Ionizing Radiation

Introduction

Ionizing radiation is electromagnetic radiation that has sufficient energy to remove electrons from atoms. Ionization results in the production of negatively charged free electrons and positively charged ionized atoms. Ionizing radiation can be classified into two categories: photons (X-radiation and gamma radiation) and particles (alpha and beta particles and neutrons). Five types or sources of ionizing radiation are listed in the Report on Carcinogens as *known to be human carcinogens*, in four separate listings:

- X-radiation and gamma radiation (included in one listing) were first listed in the *Eleventh Report on Carcinogens* (2004).
- Neutrons were first listed in the *Eleventh Report on Carcinogens* (2004).
- Radon and its isotopic forms radon-220 and radon-222, which emit primarily alpha particles, were first listed in the *Seventh Annual Report on Carcinogens* (1994).
- Thorium dioxide, which decays by emission of alpha particles, was first listed in the *Second Annual Report on Carcinogens* (1981).

Below are the profiles for the four ionizing radiation listings, covering carcinogenicity, properties, use, sources or production, exposure, and references cited separately for each profile, followed by a list of regulations and guidelines applicable to all five types or sources of ionizing radiation listed.

X-Radiation and Gamma Radiation

CAS No.: none assigned

Known to be human carcinogens

First listed in the *Eleventh Report on Carcinogens* (2004)

Also known as X-rays, gamma rays, and γ radiation

Carcinogenicity

X-radiation and gamma radiation are *known to be human carcinogens* based on sufficient evidence of carcinogenicity from studies in humans.

Cancer Studies 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, urinary 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 sarcoma (using the U.S. Surveillance, Epidemiology, and End Results cancer registry) (Yap *et al.* 2002) added angiosarcoma 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 one 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 lymphoma and melanoma.

Studies on Mechanisms of Carcinogenesis

X-radiation and gamma radiation have been shown to cause a broad spectrum of genetic damage, including gene mutations, minisatellite mutations, micronucleus formation, chromosomal aberrations, ploidy changes, 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 cause genetic damage in somatic cells and transmissible mutations in mammalian germ cells. 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 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.

Cancer Studies in Experimental Animals

X-radiation and gamma radiation are clearly carcinogenic in all species of experimental animals tested (mice, rats, and monkeys for X-radiation and mice, rats, rabbits, and dogs for gamma radiation). Among these species, radiation-induced tumors have been observed in at least 17 different tissue sites, including sites at which tumors were observed in humans (i.e., leukemia, thyroid gland, breast, and lung) (IARC 2000). Susceptibility to induction of 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 to do so. It has been suggested that radiation exposure of mice before mating increases the susceptibility of their offspring to cancer; however, study results are conflicting.

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, 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} 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 can also 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, from 1952 to 1962, about 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 is also used to sterilize products and irradiate foods (to kill bacteria and parasites) (IARC 2000).

Ionization-type smoke detectors contain americium-241, which emits gamma radiation and alpha particles. In the past, detectors with up to 3.7 MBq of americium-241 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. For all of these products, the maximum allowable radioactivity is restricted, and radiation from these products contributes little to overall exposure of the population (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 by 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, 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 (W_R; 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; W_R ranges from 1 (for low-LET radiation) to 20 (for high-LET radiation). The standard unit for the equivalent dose is the sievert. The equivalent dose formerly was expressed in rems (1 Sv = 100 rem). Because $W_R = 1$ 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 (W_T) are assigned to the various 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 exposure, 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 (range = 1 to 20 mSv) for natural background exposure and 0.4 mSv (range = 0.04 to 1 mSv) for medical diagnostic exposure. However, in countries with the highest level of health care (< 1,000 population per physician), the average radiation dose from medical X-rays was estimated at 1.2 mSv, or about half the average natural exposure level. Estimated 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).

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, about 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). Other settings with potential for occupational exposure to X-radiation or gamma radiation include the nuclear industry, military activities, research laboratories, and various industries where radioactive materials or radiography are used (IARC 2000).

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Neutrons

CAS No.: none assigned

Known to be a human carcinogen

First listed in the *Eleventh Report on Carcinogens* (2004)

Carcinogenicity

Neutrons are *known to be a human carcinogen* based on studies on 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 of carcinogenicity from studies in experimental animals.

