Organic brain damage and occupational solvent exposure

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Abstract

309 cases of organic dementia, cerebral atrophy or psycho-organic syndrome, admitted for 5 days or more to one of 18 Quebec hospitals, were individually matched to a psychiatric referent, admitted with some other diagnosis, and a general hospital referent. Lifetime occupational history was obtained by telephone. Occupational solvent exposure was assessed by (i) individual ratings blind to case status and (ii) a job-exposure matrix. Subjects working with moderate or high solvent concentrations for at least 10 years were considered exposed. With the psychiatric referent series an odds ratio of 1.44 (90% CI 1.03-2.01) was calculated for individual exposure ratings and 1.41 (90% CI 0.89-2.23) for the job matrix. The increased risk was found largely in those with diagnoses of both organic dementia or cerebral atrophy and an alcohol related condition. A similar pattern of risk was found with the general hospital referents. Adjustment for possible confounders did not appreciably alter the risk estimates.

Résumé

Trois-cent-neuf cas de démence organique, d'atrophie cerébrale et de syndrome psycho-organique, admis pour cinq jours ou plus à un de dix-huit hôpitaux quebécois, ont été appariés individuellement à un témoin psychiatrique admis pour un autre diagnostic, et à un témoin hospitalier général. On a obtenu l'histoire professionnelle complète par télephone. L'exposition professionnelle aux solvants a été évaluée par (i) des estimations individuelles, effectuées sans connaître le statut des cas, et par (ii) une matrice emploi-exposition. Les sujets travaillant à des concentrations moyennes ou élevées de solvants pour au moins 10 ans étaient considérés comme exposés. Avec la série de témoins psychiatriques, un rapport de cotes de 1,44 (I.C. à 90% = 1,03-2,01) a été calculé au moyen des estimations individuelles, et de 1,41 (I.C. à 90% = 0,89-2,23) au moyen de la matrice emploi-exposition. Le risque accru était surtout présent chez les sujets avec un diagnostic de démence organique ou d'atrophie cérébrale accompagné d'une condition reliée à l'alcool. Un pattern de risque similaire a été trouvé avec la série de témoins hospitaliers généraux. L'ajustement pour des variables de confusion potentielles ('potential confounders') n'a pas modifié de façon appréciable les estimations de risque.

Preface The work reported here forms part of a project, comprising two overlapping studies, funded by the Institut de recherche en Santé et Sécurité du Travail du Québec: principal investigators Dr NM Cherry and Dr JC McDonald. The two studies funded were carried out in parallel; one, not reported here, provided thesis material for France Labrèche who was awarded the PhD in 1989. The methods used in the studies were essentially identical. A questionnaire was developed by the team and piloted by Dr Labrèche. Individual exposure ratings for jobs in both studies, and reliability assessments of these ratings, were also carried out by Dr Labrèche. The study reported here was designed to investigate the nature of neuropsychiatric disability that might result from occupational exposure to organic solvents; the answer to this question is an original contribution to knowledge in this area.

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State of knowledge

In Denmark, Finland, Norway and Sweden a chronic organic psycho-syndrome, characterized by changes in personality, intellect and motivation, has been associated with long term exposure to organic solvents and is compensated as an occupational disease (World Health Organization, 1985). In other western countries, while concern may be expressed about adverse health effects from occupational exposure to these chemicals (National Institute for Occupational Safety and Health, 1987) the existence of a specific disease entity has been questioned (Grasso et al., 1984).

Part of the difficulty in resolving these views arises from the diverse nature of the syndromes that have been associated with solvent exposure, ranging from mild, reversible, mood changes to irreversible dementias (Cranmer and Goldberg, 1986). Further, the quality of the evidence has been very variable, including clinical descriptions of patients compensated in Nordic countries and cross-sectional studies of currently employed workers as well as planned epidemiological studies of psychiatric disability. For a very few substances, outbreaks of neurological disorders in exposed populations have been followed by confirmatory toxicological studies in experimentally exposed animals. In general, however, the nature of the exposure believed to cause organic changes has been poorly documented. Solvents used in oil based paints have been of particular concern in the Nordic countries (Cohr, 1983) but it is assumed that the lipophilic properties of all commercially useful organic solvents may put workers at risk of neurophysiological change. The mechanism by which solvents might cause a psycho-organic syndrome is also little understood but it is assumed that the syndrome results from repeated exposure over many years rather than a brief exposure initiating events that result in disability in later years.

Diagnostic criteria for a solvent induced psycho-organic syndrome differ amongst the Nordic countries, and reflect some of these uncertainties. The criteria from Sweden are specified in terms most clearly open to epidemiological investigation: the physician must be satisfied that the worker has (a) long and/or intensive exposure to organic solvents (usually more than 10 years) (b) relevant symptoms of fatiguability, bad memory, difficulties in concentration, and loss of initiative, (c) pathological findings on an objective measure, such as tests of psychological function (d) a relation in time between exposure and the development of signs and (e) no other obvious cause of disease (World Health Organization, 1985).

In Sweden, as in other Nordic countries, the diagnosis is essentially one of exclusion and subsequent follow-up may reveal causes other than solvent exposure to account for early signs of organic damage. Juntunen et al. (1982) re-assessed 80 Finnish patients previously diagnosed as suffering from a solvent induced psycho-syndrome. At this second examination 3-9 years after diagnosis, 16 of these 80 patients were judged to be suffering from a disease with a neurological component that would, if evident at the initial assessment, have excluded the diagnosis of a solvent induced syndrome. Similarly, Orbaek and Lindgren (1987), in a follow-up of 62 Swedish patients, 2-8 years after diagnosis of a solvent induced 'chronic toxic encephalopathy', found 12 to have some other disease that might have contributed to brain dysfunction.

An important difficulty in assessing whether or not a patient has a solvent related psycho-organic syndrome is thus the absence of signs and symptoms that distinguish it, at the time of presentation, from other organic syndromes such as early pre-senile or alcoholic dementias. It has been suggested (Crammer and Goldberg, 1986) that, unlike other chronic

dementias, signs and symptoms associated with solvent exposure do not progress once exposure ceases. The evidence for this is not clear cut. In three follow-up studies of patients (Bruhn et al. 1981; Juntunen et al. 1982 and Orbaek and Lindgren 1987) subjective symptoms improved after diagnosis and removal from exposure but clinical signs, psychometric test scores and degree of cerebral atrophy have either been unchanged or, in Juntunen's study, mildly deteriorated. These case series do not provide evidence of clinical or intellectual status prior to exposure, however, and the condition may have been one that had existed for many years.

Evidence such as this from patients assessed for occupational disease can, at best, be useful in discussing prognosis and tertiary prevention. Information about a causal relation between solvent exposure and a psycho-organic syndrome must be sought from other sources.

The suspicion that occupational solvent exposure might lead to central nervous system impairment was raised by a number of earlier reports about clusters of neuropsychiatric symptoms amongst workers exposed to carbon disulphide (CS_2) (Braceland, 1942). A systematic study of the effects of CS_2 was begun in Finland in 1963 and a final report published 8 years later (Hanninen, 1971). This used psychological tests to assess trends in intellectual and motor performance in workers exposed to CS_2 without known poisoning. On 20 of 26 parameters examined the exposed group did worse than the controls (non-exposed workers from the same factory) significantly so (with no allowance for multiple comparisons) on 11. On 15 parameters the value for the exposed lay between those of the control group and those of a group of men diagnosed to have acute or chronic CS_2 poisoning. The conclusion from this study was that latent poisoning was probably much more common than had been hitherto believed.

This study has a number of the deficiencies of the many investigations that followed; there is no evidence that the intellectual capacity of the control group was equal to those exposed before encountering CS_2, no "wash out" was introduced to enable a distinction to be made between acute effects and long term disablement and multiple statistics were computed without thought for statistical inference. However the long history of case reports of neuropsychiatric effects of CS_2 poisoning (the earliest in 1856), together with histological evidence of neuronal degeneration in the brain of dogs exposed experimentally to CS_2 (Lewey et al. 1941) has led to the acceptance by Grasso et al. (1984) Spencer and Schaumburg, (1985) and the National Institute for Occupational Safety and Health (1987), of CS_2 as a cause of chronic neurologic disorder even amongst those sceptical of a psycho-organic syndrome more generally associated with solvent exposures.

Other organic solvents that are reported to have central nervous system effects in man include trichloroethylene and toluene. Grandjean et al. (1955) reported that 17 of 55 workers exposed to trichloroethylene had a slight or moderate psycho-organic syndrome, in 9 of whom no alternative aetiological factor could be found. Cranial neuropathies have been also reported from both industrial exposure to trichloroethylene and its use as an inhaled analgesic and anesthetic (Cavanagh, 1983). Toluene, as a substance of abuse, has been associated with irreversible brain dysfunction with cerebellar ataxia (King, 1982) and cerebral atrophy (Lazar et al., 1983), confirmed at autopsy (Esobar and Aruffo, 1980). No comparable deficit is seen, however, in workers exposed to toluene (Elofsson et al., 1980; Cherry et al., 1985).

Damage to the peripheral nervous system has been demonstrated with occupational exposure to both n-hexane (Herskowitz et al., 1971), and methyl n-butyl ketone (Mendell et al., 1974)

and has been shown in animal work to result from a common metabolite of the two substances (Spencer et al., 1980).

In summary, it is widely accepted that occupational exposure to carbon disulphide and addictive abuse (but not occupational exposure) to toluene may cause a psycho-organic syndrome and that trichloroethylene, n-hexane, and methyl n-butyl ketone are neurotoxic, at least to the peripheral nervous system. Cross-sectional studies of workers currently exposed to other solvents (or mixtures of solvents) have failed to provide evidence of central nervous system impairment that cannot reasonably be attributed to acute effects of recent exposure or explained by inadequacies in the study design. The very considerable number of such suggestive but inconclusive studies contribute little or no evidence to questions of cause and effect.

More serious consideration must be given to planned epidemiological studies that have investigated the relation between psychiatric morbidity or mortality and solvent exposure. The earliest of these was reported some 15 years ago (Axelson et al., 1976) and considered cases of early retirement for neuropsychiatric diseases, alcoholism or cerebral atrophy amongst members of a pension fund register, in whom the pension was awarded between 1969 and 1973. Thus diagnosis was made after the possibility of a solvent related psycho-organic syndrome had been recognised (at least in Finland, where 486 cases were diagnosed between 1964 and 1979 (Juntunen et al. 1982)) but, it is argued (Axelson, 1983), before any widespread suspicion of such a disease in Sweden. Later studies, particularly those from the Nordic countries, may have been subjected to diagnostic bias or, in those where contact is made with the subject, biased reporting of exposure.

A total of ten studies of this question appear to have been published and reports from at least two others (included in this review) submitted for publication. Of these, eight have a case-referent design, two are cohort studies, and two are studies of prevalence. The results of these studies are summarised in Table 1. Details of the design and analysis of each study are given below.

In the study reported by Axelson et al. (1976), cases and referents were selected from a pension register held by the Swedish social security system for the region of Orebro. Only male subjects who were skilled workers in defined jobs in the construction industry were included, and age limits were set at 35-64 years. A subject was considered to be a case if, by this age, he had received a disability pension for certain mental disorders (excluding primary debility, schizophrenia and manic depressive psychosis) for cerebral atrophy or for alcoholism (as a primary or secondary diagnosis). Referents were selected from those on the pension register who were completely free of any kind of mental disorder or brain injury. Exposure to solvents was defined as painting, varnishing or carpet laying. Amongst the exposed about half had been working in such jobs for at least 30 years. It was found that 23% of cases (35/151) and 14% of referents (35/248) had been employed in one of the exposed jobs, giving a crude odds ratio of 1.8. Risk ratios were calculated to examine the effects of duration of exposure. Using the non-exposed as the standard, the odds ratio was 1.3 for those exposed for less than 30 years but 2.1 for those with longer exposure. The authors concluded that it was likely that exposure to solvents played an aetiological role in neuropsychiatric disorder.

A subsequent analysis of these data (Axelson, 1983) considered the crude odds ratio associated with different diagnostic groups. A ratio of 2.5 was computed for senile and pre-senile

dementia, 2.0 for nervositas and 1.8 for alcoholism. A ratio of 1.1 was associated with neuresthesia.

A Finish study (Lindström et al., 1984) attempted to duplicate this early investigation as closely as possible, using male construction workers granted a disability pension in 1978-80. Men aged 30-64 years were included in this study. Identical diagnostic categories were used with, however, alcoholism accounting for 50% of the diagnosis in the Finnish study compared with only 26% in the earlier Swedish one. Nervositas (ICD-8; category 790 excluding 790.19) accounted for 19% of the Swedish group but only 1% of the Finnish one. Exposure to solvents was defined as working as a painter or a carpet layer. Unlike the earlier study, cases and referents were matched on age and time of pension.

It was found that 36/374 cases had been exposed, compared with 23/374 of the referents. The odds ratio computed for matched pairs was 1.6, with 90% confidence interval of 1.0 to 2.5 suggesting, on a one tailed test, a probability of less than 1 in 20 that the excess observed was due to chance alone. No information was given on the length of exposure; however a cut point of 16 years was reported (without detail) as showing no dose-response relationship.

Details are, however, given of the odds ratio associated with different diagnostic groups. In this study the highest quoted rate is for neurosis, an odds ratio of 5.5 compared with one of only 1.1 in the Axelson study. Conversely the ratio for alcoholism (1.8 in the Swedish study) was only 1.1. All other neuropsychiatric diagnoses were grouped together, with a ratio of 1.5, thus providing no information on the relation of dementia to solvent exposure.

Two further case-referent studies were carried out in Denmark. The earlier study was reported by Olsen and Sabroe (1980) and considered members of the carpenter and cabinet makers trade union who received a disability pension in the period from 1971-75; a period later than that of Axelson et al., (1976) but before the results of that study were published. Cases were taken as those with disability or early (60-66 years) old age pension suffering from psychosis, neurosis, change of character, oligophrenia, mental retardation or diseases of the nervous system (including cerebral atrophy) or sense organs. Referents were pensioners matched on type of pension and age. One hundred forty-one of 171 disability pensioners and 146 of their referents were traced. In addition, of the 35 cases who had received early old age pensions, 28 were traced as were 27 of their referents.

