Ionizing Radiation Effects and Their Risk to Humans

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Radiation and DNA

Radiation is simply a mechanism whereby energy passes through space. It takes the form of an electromagnetic wave, with the frequency of the electromagnetic wave determining its position in the electromagnetic spectrum. Low-frequency waves such as radio waves lie at one end of the spectrum and high-energy, high-frequency X-rays/Gamma rays at the other end. These high-frequency, high-energy waves are termed "ionizing" (as opposed to non-ionizing) radiation because they contain sufficient energy to displace an electron from its orbit around a nucleus. The most important consequence of this displaced electron on human tissue is the potential damage it can inflict on DNA, which may occur directly or indirectly. Direct damage occurs when the displaced electron hits and breaks a DNA strand. Indirect damage occurs when the electron reacts with a water molecule, creating a powerful hydroxyl radical which then damages the cell's DNA.

Damage to a cell's DNA in either of these ways can have several consequences. A single-strand DNA break is usually repaired appropriately by the cell with no subsequent deleterious sequelae. However, a break affecting both strands of DNA allows the potential for abnormal reconnection of the strands, which likely accounts for all the adverse biological effects ionizing radiation has on humans. First, DNA may rejoin itself incorrectly, rendering the cell nonviable with cell death taking place. Second, it may rejoin as a symmetrical translocation with the potential expression of an oncogene during division (and development of subsequent malignancy) or with abnormal division in gonads, giving rise to potential hereditary disorders.

Radiosensitivity is the probability of a cell, tissue, or organ suffering an effect per unit dose of radiation. Radiosensitivity is highest in cells which are highly mitotic or undifferentiated. For this reason the basal epidermis, bone marrow, thymus, gonads, and lens cells are highly radiosensitive. Muscle, bones, and nervous system tissues have a relative low radiosensitivity.

Ionizing Radiation Effects

The deleterious effect ionizing radiation has on human tissue can be divided into two types: non-stochastic (deterministic) or stochastic effects.

Deterministic (Non-Stochastic) Effects

Deterministic effects only occur once a threshold of exposure has been exceeded. The severity of deterministic effects increases as the dose of exposure increases. Because of an identifiable threshold level, appropriate radiation protection mechanisms and occupational exposure dose limits can be put in place to reduce the likelihood of these effects occurring.

Mechanisms

Deterministic effects are caused by significant cell damage or death. The physical effects will occur when the cell death burden is large enough to cause obvious functional impairment of a tissue or organ.

Examples

1. **Skin Erythema/Necrosis/Epilation**

Erythema occurs 1 to 24 hours after 2 Sv have been received. Breakdown of the skin surface occurs approximately four weeks after 15 Sv have been received. Epilation is reversible after 3 Sv but irreversible after 7 Sv and occurs three weeks following exposure.

2. **Cataract**

Cataract occurs due to accumulation of damaged or dead cells within the lens, the removal of which cannot take place naturally. Cataract occurs after 2 to 10 Gy have been received, but may take years to develop.

3. **Sterility**

Radiation can impair oocyte function, leading to impaired or non-fertility. The radiation dose required to have this effect decreases with age due to falling total oocyte numbers. Similarly, radiation exposure to the testes can result in temporary or permanent azoospermia. Permanent sterility occurs after 2.5 to 3.5 Gy have been received by the gonads.

4. **Radiation Sickness**

Radiation sickness (correctly termed acute radiation syndrome) involves nausea, vomiting, and diarrhea developing within hours or minutes of a radiation exposure. This is due to deterministic effects on the bone marrow, GI tract, and CNS.

5. **IUGR/Teratogenesis/Fetal Death**

Deterministic radiation exposure effects during pregnancy depend not only on the radiation dose received but also on the gestational age at which it occurred. The embryo is relatively radio-resistant during its preimplantation phase but highly radiosensitive during its organogenesis (two to eight weeks) and neuronal stem cell proliferation phases (eight to 15 weeks). Fetal radiosensitivity falls after this period. High levels of radiation exposure in pregnancy can lead to growth retardation, in particular microcephaly. The threshold dose for this effect is high (>20Gy) with other deterministic effects (hypospadia, microphthalmia, retinal degeneration, and optic atrophy) having a lower threshold level of >1Gy.

Incidence

Although relatively rare, deterministic effects secondary to diagnostic imaging do occasionally occur. These have been most commonly encountered with: CT (example 1 and example 2), CT perfusion, fluoroscopy, and interventional radiology.

Stochastic Effects

Current thinking is that stochastic effect occurrence follows a linear no-threshold hypothesis. This means that although there is no threshold level for these effects, the risk of an effect occurring increases linearly as the dose increases.

Mechanism

Stochastic effects occur due to the ionizing radiation effect of symmetrical translocations taking place during cell division.

Examples

1. **Cancer**

Over time, anecdotal evidence suggested that ionizing radiation could cause cancer. However, reliable evidence has only relatively recently become available. Data from the Radiation Effects Research Foundation on individuals exposed to radiation from the atomic bombs in Hiroshima and Nagasaki have shown an increased relative risk of developing malignancy (leukemia, oral cavity, esophagus, stomach, colon, lung, breast, ovary, urinary bladder, thyroid, liver, non-melanoma skin, and nervous system) as a result of radiation exposure. As such, multiple bodies, including the U.S. Department of Health and Human Services, have classified ionizing radiation as a human carcinogen.

Unfortunately, doses which have been shown to result in this increased relative malignancy risk are similar to levels which can also be imparted by radiology studies such as CT scans, interventional radiology, and barium enema procedures. Indeed, the excessive relative risk of cancer mortality determined by the International Commission of Radiological Protection (ICRP) is 5 %/Sv. The National Research Council of the National Academies has concluded that a single CT scan with a dose of 10 mSv carries a risk of 1:1000 of producing cancer. A comprehensive list of effective doses in various other radiology and nuclear medicine procedures can be easily compared with natural background radiation levels.

The risk of developing solid cancers follows a linear pattern with increasing dose although the age at which exposure takes place is highly relevant. A decline in radiosensitivity does take place with age, making young children more susceptible to radiation-induced malignancies. Although the malignancy risk for the population as a whole is 5 %/Sv, this rises to 15 %/Sv in a young girl and falls to 1 %/Sv in a 70-year-old.

Adopting the linear no-threshold hypothesis and extrapolating the data to very low dose exposures (plain radiographs, for example) would suggest that while the risk of a radiation-induced malignancy persists, its impact becomes negligible for a single exposure. There is some controversy concerning the extrapolation of the linear no-threshold hypothesis to very low doses given that no increased incidence of cancer is seen in areas of high background radiation or in airline pilots. Caution should be exercised in multiple radiation exposures however, given that stochastic effects are cumulative. Similarly, multiple high-dose diagnostic imaging procedures such as CT can easily exceed the levels known to impart an increased relative risk for malignancy.

2. **Hereditary Defects (e.g., Down Syndrome)**

Although no increased incidence of hereditary defects in patients exposed to radiation in Japan and Chernobyl was documented, animal experiments would suggest that this risk does exist. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and ICRP propose a hereditary defect risk of between 0.3 to 0.8% per Sv.

Risk Estimation

An estimate of an individual's stochastic risk relating to ionizing radiation exposures can be obtained by applying the average effective dose of the procedure to the age at which the exposure took place. However, it is important to remember that the advantages obtained by an accurate diagnosis usually outweigh this slightly increased malignancy risk, particularly when this risk is compared to common daily activities such as driving. Such activities have a higher relative risk of dying than the 1:1000 cancer risk of having a single CT scan.