

Organic solvents and presenile dementia: a case referent study using death certificates

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ABSTRACT Occupational exposure to organic solvents has been implicated in the development of "presenile dementia" in several studies. The death certificates of all men aged under 65 dying in England and Wales bearing presenile dementia as cause of death were collected for the years 1970-9 (n = 557): control death certificates were obtained, matched for age and sex. No significant differences were found between the groups as regards estimated occupational exposure to either organic solvents or lead.

Several epidemiological studies, conducted for the most part in Scandinavia, have examined the relation between the occupational exposure to solvents of certain trades and the frequency with which individuals receive disability pensions for neuropsychiatric disorders. Some studies have suggested that the relative risk of receiving such pensions is increased in workers exposed to solvents by a factor of between 2 and 3.¹⁻³ Others have failed to detect similar increases in solvent workers except for some categories of neurosis.⁴

Reports of groups of individuals attending occupational clinics have suggested that solvent workers in general, and house painters in particular, develop a characteristic syndrome which, with severe disturbances of memory, cognition, and behaviour, is said to be a dementing illness.^{5,6} A recent case referent study of men receiving diagnoses of dementia failed to find a statistically significant excess of solvent exposed workers compared with matched controls.⁷

After an attempt to perform a case control study of Alzheimer's disease (which failed to recruit satisfactory numbers of subjects) (T D Browne *et al*, Medichem Conference, Ludwigshaven, 1986) we have examined the relation between the death certificate diagnosis of "presenile dementia" and the occupation for all men dying with this disease between 1970 and 1979 inclusive.

Method

Copies of death certificates bearing presenile demen-

tia or "Alzheimer's disease" as a cause of death were obtained for all men dying in England and Wales for the years 1970 to 1979 inclusive. In addition those dying from dementia before the age of 65 were included since, by definition, they had presenile dementia. For each case an age matched (± 2 years) male control was drawn at random. There were 557 cases during this ten year period.

The death certificates record, in addition to general demographic data, the individual's most recent full time paid employment as reported to the Registrar at the time the death was registered.

Occupations of both subjects and controls were graded into one of three categories according to probable occupational exposure to organic solvents and to lead. These categories were "no exposure," "possible exposure," and "probable exposure" (see appendix 1).

This analysis of occupations was carried out by one of us (HAW) and, independently, by an occupational hygienist. Both were "blind" as to the cause of death on the death certificate. The exposure category was agreed before final allocation. We were particularly interested to see whether painters and decorators were more frequently represented among the cases than the controls since it is this group which has attracted most attention of late. As painters and decorators are likely to have, or to have had, exposure also to lead, which was formerly a common constituent of paints, we have also extended our inquiry to see whether or not there is any suggestion that lead may be associated with presenile dementia. The occupations were categorised with respect to lead exposure in the same way as for solvent exposure (see appendix 2).

Results

A total of 557 pairs of death certificates was analysed. Thirty cases had possible exposure to solvents and 13 had probable exposure; the corresponding figures for the controls were 22 and 17 respectively (table 1). Among the group as a whole were 12 painters and decorators (six cases and six controls).

The number of cases and controls with probable or possible exposure to lead is shown in table 2 from which it may be seen that there were virtually no differences.

The relative risk (calculated using a matched pairs method) of dying from presenile dementia according to exposure to solvents or to lead is shown in table 3; there is no indication that exposure to either increases the risk of dying from presenile dementia.

In table 3 the relative risks are also shown after

Table 1 Occupational exposure to solvents

No	Case	Control
0	514	518
1	30	22
2	13	17
Total	557	557

0 = Occupation entails no exposure to solvents.

1 = Occupation entails possible exposure to solvents.

2 = Occupation entails probable exposure to solvents.

Table 2 Occupational exposure to lead

No	Case	Control
0	539	547
1	5	8
2	13	12
Total	557	557

0 = Occupation entails no exposure to lead.

1 = Occupation entails possible exposure to lead.

2 = Occupation entails probable exposure to lead.

Table 3 Relative risks of presenile dementia with respect to exposure to solvents or lead. (Figures in parentheses are relative risks obtained after removal of subjects with specific defined diagnoses on the death certificate other than Alzheimer's disease)

	\hat{R}	<i>p</i>
Probable solvent exposure	0.76	NS
Possible solvent exposure	1.53 (1.42)	NS NS
Total	1.14 (1.11)	NS NS
Probable lead exposure	1.08 (1.00)	NS
Possible lead exposure	0.63	NS
Total	0.90 (0.86)	NS NS

exclusion of those subjects in whom a specific defined pathological process, other than Alzheimer's disease, was indicated on the death certificate; these included Jacob-Creutzfeld disease, Pick's disease, and Korsakoff's psychosis. Removing these subjects had no effect at all on the relative risks.

Discussion

In this study we have been unable to show a significant difference between men receiving a death certificate diagnosis of presenile dementia and age matched controls with regard to their estimated occupational exposure either to solvents or to lead. A similar result was obtained when those with firm specific pathological diagnoses were excluded from the study.