This study differed from both previously described in that occupational exposure was obtained not only from job title but also from a questionnaire completed by the subject himself (if still alive). It appears that all members of the union were exposed to solvents and the odds ratio calculated was between those with high exposure (an estimate of at least 4,000 hours exposure working either indoors or outside) and the rest of the study subjects. An odds ratio (corrected for age, alcohol intake and previous head injuries) of 2.12 (95% CI 1.20 - 3.75) was computed for this higher exposed group when compared to the less exposed group; this rose to 2.80 when only indoor work for 4,000 hours was considered as exposure. When job title (skilled cabinet maker) was used rather than self report of exposure to define high exposure, an odds ratio of 1.34 was obtained, with a confidence interval of 0.82 - 2.19.

Odds ratios by diagnosis were presented only for those with dementia (ICD-8, category 290) and non-psychotic conditions. The odds ratios, with exposure for more than 4,000 hours, were

2.00 (95% CI 1.11 - 7.07) for dementia and 3.11 (CI 1.31 - 7.35) for non-psychotic conditions. The authors conclude that chronic neurological effect may result from exposure to organic solvents.

A second case-referent study from Denmark (Rasmussen et al., 1985) was carried out amongst men under 81 years applying for social support (nursing home accommodation). Cases were 229 men diagnosed during the assessment of their application for support as having dementia or other kinds of encephalopathy. The referents were those undergoing the same assessment but diagnosed with other conditions such as ischemic heart disease or chronic bronchitis. Referents were closely matched to cases on age. Cases or referents in whom the disease was apparent by the age of 50 were excluded, leaving 207 cases and 210 control subjects.

Information on longest held occupation, certain specific solvent exposed occupations and alcohol consumption was obtained by questionnaire with the subject or a family member. Job exposure was coded from job title, using a previously published job matrix which classified jobs as involving solvent exposure always, often, sometimes, or never. An odds ratio of 1.5 (95% CI 0.7 - 3.5) was found for those employed for at least five years in one or more of the pre-specified solvent exposed jobs. Those whose longest held job was classified as always or often solvent exposed had an odds ratio of 2.0 (95% CI 0.9 - 4.5) for senile dementia. The authors conclude that the findings are, to some degree, supportive of the hypothesis that exposure to organic solvents increases the risk of chronic encephalopathy.

The remaining case-referent studies were conducted outside the Nordic countries. O'Flynn et al. (1987) attempted a case-referent study of pre-senile dementia using death certificates

of all men in England and Wales dying under the age of 65 from 1970-79. Cases comprised 557 deaths with a diagnosis of senile or pre-senile dementia or "Alzheimer's disease". An age matched referent was drawn at random from subsequent death certificates. The most recent full time employment recorded on the death certificate was coded, blind to cause of death, by possible exposure to organic solvents. Forty-three cases and 39 referents were judged to have possible or probable exposure to solvents, with only 13 cases and 17 referents having probable exposure.

Shalat et al. (1988) in the USA also used Alzheimer patients as cases. The series consisted of all male patients with dementia of the Alzheimer type (except those with recorded excessive alcohol consumption) diagnosed in the 10 year period from July 1975 at a single Veterans hospital in Massachusetts. Five male referents per case were selected from the voters list. Occupational information was obtained by questionnaire and from the Massachusetts town books for those born after 1914. A panel of three hygienists coded the job titles according to probability of solvent exposure. It is unclear how many cases were originally selected or the success rate of locating referents but the reported analysis appears to be based on 98 cases and 162 matched referents. An odds ratio of 1.0 was computed, using logistic regression to control for years of education, when exposure was defined as "ever employed" in an occupation classified as solvent exposed on a previously developed exposure matrix. When the exposure criterion was tightened to include only those exposed for 10 years or more, the odds ratio fell to 0.8. Thus this study, somewhat incompletely reported, provided no evidence that organic solvents were a risk factor for dementia of the Alzheimer type in which alcohol was not reported as a contributing factor.

The remaining two case-referent studies have not yet been published. van Vliet et al. (submitted), have carried out a case-referent study in the Netherlands. Cases and referents were selected from members of the two workers organizations to which painters and construction workers belonged. Cases were members who had received disability benefits for mental disorders during the two year period from July 1984. Five hundred and five such cases were identified. Referents were chosen by stratified random sampling of members; 1,000 were drawn from those still in employment at the time of the subject selection. Subjects without a telephone were excluded from the study; referents who did not respond were replaced. The final sample of cooperative subjects consisted of only 252 cases (50% of those selected) and 822 referents who returned a questionnaire containing detailed information on job exposures. Various odds ratios were calculated. The crude odds ratio for solvent exposure (ever in a job identified as exposed) was 1.01 (95% CI 0.76 - 1.34). Only amongst those with a diagnosis of neurotic disorder did the odds ratio reach apparent significance (OR = 1.93, 95% CI 1.13 - 1.30). With adjustment for age, education level, marital status, smoking, alcohol consumption and quetelet index the ratio increased to 1.17 (95% CI 0.83 - 1.61). Amongst those with a diagnosis of neurotic disorder the adjusted odds ratio was 2.30 (95% CI 1.19 - 4.08). More detailed analyses by exposure indices derived from the questionnaire suggested that painters who reported higher exposure had a higher risk; however, given the relatively recent date of this study, information bias cannot be excluded.

The final case referent study, by Brackbill and Maizlish (submitted), is based on US social security administrative records. Subjects were defined as males receiving benefits from 1969 to 1976 (excluding 1974) who were aged at least 35 years and who had been employed in blue collar jobs (painting

or bricklaying) prior to disability. The cases had diagnoses of pre-senile dementia, alcoholic dementia or alcoholism, affective psychoses, neuroses, personality disorder or cerebral atrophy. Referents were eligible subjects with diagnoses other than psychiatric or nervous system disease. Exposure in this study was defined as employment as a painter prior to application for disability. The computed odds ratio for cases was 1.42 (95% CI 1.04 - 1.94). The highest odds ratio, 2.41, was for affective psychosis (95% CI 0.80 - 7.21). The authors concluded that their findings were consistent with the results of European (ie. Nordic) studies.

Mikkelsen (1980) reported the first cohort study of solvent exposed workers. A cohort of 2601 painters and 1790 bricklayers from the Copenhagen area, born before 1941, was identified retrospectively and followed for five years from January 1971. The incidence of disability pensioning was compared for the two groups, the painters being solvent exposed. Pension diagnosis was reclassified (without blinding to exposure), diagnoses containing "dementia", "cerebral atrophy" or a close equivalent were labelled as "pre-senile dementia". This group was then sub-divided by whether or not a possible cause (e.g. alcoholism) for the dementia was indicated.

The overall risk of disability pension for painters compared with bricklayers was 1.4 (95% CI 1.1 - 1.9). The risk was increased for diagnoses (before reclassification as described above) of psychoses (relative risk 2.1, 95% CI 1.1 - 4.2) and neuroses (relative risk 2.8, 95% CI 1.0 - 7.3). After reclassification a relative risk of 3.4 (95% CI 1.6 - 7.4) was found for pre-senile dementia without cause indication and 2.4 (95% CI 1.2 - 4.7) for pre-senile dementia with indication of probable cause; for all diagnoses not re-classified as dementia, the relative risk was 1.0. Thus the author

concludes that the painters had an increased risk, compared with bricklayers, for disability pension due to pre-senile dementia. Unfortunately the lack of blindness in the reclassification of diagnoses puts in question this part of the analysis. However it appears that the original diagnoses showed an increased risk in each of the broad neuropsychiatric diagnostic categories given.

A recent cohort study (Guberan et al., 1989) investigated Swiss painters and electricians; 1916 painters and 1948 electricians living in Geneva at the time of the 1970 census were followed up to 1984. Twenty pensions were awarded to painters for neuropsychiatric diseases and 10 to electricians. The age standardised incidence per 1000 man years was calculated, giving a risk of 1.8 to painters relative to electricians. This did not reach statistical significance. Among the 20 painters, alcohol was recorded as a major contributing factor in 12; among the electricians only 1 of the 10 cases of neuropsychiatric disability was recorded as having an alcoholic contribution. The painters had a significant excess of mortality from alcoholism and an excess of mortality from liver cirrhosis. The authors concluded that there was inadequate evidence to support a solvent related painters syndrome.

Finally, two prevalence studies have been reported. In the first (Cherry and Waldron, 1984) data from a study of morbidity and general practice in Britain in 1970-71 were used to examine whether the prevalence of minor psychiatric illness was higher than expected amongst those workers possibly exposed to organic solvents. Four hundred and eighty-seven women and 1974 men in the population at risk were in jobs (printers, painters, dry cleaners) designated by the authors as solvent exposed. There was no evidence of greater than expected consultations for mental disorder.

Mikkelsen et al. (1988) drew samples from cohorts of Copenhagen painters and bricklayers, born before 1941, who held membership of their trade union in January 1971; subjects who had been included in Mikkelsen's previous cohort study (Mikkelsen, 1980) were excluded. The 94 painters and 99 bricklayers agreeing to take part were assessed by a psychologist who used clinical judgement and agreed guidelines to determine whether the subject showed signs of mild, moderate or severe dementia. From a logistic regression analysis the authors concluded that painters with a medium or high self-reported solvent exposure had odds of dementia approximately 3.6 and 5.0 times as high as bricklayers of similar age and verbal intelligence. The lack of objective measure of either exposure or effect seems to put this study at particularly high risk of bias, however.

The results of the 12 studies summarised in Table 1 show an overall risk ranging from 1.0 (Shalat et al; van Vliet et al) to 2.1 (Olsen and Sabroe). Three of the case referent studies have overall odds ratios reaching a 95% level of significance and Mikkelsen's studies also provide support for this relationship between solvent exposure and psychiatric disability. The studies with the lowest estimated risk have either low power (O'Flynn et al.) or unacceptable response rates (Shalat et al.; van Vliet et al.); Shalat et al. further chose a case series (Alzheimer's disease without indication of alcohol excess) that may have selectively excluded cases of greatest interest. However, reviewing the 12 studies overall, it seems reasonable to conclude that there is a mild but consistent elevation in risk of neuropsychologic disease associated with occupational exposure to organic solvents.

The extent to which such a relation is causal is more difficult to assess. Hogstedt and Axelson (1986) have discussed some of the factors that might affect the

comparability of information between cases and referents and the possible role of confounding factors, particularly alcohol consumption. The Nordic countries have in common political systems that would tend to be sympathetic to providing social support for disabled workers and in these countries both physicians and workers' organisations are aware of the possible role of solvents in neuropsychiatric disease. Under such circumstances both diagnostic and information bias might arise. Physicians may be more ready to make a diagnosis of neuropsychiatric disability in patients known to have worked with solvents than in patients with other work histories; they may also be less willing to use labels, such as alcoholic dementia, that would decrease the chance of compensation. Similarly patients may be tempted to report higher levels of solvent exposure and to minimize reports of alcohol consumption. Such biases would be expected to increase the apparent relationship between solvent exposure and neuropsychiatric disability in countries in which compensation may be available.

A strong relationship between duration of exposure and response would strengthen the case for a causal relationship but this has been demonstrated only in the original study by Axelson et al. (1976). Olsen, Sabroe, van Vliet and Mikkelsen (1988) have produced some evidence that increased intensity of exposure, as reported by self-completed questionnaire, was associated with increased risk.

The diagnostic entity of greatest interest is unclear. Neuroses or other non psychotic diagnoses were associated with the greatest risk in the studies of Olsen and Sabroe, Lindstrom et al., van Vliet et al. and in Mikkelsen's 1980 study before diagnoses were re-classified. In the remaining studies psychotic illness was associated with the greater risk, with senile or pre-senile dementia having the highest

odds ratio in the study by Axelson et al., and in Mikkelsen's 1980 study after re-classification. Guberan's recent cohort study appears to show alcoholism or alcoholic dementia to be closely related to solvent exposure.

In summary, there is good evidence that a small number of solvents or their metabolites can cause damage to the peripheral nervous system and sufficient epidemiological and clinic data to suggest that carbon disulphide and toluene have properties that are capable of causing central nervous system damage. From the 10 case referent and cohort studies reviewed there is reasonable evidence to accept, with caution, a mildly increased risk of neuropsychiatric illness in workers exposed over many years to various solvents, a risk that may increase with longer duration and intensity of exposure. The type of neuropsychiatric disease associated with solvent exposure remains uncertain but there is at least some evidence that disabling organic dementia may result from prolonged exposure. Finally, insufficient attention may have been given to the part played by confounders, particularly alcohol consumption, the ingestion of a substance, itself an organic solvent, well documented (Ron, 1983) as causing a psycho-organic syndrome very similar to that postulated to result from occupational solvent exposure.

Background to the present study

The investigation reported here was set up as part of a larger study, designed to answer two questions. The first of these was whether men admitted to hospital because of psychiatric illness were more likely to have been exposed to organic solvents than comparable referents. This question was addressed by a case-referent study (Study A) of patients first admitted to either of two Montreal psychiatric hospitals during a four year period from 1981-1985. The study reported here (Study B) was designed to address a further question, on

the nature of the disease resulting from exposure, an issue addressed only as a supplementary analysis, with inadequate numbers, in previously reported studies.

Studies A and B were carried out by a single research team using methods of data collection and analysis that were essentially identical. Study A, which provided material for a PhD thesis for one of the team (Labrèche, 1989) was given priority in data collection but initial results from the two studies were obtained simultaneously (Cherry et al 1988). The results from Study A showed no increase in risk (odds ratio 0.96; 90% CI 0.69 - 1.38) associated with solvent exposure in psychiatric patients compared with general hospital referents. The initial analysis of Study B suggested that patients with organic brain syndromes had been more exposed to solvents than other psychiatric patients (OR 1.46; 90% CI 1.05-2.04). The present report describes the objectives and methods of Study B and the further analyses that have been carried out.

Objective

The specific objective of Study B was to determine whether occupational exposure to organic solvents is more frequent amongst patients with a diagnosis of organic psychiatric disease than amongst other psychiatric patients.

Methods

Identification of cases and referents. Cases for this study were patients whose final diagnosis, either primary or secondary, was one of the organic brain conditions included in Table 2. The primary referent series consisted of psychiatric patients with any psychiatric diagnosis other than those shown in Table 2 and who had neither a diagnosis of chronic alcoholism nor of mental retardation. Where a case was matched to a psychiatric referent with a primary or secondary diagnosis of alcoholism (as occurred in 18% of first matches) a second referent was chosen and has been used throughout the

analysis reported here. This psychiatric referent series was chosen to test the null hypothesis that there was no difference between solvent exposure in patients with organic brain damage and in other psychiatric patients. A second referent series was drawn from general hospital patients with any diagnosis other than psychiatric illness, chronic alcoholism, elective surgery or accidental injury. This series was included to allow comparison of exposures among patients with organic brain damage and those in a more general (non psychiatric) population. In order to answer more fully the first question described above, a general hospital referent was also matched to the psychiatric referent in Study B; analysis of this series is not directly relevant to the objective of the present study and is not included in this report.

