PUBLIC HEALTH

Effect of exposure of miners to aluminium powder

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'McIntyre Powder' (finely ground aluminium and aluminium oxide) was used as a prophylactic agent against silicotic lung disease between 1944 and 1979 in mines in northern Ontario. To find out whether the practice produced neurotoxic effects a morbidity prevalence study was conducted between 1988 and 1989. There were no significant differences between exposed and non-exposed miners in reported diagnoses of neurological disorder; however, exposed miners performed less well than did unexposed workers on cognitive state examinations; also, the proportion of men with scores in the impaired range was greater in the exposed than non-exposed group. Likelihood of scores in the impaired range increased with duration of exposure. The findings are consistent with putative neurotoxicity of chronic aluminium exposure.

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Introduction

Between 1944 and 1979, miners in northern Ontario, mainly underground gold and uranium miners, were exposed to a finely ground powder of aluminium ('McIntyre Powder', McIntyre Research Foundation, Toronto) as means of prophylaxis against silicotic lung disease.[1,2] The powder was said to contain 15% elemental aluminium and 85% aluminium oxide.[3] The recommended exposure was to an aluminium dust concentration of 20 000–34 000 parts per ml air in the miners' changing rooms before each underground shift for 10 min.[4]

On the basis of particle size, dispersion characteristics, and recommended concentration, the annual alveolar burden of aluminium accumulated by exposed miners would have been approximately 375 mg (Muir D, personal communication).[5]

Stored samples of McIntyre powder have recently been found to contain subspherical particles of bayerite, gibbsite, and norstrandite (polymorphs of aluminium tri-hydroxide), triangular plates of elemental aluminium, and traces of iron (as haematite, Fe_2O_3). The possibility that these findings were due to chemical changes over time could not be ruled out (Mitchell R, personal communication).

The prophylaxis programme was stopped in 1979, on the recommendation of a scientific task force commissioned to examine its value and safety.[5] Although the task force found that a fall in mortality from silicotic lung disease had coincided with the term of the programme, and that McIntyre powder did not produce apparent adverse effects, they concluded that changes in mining practices had lowered dust levels, and that there was insufficient evidence of benefit from the aluminium. They also recommended mortality and morbidity studies to determine whether the powder had caused harm.

Studies over the next few years indicated raised mortality rates for respiratory disorders among gold and uranium miners,[6] but no evidence of differential rates between gold miners exposed and those unexposed to McIntyre powder.[7] More than 95% of northern Ontario gold miners had been exposed to McIntyre powder.

In 1987, the Ontario Ministry of Labour funded the current morbidity prevalence study, conducted between July, 1988, and August, 1989, to examine whether there were differential rates of chronic disorder among miners likely to have been exposed to McIntyre powder. The objective of the field investigation was to examine the health histories and current status of a cohort of men working in northern Ontario mines between 1940 and 1979. A focus on neurodegenerative disorders was specified since aluminium may be neurotoxic under certain conditions. Although direct evidence of aluminium neurotoxicity was limited to laboratory animals,[8-10] and to dialysis encephalopathy in man,[11] aluminium had also been associated with dementia of Alzheimer type in neuropathological[12-14] studies.

The occasional reports of acute neurotoxic responses among individuals with normal renal function have been controversial.[15-17] More subtle or delayed effects from chronic aluminium exposure, however, have not been assessed in man.

We have tested the null hypothesis that there are no differences between miners exposed and those not exposed to McIntyre powder, in either proportions with neurological or cognitive disorder, or in group means for cognitive test scores.

Methods

Sampling frame and sample(s)

Between 1955 and 1979, 29 000 underground miners were examined in one of three Ontario chest clinics. From this database a sampling frame was constructed which contained a cohort of 6604 men born between 1918 and 1928 who first started underground mining between 1940 and 1959. For 2414 of these men at least one of the annual examination records indicated that they had been exposed to the aluminium prophylaxis programme some time in the year preceding that examination. Two samples were drawn from

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the sampling frame of 6604. The first was a stratified sample, with 369 exposed and 369 unexposed miners pair-matched on age and year of first mining experience in Ontario and total underground mining time. The second was a random sample of 678 miners, obtained by drawing equal numbers from the exposed and unexposed strata of the sampling frame. 63 miners (ie, 49 exposed and 14 unexposed) drawn into both samples were retained only in the random sample, so that there were two non-overlapping samples.

The correction of inaccuracies in the exposure records resulted in the redefinition of exposure status for 28 miners previously considered "exposed". With these changes, the drawn samples consisted of 631 miners exposed to McIntyre powder and 722 miners never exposed, with 308 matched pairs in the stratified sample.

Data collection procedures

Occupational history in the Ontario mining industry and periods of exposure to McIntyre powder for individuals were obtained from records on miners' annual Chest Clinic examinations and McIntyre Research Foundation records on mining companies licensed to dispense their powder.