The major criticism of the use of death certificates in epidemiological research is that the diagnoses recorded are imprecise. Several studies have compared certificated "indications of cause of death" with necropsy results and shown considerable discrepancies between them (for example⁸⁻¹⁰). Whereas there are several causes for this^{11 12} the only one which might systematically distort the frequency with which "dementia" is recorded is when an unrelated process or unrecognised complication is proposed as an immediate cause of death and the chronic condition is completely omitted from the certificate.

A second difficulty arises in occupational epidemiology when death certificate diagnoses are related to the recorded occupation. In the United Kingdom the guidance for the registrar limits the recorded occupation to "the latest full time gainful employment followed by the deceased" with an indication if the individual was retired. As the Joint Report of the Royal Colleges of Physicians and Pathologists noted, this often fails to specify the type of industry concerned and even more seriously may completely ignore the main lifetime occupation.¹³ There is, however, no reason to suppose that such information is inaccurately recorded in a systematic way in either of the two groups under consideration: indeed as Swanson and her colleagues showed the occupation given on the death certificate is certainly more accurate than that recorded in clinical records (if compared with that from interviews with relatives) and is correct in up to 80% of those dying under the age of 65.¹⁴

In clinical practice the phrase presenile dementia has been used in three confusingly interrelated ways and these are presumably represented in the certificates' "causes of death."

Classically the term refers to cases of Alzheimer's disease, a primary degenerative condition of the brain commonly presenting between the ages of 40 and

60¹⁵: this shares histopathological features with "presenile dementia of the Alzheimer's type" and may be identical with it.

The difficulty of correctly diagnosing this condition has been recognised. Follow up studies from several London centres concluded that a number of "misdiagnoses" could be shown even after vigorous investigation¹⁶⁻¹⁸: this has been confirmed by Neary and his colleagues in their recent studies of diagnostic brain biopsy.¹⁹ The major socioeconomic consequences of cognitive impairment (especially in men) in the age group under 65 ensure that detailed investigation is recognised as obligatory. Presenile dementia as an outcome to such assessment means "probable Alzheimer's disease."

Finally, the most frequent use is to describe any dementing illness occurring before the age of 65—for example, one certificate in the present study reported "presenile dementia: Pick's disease."

The current form of the death certificate does not allow the clinical review that is necessary to distinguish these three uses let alone to validate the diagnoses themselves: no attempt was made to do so beyond the second analysis of the data being performed after the exclusion of those cases and their controls where defined pathologies or firm aetiologies were recorded.

The prevalence of dementia in the "presenium" is not known with any precision. The figure of 0.1% of the population aged between 45 and 64 as being afflicted by Alzheimer's disease quoted by Whalley *et al*²⁰ is certainly higher than is to be expected from clinical practice and is perhaps the result of local environmental factors²¹ (although they specifically exclude lead as one of those factors). Our figures suggest that 0.02% of male deaths occurring in England and Wales are associated with presenile dementia: this compares favourably with that obtained by Chandra *et al* in their identically designed study of Alzheimer's disease.²²

The failure to show an excess of solvent exposed workers in those dying with a diagnosis of dementia compared with age matched controls contrasts with several epidemiological studies of the pension statistics in several countries¹⁻³ but not with two of the recent case referent studies of Alzheimer's disease^{23 24} where, similarly, no significant association could be shown. A prediction from such studies is that solvent workers would present more commonly with cognitive and neuropsychological impairment in death certificates.

Certainly in the United Kingdom there is no widespread awareness either in the medical profession or among workers exposed to solvents of the postulated link between organic solvents and neuropsychological disability and hence a source of bias probably oper-

ating in Scandinavian studies may be discounted.

Given the rarity of presenile dementia and our failure to show an excess of solvent workers among those dying with dementia, two conclusions are possible which only further research can confirm or deny. The first is that organic solvents, if they exert any aetiological effect, do so either in a few individuals genetically susceptible or operate with other environmental agents in so subtle a manner as to be swamped by them. The alternative is that occupational exposure to organic solvents has no aetiological role at all in the development of dementia. On the whole, we tend towards the latter view.

Appendix 1

OCCUPATIONS WITH PROBABLE EXPOSURE TO SOLVENTS

Builder and decorator
Builders/decorators manager
Cabinet maker
Foreman coachpainter
French polisher
Journeyman (cabinet makers)
Master painter/decorator
Motor fitter
Paint sprayer
Paint tester
Painter and decorator
Screener (silk)
Signwriter and decorator
Signwriter/painter
Watchmaker

OCCUPATIONS WITH POSSIBLE EXPOSURE TO SOLVENTS

Aero engine inspector
Aircraft fitter
Art teacher
Boiler stoker
Boot and shoe repairer
Boot and shoe operator
Builder
Builders manager
Cabinet maker
Carpenter
Carpenter and joiner
Communications engineer
Die polisher
Foreman finisher
Garage proprietor
Gear cutter
Handyman
Jeweller
Machine operator—rubber company

Machine shop labourer
 Master builder
 Master printer
 Metal polisher
 Motor mechanic
 Petrol pump attendant
 Petrol station manager
 Photocopier
 Plastics engineer
 Printer
 Printing compositor
 Process worker—plastics
 Proprietor boot/shoe company
 Rubber research operator
 Rubber worker
 School workshop technician
 Sheet metal worker
 Stenciller
 Stereotyper
 Vehicle mechanic
 Warehouseman

