Multiple sclerosis in nurse anaesthetists

U Flodin, A-M Landtblom, O Axelson

Background: Volatile anaesthetics are chemically related to organic solvents used in industry. Exposure to industrial solvents may increase the incidence of multiple sclerosis (MS).

Aim: To examine the risk among nurse anaesthetists of contracting MS.

Methods: Nurses with MS were identified by an appeal in the monthly magazine of the Swedish Nurse Union and a magazine of the Neurological Patients Association in Sweden. Ninety nurses with MS responded and contacted our clinic. They were given a questionnaire, which was filled in by 85 subjects; 13 of these were nurse anaesthetists. The questionnaire requested information about work tasks, exposure, diagnosis, symptoms, and year. The number of active nurse anaesthetists was estimated based on information from the National Board of Health and Welfare and The Nurse Union. Incidence data for women in the region of Gothenburg and Denmark were used as the reference to estimate the risk by calculation of the standardised incidence ratio (SIR).

Results: Eleven of the 13 nurse anaesthetists were exposed to anaesthetic gases before onset of MS. Mean duration of exposure before diagnosis was 14.4 years (range 4–27 years). Ten cases were diagnosed in the study period 1980–99, resulting in significantly increased SIRs of 2.9 and 2.8 with the Gothenburg and the Danish reference data, respectively.

Conclusion: Although based on crude data and a somewhat approximate analysis, this study provides preliminary evidence for an excess risk of MS in nurse anaesthetists. The risk may be even greater than observed, as the case ascertainment might have been incomplete because of the crude method applied. Further studies in this respect are clearly required to more definitely assess the risk.
women in the Gothenburg region in Sweden and from the Danish population of women as the references. The Gothenburg material is the largest dataset on incidence of MS in Sweden and consists of 253 patients diagnosed as probable or definite MS in 1950–64 in a population at about 400 000 individuals. These incidence rates are the highest ever published in Sweden. Through personal communication (O Andersen) we obtained data on which the graphs presented in the article were based. For comparison we also used incidence rates from the Danish Multiple Sclerosis Registry, which includes some 10 000 probable and definite cases of MS among women collected from 1950 to 1989. Again, the underlying numbers relating to the paper were obtained through personal communication (N Koch-Henriksen).

In calculating SIRs, we first estimated approximately the person-years of the nurse anaesthetists for the age categories 20–29, 30–39, 40–49, and 50–59 years by assuming the age distribution for 1985 to be representative for the 1980s and that of 1995 for the 1990s, respectively, and then multiplied the number of subjects in each age category by 10 years in order to obtain an approximate number of person-years under observation. The expected number of MS cases by age category was then calculated by multiplying the person-years of the nurse anaesthetists by the incidence rates of the Gothenburg and the Danish material per age group. The observed number of cases was then divided by the expected number of cases as summarised over the age categories in order to obtain the SIR. Confidence limits were calculated based on Poisson distribution.

### RESULTS

Thirteen nurse anaesthetists cases were identified. Seven of these were diagnosed in the 1990s, four during the 1980s, and two during the 1970s. The first symptoms of MS occurred in the 1990s in five subjects, in the 1980s in another five, and in the 1970s in the other three individuals. Two nurses were diagnosed with MS prior to exposure as nurse anaesthetists and were therefore excluded.

For the remaining 11 nurses, mean age at diagnosis was 43.5 years (range 32–54 years). Mean age at the start of symptoms was 40.6 years (range 29–54 years). Mean duration of exposure prior to diagnosis was 14.4 years (range 4–27 years). Considering exposure before the start of symptoms, mean duration was 11 years (range 2–26 years). The start of exposure occurred from 1963 to 1987, mean 1977. Of the 11 nurse anaesthetists that had been exposed to anaesthetic gases prior to diagnosis, 10 were diagnosed in 1980–99, while one was diagnosed in the 1970s. Since the mean survival probability 30 years after MS diagnosis is only 50%, we abstained from calculating incidence rates for the 1970s and restricted the incidence analysis to encompass the period 1980–99, leaving 10 cases to be included in the analysis. An almost threefold and significantly increased risk was obtained for nurse anaesthetists diagnosed during the period 1980–99, both when using the Gothenburg and the Danish incidence rates for reference (table 1).

### DISCUSSION

Although based on somewhat crude data and methodology, our study suggests an increased incidence of MS in Swedish nurse anaesthetists during 1980–99, whether the reference material involves the population from Gothenburg during 1950–64 or the Danish material during 1950–89. Although there is an incongruity in time between the material concerning the nurses and the reference data, to our knowledge there are no reference data on incidence for the 1990s. The Gothenburg material also covers a second period of time from 1974 to 1988. The incidence rate is lower in this latter period, possibly as a result of the opening up a few more neurological departments in the Gothenburg area, with subsequent difficulties in getting a complete collection of cases. We therefore preferred to use the higher incidence rates of the first period as the reference in order not to underestimate the expected number of cases. In the Danish material there is a slightly decreased incidence from 1950 to 1969 and a slight increase in the incidence from 1970 to 1989. Minor changes in temporal trends from other countries are also seen, for example in Finland, Norway, and Iceland. In spite of the somewhat crude methods that had to be applied in this study, the clearly increased SIRs found for the nurse anaesthetists can hardly depend on the time incongruities.

Neurologists had diagnosed all cases as MS in our material. All cases were definite MS. The reference materials on the other hand include both definitive and probable MS cases, thereby leading to some overestimation of the expected number of cases. The more specific diagnoses among the MS nurses, whose exposure preceded the onset of the disease, were relapsing remitting MS in seven patients, relapsing progressive in three patients, and primary progressive MS in one patient. This distribution is unremarkable according to our clinical knowledge.

As already emphasised, the method of collecting cases of MS among the nurses is somewhat unconventional. We asked all nurses suffering from MS independent of specialty to answer our appeal. As there was a reference to anaesthetics in the appeal, one would expect nurse anaesthetists to be more likely to answer than nurses of other specialties. This possibility of over reporting was eliminated by scrutinising the medical files of the nurse anaesthetists to confirm the MS diagnosis. It is likely, however, that some cases were missed, especially those nurses suffering from a severe state of MS and of course those who were deceased. This might explain the low number of MS cases announcing themselves diagnosed in the 1970s, having a long period of illness and progress up to the year of case collection in 1999. This consideration made us limit the period to 1980–99. Two of the nurses were diagnosed...
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ethanol nurse anaesthetists in order to more definitely assess or refute
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observed. Further studies based on more rigorous methods


acknowledge oxidation reactions in guinea pig hepatic and heart
tissue\textsuperscript{19–21}; isoflurane\textsuperscript{22} impairs the antioxidant defence system in
guinea pig kidney. Organic solvents like trichloroethylene\textsuperscript{12} and
ethanol\textsuperscript{21} cause lipid peroxidation by formation of free radicals
in animal assays. Oxidative stress from free radicals is
hypothesised to be part of a pathogenic mechanism for MS.\textsuperscript{14–17}
Mechanisms of this kind might explain our epidemiological
findings regarding the nurse anaesthetists as well as the
increased risk of MS in workers exposed to organic solvents.\textsuperscript{2}

In conclusion, this study provides preliminary evidence for
an excess risk of MS in nurse anaesthetists, although based on
 crude data and a somewhat approximate analysis. As the case
ascertainment might have been incomplete because of the
 crude method applied, the risk may be even greater than
 observed. Further studies based on more rigorous methods
should be undertaken in countries with a larger number of
nurse anaesthetists in order to more definitely assess or refute
the risk indicated in this study.

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