Patients included in the case and the two referent series were chosen from men aged 40 to 69 years admitted for at least five nights to Quebec hospitals between April 1st, 1978 and March 31st, 1985 who had a home, contact address or telephone number in Quebec or in adjacent provinces ie. Ontario, Nova Scotia or New Brunswick. For the case and psychiatric referent series the patient was eligible if the admission meeting these criteria was either the first psychiatric admission or, if this was not the first admission, if the initial admission had been (1) within the past last five years and (2) if the patient had been at least 40 years of age at the time of the first admission.

All eligible patients with a diagnosis from amongst those in Table 2 were included as cases in the study. The only exception was in certain psychiatric and general hospitals where a very large proportion of patients had been admitted with a diagnosis of alcoholic dementia. All eligible cases with this diagnosis and who had been treated in psychiatry

were identified. A random selection was then made such that the number with this diagnosis did not exceed that of cases of senile or pre-senile dementia from the same hospital.

One psychiatric and one general hospital referent was individually matched on age +/- two years and administrative year (April-March) of admission. This was done using whichever record system was most complete and accessible; in some hospitals it was practicable only to match dates of separation of referents with dates of admission of the cases.

Hospitals with more than 30 psychiatric beds were identified in six urban regions, in which the use of organic solvents might be supposed to be reasonably frequent. Where the hospital was a psychiatric one, the nearest general hospital was identified for selection of general hospital referents. Any patient meeting the selection criteria for a case at any of the 18 psychiatric or general hospitals was accepted and referents selected as shown in Table 3.

Amongst the hospitals approached two (one in Montreal and one in Quebec City) felt unable to take part, because of over work and under funding. The final list of collaborating hospitals is shown in Table 4. In Quebec City two of the hospitals agreed to participate only if they first had the agreement of the subject. At these hospitals, cases replying to the hospital request for agreement were re-matched, where necessary and possible, with referents who had also replied. In each instance this was done whether or not the reply was positive.

Fourteen cases were successfully re-matched following this procedure; 3 being re-matched to psychiatric referents and 11 to general hospital referents. Unfortunately the response rate was low (120/202) for those approached by the hospitals,

and no attempt at tracing was possible. The response rate was, however, similar for cases (59%) psychiatric referents (56%) and general hospital controls (60%). The final number of cases included from Quebec City (32) is thus less than the potential cases (67) identified.

Extraction of hospital data

For each subject (case or referent) identified a hospital extraction form was completed (Annex I) containing the final diagnoses, the destination of the subject at discharge, information (if given) on the usual occupation and any information that might be useful in tracing subjects, particularly the most recent address from hospital records and the name and address of the next of kin or other contact.

Tracing and collection of data

All study subjects - cases and referents - were initially contacted by letter (Annex 2) explaining the purpose of the study and informing the subject that an interviewer would contact them by telephone during the next few days. There were two exceptions to this rule. First, where there was no telephone at the subject's address the introductory letter asked the subject to contact the interviewer and to give a telephone number at which he might be reached. Second, at Quebec City hospitals with limited participation, an alternative introductory letter was forwarded by the hospital, explaining the study and asking the subject to reply directly to the hospital.

Attempts to interview the subject began one week after the introductory letter had been sent. If the initial attempt failed because the subject had moved, the subject was traced and a further introductory letter mailed. If a patient had died the most appropriate family member (or other contact) was interviewed. When a patient was alive and still in hospital

one of three courses was taken (1) the interview was postponed until the patient returned home (2) the patient was interviewed in hospital or (3) if, in the opinion of those closest to the patient (a family member or member of the hospital staff) the patient was never likely to recover sufficiently to be interviewed, a proxy interview was carried out.

Patients who were uncooperative were re-contacted some months later. Depending on the circumstances of the refusal this was either by further telephone call or by short letter or self completed questionnaire (Annex 3). Proxy interviews were not sought in cases where subjects refused to give information.

The telephone questionnaire used in this study is included as Annex 4. It contained sections on demographic information, occupational history including exposures to solvent, lead and pesticides, and information on alcohol intake and medical conditions particularly stroke and head trauma. The pilot work carried out in developing this questionnaire is described elsewhere (Labrèche, 1989).

Evaluation of exposure to organic solvents

Basic to this study was the comparison of exposure to organic solvents in those admitted with a diagnosis of organic brain damage with exposure of other psychiatric patients. In similar studies exposure has been estimated by job prior to disability (for example, membership of a painters' union) or by a limited range of jobs (designated 'exposed') supplemented by a self-completed questionnaire (for example, on types of paint used and conditions of ventilation). In the present study the aim was to consider solvent exposure in all types of occupation.

Because of the importance of this assessment of exposure, three approaches were adopted. First, each job reported by a

case or referent was individually assessed, blind to case status, by one of the research team (Labrèche) and a rating of exposure recorded. The replicability of this rating was assessed by two independent panels each of three raters, one in Montreal and one in Europe. The results of these replicability studies, showing good agreement, have been reported elsewhere (Labrèche, 1989).

The rating scale adopted was analogous to that used for rating changes of abnormality in chest x-rays (Liddell, 1963). In the present study a code of "0" signifies no exposure (at least not more than the average citizen), "1" light exposure (a level probably not biologically important, perhaps less than 30% of the threshold limit value (TLV)), "2" moderate exposure (levels that might need to be monitored, probably from 30 to 50% of the TLV) and "3" significant exposures (a level that is undesirable, probably over 50% of the TLV). A second, modifying digit, reflected "second thoughts". For example, a code 2/3 signifies moderate exposure which might have been considered as a code 3, a code 2/1 a moderate exposure which might have been considered as a code 1 while a code 2/2 signifies that no other exposure was considered appropriate by the rater. The rater also made an estimate, for each job period assessed, of the proportion of the working week during which the exposure took place.

Second, a job exposure matrix was developed for the present study. A four figure occupational code (Statistics Canada, 1986) was assigned to each job held, since school leaving, by a man in the study. The categories of all such jobs were tabulated by level of exposure assigned by Labrèche and, for occupations rated on at least ten occasions, the distribution of exposures examined. One hundred and thirty-one job categories were identified in which Labrèche had rated at least 10% as being exposed to level 1/0 or greater; that is,

for at least 1 in 10 job periods in this category she had considered it possible that the work had had some exposure to solvents. The descriptions supplied by Statistics Canada for each of these categories were listed in random order and submitted to three experts, occupational physicians or hygienists who had carried out research on the effects of solvent exposure, from teams in Finland, Sweden and the United Kingdom. Each expert assigned a code using the same scale as Labrèche, from 0/1 to 3/3 to the job category descriptions, and further estimated the proportion of the working week at which the worker would be exposed at that level.

The same exposure level (ie. level 0, 1, 2, 3) was recorded by all three assessors, working independently, for 63 of these job categories (Table 5) and by two of the three on all but 7 of the remaining categories. The seven types of work over which there was no agreement were discussed with the assessors as a group; in each case it was agreed that the median rating should be assigned. The matrix of job category codes and exposure levels was then merged with the job history file for each subject; job categories not assessed by the team, because the initial screen had not suggested exposure, were treated as not exposed.

Two assessments of exposure in each job were thus obtained. The individual rating took account of all the information provided by the respondent about the tasks carried out and exposures reported. This assessment was thought to be relatively sensitive but was open to bias in reporting of detail and would not be easily replicable in future studies. The second method, using the job matrix, was relatively objective and available for use in future studies, but made no use of information on individual differences in exposure in jobs within the same broad category.

As a separate task the same group of international raters compared, blind to case status, the complete job history of 98 pairs of cases and referents (in Study B) and recorded for each subject whether he had, in their judgement, received organic solvent exposure that might conceivably result in psychiatric disability. They were also asked to report on which of the pair had been more exposed, regardless of the significance of exposure.

Assessment of potential confounders

Information on attributes of the subject that might relate both to solvent exposure and to psychiatric illness were assessed from information supplied by respondents to the long questionnaire (Annex 4). Seven factors were considered. Occupational exposure to lead and pesticides, themselves suspected of being toxic to the central nervous system, was asked for each job reported. For the analyses in this report, a binary variable -ever or never occupational exposed - was used for each of these substances. Age of school leaving was asked directly (question 4) and those leaving at 14 years of age or younger were taken as being at increased risk of manual employment (and hence of solvent exposure) and, because of poor intellectual skills, of a diagnosis of organic psychosis. Similarly low socioeconomic group was defined as a score of less than 35 on the Blishen scale (Blishen and McRoberts, 1976) of social status. The rating was based on the occupation held by the father during the subject's primary school years and was not available for those raised by the mother alone (question 3).

Head trauma has been reported to be more frequent amongst those with Alzheimer's disease (Heyman et al., 1984; French et al., 1985). For this study a positive reply to the question "Has a doctor ever told you that you had had a head injury with loss of consciousness? (question 21C)" was taken to

indicate a history of head injury. Similarly a positive answer to the question "Has a doctor ever told you that you had had a stroke or other disease of that kind? (question 21D)" was taken to indicate a history of stroke, a factor of aetiological importance in multi-infarct and possibly other dementias. It was recognised that the validity of answers to these questions might be in doubt.

A particular problem for the present study was the assessment of alcohol consumption. This was potentially important because alcohol might act as a confounder, as an effect modifier or be associated with errors of classification, those with a history of drinking or solvent exposure both being diagnosed as suffering from alcoholic dementia. A detailed history of alcohol intake was collected (question 20) and from this it was determined whether the subject had ever drunk more than 14 units of alcohol a week (one unit = 12 oz beer, 5 oz of table wine or 1 1/2 oz of spirits) and whether he had ever drunk "to excess". For those with complete data an intake of more than 42 units was considered to be excessive. For those with incomplete data, the questionnaires were assessed individually, blind to case status, and intake assessed as being "excess" if some comment such as "drank like a fish", "was never sober", "a member of Alcoholics Anonymous since he was 60" had been made by the respondent and which seemed, in the judgement of the coder, to indicate a history of excess alcohol intake.

Statistical analyses

The data were analyzed using a matched case/referent comparison to test the null hypothesis that there was no difference in solvent exposure between cases and psychiatric referents. It was decided *a priori* to test this hypothesis by comparing exposures to at least moderate solvent concentration (level 2 or above) for ten years or more using first individual and then job matrix estimates of exposure. Further

analyses using conditional logistic regression were then carried out to determine whether any relation between organic brain syndrome and solvent exposure was maintained when allowance was made for possible confounding factors. These analyses first compared cases to psychiatric hospital referents. The main results were then repeated using general hospital referents.

Description of the sample

Participation rates

A total of 309 cases were identified as eligible for this study. The initial analyses, reported elsewhere (Cherry and McDonald, 1988, Cherry et al., 1988) were based on 319 cases, 10 of whom were found on review to have only alcohol related diagnoses (delirium tremens, alcohol withdrawal syndrome) not necessarily indicative of chronic organic damage; these cases were removed from the study. The success of contacting subjects is shown in Table 6. Long questionnaires were obtained for 83% of the subjects, with the proportion being marginally higher for the cases (86%) than for the psychiatric or general hospital referents (82%). Some contact with the subject or his family was made in a further 10% of cases and referents; this was achieved by short questionnaire, by letter or by telephone contact. No contact was made with 65 subjects (7%), of whom 31 refused and 34 were untraced. For the majority of these some information on occupation was available from the hospital record. No informant could be identified for two cases who had died since leaving hospital. Some occupational information was available for all but 15 of the subjects.

The rate of contact and collaboration was uniformly high, but an important difference between groups appeared when use of proxy respondents was examined (Table 7). Only in 48 of the cases (15.5%) did the patient himself complete the long

questionnaire, compared with 147 (47.6%) of psychiatric referents and 127 (41.1%) of the general hospital controls. This substantial use of proxy respondents reflects both the nature of the disease defining the cases, and the age of the participants, given the length of time since the key admission for those admitted in 1978. Many of the subjects had died either in hospital or subsequently. The large majority of proxy respondents were family members, only 9 of the interviews being conducted with a friend of the subject. The identity of respondents providing incomplete information (letters, short questionnaires, telephone conversations) was not reliably recorded.

It is recognised that proxy informants will usually not be in a good position to give detailed information about work, and this may well be reflected in ratings of job descriptions reported in this way. Job titles, however, may be relatively reliable; if so analyses based on a job exposure matrix may be less dependent on the type of respondent.

Success in matching

Cases were matched to referents on age of admission and the administrative year (from April to March) in which the admission took place. The ages of case and referents are shown in Table 8. Matching on age was less close than planned, for both referent series, with 27% of psychiatric referents and 21% of general hospital referents differing by between two and three years from the age of the case. Mean age of cases was 60.75 years (range 40-69), of psychiatric referents 60.52 years (range 40-72) and of general hospital referents 60.71 years (range 40-71). Matching was close on the administrative year of admission, only 6 psychiatric referents and 3 general hospital referents being admitted more than one year either earlier or later than that of the case. Information on the year of admission is shown in Table 9.

Distribution of diagnoses

The diagnosis for selection of cases in the study is shown in Table 10. The diagnosis for inclusion was recorded as a secondary diagnosis only for 27 of the 309 cases; for each of these the primary diagnosis was a psychiatric one, for example depression in a patient with an organic dementia.

The largest group of patients selected as cases consisted of 90 patients with a primary diagnosis of senile or pre-senile dementia. Of these about 1 in 4 had a note recorded that the dementia was of the Alzheimer type (DAT). This was recorded more frequently in more recent admissions and although it may be reasonable to assume that those for whom such a diagnosis was specified did exhibit symptoms suggestive of Alzheimer's disease, those in whom it was not specified cannot be assumed to have been free of these characteristics.

Groups 3 and 4 in Table 10 are cases with a neurological primary diagnosis of cerebral degeneration; these have been divided, in this table, between those labelled as Alzheimer's disease and those with some other ICD code.

Only 18 cases had a diagnosis of arteriosclerotic dementia. Twenty-one had other non-alcoholic psychoses. Thirty-eight were selected with a primary diagnosis of alcoholic dementia and there were a further 12 whose selection arose only from a secondary diagnosis of alcoholic dementia. Fifty-five cases were selected because of a diagnosis of an organic psycho-syndrome of non-psychotic severity.

Amongst the psychiatric referents half of those selected had been diagnosed as having a psychotic illness, the rest having a variety of disorders, shown in Table 11.