Studies on Mechanisms of Carcinogenesis

Neutrons cause a broad spectrum of genetic damage similar to that caused by X-radiation and gamma radiation, 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 causes chromosomal aberrations in human peripheral-blood lymphocytes more effectively than does gamma radiation (IARC 2000). Reciprocal translocations 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. Low-energy neutrons, such as fission neutrons (those resulting from the splitting of atomic nuclei), are significantly more potent carcinogens in experimental animals 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-LET (i.e., neutrons) and low-LET radiation differ qualitatively. 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). However, 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.

Cancer Studies in Experimental Animals

Neutrons are clearly carcinogenic in all species of experimental animals tested, including mice, rats, rabbits, dogs, and monkeys. Among these species, radiation-induced tumors have been observed in at least 20 different tissue sites, including sites at which tumors were observed in humans (i.e., leukemia, thyroid gland, breast, and lung) (IARC 2000). Susceptibility to induction of tumors depends on tissue site, species, strain, age, and sex.

Cancer Studies in Humans

The data available from epidemiological studies are inadequate to evaluate the relationship between human cancer and exposure specifically to neutron 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 cause ionization in biological 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 2001).

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 production of 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).

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, when 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 m (1 mi) is about twice that received at sea level (IARC 2000). The estimated annual effective dose of neutron radiation at sea level at 50° latitude is 80 μSv (UNSCEAR 2000). 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) (IARC 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 μSv 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 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). Workers involved in the production of nuclear weapons may be exposed to low levels of neutron radiation. 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). Oil-field workers may be exposed to low doses of neutron radiation during well logging; the average annual equivalent dose was estimated at 1 to 2 mSv (Fujimoto *et al.* 1985).

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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)

Also known as Rn

Carcinogenicity

Radon and its isotopic forms radon-222 and radon-220 are *known to be human carcinogens* based on sufficient evidence of carcinogenicity from studies in humans.

Cancer Studies 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. 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 radon exposure, supporting a causal relationship. Other prospective and retrospective cohort and case-control studies of uranium miners, together with studies of miners of iron ore (hematite), other metals, and fluorite, 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). In some cohorts, radon exposure was also 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 (IARC 1988).

Cancer Studies in Experimental Animals

There is sufficient evidence for the carcinogenicity of radon from studies in experimental animals. In male rats, inhalation exposure to 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, inhalation exposure to a combination of radon, radon decay products, and uranium ore dust caused lung cancer (epidermoid carcinoma, alveolar/bronchiolar carcinoma, and fibrosarcoma)

and nasal cancer (carcinoma). A review of studies in rats exposed to radon by inhalation also reported increased incidences of tumors of the upper lip and urinary tract. In a study in hamsters, only three animals developed features of squamous-cell carcinoma after 16 to 17 months of exposure to radon decay products or radon decay products and uranium ore dust. The International Agency for Research on Cancer (IARC 1988, 2001) concluded that there was 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. 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 isotope, 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 and is fairly soluble in water and organic solvents. It 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). Physical and chemical properties of radon are listed in the following table.

Property	Information
Density	9.73 g/L at 0°C
Melting point	–71°C
Boiling point	–61.8°C
Vapor pressure	395.2 mm Hg at –71°C

Source: 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 2009). 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. 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 by the United States (ATSDR 1990, 2012, HSDB 2009).

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 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. 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 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).

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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)

Also known as thorium oxide

ThO_2

Carcinogenicity

Thorium dioxide is *known to be a human carcinogen* based on sufficient evidence of carcinogenicity from studies in humans.

Cancer Studies in Humans

Evidence for the carcinogenicity of thorium dioxide comes from follow-up epidemiological studies of patients who received intravascular injections of Thorotrast (thorium dioxide used as a contrast agent in medical radiology; see Use, below). A large excess of liver tumors (primarily cholangiocellular tumors and hemangiosarcoma) was observed in the Thorotrast-treated patients. Excesses of other cancer, 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 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 in its evaluation of *Some Internally Deposited Radionuclides* (IARC 2001). IARC reported the results of five major cohort studies (in Germany, Denmark, Japan, Portugal, and Sweden), which followed over 10,000 patients injected with Thorotrast between the 1930s and 1950s. These studies confirmed the findings of the earlier studies and reported relative risks of liver-cancer mortality or incidence ranging from 36 to 129. Risks were correlated with the volume of injected Thorotrast. Hemangiosarcoma, typically a very rare tumor, accounted for about 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 mesothelioma and cancer of the extrahepatic bile duct, gallbladder, and pancreas were inconsistent across studies.

