

Letters to the Editor

Radon and childhood cancer

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Sir

The recent United Kingdom Childhood Cancer Study of exposure to domestic sources of ionising radiation: 1: radon gas (UKCCS Investigators, *British Journal of Cancer* (2002) 86: 1721–1726) found no evidence of increased risk in relation to exposure to domestic sources of radon, but the authors found evidence that their control houses tended to have intrinsic features resulting in higher than average indoor radon concentrations.

As the UKCCS Investigators point out, radiation risk estimates suggest that approximately 14% of the incidence of childhood leukaemia in the UK may be linked to natural background high-LET alpha-radiation (Committee on Medical aspects of Radiation in the Environment, 1996; Simmonds *et al*, 1995). Partitioning the dose to red bone marrow between the principal emitters suggests that 5% of childhood leukaemia may be linked to ²²²Rn, ²²⁰Rn and their short-lived alpha-emitting decay products, and 9% to longer-lived emitters, especially ²¹⁰Po. This suggests that for radon gas concentrations of 20, 100 and 200 Bq m⁻³, the relative risks of childhood leukaemia with respect to zero radon are respectively 1.05, 1.25 and 1.50. These values also define the resolving power of a case–control study to detect this level of risk at a given radon concentration.

Such resolving power has not been available in any previous case–control study, including those cited by the UKCCS Investigators (Stjernfeldt *et al*, 1987; Lubin *et al*, 1998; Kaletsch *et al*, 1999; Steinbuch *et al*, 1999). Even without the biases in the controls identified by the UKCCS Investigators, this was also true of their study as there were too few cases in the high radon exposure category.

However, I suggest that there are at least three other factors which limit the ability to detect a link between radon and childhood cancer in the United Kingdom Childhood Cancer Case–control Study and which pose serious challenges for the design of future studies.

Firstly, we have shown that the level of ²¹⁰Po in children's teeth, a marker for the level in the skeleton, varies considerably between children (Henshaw *et al*, 1994), in particular higher levels are associated with proximity to major sources of vehicle exhaust pollution in the UK (Henshaw *et al*, 1995). Examination of our database suggests that for children living in rural areas, the average activity concentration of ²¹⁰Po in permanent teeth extracted for orthodontic purposes is approximately 7.2 Bq kg⁻¹. Near motorways the average activity concentration is approximately 10.6 Bq kg⁻¹, but the range can extend up to 18 Bq kg⁻¹ and occasionally even high-

er concentrations have been recorded. Using the corresponding bone marrow dose estimates given in Simmonds *et al* (1995), the possible variations in ²¹⁰Po skeletal burden correspond to an equivalent spread in radon exposure of about 90 Bq m⁻³. In the UKCCS, the level of ²¹⁰Po in the skeleton of case and control children is not known, nevertheless there is potential for serious confounding of total bone marrow dose from high-LET emitters, given that the highest radon bin is only 200+ Bq m⁻³.

Secondly, according to Greaves (2002) the initiating step in childhood leukaemia is believed to take place *in utero*. This raises the question of whether radon measurements in the home of childhood cancer cases post diagnosis is the appropriate metric to employ. Kohli *et al* (2000) suggest that assessment of general radon exposure in the neighbourhood surrounding the home may be a better measure of the average exposure of the child, taking account of the time spent away from home, for example at school or play centres. This may also be a more appropriate metric for the exposure of the mother during pregnancy and of the transplacental transfer of radon and its decay products to the fetus. Kohli *et al* (2000) used measurements of radon in the ground to assess overall indoor radon exposure of childhood cancer cases in Sweden. The authors found evidence that children born and continuously living in areas with normal to high levels of radon have a significantly higher risk of childhood malignancy.

Thirdly, a number of studies have indicated an association between either childhood leukaemia or childhood cancer generally and urban air pollution, especially from motor vehicle exhausts (Savitz and Feingold, 1989; Knox and Gilman, 1997; Feychting *et al*, 1998; Harrison *et al*, 1999; Pearson *et al*, 2000). There are also studies suggesting an association between paternal exposure to hydrocarbons and increased leukaemia risk in their offspring (Savitz and Chen, 1990) and of similar exposures to mothers during pregnancy (Shu *et al*, 1999). Thus the effects of urban pollution may also act to confound radon measurement between cases and controls.

It may be that the UKCCS Investigators can address some of these issues in their existing data. However, the possibility may have to be faced that a link between radon and childhood cancer at the level suggested by radiation risk factors, as well as some geographical studies, is undetectable in a case–control design.

The impact of this is to recognise that while radon is not a major factor for childhood leukaemia or childhood cancer generally in the UK, it may be so in countries with much higher indoor radon levels, notably in Scandinavia. Also, it must be noted that the absence of an association in the UK study does not equate to the absence of an effect.

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The role of aspirin in carcinogenesis

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Sir

We read with interest the excellent paper by Akhmedkhanov *et al* (2002) regarding aspirin use and the incidence of lung cancer. We would like to offer another possible anti-cancer property of aspirin, namely, the inhibition of phenolsulphotransferase (PST) activity.

PSTs are found throughout the body, but the bowel, liver and platelets are known to contain particularly high activities of this enzyme. PSTs are cytosolic and exist in two forms: (i) P-PST, which selectively sulphates micromolar concentrations of phenols; and (ii) M-PST, which is similarly selective for aromatic amines.

The main function of this sulphation is to scavenge low concentrations of endogenous and exogenous toxins from the body, but

the lability of the phenolic sulphate-ester bond means it is liable to cause the formation of electrophilic free radicals. These react chemically with DNA which may cause mutations leading to neoplasia (Coughtrie, 1996).

Food cooking can result in a wide variety of mutagenic compounds, including polyaromatic hydrocarbons and heterocyclic amines, especially if the food becomes charred when grilled or barbecued. Certainly, several polyaromatic hydrocarbons have been shown to be activated by hydroxylation to phenols followed by sulphation via P-PST to the final mutagenic form (Grover, 1986). P-PST has also been found to be responsible for the activation of heterocyclic amines by N-sulphation, for example, the bladder carcinogen 2-naphthylamine (Hernandez *et al*, 1991) and a wide variety of carcinogenic N-hydroxy arylamines (Chou *et al*, 1995).

Thus, inhibition of P-PST would block one route of activation for both main groups of carcinogen found in food. Indeed, Rao

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