Distribution of potential confounders

Information on confounders was available only for the 86% of cases and 82% of psychiatric and general hospital controls who had completed the long questionnaire. The proportions with attributes coded for each of the possible confounders is shown in Table 12. The distribution of the three factors thought to be associated with a particular diagnostic group (head trauma with Alzheimer's disease, stroke with arteriosclerotic dementia, alcohol excess with alcohol dementia) is shown in Table 13 by diagnostic group. The highest rate of reporting of each of these three factors was indeed in the group predicted.

Results

Exposure to solvents

It had been decided a priori to consider as exposed those subjects exposed to solvents at level 2 or above for at least 10 years, and carry out a matched analysis. The results of this analysis are given in Table 14. In this, and in all subsequent tables, results are given for both the individual ratings of exposure, based on the job description obtained from the subject, and for estimate of exposure based on the job matrix. This allows the greater sensitivity of the first method to be balanced against the greater objectivity of the second. In Table 14 it can be seen that for each method of exposure assessment, the odds ratio computed is greater than 1, both for the complete sample, and for those with long questionnaires. This increase in odds ratio supports the hypothesis of an increased risk of organic psychosis amongst those exposed to solvents. However the increase reaches statistical significance at the 5% level in a one sided test (a 90% confidence interval with a lower bound greater than 1.0) only when all respondents are included, using the individual rating of exposure. The greater power of this comparison is a reflection of the relatively high number of pairs in which long questionnaire data was not available for

either the case or for the referent (29% of pairs had missing data) and the lower rate of exposure in cases and referents when estimates of exposure were based on the job matrix rather than the individual job description.

The next stage of the analysis was to examine odds ratios by diagnostic groups, shown for individual ratings in Table 15a and for job matrix ratings in Table 15b. By both methods of assessment the highest risk is in the group diagnosed as suffering from alcoholic dementia. Discrepancies between the two methods of exposure assessment in the estimate of risk in other groups are difficult to interpret in view of the small numbers of discordant pairs.

Review of the secondary diagnosis of cases identified an additional 25 patients who had a secondary diagnosis of alcoholic dementia or alcoholic dependency, although their primary diagnosis was not labelled as associated with alcohol consumption, In order to simplify the analysis, and to reduce the problem of small numbers in any one diagnostic group, the cases were then re-classified to take account of both whether they had any alcoholic diagnosis and whether the diagnosis on which they had been selected as eligible for the study was either one of organic psychosis or cerebral degeneration or a diagnosis of less severity, namely an organic syndrome of non psychotic severity (ICD-8 309.6 or ICD-9 301.1). Results of this analysis can be seen in Table 16a (individual ratings) and Table 16b (job exposure matrix). It will be seen that, by either method of exposure assessment, the odds ratio is markedly elevated in the group with organic psychosis or cerebral degeneration in which an alcohol related diagnosis is also present. Those with a diagnosis of this type were five times more likely than their individually matched referent to have a job history suggestive of extended occupational exposure to organic solvents.

The results in Table 14 and 16 represent the basic a priori (Table 14) and post hoc (Table 16) results of this study. They are shown for the second referent series, that of general hospital patients, in Tables 17 and 18. The odds ratios for the individual assessment, but not for the job exposure matrix, are lower than for the psychiatric referent series. However the higher risk amongst those with organic dementia or cerebral degeneration and an alcohol related diagnosis remains in evidence.

Effects of confounders

Assessment of effects adjusted for potential confounders was limited in the present study; only pairs in which both case and referent had completed the long questionnaire were included in the analysis and, for this sub-group, the odds ratio associated for solvent exposure did not attain statistical significance. Thus the question was not whether the results still "held" having allowed for possible confounders, but rather to estimate whether the (non-significant) risk estimate was modified. The increase in risk with alcohol related diagnoses demanded that the confounding or modifying effects of reported alcohol consumption should be considered in detail.

A. Alcohol In the present study there is no clear relation between solvent exposure and reported alcohol consumption. Comparison of consumption between cases and referents is not meaningful in the present study because of the exclusion of alcoholics from the referent series. However neither in the cases (Table 19a) nor psychiatric referents (Table 19b) is there an important difference between exposed and non-exposed in reported alcohol consumption. It is unlikely, therefore, that alcohol acts as a confounder. Its role as a possible effect modifier is more interesting, as those with hepatic function impaired by alcohol might well be less able to

detoxify solvents, or those exposed to solvents for many years may become demented under the additional burden of alcohol. Table 20 demonstrates the odds ratios associated with solvent exposure, in a paired analysis, where the pairs are stratified by the reported alcohol consumption of the case. Here the excess risk seems, on both estimates of solvent exposure, to be largely confined to the heavy drinkers. An unmatched analysis (Table 21) suggests that the risk of receiving a diagnosis of organic brain damage is greatest amongst those who are both exposed to solvents and who drink heavily. On these data it appears that the effects are more than additive; results from the job exposure matrix suggest more strongly than those of the individual ratings that a multiplicative model might be appropriate.

Logistic regression analysis, using a matched pair analysis and multiplicative model, demonstrated a marked main effect for reported alcohol consumption (as would be expected from the exclusion of alcoholics from the referent series) but no significant interaction between solvent exposure and excess alcohol consumption with either method of exposure assessment.

Investigation of patterns of drinking and solvent exposure amongst cases and referents gave little insight into the circumstances in which the combination was likely to lead to an organic diagnosis. In the rather small number of subjects with both significant alcohol consumption (greater than 14 units per week) and exposure to solvents, solvent exposure was reported to precede alcohol consumption in the majority of both cases and referents (Table 22).

Amongst cases who reported drinking to excess, those who were also exposed to solvents were admitted to hospital some 5 years or so earlier in their drinking history than excess drinkers not exposed to solvents. This difference did not

reach statistical significance but was not in evidence in the referent series (Table 23).

B. Other confounders Odds ratios for each of the six potential confounders other than alcohol consumption are given in Table 24. The two variables reflecting socioeconomic group, age at leaving school and the social status of the father's job, were not related to the probability of developing organic brain disease rather than other psychiatric illness. Exposure to other neurotoxic substances at work, namely lead and pesticides, was not greater in the case series; indeed those exposed to pesticides were significantly less likely to given a diagnosis of organic brain disease. Reported head trauma and, particularly, stroke were more frequent in the case series; this relationship with stroke persists when cases with a diagnosis of arteriosclerotic dementia were excluded (OR 3.6 CI 1.8 - 7.2).

Logistic regression analysis including all six confounders is shown in Table 25. The odds ratio for solvent exposure, using individual ratings, in the group with data on all these variables was 1.2 (CI 0.8 - 2.0); this was unchanged (OR = 1.2 CI 0.8 - 2.1) when allowance was made for all potential confounders other than alcohol consumption. Comparative figures for solvent exposure assessed by the job matrix were 1.1 (CI 0.6 - 2.1) before adjustment and 1.1 (CI 0.5 - 2.2) after allowance for other confounders. When alcohol excess was added to the equation the odds ratios were reduced only very marginally, remaining after rounding the second decimal place at 1.2 (CI 0.7 - 1.9) for individual ratings and 1.1 (CI 0.5 - 2.1) for the job matrix assessment. Thus adjustment for confounders had no important influence on the estimate of risk amongst those pairs in which both subjects had supplied full information.

The final stage of this analysis was to consider the effects of confounders on the odds ratios obtained for the group of 61 men with both a diagnosis of organic dementia or cerebral degeneration and an alcohol related diagnosis. For this group, only reported alcohol consumption was significantly related to case status (alcohol excess OR 9.5 CI 2.8 - 32.3). The odds ratios for pesticide exposure was again low and that for head trauma (but not stroke) high (Table 26). With small numbers, these effects did not reach statistical significance.

Logistic regression on the 23 pairs with data on all potential confounders failed to converge. However for the 25 pairs with data on head injury, pesticide exposure and alcohol consumption, an estimate was achieved (Table 27). The inclusion of head trauma and pesticide exposure reduced the odds ratio for solvent exposure in these 25 pairs from 6.0 (CI 1.0 - 35.5) to 5.2 (CI 0.8 - 34.2) using individual estimates of exposure. With exposure ratings from the job matrix an odds ratio of 5.0 (CI 0.8 - 30.3) was increased slightly to 5.8 (CI 0.9 - 38.2). Inclusion of the variable reflecting excess alcohol consumption further increased the odds ratio to 6.6 (CI 0.8 - 55.2) for individual ratings and 6.2 (CI 0.7 - 56.4) for exposure estimates from the job matrix. However the low proportion in this group giving complete data on confounding variables makes any such analysis of dubious value.

Other estimates of exposure

1. Weighted indices The exposure variable used to this point was that chosen *a priori* as being most likely to distinguish between exposure of possible biological significance and exposure unlikely to result in long term damage. However the model used does not reflect all the information, further detail being available on both duration and level of exposure and the proportion of the working week

during which exposure was thought to have occurred. For both the individual ratings and the job exposure matrix it was possible to compute indices which made some allowance for these additional aspects of exposure. The sum of years exposed at each level, weighted by the exposure level (ie. years at level one + 2 x years at level 2 + 3 x years at level 3) was computed. A second index was computed, in which the years at each level were weighted by the estimated proportion of a working week during which the exposure occurred. This was slightly more detailed for the job title matrix than for the individual exposure estimates; a scale from 0/0 (=0) to 3/3 (=9) was weighted by each assessors' estimate of the proportion of the week exposed.

The values on these indices were compared for cases and psychiatric referents using a paired t-test both for the raw indices (Table 28a) and the logarithmic transformation (Table 28b). All comparisons suggested, at least at the 10% level, that the cases had been more exposed than the referents. No attempt has been made to test, using these data, the assumption of a threshold effect of 10 years exposure at level 2 or above. However an index calculated excluding level 1 exposures and exposures to level 2 or above for less than 10 years showed t values (t = 1.6 individual ratings; t = 1.2, job matrix) comparable with those taking account of all years at all levels of exposure.

2. <u>Comparative evaluation of job histories</u> A quite different approach was adopted by asking the three international experts to assess, blind to case status, the job histories of pairs of cases and referents, and to judge which of the pair had received the greater exposure. Further, they were asked to decide whether either or both had, in their judgement, been exposed to solvents at a level compatible with reported organic effects. For the subjects selected for this exercise

the job descriptions and dates were translated into English, if necessary, and transcribed in a standard form.

Because of the time required for preparing and carrying out this evaluation only pairs in which either the case or referent (or both) had been assessed by Labrèche as receiving exposure to level 2 or greater for at least 10 years were considered. Further, to enable comparison to be made with the companion study of Montreal psychiatric patients and general hospital referents, only the general hospital referent series was used. Thus assessment was made of a total of 98 pairs of cases from the present study and their matched referents from the general hospital series.

Amongst the 98 pairs were 19 in which Labrèche had assessed that both were exposed to level 2 or above for at least 10 years, 41 in which the case only had been exposed to this degree and 38 in which the referent only had been exposed. Thus of the 196 subjects involved in this exercise, 117 were judged, using indices derived from the individual ratings, to have been exposed.

The three assessors varied in the number of subjects they considered significantly exposed, with the most liberal (RR) judging 54 to be significantly exposed and the more conservative pair of assessors with roughly equal numbers 30 (HAW) and 27 (OA). Table 29 shows the agreement between the criteria used in earlier analyses (exposure for 10 years or more to at least moderate levels of solvents, based on individual ratings) and the international assessors judgement of exposures that they believed might conceivably lead to a psycho-organic syndrome. Amongst the 117 subjects assessed on individual ratings as being exposed for 10 years or more to level 2 or above, 60 were not judged by any of the three assessors as receiving important exposure, 30 were judged to

have such exposure by one assessor, 7 by two and 20 all three. Amongst the 79 subjects previously judged as not being exposed, 73 were thought by all three assessors not to be importantly exposed, 5 were judged by just one assessor to be importantly exposed and 1 subject was felt by all three judges to have received an important degree of exposure. Thus, if the international assessors were to be used as the gold standard, the criterion of 10 years exposure to at least moderate levels of solvent appears to be highly sensitive (0.96) but not highly specific (0.46).

Amongst the 21 pairs in which all three judges felt that one subject was importantly exposed, and the other not, 16 were cases and 5 were referents. If the criterion was relaxed to include also the 7 subjects judged by two of the three assessors to be importantly exposed, numbers rise to 19 cases and 9 referents, one pair containing both case and referent judged by at least two assessors to have had significant exposure. The odds ratio for the more stringent criterion is thus 3.2 (90% CI 1.4 - 7.1) and for the rather less stringent, based on 18 cases and 8 referents in discordant pairs, 2.25 (90% CI 1.1 - 4.4). This compares with the odds ratio, based on discordant pairs, of 1.1 for individual ratings of these cases and general hospital referents.

Discussion

The null hypothesis for this study was that solvent exposure would be no more frequent amongst patients with a diagnosis of organic brain damage (dementia, cerebral degeneration or non-psychotic changes) than among those with other psychiatric diagnoses. This hypothesis was not supported by the data; those with organic brain damage were more likely to have been exposed. The observed excess was found to be significant (on a one-tailed test, with a 5% probability level) only in the largest group of 297 pairs (all respondents for whom at least

basic employment data was available) and only for one of the two indices of exposure, that based on individual ratings; on this index some 15% of referents were judged to be exposed to solvents. Sample size calculations, at the time the study was designed, suggested that a sample size of 322 would be needed to detect an odds ratio of 1.8, assuming exposure in 10% of referents. With smaller numbers (219 pairs) providing complete data and a lower estimate of exposure (8%) using the job matrix the study was not sufficiently powerful to demonstrate a significant excess on the other comparisons. However the consistency of findings, together with the clear excess of cases among those judged importantly exposed by the international panel, requires that the null hypothesis be re-considered.

More detailed analysis suggested that the excess risk is largely restricted to those with severe disease (organic psychosis and cerebral degeneration) who have an associated diagnosis indicating an alcohol problem. Here the odds ratios were of the order of 5, with either method of exposure estimate. A smaller excess of about 1.5 was observed for those with less serious, non-psychotic disease for whom no alcohol related diagnosis was reported. This group of cases, included because of the closer parallels to previous studies of mild neuropsychiatric disease, was too small for detailed analysis, but the risk is consistent with reports from these earlier Scandinavian studies.