Cancer Studies in Experimental Animals

There is sufficient evidence for the carcinogenicity of thorium dioxide from studies in experimental animals. When administered by intravenous injection, thorium dioxide caused cancer of the blood vessels (hemangiosarcoma) or reticuloendothelial system (sarcoma) in the liver, spleen, and lung in rabbits; liver cancer (cholangiocellular carcinoma) in hamsters; and benign liver tumors (hepatocellular adenoma) in rats. Subcutaneous injection of thorium dioxide caused cancer at the injection site (fibrosarcoma) in rats and mice, and intraperitoneal injection caused cancer (sarcoma) in rats, mice, hamsters, rabbits, and guinea pigs (Wegener 1979, EPA 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; 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 with 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 alkalis and slightly soluble in acids and biological fluids. Thorium dioxide is incandescent when heated. It is available in the United States in stocks of various 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 (IARC 2001, Clark *et al.* 2006, HSDB 2009). Thorotrast was fomerly a registered trademark of the Heyden Chemical Corporation.

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 non-fuel 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, non-silica optical glass, and thoriated tungsten filaments, and as a catalyst. It has also been used as a diagnostic aid (radiopaque medium) in feline medication (HSDB 2009).

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 was also injected directly into the nasal cavity, paranasal sinus, spleen, brain, and other sites. Thorotrast treatment led to deposition of thorium and its decay products in body tissues and organs, especially reticuloendothelial tissue and bone, which resulted in continuous lifelong alpha-particle irradiation (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 of 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, all of which was exported. U.S. production of thorium-bearing monazite ended in the United States in 1994; since then, all U.S. production of thorium-containing products has relied on imports and existing industry and government stocks. About seven U.S. companies continue to process or fabricate various forms of thorium for non-energy uses such as described above (Hedrick 2002). In 2009, thorium dioxide was available from 12 U.S. suppliers (ChemSources 2009). From 1983 to 1987, annual U.S. imports of thorium dioxide equivalent ranged from 19.7 metric tons (43,000 lb) to 69.3 metric tons (153,000 lb) (ATSDR 1990). From 1996 to 2002, imports of thorium compounds, expressed as thorium dioxide equivalent, declined from 26,400 kg (58,200 lb) to 480 kg (1,060 lb) (Hedrick 2000, 2002). U.S. exports of thorium metal waste and

scrap (thorium dioxide equivalent) from 1983 to 1987 ranged from 1.0 metric tons (2,200 lb) to 20.4 metric tons (45,000 lb) (ATSDR 1990). Between 1996 and 2002, exports of thorium compounds (thorium dioxide equivalent) ranged from a low of 58 kg (128 lb) in 1996 to a high of 5,390 kg (11,900 lb) in 2001 (Hedrick 2000, 2002). No more recent data on U.S. imports or exports were found.

Exposure

The primary routes of potential human exposure to thorium dioxide are inhalation, intravenous injection, ingestion, and dermal contact. 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, resulting in lifelong exposure (BEIR IV 1988).

According to the U.S. Environmental Protection Agency's Toxics Release Inventory, environmental releases of thorium dioxide declined from 679,129 lb in 1988 to 42,000 lb in 1993. In 1995 and 1996, 1 lb of thorium dioxide was released, and no releases were reported from 1997 to 2007 (TRI 2009). 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 among people living near hazardous-waste sites or mining areas that contain thorium (ATSDR 1990).

Occupational exposure to thorium 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). Exposure could also have occurred during the formulation, packaging, preparation, or administration of thorium dioxide as a pharmaceutical.

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Ionizing Radiation

Regulations

Department of Energy (DOE)

A comprehensive set of protection standards and program requirements has been developed for protecting individuals from ionizing radiation resulting from the conduct of DOE activities.

Radiation Dose Limits

Annual occupational dose limits for adults (the more limiting of the following): Total effective dose = 5 rem (0.05 Sv); sum of the equivalent dose to the whole body for external exposures and the committed equivalent dose to any organ or tissue other than the skin or the lens of the eye = 50 rem (0.5 Sv); eye-lens dose equivalent = 15 rem (0.15 Sv); sum of the equivalent dose to the skin or to any extremity for external exposures and the committed equivalent dose to the skin or to any extremity = 50 rem (0.5 Sv).

Dose equivalent to an embryo or fetus due to the occupational exposure of a declared pregnant woman: Shall not exceed 0.5 rem (5 mSv) during the entire pregnancy.

Annual total effective dose equivalent for individual members of the public: Shall not exceed 0.1 rem (1 mSv).

