intake of radionuclides for embryo-fetus exposures once the pregnancy is known = 1/20 of Annual Limit on Intake (ALI)

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