An apparent excess of solvent exposure amongst the cases might arise in a number of ways. First, the possibility of bias must be considered. Subjects with organic conditions might have tended to over-report solvent exposure. Such an explanation is unlikely in Canada where solvent related brain damage has had little recognition. Indeed pesticides, apparently associated with lower risk, might have been more

likely perceived as a causal factor. The use of proxy respondents may also have lead to bias in a direction and to a degree that is difficult to assess; in 82 pairs where both case and referent were interviewed by proxy, the odds ratio was 1.46, almost identical to that of the whole sample. It might be anticipated that any bias in reporting, whether or not associated with proxy interviews, would be less when job title, rather than job content, was used to assess exposure. In the present study the absolute level of risk, using the psychiatric referents, was similar by the two methods.

A second problem arises with the diagnostic label attached by a psychiatrist to patients who have been exposed to solvents. If solvent exposure does indeed cause even minor brain damage this may have affected the assessment of the psychiatrist and lead, particularly in the presence of at least moderate alcohol consumption, to a diagnosis of an alcohol associated psychosis. Further those with organic brain damage may be less able to tolerate even small amounts of alcohol (Lishman, 1987) and present after moderate drinking with the appearance of alcohol related dementia.

Using the data presented here it is not possible to demonstrate whether solvent exposure is associated with greater numbers of patients with psychiatric illness (ie. the onset of psychiatric illness in those who would not otherwise present) or with simply a shift in diagnosis within the same patient population. However, if the numbers of psychiatric patients were unchanged but a diagnosis of organic brain damage more frequently attached to the solvent exposed, it would be expected that a deficit of solvent exposure would be found amongst psychiatric patients with other (ie. non organic) diagnoses. In conjunction with the present study, an additional series of general hospital referents was individually matched with the psychiatric referents. When

exposure was compared, using individual and job matrix ratings for the psychiatric referents and their general hospital controls there was indeed a mild (non significant) reduction in the odds ratios for the psychiatric referent and their controls (odds ratio (individual) 0.81, 90% CI 0.56-1.18; odds ratio (job matrix) 0.95, 90% CI 0.55-1.62). However the excess risk cannot simply be attributed to such a small deficit in exposure amongst the psychiatric referents; an excess risk was also found, in the main study reported here, when those with an organic diagnosis were compared to the general hospital referent series.

The finding that increased risk is largely confined to those with an alcohol related diagnosis is potentially of some importance and merits consideration of mechanisms in addition to simple bias. Analysis of reported consumption suggests that those who have had a period of heavy alcohol consumption are at greatest risk. The most straightforward explanation of this finding is that, for those with both exposures, the increased load of circulating solvents - the sum of alcohol ingestion and industrial exposure - puts the nervous system at greater risk. Second, it may be that the presence of one substance alters the time course of metabolism of the other. Exposure to alcohol before the elimination of a recently inhaled solvent is known to delay the metabolism of the solvent (Wilson et al. 1983) while those with moderate drinking habits appear to metabolise solvents more quickly than non-drinkers, presumably by enzyme induction (Waldron et al. 1983; Cherry and Gautrin, 1990). With chronic alcohol abuse, cirrhosis may be expected to result in a decreased capacity to detoxify solvents and hence enhance the potential for nervous system damage.

Confounding of solvent exposure by alcohol consumption does not appear to have been an issue in the present study,

although it is recognised that the information on drinking habits is imperfect; it has not been validated and is available for only 85% of cases and 81% of referents. However other recent reports also find little relation between degree of exposure and reported drinking habits. Both Mikkelsen et al. (1988) and van Vliet et al. (submitted) show somewhat lower reported consumption among the exposed (painters) than referents (other construction workers). These reports contrast with findings from mortality studies in Geneva (Guberan, 1989) and Stockholm (Lundberg et al. 1990 and personal communication). In Geneva painters had excess mortality from alcohol related diagnosis (alcoholism, liver cirrhosis in house painters) when compared to electricians. In Stockholm painters had a higher mortality rate from alcoholism than did carpenters.

In considering these results it might be thought helpful to review the ways in which alcohol and alcoholic diagnoses, have been treated in the previous studies summarised in Table 1. The final table (Table 30) lists the 12 studies indicating whether the criteria for a case included a diagnosis of alcoholism (ICD 303) or alcoholic dementia (ICD 291) and whether information on alcohol consumption was used in the analysis.

Alcoholism (ICD 303) was included in specification of the case series in five of eight case-referent studies. In those of Axelson (1983) Lindstrom et al. and van Vliet et al. the odds ratio was calculated separately for this diagnosis. In Axelson's re-analysis the odds ratio for alcoholism was identical to that overall (1.8). For van Vliet et al the odds ratio was marginally lower for alcohol (1.0 overall; 0.9 for alcoholism) and for Lindstrom et al. considerably lower (1.6 overall; 1.1 for alcoholism). Brackbill et al. present risk estimates only for alcoholism and alcoholic dementia combined.

In the remaining case-referent study using this diagnosis (Olsen & Sabroe), in Mikkelsen's cohort study and Cherry and Waldron's prevalence study no separate estimate of risk is given.

Alcoholic dementias were included in only three of the case-referent studies. In Olsen and Sabroe there is again no separate analysis. Rasmussen et al. present odds ratios in which cases and referents with alcohol related diagnoses are excluded. Such an exclusion leads to a mild decrease in risk (from 1.8 to 1.5) consistent with a slightly greater risk in alcohol related than other cases of dementia. Brackbill et al. provide odds ratios only for alcoholism and alcoholic dementia combined. They compute a risk of 1.2 (overall risk 1.4) when the non-exposed group are taken as bricklayers and 1.5 when all blue collar workers other than painters are considered non-exposed. Again Mikkelsen and Cherry and Waldron do not present separate analyses for the alcoholic dementias. Mikkelsen does, however, include alcohol as one 'indication of cause' of dementia when re-classifying the diagnoses in his cohort study. The relative risk for dementia for those with 'cause indication' was lower (2.4) than those without (3.4), suggesting a lower risk for those with dementia associated with alcohol. Alcoholism and alcoholic dementia were also combined in the study of Guberan et al. As previously discussed, these authors report that there were associated alcohol related diagnoses in 12 of the 20 painters but only 1 of 10 electricians receiving disability pension for neuropsychiatric disease.

In four of the studies information on alcohol consumption was collected by questionnaire and used to adjust the odds ratio for solvent exposure. Olsen and Sabroe, Rasmussen and van Vliet et al. give no detail of the effects of adjustment for this factor alone. Mikkelsen et al (1988) report that adjust-

ment for alcohol consumption (higher in the referent group) had no effect on the estimated odds ratio for solvent exposure

It must be concluded that published studies add little to our understanding of the relation between alcohol consumption and the risk of dementia in solvent exposed workers. On balance alcoholism alone does not appear to be associated with increased risk and there are too few data to reach a conclusion from previous studies of alcoholic dementia. One possibility, untestable in the present study, is that signs of organic brain damage resulting from solvent exposure lead to more frequent diagnoses of alcoholic dementia (rather than simply alcoholism) in solvent workers presenting with psychiatric problems related to drinking. Those studies including alcoholism but excluding alcoholic dementia would then systematically underestimate the impact of solvent exposure.

The present study has limitations in a number of ways. It is limited in that cases are drawn only from patients admitted to hospital; such admissions will depend in part on social and other circumstances that may be particular to the family, the local community or to the Province of Quebec. Second, the decisions to include only a reduced sample of the cases with a diagnosis of alcoholic dementia, and to exclude alcoholics from the referent series, makes estimates of the social impact of solvent exposure difficult, even for this population. In the first two hospitals visited alcoholic dementia, treated in psychiatry, constituted approximately half the eligible cases; after sampling, and in the whole case series, they constitute 15%. Thus, without sampling and given the high risk associated with this diagnosis, the overall risk would be expected to be appreciably higher than the odds ratio of 1.4 reported here.

A second important limitation arises from the use of proxy respondents. These were used in a high proportion of

subjects, particularly cases, and the impact of this on the results presented here cannot be adequately assessed. Third, the analysis of the effects of confounders was seriously limited by the reduced, and probably non representative, sample with complete data on even the fairly small set of variables considered.

Some inconsistent or unexpected results could not be adequately explained. Particularly troublesome was the lack of evidence of increased risk when cases were compared to the general hospital series, using the individual ratings of exposure. It was evident that interviewers seldom mistook the general hospital referents for a case; however, if there were subconscious bias in the interviewers to produce a positive study result, this might be expected to lead to reduced prompting rather than over prompting for exposure. It may be that the nature of the disease in cases and psychiatric referents made them less responsive to prompting than the general hospital referents and that this lead to under reporting amongst cases and psychiatric referents rather than over reporting amongst the general hospital series. It is important to remember, in this context, that use of the job exposure matrix, believed to be less subject to bias, showed an excess of solvent exposure in the cases, compared with general hospital referents, that was consistent with the finding from the psychiatric referent series.

The significantly reduced risk amongst those with pesticide exposure was also unexpected. It may be that agriculture workers have less exposure to other environmental or lifestyle factors and that this reduces their risk of organic brain damage but not other psychiatric disease. Alternatively the clinical pattern of pesticide induced psychiatric illness may resemble affective rather than organic disease.

Despite the imperfections of the study, the results presented here suggest that solvent exposure is indeed associated with an increased risk of disease labelled as organic psychosis or cerebral degeneration, particularly when there is suspicion of alcohol abuse. Earlier studies have not, in general, concentrated on disease of this severity and may have systematically excluded cases in which alcohol abuse was suspected. The present study, and the recent reports from Switzerland and Sweden, suggest that the inter-relation of the two types of exposures in the aetiology of organic brain damage may be more important than previously suspected. Studies will need to be designed with some care to establish the degree of mis-diagnosis and the true pattern of interaction of solvents and alcohol in the epidemiology of this disease.

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Table 1

Risks reported in previous studies

		Overall		Group with highest risk		
A) Case-referent						
		OR	95% CI	Diagnosis	OR	95% CI
Axelson et al.	1976	1.8	1.1-3.1	senile & pre-senile dementia	2.5	1.0-6.3 (estim.)
Olsen & Sabroe	1980	2.1	1.2-3.8	non-psychotic conditions	3.1	1.3-7.4
Lindstrom et al.	1984	1.6	1.0-2.5*	neurosis	5.5	1.8-16.9*
Rasmussen et al.	1985	1.5	0.7-3.5	psychosis	5.3	0.7-33.3
O'Flynn et al.	1987	1.1	0.7-1.7 (estim.)	(all cases dementia)		
Shalat et al.	1988	1.0	0.5-1.9	(all cases Alzheimer's disease)		
van Vliet et al.	subm.	1.0	0.7-1.3	neurosis	1.9	1.1-1.3
Brackbill & Maizlish	subm.	1.4	1.0-1.9	affective pyschosis	2.4	0.8-7.2
B) Cohort studies						
		RR	95% CI	Diagnosis	RR	95% CI
Mikkelsen	1980	1.4	1.1-1.9	neurosis**	2.8	1.0-7.3
Guberan	1989	1.8	not given (NS)	alcoholism	not given - see text	
C) Prevalence studies						
Cherry & Waldron	1984	No evidence of increased psychiatric morbidity				
Mikkelsen et al.	1988	Increasing prevalence of dementia with greater exposure				

* 90% CI
** On re-classification risk highest for pre-senile dementia

Table 2

Case definition

ICD-8	Description of Diagnosis	ICD-9
290.0	Senile dementia	290.0
290.1	Pre-senile dementia	290.1
	Senile dementia, depressed or paranoid	290.2
	Senile dementia with acute confusional state	290.3
293.0	Arteriosclerotic dementia	290.4
	Other senile and pre-senile organic conditions	290.8
	Unspecified senile and pre-senile organic psychotic conditions	290.9
299	Korsakoff's psychosis or syndrome (non alcoholic)	294.0
293.4	Dementia in conditions classified elsewhere	294.1
	Other organic psychotic conditions (chronic)	294.8
	Unspecified organic psychotic conditions (chronic)	294.9
294.9	Psychosis associated with unspecified physical conditions	
347.1	Unspecified psychosis (incl. dementia N.O.S.)	
309.6	Mental disorders with senile or pre-senile brain disease	
	Cognitive or personality change ('organic psycho-syndrome of non psychotic severity')	310.1
290.1	Alzheimer's disease	331.0
290.1	Pick's disease	331.1
794	Senile degeneration of the brain	331.2
347.1	Unspecified cerebral degeneration	331.9
291.1	Korsakoff's psychosis (alcoholic)	291.1
291.2	Other alcoholic dementia	291.2
291.9	Unspecified alcoholic psychoses	291.9

Table 3

Provenance of referents for cases from psychiatric and general hospitals

Case	Referent	
	Psychiatric	General Hospital
Psychiatric hospital	Same hospital as case	Nearest general hospital
Psychiatric bed, general hospital	Same hospital as case (exceptionally, nearest collaborating psychiatric hospital)	Same hospital as case
Neurological bed, general hospital	Same hospital as case (exceptionally nearest collaborating psychiatric hospital)	Same hospital as case

Table 4

Hospitals participating in the study

Montreal region

Louis-H. Lafontaine

Douglas Hospital

Charles LeMoyne

Sacré-Coeur

Maisonneuve-Rosemont

Montreal General

Jewish General

Royal Victoria

Verdun General

Quebec City Region

St-François d'Assise

L'Enfant-Jesus

Robert Giffard

Clinique Roy-Rousseau

Other Regions

CHR de Lanaudière (Joliette)

Ste-Marie (Trois Rivières)

Ste-Croix (Drummondville)

Hotel-Dieu (Sherbrooke)

CH Universitaire de Sherbrooke (Sherbrooke)

Table 5

Job matrix ratings. Level of exposure assigned to 131 possibly exposed job categories by number of raters in agreement.

