Special Report: Policy

A review of human carcinogens—Part D: radiation

In June 2009, 20 scientists from nine countries met at the International Agency for Research on Cancer (IARC) to reassess the carcinogenicity of the types of radiation previously classified as "carcinogenic to humans" (Group 1) and to identify additional tumour sites and mechanisms of carcinogenesis (table and panel). These assessments will be published as part D of Volume 100 of the IARC Monographs.[1]

Alpha particles, consisting of two protons and two neutrons, are a densely ionising type of radiation with low capacity to penetrate living tissue (less than 0·1 mm). Beta particles are electrons or positrons that are less ionising, but more penetrating (up to a few milimetres). The health hazards resulting from radionuclides that emit these particles largely occur after internal deposition. Epidemiological evidence shows a number of radionuclides that emit alpha or beta particles increase cancer risks at several anatomical sites (table). The Working Group reaffirmed the carcinogenicity of internally deposited radionuclides that emit alpha or beta particles (Group 1).

After the Chernobyl accident, a sharp increase in the risk of thyroid cancer was found with exposure to radioiodines, particularly iodine-131, during childhood and adolescence.[2,3] This increased risk might be due to higher milk intake per unit of body weight among children; a higher thyroid dose per unit of iodine-131 intake from milk; a higher susceptibility per unit of thyroid dose; or a combination of these.

Radon exposure occurs mainly through contamination of indoor air by radon released from soil and building materials. Combined analyses of case–control studies now estimate that residential exposure to radon gas is the leading cause of lung cancer after tobacco smoke (8–15% attributable risk in Europe and North America).[4,5]

X-rays and gamma-rays are sparsely ionising electromagnetic radiation that penetrate living tissue, typically producing fast electrons that deposit energy, resulting in tissue damage. Extensive study of atomic-bomb survivors shows increased cancer risks at multiple anatomical sites.[6] Current evidence adds to the list of tumours caused by x-rays and gamma-rays (table), and also establishes that in-utero exposure increases the risk of cancer at multiple sites.[7,8] The Working Group reaffirmed the carcinogenicity of x-radiation and gamma-radiation (Group 1).

Neutrons are produced by nuclear reactions and are a main component of cosmic radiation. They are highly penetrating and interact with the traversed tissue, producing protons, other charged particles, and gamma-radiation. Epidemiological evidence is inadequate to assess the carcinogenicity of neutrons, because of co-exposures to other types of radiation. However, the evidence of cancer in experimental animals is sufficient, and mechanistic data show that neutrons transfer their energy in clusters of ionising events—resulting in similar, but more severe, local damage than that induced by x-rays or gamma-rays. On the basis of this evidence, the Working Group reaffirmed the carcinogenicity of neutron radiation (Group 1).

Each type of ionising radiation (panel) transfers energy in the form of highly structured tracks of

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Radiation type	Major study populations	Tumour sites (and types) on which sufficient evidence is based
Alpha-particle and beta-particle emitters		
Radon-222 and decay products	General population (residential exposure), underground miners	Lung
Radium-224 and decay products	Medical patients	Bone
Radium-226, radium-228, and decay products	Radium-dial painters	Bone, paranasal sinus and mastoid process (radium-226 only)
Thorium-232 and decay products	Medical patients	Liver, extrahepatic bile ducts, gall bladder, leukaemia (excluding CLL)
Plutonium	Plutonium-production workers	Lung, liver, bone
Phosphorus-32	Medical patients	Acute leukaemia
Fission products, including strontium-90	General population, following nuclear reactor accident	Solid cancers, leukaemia
Radioiodines, including iodine-131	Children and adolescents, following nuclear reactor accident	Thyroid
X-radiation or gamma-radiation	Atomic-bomb survivors, medical patients; in-utero exposure (offspring of pregnant medical patients and of atomic-bomb survivors)	Salivary gland, oesophagus, stomach, colon, lung, bone, skin (BCC), female breast, urinary bladder, brain and CNS, leukaemia (excluding CLL), thyroid, kidney (atomic-bomb survivors, medical patients); multiple sites (in-utero exposure)
Solar radiation	General population	Skin (BCC, SCC, melanoma)
UV-emitting tanning devices	General population	Skin (melanoma), eye (melanoma, particularly choroid and ciliary body)

CLL=chronic lymphocytic leukaemia. BCC=basal-cell carcinoma. SCC=squamous-cell carcinoma.

Table: **Radiation exposures with sufficient evidence in humans**

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Conflicts of interest
NP works for, and RM is a consultant to, Atomic Energy of Canada Ltd. CM receives funding from the UK Ministry of Defence. JH receives funding from Electricité de France. AG receives funding from L'Oreal Recherche.

Invited Specialists
None

***Panel:* Types of radiation classified in Group 1**

- Ionising radiation
  - Alpha-particle emitters
  - Beta-particle emitters
  - X-rays and gamma-rays
  - Neutron radiation
- Solar radiation
- Ultraviolet radiation (wavelengths 100–400 nm, encompassing UVA, UVB, and UVC)

ionisation and excitation events that can produce a variety of molecular lesions and clustered, complex DNA damage.[9] Subsequent processing of this damage induces many responses (eg, cell killing, chromosomal aberrations, mutations, genomic instability, cell transformation, and bystander effects) that contribute to carcinogenesis. Based on these mechanistic considerations, all types of ionising radiation were classified by the Working Group as "carcinogenic to humans" (Group 1).

Solar radiation is the main source of human exposure to ultraviolet (UV) radiation, which is further subdivided into UVA, UVB, and UVC. The ultraviolet component that reaches the earth's surface comprises around 95% UVA and 5% UVB; UVC is blocked by stratospheric ozone. Epidemiological studies have established a causal association between exposure to solar radiation and all major types of skin cancer (table). The Working Group reaffirmed the carcinogenicity of solar radiation (Group 1).

Exposure to solar radiation causes a specific mutation fingerprint (cytidine to thymidine transition), as a result of cyclobutane pyrimidine dimers in DNA. This pattern had long been attributed to UVB.[10] However, this same cytidine to thymidine transition has been detected in the skin of UVA-treated mice[11] and in the *Tp53* gene of UVA-induced or UVB-induced skin tumours in hairless mice.[10] In humans, this transition has been seen in *TP53* in premalignant solar keratosis and in malignant skin tumours.[12] Based on these mechanistic data, the Working Group classified UV radiation as "carcinogenic to humans" (Group 1).

The use of UV-emitting tanning devices is widespread in many developed countries, especially among young women. A comprehensive meta-analysis concluded that the risk of cutaneous melanoma is increased by 75% when use of tanning devices starts before 30 years of age.[13] Additionally, several case–control studies provide consistent evidence of a positive association between the use of UV-emitting tanning devices and ocular melanoma.[14,15] Therefore, the Working Group raised the classification of the use of UV-emitting tanning devices to Group 1, "carcinogenic to humans".

While reviewing the studies of occupational UV exposure, the Working Group concluded that there is "sufficient evidence" for ocular melanoma in welders.[16,17] However, because welders are also exposed to other harmful agents, this association could not be attributed specifically to UV radiation. A full review of the carcinogenic hazards of welding will be undertaken by IARC with high priority.

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