Learning difficulties in children born to male UK nuclear industry employees; analysis from the nuclear industry family study

A Burt, N Maconochie, P Doyle, E Roman

There has been much debate about paternal pre-conceptual exposure to low level ionising radiation and possible increased risk of ill health among the children subsequently conceived. The prevalence of reported learning difficulties was examined in over 16 000 children born to UK nuclear industry workers, using fathers’ information on exposure from the workers’ individual employment and dosimetry records. There was no evidence that paternal exposure to low level ionising radiation at work influences the prevalence of learning difficulties in otherwise healthy children conceived after exposure.

The majority of the work in the area of paternal occupational exposure to ionising radiation has looked at possible links with childhood cancer. Recently fetal mortality, congenital malformations, and cancer in the children of UK nuclear industry employees exposed to chronic low dose ionising radiation before conception have been analysed as part of the nuclear industry family study. No evidence of an effect was found for offspring of male nuclear industry employees. The possibility of increased minor neurological damage in the offspring of males exposed to ionising radiation which may be manifest in conditions such as learning difficulties still, however, remains.

Studies of surviving children exposed in utero to the atomic bombing of Hiroshima and Nagasaki have shown an increased incidence of neurological abnormalities including mental retardation, small head size, seizures, and poor performance on conventional tests of intelligence and in school. In addition, cranial radiation therapy for brain tumours and acute lymphatic leukaemia in children has shown association with long term intellectual effects. It is estimated that between 30% and 50% of cases of learning disability may be genetic in origin and it has been suggested that small chromosomal rearrangements may be behind idiopathic learning disability. It is biologically plausible that low dose ionising radiation could cause germ line mutations, including chromosomal rearrangements. To our knowledge, however, no studies have been conducted which have specifically investigated the association between learning difficulties and chronic pre-conceptual exposure to low dose ionising radiation. The aim of this study is to examine the relation between paternal exposure to chronic low level pre-conceptual ionising radiation at work and learning difficulties requiring special educational provision in otherwise healthy children.

“Learning difficulties” is a broad term used for different conditions that affect the normal learning ability of individuals. The causes of many specific learning disorders are unknown, but it is likely that more than one mechanism is responsible. In addition to genetic factors, factors implicated in the predisposition to learning disorders include low birth weight, preterm delivery, maternal alcoholism and smoking, cerebral palsy, inadequate development of brain lateralisation, early protracted poor nutrition, and thyroid disorders. The number of people in England with severe and profound learning difficulties is currently estimated to be approximately 210 000, a prevalence of 0.44%, with an estimated 1.2 million having some form of mild to moderate learning difficulty, a prevalence of around 2.5%.

METHODS
Detailed information about the study is reported elsewhere. Briefly, the nuclear industry family study is an occupational cohort study of the reproductive health and the health of the children of nuclear industry workers in the UK. The study population consisted of the employees of establishments operated by the three nuclear authorities, the UK Atomic Energy Authority (UKAEA), Atomic Weapons Establishment (AWE), and British Nuclear Fuels Limited (BNFL) at a total of 15 different sites around Great Britain. All current employees of these three authorities, and past employees of UKAEA and BNFL less than 75 years of age whose details were recorded on the pensions database, were surveyed between 1993 and 1996. For each employee the employer provided individual employment and radiation monitoring data (including annual radiation dose). Employees were surveyed by postal questionnaire which requested details of all live born children, including sex, date and place of birth, birth weight, whether the child was born with, or had since developed any medical problem, and whether the child had any learning difficulty requiring special educational provision. The data from the employer were linked to data collected from each individual employee using a unique personal identifier.

The nuclear industry has a predominantly male employment population, and for this reason the analysis for this study has been limited to the children of male employees only. After undelivered post was excluded, the response rate was 83% among male employees. Reporting of illness in children by the parents proved very accurate, as shown by reporting of cancer in the children where 97% were clinically validated.

Main messages

- There was no evidence that paternal exposure to low level ionising radiation at work influences the prevalence of learning difficulties in otherwise healthy children conceived after exposure.