Level of exposure finally assigned	Number of raters in agreement			
	All	2/3	Agreement only after discussion	Total
0	52	28	0	80
1	6	23	6	35
2	3	7	1	11
3	2	3	-	5
Total	63	61	7	131

Table 6

Participation rates

	Cases	Referents		Overall
		Psychiatric	General Hospital	
Long questionnaire	86.1%	81.6%	82.2%	83.3%
N	266	252	254	772
Some contact: limited information	8.1%	10.4%	10.4%	9.6%
N	25	32	32	89
Untraced: some information	2.9%	3.2%	3.6%	3.2%
N	9	10	11	30
Untraced: no information	0.6%	0.3%	-	0.3%
N	2	1	0	3
Refusal: some information	1.6%	4.5%	3.9%	3.1%
N	5	14	12	31
Refusal: no information	-	-	-	-
N	0	0	0	0
No informant available	0.6%	-	0	0.2%
N	2	0	0	2
Total	100%	100%	100%	100%
N	309	309	309	927

Table 7

Use of proxy informants (long questionnaire)

	Cases	Referents		Overall
		Psychiatric	General Hospital	
No proxy (i.e. subject himself)	18.0%	58.3%	50.0%	41.7%
N	48	147	127	322
Family member	80.5%	39.7%	49.6%	57.0%
N	214	100	126	440
Some other proxy	1.5%	2.0%	0.4%	1.3%
N	4	5	1	10
Total	100%	100%	100%	100%
N	266	252	254	772

Table 8

Age at admission

	Cases	Referents		Overall
		Psychiatric	General Hospital	
38 < 50 yrs	10.0%	10.0%	10.4%	10.1%
N	31	31	32	94
50 < 60 yrs	31.1%	32.7%	30.7%	31.5%
N	96	101	95	292
60 < 72 yrs	58.9%	57.3%	58.9%	58.4%
N	182	177	182	541
Total	100%	100%	100%	100%
N	309	309	309	927

Table 9

Administrative year* of admission

	Cases		Referents	
Overall		Psychiatric	General Hospital	
1977-78	-	1.9%	-	0.6%
N	0	6	0	6
1978-79	15.5%	14.2%	14.6%	14.8%
N	48	44	45	137
1979-80	14.2%	12.6%	14.9%	13.9%
N	44	39	46	129
1980-81	14.6%	15.5%	15.2%	15.1%
N	45	48	47	140
1981-82	17.8%	14.9%	17.2%	16.6%
N	55	46	53	154
1982-83	17.5%	19.1%	18.8%	18.4%
N	54	59	58	171
1983-84	10.4%	12.3%	11.7%	11.4%
N	32	38	36	106
1984-85	10.0%	9.1%	7.8%	9.0%
N	31	28	24	83
1985-86	-	0.3%	-	0.1%
N	0	1	0	1
Total	100%	100%	100%	100%
N	309	309	309	927

* April 1 - March 31

Table 10

Cases - Diagnoses

		N	%
Main Diagnosis			
1.	Senile or pre-senile dementia (ICD-8, 290.0,290.1; ICD-9 290.0-.3,.8,.9) not specified as DAT	67	21.7
2.	Senile or pre-senile dementia (ICD-8 290.0, 290.1; ICD-9 290.0-.3,.8,19) specified as DAT	23	7.4
3.	Cerebral degeneration 'Alzheimer' (ICD-9 only 331.0)	21	6.8
4.	Other cerebral degeneration (ICD-8, 347.1, 794; ICD-9, 331.1-331.9)	35	11.3
5.	Arteriosclerotic dementia (ICD-8 293.0; ICD-9 290.4)	18	5.8
6.	Other organic psychoses (non-alcoholic) (ICD-8 293.4, 299; ICD-9 294.0,.1,.8,.9)	21	6.8
7.	Alcoholic dementia (ICD-8, ICD-9; 291.1,291.2,291.9)	38	12.3
8.	Organic psychosyndrome of non-psychotic severity (ICD-8 309.6; ICD-9 310.1)	49	15.9
Secondary diagnosis only			
	Organic dementia (non-alcoholic) (i.e. groups 1-6 above)	19	6.1
	Alcoholic dementia (group 7)	12	3.9
	Organic psychosyndrome of non-psychotic severity (group 8)	6	1.9
	Total	309	100%

Table 11

Psychiatric Referents - Diagnoses

Main diagnosis only	N	%
Psychosis (not organic/alcoholic) ICD-8,9 (293-299)	158	51.1
Neurotic and personality disorders (ICD-8 300-306; ICD-9 300-307)	85	27.5
Acute reaction to stress and adjustment disorders (ICD-8 307; ICD-9 308-309)	35	11.3
Depressive disorders (ICD-9 311)	26	8.4
Disturbance of conduct (ICD-9 312)	5	1.6
Total	309	100%

Table 12

Distribution of potential confounders

	Cases	Referents		Overall
		Psychiatric	General Hospital	
% reporting				
Head trauma	17.1%	13.2%	10.1%	13.4%
N	234	235	247	716
Stroke	14.9%	5.3%	10.0%	10.1%
N	248	246	251	745
Alcohol - ever > 14 drinks/week	41.4%	29.9%	27.7%	33.3%
N	262	251	253	766
Alcohol - ever 'excess'	21.0%	13.9%	7.5%	14.2%
N	262	251	253	766
Lead - ever (at work)	9.4%	7.5%	8.3%	8.4%
N	266	252	254	772
Pesticides - ever (at work)	3.5%	8.7%	9.1%	7.0%
N	266	252	254	772
School leaving ≤ 14 years	52.1%	44.4%	46.3%	47.6%
N	238	239	240	717
Father's job 'low status'	31.0%	34.8%	32.4%	32.7%
N	236	233	238	707

Table 13

Head trauma, stroke, alcohol excess by diagnostic group

		Head trauma	Stroke	Excess Alcohol
Senile/pre-senile dementia DAT not specified; Group 1		18.5%	16.7%	10.0%
	N	54	60	60
Senile/pre-senile dementia DAT specified; Group 2		30.0%	4.5%	13.0%
	N	20	22	23
Neurological, cerebral degeneration; Group 3, 4		17.0%	15.1%	18.5%
	N	53	53	54
Arteriosclerotic dementia Group 5		7.1%	40.0%	6.7%
	N	14	15	15
Other (non alcoholic) dementia; Group 6		11.8%	27.7%	31.8%
	N	17	18	22
Alcoholic dementia Group 7		12.9%	0.0%	50.0%
	N	31	37	40
Non-psychotic organic syndrome; Group 8		17.8%	16.3%	16.7%
	N	45	43	48
Overall		17.1%	14.9%	21.0%
	N	234	248	262

Table 14

Exposure to solvents amongst cases and psychiatric referents

	Pairs with data	% exposed Cases	% exposed Referents	Discordant Pairs	Odds Ratio	90% CI
Exposure to level 2 or above for at least 10 yrs						
(i) **Individual ratings**						
All respondents	297	21.2%	15.2%	59/41	1.44	1.03-2.01
Subjects with long questionnaires	219	22.4%	16.4%	45/32	1.41	0.96-2.06
(ii) **Job matrix ratings**						
All respondents	300	10.7%	7.7%	31/22	1.41	0.89-2.23
Subjects with long questionnaires	219	9.6%	8.2%	20/17	1.18	0.68-2.02

Table 15a

Odds ratios by diagnosis for inclusion
= Exposure to level 2 or greater for at least 10 years

Exposure assessment from individual ratings

Diagnosis	No of pairs	Pairs with missing data	Discordant pairs	Odds ratios	90% CI
Senile or pre-senile dementia DAT not specified	72	2	14/13	1.1	0.6-2.0
Senile or pre-senile dementia DAT specified	25	0	3/1	3.0	0.4-20.1
Cerebral degeneration (Alzheimer or other)	61	1	12/8	1.5	0.7-3.2
Arteriosclerotic dementia	18	1	5/2	2.5	0.6-9.9
Other, non alcoholic, organic psychosis	28	2	7/6	1.2	0.5-2.9
Alcoholic dementia	50	4	11/3	3.7	1.3-10.7
Organic psycho-syndrome of non-psychotic severity	55	2	7/8	0.9	0.4-2.1
Overall	309	12	59/41	1.44	1.03-2.01

Table 15b

Odds ratios by diagnosis for inclusion
- exposure to level 2 or greater for at least 10 years

Exposure assessment from job title matrix

Diagnosis	No of pairs	Pairs with missing data	Discordant pairs	Odds ratios	90% CI
Senile or pre-senile dementia DAT not specified	72	1	7/5	1.4	0.5-3.7
Senile or pre-senile dementia DAT specified	25	0	2/1	2.0	0.3-15.0
Cerebral degeneration (Alzheimer or other)	61	0	7/3	2.3	0.7-7.3
Arteriosclerotic dementia	18	0	0/2	0.0	- -
Other, non alcoholic, organic psychosis	28	2	1/5	0.2	0.0-1.2
Alcoholic dementia	50	4	8/?	4.0	1.1-14.7
Organic psycho-syndrome of non-psychotic severity	55	2	6/4	1.5	0.5-4.3
Overall	309	9	31/22	1.41	0.89-2.23

Table 16a

Odds ratios by psychotic and alcohol related diagnoses - exposure to level 2 or greater for at least 10 years

Exposure assessment based on individual ratings

Diagnosis (to include)		Alcohol related diagnosis (1° or 2°)		
		No	Yes	Overall
Organic psychosis or cerebral degeneration				
	OR	1.20	5.33	1.58
	90% CI	0.80-1.80	1.90-15.01	1.09-2.27
	No of pairs	183	61	244
Organic syndrome -non psychotic				
	OR	1.50	0.25	0.88
	90% CI	0.52-4.34	0.04-1.57	0.37-2.05
	No of pairs	44	9	53
Overall	OR	1.24	2.43	1.44
	90% CI	0.85-1.81	1.16-5.08	1.03-2.01
	No of pairs	227	70	297

Table 16b

Odds ratio by psychotic and alcohol related diagnoses - exposure to level 2 or greater for at least 10 years

Exposure assessment based on job title exposure matrix

Diagnosis (to include)		Alcohol related diagnosis (1° or 2°)		
		No	Yes	Overall
Organic psychosis or cerebral degeneration				
	OR	0.88	5.50	1.39
	90% CI	0.48-1.60	1.59-19.48	0.84-2.31
	No of pairs	185	62	247
Organic syndrome -non psychotic				
	OR	1.67	1.0	1.50
	90% CI	0.50-5.54	0.10-10.25	0.52-4.30
	No of pairs	44	9	53
Overall	OR	1.00	4.00	1.41
	90% CI	0.59-1.71	1.38-11.57	0.89-2.23
	No of pairs	229	71	300

Table 17

Exposure to solvent amongst cases and general hospital referents

	Pairs with data	% exposed Cases	% exposed Referents	Discordant Pairs	Odds Ratio	90% CI
Exposure to level 2 or above for at least 10 yrs						
(i) **Individual ratings**						
All respondents	287	22.3%	20.9%	45/41	1.10	0.77-1.57
Subjects with long questionnaires	221	22.2%	23.1%	31/33	0.94	0.62-1.42
(ii) **Job matrix ratings**						
All respondents	292	11.3%	7.5%	30/19	1.58	0.97-2.56
Subjects with long questionnaires	221	10.9%	7.7%	23/16	1.43	0.84-2.46

Table 18a

Odds ratio by psychotic and alcohol related diagnoses - exposure to level 2 or greater for at least 10 years

Exposure assessment based on individual ratings

General Hospital Referents

Diagnosis (to include)		Alcohol related diagnosis (1° or 2°)		
		No	Yes	Overall
Organic psychosis or cerebral degeneration				
	OR	0.87	2.0	1.08
	90% CI	0.56-1.35	0.93-4.28	0.74-1.57
	No of pairs	179	60	239
Organic syndrome -non psychotic				
	OR	1.25	-	1.25
	90% CI	0.41-3.77	-	0.41-3.77
	No of pairs	41	7	48
Overall	OR	0.91	2.0	1.10
	90% CI	0.61-1.37	0.93-4.28	0.77-1.57
	No of pairs	220	67	287

Table 18b

Odds ratio by psychotic and alcohol related diagnoses - exposure to level 2 or greater for at least 10 years

General Hospital Referents

Exposure matrix based on job title exposure matrix

Diagnosis (to include)		Alcohol related diagnosis (1° or 2°)		
		No	Yes	Overall
Organic psychosis or cerebral degeneration				
	OR	1.08	5.0	1.60
	90% CI	0.57-2.03	1.40-17.88	0.93-2.75
	No of pairs	183	60	243
Organic syndrome -non psychotic				
	OR	1.25	-*	1.50
	90% CI	0.42-3.77	-	0.52-4.34
	No of pairs	42	7	49
Overall	OR	1.12	5.50	1.58
	90% CI	0.64-1.94	1.55-19.48	0.97-2.56
	No of pairs	225	67	292

* did not converge; discordant pairs 1/0

Table 19a

Reported alcohol consumption by exposure to solvents among cases

1) Individual ratings by exposure

Maximum reported weekly consumption of alcoholic drinks

Exposure to solvents for at least 10 years	None	< 14	≥14<42	'excess'	Total %	N
Not exposed	36.3%	22.1%	21.1%	20.6%	100%	204
Exposed	32.8%	24.1%	20.7%	22.4%	100%	58
Total	35.5%	22.5%	21.0%	21.0%	100%	262

2) Job matrix ratings of exposure

Maximum reported weekly consumption of alcoholic drinks

Exposure to solvents for at least 10 years	None	< 14	≥14<42	'excess'	Total %	N
Not exposed	35.7%	23.0%	21.3%	20.0%	100%	235
Exposed	33.3%	18.5%	18.5%	29.6%	100%	27
Total	35.5%	22.5%	21.0%	21.0%	100%	262

Table 19b

Reported alcohol consumption by exposure to solvents among psychiatric referents

1) Individual ratings by exposure

Maximum reported weekly consumption of alcoholic drinks

Exposure to solvents for at least 10 years	None	< 14	≥14<42	'excess'	Total %	N
Not exposed	45.4%	24.6%	15.9%	14.0%	100%	207
Exposed	50.0%	20.5%	15.9%	13.6%	100%	44
Total	46.2%	23.9%	15.9%	13.9%	100%	251

2) Job matrix ratings of exposure

Maximum reported weekly consumption of alcoholic drinks

Exposure to solvents for at least 10 years	None	< 14	≥14<42	'excess'	Total %	N
Not exposed	48.3%	22.2%	15.2%	14.4%	100%	230
Exposed	23.8%	42.9%	23.8%	9.5%	100%	21
Total	46.2%	23.9%	15.9%	13.9%	100%	251

Table 20

Exposure to solvents: Odds ratio stratified by drinking habits reported by case

	No of pairs	Discordant pairs	Odds ratio	90% CI
(1) Individual ratings				
Always drank < 1 drink/week	74	14/9	1.56	0.77-3.14
At most drank < 14/week	50	12/11	1.09	0.55-2.17
At most drank ≥ 14 < 42/week	47	9/9	1.00	0.46-2.17
At most drank ≥ 42 week or "excess"	43	9/3	3.00	1.00-8.98
Overall	214	44/32	1.38	0.94-2.02
(2) Job matrix ratings				
Always drank < 1 drink/week	74	6/6	1.00	0.39-2.59
At most drank < 14/week	50	4/5	0.80	0.27-2.41
At most drank ≥ 14 < 42/week	47	4/4	1.00	0.31-3.20
At most drank ≥ 42/week or "excess"	43	6/2	3.00	0.78-11.49
Overall	214	20/17	1.18	0.68-2.02

