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Factsheet 2: Cancer/non-cancerous causation

Evidence of cancer causation by ionising radiation

Evidence that ionising radiation can cause human cancer has come from several sources. These include the follow-up of patients therapeutically irradiated for malignant conditions, such as cancer of the cervix, and, as was the practice years ago, for non-malignant conditions like ankylosing spondylitis; follow-up studies on UK, US, Australian and New Zealand service personnel present at atmospheric nuclear test sites; and, most notably, from the Japanese atomic bomb survivor studies.

The Japanese atomic bomb survivor data show evidence of an increase in cancer incidence, but only in individuals exposed to levels of ionising radiation of 50 mSv and above. (The UK natural background radiation is 2.2 milliSieverts per annum average). There have been no human low-dose epidemiological studies that unequivocally demonstrated an increase in cancer incidence.

Since everyone is exposed to ionising radiation and not everyone develops cancer, other factors must be involved. Cancers induced by ionising radiation are indistinguishable from those due to other more common causes such as diet, tobacco, alcohol, etc. In addition to the dose of radiation delivered, the *type* of radiation, its duration or exposure i.e. an acute high dose or a chronic low dose, the particular tissue irradiated and the age of the individual at the time of the irradiation are all known to be important. Taking the overall evidence on these matters into account and in the absence of a positive threshold dose of ionising radiation, the convention is to accept that no dose of ionising radiation is completely free from risk of cancer and that the risk increases linearly with dose.

There is, however, a spectrum of risk dependent on the factors discussed above and a standard international approach to estimation of the probability that a particular cancer in a particular patient is causally linked to ionising radiation has been established. (IAEA – Tech – Doc 870 (1996)). The "probability of causation" approach requires dosimetry information on the individual's exposure. There is reliable evidence sufficient to generally recognise a causal link between ionising radiation exposure and the following cancers:

leukaemia (other than chronic lymphatic leukaemia)
multiple myeloma
female breast
lung
stomach
colon
thyroid
urinary bladder
brain
ovary

Evidence of radiation induction of non-cancer conditions

Reports of the atomic bomb survivor follow-up studies suggest that ionising radiation exposure may also be associated with non-cancer diseases. (Kodama (1996): Schull et al (1998)). Associations have been described with uterine fibroids and certain non cancerous thyroid and para-thyroid tumours. A review of the current evidence on atherosclerosis and coronary disease follows.

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Ionising radiation and heart disease

Until the 1960s the heart and blood vessels were thought to be completely resistant to ionising radiation (Warren 1942). Since then reports have appeared describing inflammation of the heart lining, and conduction disorders from damage to the electrical system following high dose mediastinal irradiation of malignant tumours. Today these effects of high-dose ionising radiation exposure are generally accepted. (Stewart et al 1984).

The situation regarding a link between ionising radiation - particularly low-dose ionising radiation - and atherosclerotic disease is less clear. An association between ionising radiation and atherosclerosis has not been established. (Corn et al 1990).

In animal studies, coronary sclerosis has been found in rabbits, rats and pigeons which have been irradiated **and** which have high serum cholesterol. The evidence is that both elements are required (Gold 1961).

In 1958 a human case study reported a myocardial infarction following deep X-ray therapy and since then there have been further reports linking death due to coronary disease following radiotherapy for medical conditions including Hodgkin's disease, breast cancer, and seminoma (Prentice 1965: Stewart et al 1967: Tracy et al 1974: McReynolds et al 1976). In these studies, confounders were present e.g. they did not control for serum cholesterol, blood pressure or cigarette smoking. In addition, the study subjects were already ill. The reports do not prove a causal relation between ionising radiation and ischaemic heart disease.

Further information from long-term follow-up studies of heavily irradiated populations (Host and Loeb 1986) has shown excess mortality from myocardial infarction in these populations. There are also case reports of cerebral infarction following radiotherapy to head and neck and of peripheral vascular disease of the lower limbs following pelvic irradiation. However, these effects have been reported only where the irradiation procedure delivered a very large dose of ionising radiation (20,000-60,000 mSv), and the results cannot be extrapolated to populations exposed to low doses of radiation. Studies involving up to 20 years follow-up of patients irradiated according to more recent radiotherapy procedures, i.e. using much lower doses, have shown no significant difference in myocardial infarction death rate between irradiated and control populations (Hancock et al 1988). A detailed discussion of these studies was presented in a review paper by Kodama (1995).

An American 50-year follow-up study of 30,000 radiologists suggested that in those who started practice between 1920 and 1929 there was an excess of coronary deaths compared with other medical specialists. However, a British 60-year follow-up study of 25,000 radiologists did not confirm this effect, and similarly follow-up studies of 14,500 patients treated with deep X-ray therapy for ankylosing spondylitis over 30-50 years suggested no increase in coronary deaths. Results are therefore inconsistent.

Most follow-up studies have focussed on mortality rates, which are subject to many uncertainties and inaccuracies. A more accurate estimate of the association would come from incidence studies in large populations with lengthy follow-up and controlled risk factors.

The issue of association between ionising radiation and stroke or coronary heart disease in non-medical settings has been addressed periodically in the atomic bomb studies, in particular in the Radiation Exposure Research Foundation Life Span Study (RERF LSS) technical reports. Until the report LSS6, summarising the results for the period 1950-70, there was no suggestion of a relation between atomic bomb radiation exposure and mortality from stroke or coronary disease. That analysis reported an increased mortality from coronary disease in women exposed to 100 mSv or more. The increase was particularly marked where dose exceeded 500 mSv. The trend was not, however, confirmed in the subsequent report, LSS9 for the period 1950 - 1978, although this did show increased mortality from "all diseases other than cancer" where exposure exceeded 2000 mSv.