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Our interest in this paper is in mild to moderate learning difficulties. We thus restricted the analysis to specified learning difficulties in children who were otherwise healthy—that is, they did not have any reported medical or genetic conditions which may be associated with learning difficulties (for example, cerebral palsy or Down’s syndrome).

Table 1 lists the ICD10 codes used to classify cases of learning difficulties, and the conditions which were used to exclude individuals. The analysis was restricted to specified learning difficulties (for example, cerebral palsy or Down’s syndrome).

All statistical analyses were performed using Stata software. All p values quoted are two sided, with values less than 0.05 taken to indicate statistical significance. The unit of analysis was the child. The effect of pre-conceptual exposure to ionising radiation on the risk of outcome (learning difficulties) was estimated by odds ratios (OR) with 95% confidence intervals (CI) using random effects logistic regression which allowed for the fact that many of the workers had more than one child in the study. The reliability of the numerical approximations used to obtain the parameter estimates was checked using different quadrature. Likelihood ratio tests were then used to ascertain statistical significance of the parameters.

All employees designated potentially at risk of exposure to external ionising radiation are required to wear personal dosimeters (film badges or thermoluminescent devices) to record the amount of exposure, and for regulatory and managerial purposes nuclear establishments maintain records of all such monitoring. The main exposure of interest in this analysis was paternal pre-conceptual monitoring for low dose ionising radiation, taking the baseline as the group whose father had not been monitored before their estimated date of conception.

RESULTS
A total of 16 918 children reported by male employees were aged between 5 and 24 years at survey (or death). Of these,

<table>
<thead>
<tr>
<th>Table 1</th>
<th>List of ICD10 codes used to classify cases learning difficulties in the cohort and conditions which excluded individuals from the analysis</th>
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</thead>
<tbody>
<tr>
<td>ICD10 codes used to classify cases of learning difficulties</td>
<td>Specific developmental disorders of speech and language, specific speech articulation disorder, expressive language disorder, and developmental disorder of speech and language unspecified</td>
</tr>
<tr>
<td>F80, F80.0, F80.1, F80.9</td>
<td>Specific developmental disorders of scholastic skills, specific reading disorder, specific spelling disorder, specific disorder of arithmetical skills, mixed disorder of scholastic skills, other developmental disorders of scholastic skills, and developmental disorder of scholastic skills, unspecified</td>
</tr>
<tr>
<td>F81, F81.0, F81.1, F81.2, F81.3, F81.8, F81.9</td>
<td>Specific developmental disorder of motor function and mixed specific developmental disorders</td>
</tr>
<tr>
<td>F82, F83</td>
<td>Dyslexia and other symbolic dysfunctions, not elsewhere classified and dyslexia and alexia</td>
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<td>R48, R48.0</td>
<td>Mental retardation</td>
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<tr>
<td>E70</td>
<td>Brain tumour, if diagnosed under the age of 16 (astrocytoma, benign brain tumours, etc.) and accidental brain damage</td>
</tr>
<tr>
<td>F64, F07.3, F90, F90.9, F99</td>
<td>Phenyketonuria</td>
</tr>
<tr>
<td>Q00-G03, A87, A39.9, A86.0, G04.8, G04.9</td>
<td>Meningitis, meningococcal infection, unspecified viral encephalitis and encephalitis</td>
</tr>
<tr>
<td>G40, G41</td>
<td>Epilepsy</td>
</tr>
<tr>
<td>G80, G81.1, G93.7</td>
<td>Cerebral palsy and possibly spastic diplegia, facioid hemiplegia, Reye’s syndrome</td>
</tr>
<tr>
<td>H54</td>
<td>Blindness</td>
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<tr>
<td>H90, H91 H66.9, H70, H71, H72, H74, H93, Q16.1</td>
<td>Deafness and hearing disorders, including glue ear (chronic otitis media) and congenital malformation of ear affecting hearing</td>
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<tr>
<td>P10, P11.1, P11.2, Q04, Q06.2, Q06.9, Q07.0, Q07.8</td>
<td>Brain haemorrhage, brain damage (perinatal) and congenital malformations affecting the brain and nervous system</td>
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<tr>
<td>P21, P22.5</td>
<td>Birth asphyxia and anoxia</td>
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<tr>
<td>Q02, Q03, Q05, Q75.3, Q87.0, Q87.1, Q90-Q99</td>
<td>Microcephaly, hydrocephaly, spina bifida, macrocephaly, Pierre-Robin syndrome, Prader-Willi syndrome, chromosomal syndromes (e.g. Turner, Down’s, Klinefelter’s)</td>
</tr>
</tbody>
</table>