Table 21

Odds ratios by exposure and excess alcohol consumption - unmatched analysis from Table 19 (approximate 90% CI)

(a) Individual ratings of exposure

Alcohol consumption	Not exposed	Exposed
Never "excess"	1.00	1.30 (0.87-1.94)
"Excess"	1.59 (1.03-2.45)	2.38 (1.06-5.33)

(b) Job matrix ratings of exposure

Alcohol consumption	Not exposed	Exposed
Never "excess"	1.00	1.05 (0.59-1.88)
"Excess"	1.49 (0.99-2.24)	4.19 (1.25-14.03)

Table 22

Time pattern of drinking and exposure

Subjects who at some point drank more than 14 drinks/week and were exposed to level 2 or more for at least 10 years (individual ratings)

Began drinking	Cases	Psychiatric Referents
	N	N
At least 5 years before first exposure	4	1
Within 5 years of first exposure	4	4
At least 5 years after first exposure	15	6
Information incomplete	2	2
	25	13

Table 23

Mean years from starting drinking to hospital admission by exposure to level 2 or above for at least 10 years

- men reporting excess drinking

(1) Individual ratings

	Not exposed to solvents			Exposed				
	Mean	SD	N	Mean	SD	N	t-test	p <
Cases	32.3	12.3	37	27.6	12.4	12	1.14	NS
Referents	30.1	9.4	25	34.9	15.5	5	0.92	NS

(2) Job matrix ratings

Cases	32.1	11.9	41	25.9	14.0	8	1.32	NS
Referents	31.0	10.5	28	30.2	14.8	2	0.11	NS

Table 24

Odds ratio for selected potential confounders: all pairs with data

	No of pairs	OR	90% CI
Head trauma	184	1.56	0.95-2.56
Stroke	200	3.33	1.78-6.23
Lead - ever (at work)	219	1.50	0.81-2.77
Pesticide - ever (at work)	219	0.45	0.23-0.87
School leaving ≤ 14 years	187	1.15	0.83-1.57
Father's job 'low status'	180	1.05	0.73-1.51

Table 25

Odds ratios for exposure, allowing for potential confounders other than alcohol consumption. Logistic regression analysis (N of pairs = 139)

	Exposure ratings			
	Individual		Job matrix	
	OR	90% CI	OR	90% CI
Head trauma	1.65	0.90-3.03	1.66	0.90-3.04
Stroke	2.44	1.12-4.87	2.41	1.21-4.81
Lead exposure	1.53	0.64-3.62	1.58	0.67-3.74
Pesticide exposure	0.42	0.20-0.88	0.43	0.21-0.89
School leaving	1.13	0.75-1.70	1.14	0.76-1.72
Father's job status	1.07	0.68-1.68	1.09	0.69-1.70
Exposure to solvents	1.24	0.75-2.05	1.07	0.53-2.15

Table 26

Odds ratio for selected potential confounders: pairs in which the case has both an organic psychosis and an alcohol related diagnosis

	No of pairs	OR	90% CI
Head trauma	30	3.00	0.78-11.49
Stroke	35	0.50	0.67-3.75
Lead - ever (at work)	42	1.25	0.41-3.77
Pesticide - ever (at work)	42	0.25	0.04-1.57
School leaving ≤ 14 years	38	1.17	0.61-2.23
Father's job 'low status'	36	1.00	0.46-2.17

Table 27

Odds ratios for exposure, allowing for head injury and pesticide exposure; pairs in which the case has both an organic psychosis and an alcohol related diagnosis.
Logistic regression analysis (N of pairs = 25)

	Exposure ratings			
	Individual		Job matrix	
	OR	90% CI	OR	90% CI
Head trauma	2.57	0.64-10.28	3.20	0.73-14.10
Stroke	0.86	0.10-7.34	0.42	0.06-2.92
Exposure to solvents	5.20	0.79-34.19	5.76	0.87-38.19

Table 28a

Mean estimated cumulative solvent exposure; matched pair comparisons

	N of pairs	Mean Cases	Mean Psychiatric referents	t	p (1 tailed)
1. Individual exposure estimates					
Years weighted by intensity	291	20.8	17.7	1.3	p<.10
Years weighted by intensity and proportion of working week	291	4.8	3.4	1.7	p<.05
2. Exposure estimates based on job title matrix					
Years weighted by intensity	292	13.2	9.7	1.9	p<.05
Years weighted by intensity (0/1-3/3) and proportion of working week	281	11.1	7.8	1.4	p<.10

Table 28b

Mean log estimated cumulative solvent exposure; matched pair comparisons

	N of pairs	Mean Cases	Mean Psychiatric referents	t	p (1 tailed)
1. Individual exposure estimates					
Log years weighted by intensity	291	0.5	0.2	1.4	p<.10
Log years weighted by intensity and proportion of working week	291	-0.6	-1.0	1.9	p<.05
2. Exposure estimates based on job title matrix					
Log years weighted by intensity	292	-0.3	-0.8	2.1	p<.05
Log years weighted by intensity (0/1-3/3) and proportion of working week	281	0.2	-0.2	2.1	p<.05

Table 29

Job history assessments; individual ratings compared with international assessors

Exposure for at least 10 years to level 2 or more (individual ratings)	Number of assessors judging exposure 'significant'*				
	0	1	2	3	Total
Yes	60	30	7	20	117
No	73	5	0	1	79
Total	133	35	7	21	196

*i.e. might conceivably cause an organic brain syndrome

Table 30

Treatment of alcohol/alcoholism in previous analyses

A) Case referent		Diagnoses include: Alcoholism	Alc. Dementia	Info. on alc. intake	Comments
Axelson et al.	1976	Yes	No	No	Analysis with/without alcoholism
Olsen and Sabroe	1980	Yes	Yes	Yes	Odds ratios adjusted for alcohol intake
Lindstrom et al.	1984	Yes	No	No	Odds ratio calculated for alcoholics
Rasmussen et al.	1985	No	Yes	Yes	Odds ratio calculated with/without alcoholism
O'Flynn et al.	1987	No	No	No	-
Shalat et al.	1988	No	No	No	Cases excluded if evidence of alcohol excess
van Vliet et al.	subm.	Yes	No	Yes	Odds ratio adjusted for alcohol intake
Brackbill et al.	subm.	Yes	Yes	No	Odds ratio calculated for alcoholism
B) Cohort studies					
Mikkelsen	1980	Yes	Yes	No	RR calculated for dementia with/without cause (e.g. alcohol)
Guberan et al.	1989	Yes	Yes	No	'Exposure confounded with alcoholism'
C) Prevalence studies					
Cherry & Waldron	1984	Yes	Yes	No	No separate analysis
Mikkelsen et al.	1988	No	No	Yes	Analysis adjusted for alcohol consumption

ANNEXES

Annex 1	Hospital extraction form
Annex 2	Initial contact letter
Annex 3	Short questionnaire - self-completed
Annex 4	Full questionnaire - completed by interviewer

ANNEX 1 - HOSPITAL EXTRACTION FORM

No dossier médical _____ No d'identification ☐☐☐☐☐

Nom de l'hôpital _____ ☐ Homme ☐ 40-69 ans ☐ 5 jours + ☐ 1ère admission ☐ Diagnostic final ☐ Dx associé

Adresse _____

Cas-étude A ☐
étude B ☐
Témoin-étude A ☐
étude B ☐

Cas et témoins hospitaliers

Informations extraites du dossier médical

Nom du patient _____ Date de naissance |___|___|___|
(Apparié à.) An Mois Jour

Adresse à la 1ère admission _____ Tél : (___) ___-____

_____

Langue maternelle: ☐ français ☐ anglais ☐ autre

1ère admission: |___|___|___| An Mois Jour Radiation: |___|___|___| An Mois Jour

Destination au congé: ☐ Domicile
☐ Autre _____

Diagnostic - final au congé (ou actuel): _____ ☐☐☐.☐

(CIM-) - secondaires _____ ☐☐☐.☐

_____ ☐☐☐.☐

_____ ☐☐☐.☐

Nom du (des) médecin(s) traitant(s): _____

Occupation habituelle mentionnée.
feuille d'admission oui ↓ non anamnèse / notes infirmières ↓

Poste _____ _____

_____ _____

Consommation d'alcool: _____

Hospitalisations subséquentes: ☐ Aucune au même endroit

2ème admission |___|___|___| An Mois Jour Radiation. |___|___|___| An Mois Jour

3ème admission |___|___|___| An Mois Jour Radiation |___|___|___| An Mois Jour

4ème admission: |___|___|___| An Mois Jour Radiation. |___|___|___| An Mois Jour

5ème admission: |___|___|___| An Mois Jour Radiation |___|___|___| An Mois Jour

Autres remarques pouvant servir à retracer le sujet:

Adresse la plus récente _____ Tél : (___) ___-____

_____

Autre(s) contact(s) Nom _____ Tél : (___) ___-____

Adresse _____

Lien avec le sujet _____

Nom: _____ Tél : (___) ___-____

Adresse _____

Lien avec le sujet _____

Autres remarques _____

_____

_____

_____

_____

Informations extraites le _____ par _____

ANNEX 2 - INITIAL CONTACT LETTER

McGill University

School of Occupational Health
Ecole de Santé au Travail
Charles Meredith House (514) 392-4568

Dear Sir,

A research team of McGill University is carrying out a survey on health and occupation. The purpose of this study is to look at the work history of people and find out if some occupational exposures are related to certain health problems.

Your name has been chosen, using scientific methods of sampling, from hospital listings. Your participation in this study is very important; however, your collaboration is entirely voluntary.

In a few days, a member of our team will telephone and ask you to answer a 15-30 minute questionnaire. Most of the questions will be about the kinds of work you have done since leaving school, but there will also be some questions about hobbies, lifestyle, and health. If the interviewer calls when you are busy, please do not hesitate to suggest another time so that the questionnaire can be completed in the most convenient manner for you. The information that will be collected is entirely confidential and only an identification number will appear on the questionnaire itself.

We hope that you will be able to spare the amount of time required to answer this questionnaire If you have any question on the study, you can talk to one of the team at 392-8932.

Yours sincerely,

Si vous désirez les informations en français, s.v.p. téléphonez à 392-8932.

Postal address 1130 Pine Avenue West, Montreal, PQ, Canada H3A 1A3

ANNEX 3 - SHORT QUESTIONNAIRE - SELF-COMPLETED

McGill University

Identification number ☐☐☐☐☐

Date questionnaire is completed _____

Day Month Year

STUDY ON OCCUPATION AND HEALTH

For this study, it is very important for us to know about your jobs. Could you spare a few minutes to answer the questions on this side and send us back this questionnaire in the self-addressed envelope. If you have a few more moments, please turn over and complete the back of this sheet.

1. We believe your present age to be ____ years. Is it correct? _____

   Could you give us your date of birth? _____

   Day Month Year

2. What was your main job during most of your working life? _____

   _____

3. How old were you when you started your first full-time job? _____ years old.

4. In the course of any of your jobs, were you exposed to (i.e. handle, breathe or swallow) any of the following chemical substances? If yes, what year did this start, and for how many years did it last?

   - Glues or adhesive substances ☐ No ☐ Yes → started in 19___, for ___ years.
   - Lead ☐ No ☐ Yes → started in 19___, for ___ years.
   - Gasoline, oils ☐ No ☐ Yes → started in 19___, for ___ years.
   - Paints, varnishes, dyes ☐ No ☐ Yes → started in 19___, for ___ years.
   - Solvents, alcohols ☐ No ☐ Yes → started in 19___, for ___ years.
   - Pesticides, herbicides ☐ No ☐ Yes → started in 19___, for ___ years.
   - Metal cleaners, or degreasers ☐ No ☐ Yes → started in 19___, for ___ years.
   - Other chemical substances ☐ No ☐ Yes → started in 19___, for ___ years.
     - If yes, which one(s)? _____

5. Please list below all the jobs you have held for one year or more since you finished school. If more than 5 jobs, please start with those you held for the longest time.

	What type of company was it?	What was your job title?	Can you briefly describe what you did in this job?	When did you start this job? For how many years did you do it?
A				From 19__ to 19__ For _____ years _____ hours/week
B				From 19__ to 19__ For _____ years _____ hours/week
C				From 19__ to 19__ For _____ years _____ hours/week
D				From 19__ to 19__ For _____ years _____ hours/week
E				From 19__ to 19__ For _____ years _____ hours/week

6. Do you think that any of your jobs has affected your health? If so, please explain _____

_____

_____

_____

THANK YOU FOR YOUR HELP WITH THIS STUDY.

McGill University

Je vous ai téléphoné il y a quelques semaines, au sujet de notre important projet médical concernant les effets du travail sur la santé. Malheureusement, vous étiez trop occupé à ce moment pour nous parler de votre travail. Tout ce que nous désirons vraiment savoir est quels ont été vos principaux emplois et si, au cours de votre travail, vous avez souvent été exposé à des vapeurs de colles, de peintures, de vernis, de solvants ou de dégraisseurs. Si vous pouviez nous faire connaître la réponse à ces deux questions, ceci contribuerait énormément à notre recherche et nous vous en serions très reconnaissants.

Bien vôtre,

Donna Amyot, infirmière
Assistante de recherche
No. tél.: 392-8932

Répondez simplement aux deux questions ci-après et retournez-nous cette feuille dans l'enveloppe adressée et timbrée ci-jointe. Lorsque nous recevrons votre réponse, nous serons heureux de vous faire parvenir $ 10.00 pour vos frais.

Mes principaux emplois ont été: _____

_____

Ces emplois m'ont souvent exposé à des: [Si oui, cochez s.v.p.: ✓]

colles/ adhésifs ___

peintures/ vernis/ teintures ___

solvants/ alcools ___

nettoyeurs à métal/ dégraisseurs ___

Ou si à aucune de ces substances, cochez ici ___

Signé: _____

P.S. Si vous accepteriez de répondre à quelques autres questions sur vos emplois, veuillez cocher ici pour indiquer si vous préférez le faire par la poste ___, ou au téléphone (au no. ___ - ___) ___.

ANNEX 4 - FULL QUESTIONNAIRE - COMPLETED BY INTERVIEWER

McGill University
School of Occupational Health

Identification number ☐☐☐☐☐

Date of Interview _____

Beginning ____ ___h End____ ___h

Length of interview ☐☐☐ min.

Study on occupation and mental health

A. GENERAL INFORMATION

1. a) I would first like to make sure that I am speaking to the right person I have here that your age is ____ years. Is that correct? ☐ Does not know

b) Can you give me your date of birth ___ ___ ___ (D M YR) ☐ Does not know

[Date of birth given by 1 Subject 2 Other]

I would now like to ask you a few general questions.