Appendix 2

OCCUPATIONS WITH PROBABLE EXPOSURE TO LEAD

Battery attendant
 Battery worker
 Master plumber
 Plumber
 Plumber and engineer
 Plumbers mate
 Scrapmetal merchant
 Painter and decorator

OCCUPATIONS WITH POSSIBLE EXPOSURE TO LEAD

Car factory worker
 Engineers fitter
 Garage proprietor
 Machinist
 Master printer
 Motor car engine fitter
 Petrol pump attendant
 Petrol station manager
 Precision engineer
 Printer
 Printers compositor

We are grateful to the Office of Population Censuses and Surveys for providing us with the death certificates. The study was supported by a grant from the European Chemical Industry Ecology and Toxicology Centre and the Paintmakers Association of Great Britain to whom we are very grateful.

References

- 1 Axelson O, Hane M, Hogstedt C. A case-referent study of neuropsychiatric disorders among workers exposed to solvents. *Scand J Work Environ Health* 1976;2:14-20.
- 2 Mikkelsen S. A cohort study of disability pension and death among painters with special regard to disabling pre-senile dementia as an occupational disease. *Scand J Soc Med* 1980;16 suppl 16:34-43.
- 3 Olsen J, Sabroe S. A case referent study of neuropsychiatric disorders among workers exposed to solvents in the Danish wood industry. *Scand J Soc Med* 1980;16:suppl 16:44-9.
- 4 Lindstrom K, Riihimaki H, Hanninen K. Occupational solvent exposure and neuropsychiatric disorders. *Scand J Work Environ Health* 1984;10:321-3.
- 5 Arlien-Soborg P, Bruhn P, Gyldensted C, Melgaard B. Chronic painters syndrome: chronic toxic encephalopathy in house painters. *Acta Neurol Scand* 1979;60:149-56.
- 6 Bruhn P, Arlien-Soborg P, Gyldensted C, Christensen EL. Prognosis in chronic toxic encephalopathy: a two year follow-up study in 26 painters with occupational encephalopathy. *Acta Neurol Scand* 1981;64:259-72.
- 7 Rasmussen H. Risk of encephalopathia among retired solvent workers. *J Occup Med* 1985;27:561-74.
- 8 Britton M. Diagnostic errors discovered at autopsy. *Acta Med Scand* 1974;196:203-10.
- 9 Medical Services Study Group of the Royal College of Psychiatrists. Death certification and epidemiological research. *Br Med J* 1978;ii:1063-5.
- 10 Waldron HA, Vickerstaff L. *Intimations of quality*. London: Nuffield Provincial Hospitals Trust, 1977.
- 11 Aldersen MR, Baylis RIS, Clarke CA, Whitfield AGW. Death certification. *Br Med J* 1983;287:444-5.
- 12 Cochrane AL, Moore F. Death certification from the epidemiological point of view. *Lancet* 1981;ii:742-3.
- 13 Joint Report of the Royal College of Physicians and the Royal College of Pathologists. Medical aspects of death certification. *J R Coll Physicians London* 1982;16:206-18.
- 14 Swanson GM, Schwarz AG, Burrows RW. An assessment of occupation and industry data from death certificates and hospital medical records for population-based cancer surveillance. *Am J Public Health* 1984;74:464-7.
- 15 Lishman WA. *Organic psychiatry*. Oxford: Blackwell, 1978.
- 16 Marsden CD, Harrison MJG. Outcome of investigation of patients with pre-senile dementia. *Br Med J* 1972;ii:249-52.
- 17 Nott PN, Fleminger JJ. Presenile dementia: the difficulties of early diagnoses. *Acta Psychiatr Scand* 1975;51:210-7.
- 18 Ron MA, Toone BK, Garralda ME, Lishman WA. Diagnostic accuracy in presenile dementia. *Br J Psychiatr* 1979;134:161-8.
- 19 Neary D, Snowden JS, Mann DM, et al. Alzheimer's disease: a correlative study. *J Neurol Neurosurg Psychiatry* 1986;49:229-37.
- 20 Whalley LJ, Caruthers AD, Collyer S, De May R, Frankievicz A. A study of familial factors in Alzheimer's disease. *Br J Psychiatry* 1982;140:249-56.
- 21 Whalley LJ, Holloway S. Non-random geographical distribution of Alzheimer's presenile dementia in Edinburgh. *Lancet* 1985;i:578.
- 22 Chandra V, Bharucha NE, Schoenberg BS. Conditions associated with Alzheimer's disease at death. *Neurology* 1986;36:209-11.
- 23 French RL, Schuman LM, Mortimer JA, Hutton JT, Boatman RA, Christians B. A case controlled study of dementia of the Alzheimer type. *Am J Epidemiol* 1985;121:414-21.
- 24 Arnaducci LA, Fratiglioni L, Rocca WA, et al. Risk factors for clinically diagnosed Alzheimer's disease. *Neurology* 1986;36:922-31.