British Journal of Cancer (2002) 87, 1336 – 1338

www.bjcancer.com

Letters to the Editor

Radon and childhood cancer

DL Henshaw*[1]

[1]HH Wills Physics Laboratory, University of Bristol, Tyndall Avenue, Bristol BS8 1TL, UK

British Journal of Cancer (2002) **87,** 1336 – 1337. doi:10.1038/sj.bjc.6600671 www.bjcancer.com

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 ^{222}Rn, ^{220}Rn and their short-lived alpha-emitting decay products, and 9% to longer-lived emitters, especially ^{210}Po. 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 ^{210}Po 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 ^{210}Po 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 higher concentrations have been recorded. Using the corresponding bone marrow dose estimates given in Simmonds *et al* (1995), the possible variations in ^{210}Po skeletal burden correspond to an equivalent spread in radon exposure of about 90 Bq m^{-3}. In the UKCCS, the level of ^{210}Po 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.

*Correspondence: DL Henshaw; E-mail: d.l.henshaw@bris.ac.uk

REFERENCES

Committee on Medical Aspects of Radiation in the Environment (1996) The incidence of cancer and leukaemia in young people in the vicinity of the Sellafield site, West Cumbria: further studies and an update of the situation since the publication of the report of the Black Advisory Group in 1984 COMARE 4th Report, London: HMSO

Feychting M, Svensson D, Ahlbom A (1988) Exposure to motor vehicle exhaust and childhood cancer. *Scand J Work Environ Health* **24:** 8 – 11

Greaves M (2002) Clinical Review: Science, medicine and the future – Childhood leukaemia. *Br Med J* **324:** 283 – 287

Harrison RM, Leung PL, Sommervaille L, Smith R, Gilman E (1999) Analysis of incidence of childhood cancer in the West Midlands of the United Kingdom in relation to proximity to main roads and petrol stations. *Occup Environ Med* **56:** 774 – 780

Henshaw DL, Allen JE, Keitch PA, Randle PH (1994) The spatial distribution of naturally occurring ^{210}Po and ^{226}Ra in children's teeth. *Int J Radiat Biol* **66:** 815 – 826

Henshaw DL, Keitch PA, James PR (1995) Lead-210, polonium-210 and vehicle exhaust pollution. *Lancet* ***245:*** 324 – 325

Kaletsch U, Kaatsch P, Meinert R, Schüz J, Czarwinski R, Michaelis J (1999) Childhood cancer and residential radon exposure – results of a population-based case-control study in Lower Saxony (Germany). *Radiat Environ Biophys* **38:** 211 – 215

Knox EG, Gilman EA (1997) Hazard proximities of childhood cancers in Great Britain from 1953 – 80. *J Epidemiol Community Health* **51:** 151 – 159

Kohli S, Brage HN, Löfman O (2000) Childhood leukaemia in areas with different radon levels: a spatial and temporal analysis using GIS. *J. Epidemiol. Community Health* **54:** 822 – 826

Lubin JH, Linet MS, Boice Jr JD, Buckley J, Conrath SM, Hatch EE, Kleinerman RA, Tarone RE, Wacholder S, Robison LL (1998) Case-control study of childhood acute lymphoblastic leukaemia and residential radon exposure. *J Nat Cancer Inst* **90:** 294 – 300

Pearson RL, Wachtel H, Ebi KL (2000) Distance-weighted traffic density in proximity to a home is a risk factor for leukaemia and other childhood cancers. *J Air Waste Manag Assoc* **50:** 175 – 180

Savitz DA, Chen J (1990) Parental occupation and childhood cancer: review of epidemiologic studies. *Environ Health Perspectives* **88:** 325 – 337

Savitz DA, Feingold L (1989) Association of childhood cancer with residential traffic density. *Scand J Work Environ Health* **15:** 360 – 363

Shu XO, Stewart P, Wen W, Han D, Potter JD, Buckley JD, Heineman E, Robison LL (1999) Parental occupational exposure to hydrocarbons and risk of acute lymphocytic leukaemia in offspring. *Cancer Epidemiol Biomarkers Prev* **8:** 783 – 791

Simmonds JR, Robinson CA, Phipps AW, Muirhead CR, Fry FA (1995) *Risks of Leukaemia and other cancers in Seascale from all sources of ionising radiation exposure.* Didcot: HMSO

Stjernfeldt M, Samuelsson L, Ludvigsson J (1987) Radiation in dwellings and cancer in children. *Paediatr Haematol Oncol* **4:** 55 – 61

Steinbuch M, Weinberg CR, Buckley JD, Robison LL, Sadler DP (1999) Indoor residential radon exposure and risk of childhood acute myeloid leukaemia. *Br J Cancer* **81:** 900 – 906

UKCCS Investigators (2002) The United Kingdom Childhood Cancer Study of exposure to domestic sources of ionising radiation: 1: radon gas. *Br J Cancer* **86:** 1721 – 1726

The role of aspirin in carcinogenesis

GJ Caine*[,1,2], ST Kehoe[2] and GYH Lip[1]

[1]University Department of Medicine, City Hospital, Birmingham B18 7QH, UK; [2]Department of Gynaecological Oncology, Birmingham Women's Hospital, Birmingham B15 2TG, UK

British Journal of Cancer (2002) **87,** 1337 – 1338. doi:10.1038/sj.bjc.6600670 www.bjcancer.com

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 barbequed. 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-napthylamine (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

*Correspondence: GJ Caine; University Department of Medicine, City Hospital, Birmingham B18 7QH, UK; E-mail: grahamcaine@hotmail.com