Department of Transportation (DOT)

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

Environmental Protection Agency (EPA)

Clean Air Act

National Emission Standards for Hazardous Air Pollutants: Radionuclides are listed as hazardous air pollutants.

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 ≥ 10 mrem (0.1 mSv).

Emissions of radon-222 from an underground uranium mine shall not exceed the amount that would cause a member of the public to receive in a year an effective dose > 10 mrem (0.1 mSv).

No source at a DOE facility shall emit into the air more than 20 pCi/m^2 per sec of radon-222 as an average for the entire source.

Each stack used in the generation of phosphogypsum shall not emit more than 20 pCi/m^2-sec (1.9 pCi/ft^2-sec) of radon-222 into the air.

Emissions to the ambient air from an existing uranium mill tailings pile shall not exceed 20 pCi/m^2-sec (1.9 pCi/ft^2-sec) of radon-222.

Comprehensive Environmental Response, Compensation, and Liability Act

Reportable quantity (RQ): range for 758 radionuclides = 0.001 to 1,000 Ci; for radon-220 and radon-222 = 0.1 Ci.

Emergency Planning and Community Right-To-Know Act

Toxics Release Inventory: Thorium dioxide is a listed substance subject to reporting requirements.

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.

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 containment requirements have been set that will limit the total amount of radiation entering the environment from the Yucca Mountain (Nevada) nuclear waste repository 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 (0.15 mSv).

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

Radiation Protection Programs

Environmental radiation protection standards for nuclear power operations have been established to limit human and environmental exposure to radiation.

Resource Conservation and Recovery Act

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

Safe Drinking Water Act

Maximum contaminant level (MCL) = The average annual concentration of beta particle and photon radioactivity from manmade radionuclides in drinking water must not produce an annual dose equivalent to the total body or any internal organ greater than 4 mrem (0.04 mSv).

Uranium Mill Tailings Radiation Control Act

A comprehensive set of regulations have been established to guard against exposure to radon from uranium and thorium mill tailings.

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

Food and Drug Administration (FDA, an HHS agency)

Rules have been established 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 diagnostic and therapeutic products and procedures and for accreditation and certification of facilities and personnel.

Rules have been established for use of radioactive drugs in research.

An approved new drug application is required for marketing thorium dioxide drugs.

Mine Safety and Health Administration (MSHA, Dept. of Labor)

Regulations have been established to protect workers in underground metal and nonmetal mines against exposure to gamma radiation, including annual radiation surveys and an annual individual gamma radiation limit of 5 rem (0.05 Sv).

Regulations have been established to protect workers in underground metal and nonmetal mines against exposure to radon and radon daughters, including monitoring and record keeping requirements and various exposure limits.

Nuclear Regulatory Commission (NRC)

Comprehensive regulations have been developed to control the receipt, possession, use, transfer, and disposal of radioactive material in such a manner that the total dose to an individual does not exceed the Standards for Protection Against Radiation (see DOE Radiation Dose Limits, above). The regulations apply to entities licensed to receive, possess, use, transfer, or dispose of by-product, source, or special nuclear material or to operate a production or utilization facility, and to exposure associated with nuclear power plants and other uses of radioactive materials, including medical, veterinary, industrial, academic, and research.

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

Rules have been established 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.

Occupational Safety and Health Administration (OSHA, Dept. of Labor)

Comprehensive regulations have been set to limit worker exposure to ionizing radiation which include monitoring requirements, restricting access to areas with radiation, established exposure limits, and various precautionary procedures.

Guidelines

American Conference of Governmental Industrial Hygienists (ACGIH)

Effective dose = 50 mSv for a single year; = 20 mSv per year averaged over 5 years.

Annual equivalent dose = 150 mSv for the lens of the eye; = 500 mSv for the skin, hands, and feet.

Embryo/fetus monthly equivalent dose = 0.5 mSv.

Recommended dose limit for radon daughters = 4 working level months per year (WLM/yr).

Food and Drug Administration (FDA, an HHS agency)

Radiation protection recommendations have been established for the protection of patients from radiation during diagnostic and therapeutic procedures.

National Institute for Occupational Safety and Health (NIOSH, CDC, HHS)

Recommended exposure limit (REL) for radon progeny in underground mines = 1 working level month (WLM) per year; average workshift concentration = 1/12 of 1 WL (0.083 WL).

A comprehensive set of recommended standards for occupational exposure to radon progeny in underground mines has been developed.