SHORT REPORT

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

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Occup Environ Med 2004;**61**:786–789. doi: 10.1136/oem.2004.012906

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.^{1–4} Recently fetal death, 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.^{4–5} 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.^{6–8} In addition, cranial radiation therapy for brain tumours and acute lymphatic leukaemia in children has shown association with long term intellectual effects.⁹

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.¹⁰ 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.^{11–12} 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%.¹³

METHODS

Detailed information about the study is reported elsewhere.¹⁴ 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.⁴

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.

Table 1 List of ICD10 codes used to classify cases learning difficulties in the cohort and conditions which excluded individuals from the analysis**ICD10 codes used to classify cases of learning difficulties**

F80, F80.0, F80.1, F80.9	Specific developmental disorders of speech and language, specific speech articulation disorder, expressive language disorder, and developmental disorder of speech and language unspecified
F81, F81.0, F81.1, F81.2, F81.3, F81.8, F81.9	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
F82, F83	Specific developmental disorder of motor function and mixed specific developmental disorders
R48, R48.0	Dyslexia and other symbolic dysfunctions, not elsewhere classified and dyslexia and alexia

ICD10 codes for conditions which excluded individuals from the analysis

F70–F79, F99, F89.0–89.9	Mental retardation
C71, C72.8, C72.9 D33, S09, V89 E70	Brain tumour, if diagnosed under the age of 16 (astrocytoma, benign brain tumours, etc.) and accidental brain damage
F84, F07.3, F90, F90.9, F99	Behavioural disorders, including autism and hyperkinetic disorders
G00–G03, A87, A39.9, A86.0, G04.8, G04.9	Meningitis, meningococcal infection, unspecified viral encephalitis and encephalitis
G40, G41	Epilepsy
G80, G81.1, G93.7	Cerebral palsy and possibly spastic diplegia, flaccid hemiplegia, Reye's syndrome
H54	Blindness
H90, H91 H65, H66.9, H70, H71, H72, H74, H93, Q16.1	Deafness and hearing disorders, including glue ear (chronic otitis media) and congenital malformation of ear affecting hearing
P10, P11.1, P11.2, Q04, Q06.2, Q06.9, Q07.0, Q07.8	Brain haemorrhage, brain damage (perinatal) and congenital malformations affecting the brain and nervous system
P21, P02.5	Birth asphyxia and anoxia
Q02, Q03, Q05, Q75.3, Q87.0, Q87.1, Q90–Q99	Microcephaly, hydrocephaly, spina bifida, macrocephaly, Pierre-Robin syndrome, Prader-Willi syndrome, chromosomal syndromes (e.g. Turner, Down's, Klinefelter's)

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 difficulty, and the conditions which were used to exclude individuals.¹⁵ The analysis was restricted to children aged between 5 and 24 years at survey (up to, but not including their 25th birthday), and included those who had died at 5 years or more. This allowed all children in the analysis the chance to be diagnosed with learning difficulties, which are frequently identified once the child has reached school age.

All statistical analyses were performed using Stata software.¹⁶ 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.¹⁷ The reliability of the numerical approximations used to obtain the parameter estimates was checked using different numbers of cut points for the 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 2 Characteristics of live born children of male employees over 5 years and under 25 years at survey for analysis of learning difficulties

	n	(%)
Total children	16579	(100)
Sex of child		
Male	8509	(51)
Female	8053	(49)
Unknown	17	(0.1)
Year of birth		
Before 1975	4795	(29)
1975–84	8369	(50)
1985–96	3415	(21)
Age of child at survey (years)		
5–9	4119	(25)
10–14	4339	(26)
15–19	3941	(24)
20–24	4180	(25)
Industrial status of parent (proxy measure of social class)		
Non-industrial	10117	(61)
Industrial	6037	(36)
Unknown	425	(3)
Most recent authority of parental employment at time of survey		
Atomic Weapons Establishment	2676	(16)
UK Atomic Energy Authority	5158	(31)
British Nuclear Fuels Limited	8745	(52)
Parent ever employed before estimated date of conception		
No	7040	(42)
Yes	9539	(58)
Parent ever monitored before estimated date of conception		
No	9472	(57)
Yes	7107	(43)
Type of monitoring		
Monitored, external only	4155	(25)
Monitored, external and internal	2952	(19)
Monitored external lifetime cumulative whole body dose before estimated date of conception (mSv)		
0.00–	1500	(9)
2.50–	1551	(9)
10.00–	2347	(14)
≥50.00	1477	(9)
Uncertain	232	(1)

Table 3 Learning difficulties in children of male employees classified by parental history of employment and monitoring for potential exposure to ionising radiation

	Number of cases (prevalence %)	Crude OR (95% CI)	Adjusted OR* (95% CI)
Parent ever employed by the nuclear industry before estimated date of conception			
No	118 (1.68)	1.00	1.00
Yes	217 (2.27)	1.45 (1.10 to 1.90)	1.19 (0.85 to 1.68)
Parent ever monitored before estimated date of conception			
No	171 (1.81)	1.00	1.00
Yes	164 (2.31)	1.38 (1.05 to 1.80)	1.09 (0.79 to 1.50)
Type of monitoring			
Monitored, external only	94 (2.26)	1.34 (0.99 to 1.83)	1.05 (0.72 to 1.52)
Monitored, external and internal	70 (2.37)	1.43 (1.01 to 2.02)	1.15 (0.76 to 1.73)
Monitored external lifetime cumulative whole body dose before estimated date of conception (mSv)†			
0.00–	43 (2.87)	1.72 (1.14 to 2.59)	1.37 (0.84 to 2.24)
2.50–	32 (2.06)	1.18 (0.75 to 1.85)	0.94 (0.55 to 1.61)
10.00–	57 (2.43)	1.46 (1.01 to 2.10)	1.14 (0.73 to 1.76)
≥50.00	31 (2.10)	1.29 (0.81 to 2.05)	1.02 (0.50 to 1.74)

*Adjusted for 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.

†The monitored external lifetime cumulative whole body dose before estimated date of conception has a total number of 163 case children as one child's father had uncertain lifetime cumulative whole body dose prior to their 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, no significant effect of pre-conceptual monitoring was seen on risk of learning difficulties in these children (adjusted OR 1.09, 95% CI 0.79 to 1.50), and there was no evidence of a relation between risk of learning difficulties and pre-conceptual radiation dose (p value for trend with cumulative lifetime external parental dose before conception = 0.58). Furthermore, there was no evidence that the pattern of ORs varied with history of pre-conceptual parental employment in the nuclear industry in general. There was a slight increase in learning difficulties in children whose fathers had been additionally monitored for exposure to internal sources of radiation (radionuclides), but this difference was not statistically significant (adjusted OR 1.15, 95% CI 0.76 to 1.73).

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%)¹² (the slightly lower prevalence being most likely due to the fact that this was a retrospective cohort (median date of birth 1971)^{4,5} 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

We thank members of the study team at LSHTM, in particular Graham Davies, Patrick Sampson, Juliet Jain, and Tuyet Ngyen; our Scientific Steering Group; all members of the industry who helped us, and the study participants themselves. The study was funded by the Department of Health and the Health and Safety Executive.

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Accepted 31 January 2004

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