Journal of Labelled Compounds and Radiopharmaceuticals *J Label Compd Radiopharm* 2007; **50**: 388–391. Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/jlcr.1256



### Short Research Article

## The risks of exposure to internal emitters<sup> $\dagger$ </sup>

### **RICHARD WAKEFORD\***

The Dalton Nuclear Institute, The University of Manchester, Pariser Building-G Floor, PO Box 88, Sackville Street, Manchester M60 1QD, UK

Received 31 August 2006; Revised 7 January 2007; Accepted 10 January 2007

**Abstract:** The risks to health from internally deposited radionuclides have received considerable attention in recent years. There are significant issues concerned with exposure to internal emitters beyond those associated with the risks posed by external sources of penetrating ionizing radiations, and these issues lead to additional uncertainty in risk estimates pertaining to internal emitters. There is, however, no firm evidence that the risks from internally deposited radioactive material have been seriously underestimated by scientific review groups, but the uncertainties associated with the risks of exposure to internal emitters need to be taken into account in radiological protection. Copyright © 2007 John Wiley & Sons, Ltd.

Keywords: internally deposited radionuclides; uncertainty; epidemiology; cancer

### Introduction

It is established beyond reasonable doubt that exposure to ionizing radiation causes deterministic effects when doses are sufficiently high and stochastic effects when doses are moderate or high.<sup>1</sup> These effects are due, respectively, to significant cell killing leading to tissue reactions, and to non-lethal cell modification leading to an increased risk of cancer in the exposed individual and hereditary anomalies in subsequent generations. Radiological protection aims to limit doses such that deterministic effects do not occur and that the risk of stochastic effects that is presumed to exist at low doses is broadly acceptable when compared with risks from other hazards.

The risks of exposure to low levels of radiation are derived from the epidemiological study of appropriate groups of humans and the experimental study of laboratory animals and of tissue and cellular systems.<sup>1</sup> The quantitative estimation of the risk of cancer among exposed individuals is obtained principally from epidemiological studies supported by experimental evidence. No epidemiological study has provided unequivocal

E-mail: richard.wakeford@manchester.ac.uk

Copyright © 2007 John Wiley & Sons, Ltd.

evidence of radiation-induced hereditary effects, so hereditary risk estimates are obtained from experimental evidence suitably generalized to humans.

Cancer risk estimates are determined primarily, but not exclusively (see below), from epidemiological studies of those briefly exposed to external sources of gamma or X rays - individuals who have received external, penetrating, low linear-energy-transfer (LET) radiation exposures at high dose rates. Prominent among these epidemiological studies is the impressive follow-up study of almost 90 000 Japanese survivors of the atomic bombings of Hiroshima and Nagasaki in 1945, and considerable scientific effort has been expended in deriving risk estimates from this study. The evidence from the study of the Japanese atomic bomb survivors is supported by other epidemiological studies, notably the studies of those irradiated for medical reasons, such as ankylosing spondylitis and cervical cancer patients who received radiotherapy.

When radioactive material is taken into the body it distributes among tissues, and is removed in a characteristic time scale, that depends on the chemical nature of the material.<sup>2</sup> For example, when plutonium is inhaled, it resides in the lung for a period determined by the solubility of the chemical form, and when plutonium enters the bloodstream it concentrates preferentially on bone surfaces and in the liver from where it is excreted slowly in urine over a period of decades. Other radionuclides, such as the radioisotopes of caesium, are distributed much more



<sup>\*</sup>Correspondence to: Richard Wakeford, The Dalton Nuclear Institute, The University of Manchester, Pariser Building-G Floor, PO Box 88, Sackville Street, Manchester M60 1QD, UK.

<sup>&</sup>lt;sup>†</sup>Proceedings of the Ninth International Symposium on the Synthesis and Applications of Isotopically Labelled Compounds, Edinburgh, 16–20 July 2006.

homogeneously within the body and are excreted more rapidly. Radionuclides deposited internally pose a challenge to radiological protection that is, in general, greater than that posed by external sources of radiation for a number of reasons. For example, whereas doses from external sources of radiation can usually be measured (say, by a film badge) or reconstructed comparatively easily, the measurement or reconstruction of exposure to internal emitters can be more problematical. Although gamma rays from internal emitters such as radiocaesium can be measured outside the body by suitable monitors (such as whole-body monitors), radionuclides emitting short-range radiations, once inside the body, can only be detected by indirect techniques such as urinalysis. The derivation of, say, a lung dose from the measured concentration of a radionuclide excreted in urine will depend, among other things, on the solubility of the inhaled material, and some degree of uncertainty will inevitably arise from the assumptions that are required to be made. This paper examines some of the issues surrounding the risks associated with exposure to internal emitters.