2. Were you born in Canada? a) Yes —> Was this to an anglophone family?
   1 Francophone
   2 Anglophone
   3 Other (specify) _____
   b) No —> If not, where were you born? _____
   c) —> What year did you come to Canada? 19____

3. a) Can you remember what your father or guardian's job was when you were a child? (What type of work did he do?)
   1 yes (specify) _____
   7 female parent or guardian
   8 does not know
   9 refusal

   b) Can you remember what type of company he worked for? (What did they do?)
   1 yes _____
   7 female parent or guardian
   8 does not know
   9 refusal

4. a) At what age did you leave primary school _____ Years

   b) Did you go on to secondary school?
   1 yes —> at what age did you leave it? _____ Years
   2 no —> (GO TO QUESTION 4d)

   c) After secondary school, did you go on to college, university or other studies?
   1 yes —> When was this? 19___ to 19___
   Was it full-time ☐, or part-time ☐ ?
   2 no

   d) Did you receive any technical training or a trade course?
   1 yes: _____ When was this? 19___ to 19___
   Was it full-time ☐, or part-time ☐?
   2 no

Check approximate year ended full time schooling: 19____

B. OCCUPATIONAL HISTORY

Now I would like to know some details about every job you held since you finished school in 19____, starting with the first and going up to the present day.

5. What type of company were you working for? In what city was it located? Do you remember its name?	6. Did you have more than one job with this company?	7. Can you describe to me in a few sentences, what you did in this job? (during a typical work day/week)	8. When did you start this job? When did you finish it?
Type of Co.: _____ _____ City (Location) _____ _____ Name of Co. _____ _____ A)	Title (starting by the first) _____ _____ _____ Other job : If yes →	_____ _____ _____ _____ _____ _____	From 19___ To 19___ ____ mths /yrs. [ ] Full-time [ ] Part time ____h/wk.
Type of Co.: _____ _____ City (Location) _____ _____ Name of Co.: _____ _____ B)	Title: _____ _____ _____ Other job If yes →	_____ _____ _____ _____ _____ _____	From 19 __ To 19_ ____ mths./yrs. [ ] Full-time [ ] Part-time ____h/wk.
Type of Co. _____ _____ City (Location) _____ _____ Name of Co. _____ _____ C)	Title _____ _____ _____ Other job If yes →	_____ _____ _____ _____ _____ _____	From 19 __ To 19 __ ____ mths./yrs. [ ] Full-time [ ] Part-time ____h/wk.
Type of Co. _____ _____ City (Location) _____ _____ Name of Co.: _____ _____ D)	Title _____ _____ _____ Other job If yes →	_____ _____ _____ _____ _____ _____	From 19___ To 19___ ____mths./yrs. [ ] Full-time [ ] Part-time ____h/wk.
Type of Co. _____ _____ City (Location): _____ _____ Name of Co. _____ _____ E)	Title _____ _____ _____ Other job If yes —> Page 4	_____ _____ _____ _____ _____ _____	From 19___ To 19___ ____mths /yrs [ ] Full-time [ ] Part-time ____h/wk.

Now I would like to ask some questions about your exposure to chemicals and similar substances in the course of your work. This question is very important to the study, so I hope you will be able to give us the details we need for <u>each</u> of your jobs. It should not take too long.

12. In the course of your normal work, did you handle, inhale or ingest any of the following substances?

	(a) Glues	(b) Plastic or Rubber Fumes	(c) Lead	(d) Gasoline Oils	(e) Paints Lacquers Dyes	(f) Solvents Alcohols	(g) Pesticides or Herbicides	(h) Metal Cleaners or Degreasers
Yes	1	1	1	1	1	1	1	1
No	2	2	2	2	2	2	2	2
Doesn't know	8	8	8	8	8	8	8	8

Specify _____

A)

Yes	1	1	1	1	1	1	1	1
No	2	2	2	2	2	2	2	2
Doesn't know	8	8	8	8	8	8	8	8

Specify _____

B)

Yes	1	1	1	1	1	1	1	1
No	2	2	2	2	2	2	2	2
Doesn't know	8	8	8	8	8	8	8	8

Specify _____

C)

Yes	1	1	1	1	1	1	1	1
No	2	2	2	2	2	2	2	2
Doesn't know	8	8	8	8	8	8	8	8

Specify _____

D)

Yes	1	1	1	1	1	1	1	1
No	2	2	2	2	2	2	2	2
Doesn't know	8	8	8	8	8	8	8	8

Specify _____

E)

Examples
Glues Industrial adhesives, rubber or spirit based glues, epoxy.
Solvents Acetone, carbone tetrachloride, varsol, mineral spirits, methanol
Cleaners or degreasers Trichlorethylene or products such as "cleaning fluid" or "neutri".

9 During these years, did you ever stop working for 6 months or more for other reasons like strikes, military service, etc.?

1 yes a) in 19____ for ____ mths./yrs.
because of _____
b) in 19____ for ____ mths./yrs.
because of _____
c) in 19____ for ____ mths./yrs.
because of _____

2 no, never
8 does not know
9 refusal

10. During these working years, did you ever hold a part-time job along with your main job?

1 yes a) in 19____ for ____ mths./yrs.
work _____ ____hrs./week
b) in 19____ for ____ mths./yrs.
work _____ ____hrs./week
c) in 19____ for ____ mths./yrs.
work _____ ____hrs./week

2 no
8 does not know
9 refusal

11. Since you have been working, did you ever hold a job where you were regularly laid off for several months each year?

1 yes a) in 19____ for ____ mths./yrs.
work _____
b) in 19____ for ____ mths./yrs.
work _____
c) in 19____ for ____ mths./yrs.
work _____

2 no
8 does not know
9 refusal

11A. Check
Last day at work
_____month _____year

5a) What type of company were you working for? In what city was it located? Do you remember its name?	6a). Did you have more than one job with this company?	7a). Can you describe to me in a few sentences, what you did in this job? (during a typical work day/week)	8a) When did you start this job? When did you finish it?
Type of Co _____ _____ City (Location) _____ _____ Name of Co _____ _____ F)	Title (starting by the first) _____ _____ _____ Other job If yes →		From 19 __ To 19___ ____ mths, yrs [ ] Full time [ ] Part time ___ h/wk.
Type of Co. _____ _____ City (Location) _____ _____ Name of Co. _____ _____ G)	Title _____ _____ _____ Other job If yes →		From 19 __ To 19___ ____ mths./yrs. [ ] Full-time [ ] Part-time ____ h/wk.
Type of Co. _____ _____ City (Location) _____ _____ Name of Co. _____ _____ H)	Title _____ _____ _____ Other job If yes →		From 19 ___ To 19__ ___ mths./yrs [ ] Full-time [ ] Part-time ___ h/wk.
Type of Co. _____ _____ City (Location) _____ _____ Name of Co. _____ _____ I)	Title _____ _____ _____ Other job If yes →		From 19 ___ To 19__ ____ mths./yrs. [ ] Full time [ ] Part-time ___ h/wk.
Type of Co. _____ _____ City (Location) _____ _____ Name of Co. _____ _____ J)	Title _____ _____ _____ Other job If yes → Check and use additional [ ] sheet		From 19 __ To 19__ ____ mths./yrs. [ ] Full time [ ] Part time ____ h/wk.

12a) In the course of your normal work, did you handle, inhale or ingest any of the following substances?

	(a) Glues	(b) Plastic or Rubber Fumes	(c) Lead	(d) Gasoline Oils	(e) Paints Varnishes Dyes	(f) Solvents Alcohols	(g) Pesticides or Herbicides	(h) Metal Cleaners or Degreasers
Yes	1	1	1	1	1	1	1	1
No	2	2	2	2	2	2	2	2
Doesn't know	8	8	8	8	8	8	8	8

Specify _____

F)

Yes	1	1	1	1	1	1	1	1
No	2	2	2	2	2	2	2	2
Doesn't know	8	8	8	8	8	8	8	8

Specify _____

G)

Yes	1	1	1	1	1	1	1	1
No	2	2	2	2	2	2	2	2
Doesn't know	8	8	8	8	8	8	8	8

Specify _____

H)

Yes	1	1	1	1	1	1	1	1
No	2	2	2	2	2	2	2	2
Doesn't know	8	8	8	8	8	8	8	8

Specify _____

I)

Yes	1	1	1	1	1	1	1	1
No	2	2	2	2	2	2	2	2
Doesn't know	8	8	8	8	8	8	8	8

Specify _____

J)

13. During all these years at work, did 5 you ever stop working for 5 months or more because of health-related problems (accident, illness, etc.)?

1 yes a) in 19___ for ___ mths/yrs.
because of _____
b) in 19___ for ___ mths/yrs.
because of _____
c) in 19___ for ___ mths/yrs.
because of _____

2 no, never

8 does not know

9 refusal

11A. Check
Last day at work
_____month _____year

I would now like to check with you some types of jobs and activities which are particularly important in our study.

14. Whether at work, at home or anywhere else were you ever involved in		15. Was this as part of your job? If no, specify.	16. When was that? (In what years?)	17. How many hours a week were you doing this?
a) Cabinet making or wood working	1 yes 2 no	1 yes 2 no _____	from 19__ to 19__ from 19__ to 19__	____h/week ____h/week
b) Diesel engine operation	1 yes 2 no	1 yes 2 no _____	from 19__ to 19__ from 19__ to 19__	____h/week ____h/week
c) Machine or engine maintenance	1 yes 2 no	1 yes 2 no _____	from 19__ to 19__ from 19__ to 19__	____h/week ____h/week
d) House painting, paid by someone else	1 yes 2 no	1 yes 2 no _____	from 19__ to 19__ from 19__ to 19__	____h/week ____h/week
e) Dry cleaning	1 yes 2 no	1 yes 2 no _____	from 19__ to 19__ from 19__ to 19__	____h/week ____h/week
f) Manufacturing of fibre glass boats	1 yes 2 no	1 yes 2 no _____	from 19__ to 19__ from 19__ to 19__	____h/week ____h/week
g) Fur or leather processing, stuffing animals	1 yes 2 no	1 yes 2 no _____	from 19__ to 19__ from 19__ to 19__	____h/week ____h/week
h) Spraying of trees or weeds	1 yes 2 no	1 yes 2 no _____	from 19__ to 19__ from 19__ to 19__	____h/week ____h/week
i) Processing of photographs	1 yes 2 no	1 yes 2 no _____	from 19__ to 19__ from 19__ to 19__	____h/week ____h/week
j) Printing (textile, paper)	1 yes 2 no	1 yes 2 no _____	from 19__ to 19__ from 19__ to 19__	____h/week ____h/week

C. HOBBIES

18a. During your adult life, did you have any practical hobby that involved the use of paints ☐, glues ☐, solvents ☐, cleaners ☐, or other similar products? _____

1 yes 2 no 8 does not know 9 refusal

18b. What was the hobby?	18c. The chemical product?		
1) _____	1) _____	From 19__ to 19__	____h/week
2) _____	2) _____	From 19__ to 19__	____h/week
3) _____	3) _____	From 19__ to 19__	____h/week

D. PERSONAL HABITS

Here are a few questions on smoking and drinking habits

19.a) Have you ever smoked cigarettes regularly?

1 yes 2 no (—> Q 20)

b) Do you still smoke?

1 yes 2 no ——————> stopped _____ year(s) ago.

c) On average, how many cigarettes do (did) you smoke a day? _____ cig./day

20 a) Have you ever drunk beer, cider, wine or alcohol regularly, that is once a week or more?

1 yes 2 no 8 does not know 9 refusal

		Beer/Cider	Wine	Alcohol (Spirits)
b)	During the last 10 years or so, did you drink beer, cider, wine or alcohol once a week or more?	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
c)	If yes —> How many bottles/glasses did you drink approximately on average each week? No ⌐	_____ bottles per week	_____ glasses per week	_____ glasses per week
d)	For how many years have you been drinking (did you drink) approximately this amount?	_____ years	_____ years	_____ years
e)	Since you were 21 years old, was there there ever a time when you drank much more?	1 yes 2 no 8 does not know 9 refusal	1 yes 2 no 8 does not know 9 refusal	1 yes 2 no 8 does not know 9 refusal
f)	What age were you when you started to drink more?	_____ years	_____ years	_____ years
g)	How much did you drink then?	_____ bottles per week	_____ glasses per week	_____ glasses per week
h)	For how long?	_____ years	_____ years	_____ years

Comments on alcohol consumption history _____

E. MEDICAL HISTORY

I will finish by asking you about some ailments or diseases that you may have had.

21. Has a doctor ever told you that you had		22. What treatment did you receive for this problem?	23. In what year was this?
a) Meningitis or infection of the brain	1 yes 2 no	_____ ☐ none ☐ does not know	in 19____
b) Convulsions			
1. as an infant	1 yes 2 no	_____ ☐ none ☐ does not know	in 19____
2. as a child	1 yes 2 no	_____ ☐ none ☐ does not know	in 19____
3. since then	1 yes 2 no	_____ ☐ none ☐ does not know	in 19____
c) A head injury with loss of consciousness	1 yes 2 no	_____ ☐ none ☐ does not know	in 19____
d) Stroke or other illness of that kind	1 yes 2 no	_____ ☐ none ☐ does not know	in 19____

24. Since you were 21 years old, have you ever been hospitalized?

1 yes 2 no 8 does not know 9 refusal

a) When? _____ What was the medical problem? _____

b) When? _____ Medical problem _____

d) When? _____ Medical problem _____

d) When? _____ Medical problem _____

25. Finally, do you think that any of your jobs has affected your health?

This ends the questionnaire. Thank you very much for the time you took for this interview. Your cooperation in this study will be very useful. You can be assured that all information obtained from this questionnaire will be kept strictly confidential. If ever we need additional information, can we call you? ☐ Yes ☐ No

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F. INTERVIEWER'S REMARKS

1) - Persons who gave information (Relationship with subject)

2) - Type of interview:
1 - Telephone/home
2 - Telephone/hospital
3 - Personal/home
4 - Personal/hospital
5 - Other _____

3) - Language of interview
1 - French
2 - English

4) - Was the cooperation of person interviewed:
1 - very good 2 - good 3 - fair 4 - poor

5) - Interview seems:
1 - very reliable 2 - reliable
3 - questionable 4 - unreliable

6) - Other comments (problems, etc.)

7) ☐ The subject revealed where he was hospitalized before Question 24
☐ The interviewer thinks she knows the subject status (case or referant)
☐ The interviewer has no idea of the subject status

Interviewer's initials ☐☐