The report on the period 1950-85 (Shimuzu et al 1992) used a new method of exposure dose estimate and showed clearly increased mortality from circulatory disease - including stroke and cardiac disease again in heavily-exposed survivors.

The issue of accuracy of death certificates for the RERF studies has been examined (Carter et al 1991) and it is apparent that death certification for cardiovascular disease is less accurate than for malignancies. In addition, it is the case in these mortality studies that other known cardiac risk factors cannot be controlled.

Only a few studies have yet been published which look at the **incidence** of coronary heart disease and stroke in relation to ionising radiation exposure associated with the atomic bombs. For the period 1958-1964, Johnson et al (1966) found no association. A later report covering the period 1958-1974 suggested an increase of stroke and coronary disease in females heavily exposed (over 2000 mSv) in Hiroshima. The effect was not seen in men or in Nagasaki survivors.

Kodama's 1994 study, now covering the period up to 1990, again confirmed an increase in myocardial infarction incidence in heavily-exposed survivors regardless of age, gender or location, although the excess of myocardial infarction was very small compared with cancers. (The relative risk of myocardial infarction at 1,000 mSv exposure was 1.17. The associated p value is 0.02 with a confidence interval (95%) of 1.01 - 1.36). Lifestyle risk factors for coronary disease were not adjusted for. At this date, therefore, further studies are needed to determine the matter.

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Glossary

Absorbed dose See **dose.**

Acute radiation syndrome (ARS) The onset, within hours of high **dose** whole body **irradiation,** of nausea and vomiting followed by destruction and diminished (or absent) replacement of essential blood cells resulting in vulnerability to serious infection and bleeding; recovery is possible but with increasing **doses** these effects are more severe and death is more likely.

Alpha particle A particle consisting of two protons plus two neutrons; emitted by a radionuclide.

Background radiation **Ionising radiation** from naturally occurring **radionuclides** both in the environment (from soil, rock and building materials and from space – cosmic radiation) and in the body.

Beta particle An electron emitted by the nucleus of a radionuclide. The electric charge may be positive, in which case the beta particle is called a positron.

Contamination The suspension in air or deposition of **radionuclides** upon, or in, the ground, water and other surfaces, and personnel and equipment

- **External contamination** Of a person or equipment - deposition, general or localised, of **radionuclides** upon all or any of clothing, hair, skin and/or equipment
- **Internal contamination** Of a person - deposition within the body, usually by inspiration, by ingestion or sometimes through penetration of (usually broken) skin by **radionuclides** which will then **irradiate** the cells of surrounding body tissues.

Cosmic rays High-energy ionising radiation from outer space.

Decay The process of spontaneous transformation of a radionuclide; the decrease in the activity of a radioactive substance.

Dose The amount of **ionising radiation** received, as deduced from the energy absorbed from an external radiation source

- **Absorbed dose** Quantity of energy imparted by ionising radiation to unit mass of matter such as tissue. Unit is the gray, symbol Gy. 1Gy = 1 joule per kilogram
- **Equivalent dose** The quantity obtained by multiplying the absorbed dose by a factor to allow for the different effectiveness of the various ionising radiations in causing harm to tissue. Unit is the sievert, symbol Sv
- **Effective dose** The quantity obtained by multiplying the equivalent dose to various tissues and organs by a weighting factor appropriate to each and summing the products. Unit is the sievert, symbol Sv.

Dosemeter A small device worn on the person to measure absorbed energy and from which a record of **Absorbed Dose** may be obtained.

Dosimetry The estimating, recording and maintaining of records of **dose.**

Emitter A **radionuclide** decays by emission of certain radioactive particles and/or electromagnetic radiation. A particular **radionuclide** may be described as an **alpha** or **beta** or **beta/gamma** emitter.

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Fallout The transfer of radionuclides produced by nuclear weapons from the atmosphere to earth; the material transferred.

Fission products The two, invariably radioactive, fragments remaining after an atom has been split (undergone fission).

Gamma ray A discrete quantity of electromagnetic energy without mass or charge, emitted by a radionuclide; similar to an X-ray but with higher energy.

Ionising radiation Radiation that produces ionisation in matter; examples include alpha particles, gamma rays, X-rays and neutrons. When these radiations pass through the tissues of the body, they have sufficient energy to damage the DNA.

Ionisation The process by which a neutral atom or molecule acquires or loses an electric charge; the production of ions.

Monitoring The process of searching for the presence of radiation and then measuring, reporting and recording radiation **dose rates** found within a given area or on a person.

Neutron A nuclear particle (similar to a proton but without electrical change); emitted during fission and fusion by only a few **radionuclides;** long range (kilometres) in air and highly penetrating; an external **hazard** only at detonation; densely **ionising.**

Non-ionising radiation Radiation that does not produce ionisation in matter; examples include ultraviolet radiation, light, infrared radiation and radiofrequency radiation. When these radiations pass through the tissues of the body they do not have sufficient energy to damage the DNA directly.

Radiation weighting factor (RWF) A factor intended to take account of the relative biological effectiveness of different types of radiation according to both their energies and how densely ionising they are.

Radionuclide An unstable nuclide (atomic nucleus) that emits ionising radiation.

X-ray A discrete quantity of electromagnetic energy without mass or charge, emitted by an X-ray machine; similar to a gamma ray but with lower energy.