# Childhood leukaemia 'clusters' and nuclear installations

Although the risks to health posed by internal emitters have been the subject of much research and discussion for a considerable time, public attention was focussed on this issue by the report in a television documentary broadcast in 1983 of a pronounced (around tenfold) excess of childhood leukaemia in the Cumbrian coastal village of Seascale, adjacent to the Sellafield nuclear complex. Suspicion immediately fell upon the seemingly obvious causal candidate - radioactive material discharged into the environment from Sellafield since nuclear operations commenced there in 1950. The childhood leukaemia 'cluster' in Seascale (consisting of less than a dozen cases over around 30 years) was confirmed by an independent inquiry established by the UK Government, but this inquiry also found that radiation doses received by children in Seascale as a result of Sellafield discharges were generally less than the doses received from natural background radiation, and a factor of at least 100 too low to be able to account for the excess cases. This conclusion led some to believe that radiation risk models for internal emitters must be seriously in error, and this belief was reinforced by the discovery of an excess of childhood leukaemia around the Dounreay nuclear establishment in northern Scotland, the only other place in Great Britain where large-scale irradiated nuclear fuel reprocessing takes place.

Despite extensive research into potential ways in which radioactive discharges might have caused the excess cases of childhood leukaemia, no serious candidate has been found,<sup>3</sup> and alternative explanations - in particular, an infective basis for childhood leukaemia that results in a higher risk when unusual population mixing occurs, as it has in Seascale and around Dounreay - now appear more likely. However, nuclear power is an emotive issue, and some individuals with especially strong motivation (e.g. as members of anti-nuclear pressure groups) have stood by their belief that radiation must be involved and that risk models for internal emitters are grossly inaccurate. Unconventional radiobiological mechanisms that result in a greatly enhanced effect of internally deposited radionuclides have been proposed (usually outside the recognized scientific literature), although these are, in general, far removed from the scientific mainstream and are of doubtful validity. Nonetheless, this is not to say that such marginal views are without influence, and when Mr Michael Meacher was Environment Minister he was persuaded that these ideas should be formally examined by a group of individuals drawn from a spectrum of opinion. Thus, in 2001, the UK Government established what came to be called the Committee Examining Radiation Risks of Internal Emitters (CERRIE).<sup>2</sup> Although professional scientists were represented on CERRIE - including three from the then National Radiological Protection Board, me (the only member employed, at that time, in the nuclear industry) and five from universities or other research institutions - it is notable that among the 12 members two, Dr Chris Busby and Mr Richard Bramhall, were representatives of a small, but vocal, campaigning group (the Low Level Radiation Campaign) advocating the serious underestimation of internal emitter risk models. CERRIE reported in October  $2004^2$ ; but Dr Busby and Mr Bramhall withdrew from the production of the report when it became clear that the rest of the Committee would not support their position and that they would not be permitted a substantial proportion of the report to promulgate their views. Despite the marginalization within CERRIE of this particular wing of opinion, Mr Meacher (by then an ex-minister) was quite prepared to write a forward to an 'alternative report' produced by Dr Busby and Mr Bramhall, supporting their position rather than the published CERRIE report that satisfied ten members of the Committee representing various shades of opinion. Mr Meacher wrote an article for a national newspaper critical of the Committee and its Chairman, the strongly independent Professor Dudley Goodhead, and became embroiled in unseemly correspondence in newspaper columns. It is difficult to avoid the

impression that Mr Meacher advocated the establishment of CERRIE to give credence to the fringe views of Dr Busby and Mr Bramhall, and was frustrated by the failure of the Committee to find scientific support for their position.

### The CERRIE report

Despite the acrimony associated with the CERRIE process, the CERRIE report provides a useful summary of what is (and is not) known about the action of internal emitters.<sup>2</sup> As noted above, the presence within tissues of radionuclides that do not emit radiations that penetrate to the exterior of the body must be determined by indirect means, such as urinalysis and a biological model for the behaviour of a radionuclide in the body, leading to uncertainty in the assessed quantities present in tissues. The degree of this uncertainty will depend on the radionuclide and its chemical form. For radionuclides that are short lived or are excreted quickly it may not be possible to determine exposure by bioassay, and retrospective exposure reconstruction is required if doses are to be determined. For example, underground hard rock miners inhale radon and its radioactive decay products, but individual exposure estimates are almost always obtained by the knowledge of work histories and the mine environment (e.g. radon in air concentrations when available). It will be appreciated that under some circumstances the uncertainty associated with the intake of a particular radionuclide in a certain chemical form, and the consequent uncertainty in tissue concentrations, can be relatively large.

The determination of the degree of internal exposure to a particular radionuclide is an important, but basically practical, consideration. More fundamental is the uncertainty associated with the concept of local dose to tissues from internal emitters and its relationship to risk. Much of the concern over the risks associated with internally deposited radioactive material centres on those short-range radiations that are largely irrelevant to radiological protection if prevented from entering the body

- Alpha particles (<sup>4</sup>He<sup>2+</sup>) emitted from radionuclides such as <sup>226</sup>Ra and <sup>239</sup>Pu.
- Low-energy beta particles (e<sup>-</sup>) emitted from radionuclides such as <sup>3</sup>H.
- Auger electrons emitted from radionuclides such as <sup>125</sup>I and <sup>59</sup>Ni.