Our interest in this paper is in mild to moderate learning difficulties. We thus restricted the analysis to specified learning difficulties in children who were otherwise healthy—that is, they did not have any reported medical or genetic conditions which may be associated with learning difficulties (for example, cerebral palsy or Down’s syndrome).

Table 2 lists the ICD10 codes used to classify cases of learning difficulties, and the conditions which were used to exclude individuals. The analysis was restricted to specified learning difficulties (for example, cerebral palsy or Down’s syndrome).

All statistical analyses were performed using Stata software. All p values quoted are two sided, with values less than 0.05 taken to indicate statistical significance. The unit of analysis was the child. The effect of pre-conceptual exposure to ionising radiation on the risk of outcome (learning difficulties) was estimated by odds ratios (OR) with 95% confidence intervals (CI) using random effects logistic regression which allowed for the fact that many of the workers had more than one child in the study. The reliability of the numerical approximations used to obtain the parameter estimates was checked using different quadrature. Likelihood ratio tests were then used to ascertain statistical significance of the parameters.

All employees designated potentially at risk of exposure to external ionising radiation are required to wear personal dosimeters (film badges or thermoluminescent devices) to record the amount of exposure, and for regulatory and managerial purposes nuclear establishments maintain records of all such monitoring. The main exposure of interest in this analysis was paternal pre-conceptual monitoring for low dose ionising radiation, taking the baseline as the group whose father had not been monitored before their estimated date of conception.
339 children were excluded (table 1). Table 2 presents the characteristics of the 16579 children included in the analysis. The proportion of children whose father was monitored for exposure to ionising radiation before the child’s conception was 43%. Mean age at survey (or death) was 16.0 (SD 5.6) years for children of non-monitored workers and 13.4 (SD 5.7) years for children of monitored workers.

In total, 335 children were reported to have learning difficulties, a prevalence of 2.02%. Table 3 presents crude and adjusted ORs for learning difficulties. Among the children of male workers, there was a small increase in the crude odds of learning difficulties in children of monitored employees (crude OR 1.38, 95% CI 1.05 to 1.80), based on 164 exposed cases. However, after adjusting for the confounding effects of sex of child, age of child at survey, birth weight of child, pregnancy order, and paternal age at conception, plus for interaction between age of child at survey and pregnancy order.

### DISCUSSION AND CONCLUSIONS

This study found no evidence of an association between paternal pre-conceptual exposure to low level ionising radiation and increased risk of mild to moderate learning difficulties in otherwise healthy children. Overall, the prevalence of learning difficulties observed in this cohort of 5–24 year olds (2.0%) was similar to the current estimated prevalence of mild to moderate learning difficulties in the general population of England (2.5%) and the slighter lower prevalence being most likely due to the fact that this was a retrospective cohort (median date of birth 1971) and diagnosis of mild to moderate learning difficulties has improved over time.

The nuclear industry study is the largest survey ever undertaken of children born to radiation workers. With over 16 500 children in the analysis, the power to detect an association, should it exist, was high. The response rate was very high, and any hypotheses at the time of survey likely to be known to the workers related to childhood leukaemia. Known confounding factors have been adjusted for either in the analysis or through restriction. It is thus unlikely that bias or confounding could explain the finding. Thus our conclusion is that these data do not support the hypothesis that exposure of men to low level ionising radiation at work has any influence on the risk of mild to moderate learning difficulties among otherwise healthy children conceived after exposure.

### ACKNOWLEDGEMENTS

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