These radiations define the central difference between external and internal irradiation. The nub of the issue is how energy deposited in cells as tracks of relatively dense ionizations may be compared with the sparsely ionizing tracks produced by penetrating low-LET radiations - what conversion factor should be applied to the absorbed dose to account for the potentially greater radiobiological effectiveness of, to some degree, higher ionization density? Of course, for alpha particles this greater relative biological effectiveness per unit absorbed dose is recognized through the radiation weighting factor  $(w_R)$  of 20 – at low doses, a given absorbed dose of alpha particles is assumed to be 20 times as effective at producing the biological damage relevant to stochastic health effects as the same absorbed dose of gamma rays. This  $w_{\rm R}$  of 20 for alpha particles has been challenged, however, as has the  $w_{\rm R}$ of 1 for low-energy beta particles and Auger electrons. Indeed, persuasive evidence was presented to CERRIE that the relative biological effectiveness of tritium beta particles might be 2-3 when compared to gamma rays.<sup>2</sup>

### Epidemiological studies of internal emitters

Epidemiological studies of suitably exposed groups offer direct estimates of the risk coefficients (risk per unit dose) for internal emitters that incorporate all the radiobiological mechanisms of relevance to the causation of the adverse health effect under consideration. It must be borne in mind, however, that, guite apart from the difficulties that might be encountered in determining the pertinent dose to tissues, epidemiology is predominantly an observational (i.e. non-experimental) science that draws its findings from the uncontrolled conditions of everyday life, which leads to difficulties in reliably interpreting epidemiological associations. Nonetheless, at present epidemiology offers the most appropriate means of assessing the risks arising from exposure to radiation, including that from internal emitters.<sup>4</sup> Epidemiological evidence relating to internal emitters is obtained from a number of sources, which will be briefly considered.

Although a pronounced excess of childhood thyroid cancer has been found in those areas of the former USSR that experienced the heaviest contamination from the Chernobyl nuclear reactor accident in 1986, thyroid doses to many infants and young children were high due to the intake of significant quantities of radioiodine released during the accident. Further, it is known from studies of infants and children exposed to sources of external radiation that the thyroid gland of young children is particularly sensitive to the induction of cancer by radiation. Consequently, the excess of childhood thyroid cancer observed after the Chernobyl accident cannot be taken as indicative of an underestimation of the risk of childhood thyroid cancer from internally deposited radioiodine relative to the risk from external irradiation. Although there are

suggestions of excess risks of other cancers following exposures to radionuclides released from Chernobyl, the evidence is not, as yet, convincing, and risk estimates are unreliable.

A number of epidemiological studies of internal exposure to various alpha particle emitters have been conducted<sup>4</sup>:

- Underground hard rock miners inhale radon gas and its radioactive decay products leading to alpha particle doses, sometimes large, to the bronchial epithelium. A clear excess risk of lung cancer has been established in many miner studies, although there is little evidence for a radon-related excess risk of other cancers.
- Case–control studies of lung cancer and residential exposure to radon daughters have produced risk estimates that are consistent with the miner studies.
- Workers, mainly young women, who applied to instrument dials, and inadvertently ingested, radium-based luminous paint, accumulated internally large quantities of <sup>226</sup>Ra and, as a consequence, experienced large excesses of bone and head tumours.
- German patients who were injected with <sup>224</sup>Ra as radiotherapy subsequently experienced a large excess risk of bone cancers.
- Large excesses of liver cancer and leukaemia were manifested in patients injected with the contrast medium Thorotrast, containing <sup>232</sup>Th.
- Nuclear industry workers have been exposed to a variety of internal emitters, particularly the isotopes of uranium and plutonium. Of some importance are the workers from the Mayak nuclear facility in Russia who inhaled large quantities of plutonium.

These epidemiological studies produce risk estimates that are, in general, consistent with those derived from the studies of external irradiation, once a  $w_{\rm R}$  of 20 for

alpha particles is taken into account. However, the uncertainties associated with exposures to internal emitters, such as the accuracy of the estimates of doses to tissues, must be borne in mind. Other studies of groups exposed to internal emitters are underway or planned, which will provide further evidence on risk coefficients. For example, the monitored exposures to internal emitters of workers in the nuclear weapons and energy industries provide the basis for studies of exposure to tritium and other radionuclides.

#### Conclusions

The uncertainties surrounding the risks posed by internally deposited radioactive material are inevitably greater, to some degree, than those associated with external sources of penetrating radiation. While there is no firm evidence that the risks of exposure to internal emitters have been seriously underestimated, the additional uncertainties associated with such exposures should be taken into account in radiological protection. Further research findings will augment the evidence on the risks of internal exposure to specific radionuclides.

### REFERENCES

- 1. Committee to Assess Health Risks from Exposures to Low Levels of Ionizing Radiation. *Health Risks from Exposure to Low Levels of Ionizing Radiation – BEIR VII Phase 2.* The National Academies Press: Washington, DC, 2006.
- 2. Committee Examining Radiation Risks of Internal Emitters (CERRIE). *Report.* National Radiological Protection Board: Chilton, 2004.
- 3. Committee on Medical Aspects of Radiation in the Environment (COMARE). *Fourth Report*. Department of Health: Wetherby, 1996.
- 4. Wakeford R. Oncogene 2004; 23: 6404.