Miners who could be traced were interviewed at home for life-style information, occupational history outside the mining industry, family history, personal medical history, and current state. They were also given three cognitive state tests—the Mini-Mental State Examination (MMSE) for general cognitive function;[18] Ravens coloured progressive matrices test (CPM)[19] for reasoning; and the Symbol Digit Modalities Test (SDMT)[20] for spatial perceptual accuracy and information processing. This battery of tests was selected because of its sensitivity in detecting cognitive impairment from any cause in an elderly, community-living population.[21] The criterion for impairment on the MMSE was a score of $\leqslant 17$ out of a possible maximum of 30; this cut off was the score for the bottom 5% of a community population aged 65+ in Baltimore;[22] for CPM the criterion was a score of $\leqslant 14$ out of a possible maximum of 36 (bottom 5% of a normative sample with mean age 65[19]); and for SDMT it was $\leqslant 12$ out of 110 (2·5 SD below mean in a normative population aged 65+ with $\leqslant 12$ years' education[20]).

Findings were analysed by subjecting to unweighted linear regression adjusted differences in mean scores for the total of the three cognitive examinations, and adjusted differences in proportions "impaired" on at least one of the three cognitive tests.

Results

1027 (76%) of the sampled men were traced, and 647 (63%) of those traced completed all components of the examination protocol. Approximately 15% of those traced had died (ie, 19% of the traced exposed men and 13% of the traced unexposed men), 12% were traced to areas not accessible to interviewers, and slightly less than 10% in each group refused or could not complete the interview. Of the 647 miners who completed the interview, 40 were excluded from final analyses because of a history of stroke, head injury, or other brain trauma from which recovery was partial.

Failures at tracing miners, deaths, and refusals greatly reduced the number of pairs in the stratified sample. Of 514 men traced, and 323 completing all tests in this sample, only 42 pairs remained intact. This sample size was too small for planned paired comparisons, so both the random and stratified samples were analysed as independent samples (ie, ignoring the matching of the stratified sample). Findings for these two samples were similar despite differences in initial sampling strategy, so the results given here have been obtained by combining the stratified and random samples.

TABLE I—DIFFERENCES BETWEEN EXPOSED AND UNEXPOSED GROUPS IN INDICATORS OF COGNITIVE FUNCTION

—	Mean sum of three test scores		Proportion impaired on at least 1 test	
	Unadjusted	Adjusted	Unadjusted	Adjusted
Exposed (n = 261)	77·4	78·6	0·14	0·13
Unexposed (n = 346)	83·7	82·8	0·04	0·05
Difference (SE)	6·3 (1·1)	4·2 (1·1)	0·10 (0·02)	0·08 (0·02)
p*	0·0001	0·0001	0·0001	0·0002

*Significance of difference between exposed and non-exposed miners

TABLE II—PROPORTION WITH IMPAIRED COGNITIVE FUNCTION IN RELATION TO DURATION OF EXPOSURE

—	Duration of exposure (yr)			Un-exposed
	⩾20	10–19·9	0·5–9·9	
Number in group	50	106	105	346
Unadjusted values				
Proportion impaired	0·20	0·15	0·10	0·04
Difference (SE)*	0·16 (0·04)	0·11 (0·03)	0·06 (0·03)	..
Pr	0·0002	0·0004	0·089	..
Adjusted values				
Proportional impaired	0·18	0·14	0·10	0·05
Difference (SE)*	0·14 (0·04)	0·09 (0·03)	0·05 (0·03)	..
p	0·002	0·003	0·087	..

*Difference from unexposed group.

Observed and adjusted differences between exposure groups

There were no significant differences between traced members of the exposure groups in proportions with self or proxy reported neurological disorder. Among the miners exposed to McIntyre powder, one man had a reported diagnosis of "probable" dementia of Alzheimer type and 3 had reported diagnoses of Parkinson's disease. One unexposed miner was reported by a proxy respondent to have a diagnosis of "probable"' dementia of Alzheimer type and could not complete the cognitive tests.

Cognitive test scores and proportions impaired on at least one test indicated a disadvantage for exposed miners (table I). Differences in the proportions "impaired" were considered the more important of the two indicators. Adjustments were made for factors shown to influence the effect estimate—ie, years of underground mining time; age at starting to mine in Ontario; age at the time of interview; immigrant status; self-reported head injury resulting in a loss of consciousness; grades of education completed; raised blood pressure at the time of interview (ie, >165 mm Hg systolic or >95 mm Hg diastolic); and interviewer-rated subject cooperation, tremors, and hearing and vision impairment. With these adjustments, the estimated relative risk of impairment of cognitive function among exposed miners was 2·6. Occupational history outside the mining industry, family history of dementia, history of alcohol use, and other features of personal medical history did not influence the magnitude or precision of effect estimates.

Gradation of effect

Exposure to aluminium powder ranged from 6 months to 36 years. With adjustment for factors listed above; the regression coefficient relating years of aluminium programme participation to probability of impairment was 0·006 (SE 0·001). This gradation of effect with exposure was clearly shown when proportions impaired were listed according to arbitrary strata (10 years) of aluminium exposure (table II). Comparisons across strata were made between groups at each exposure level and the unexposed group of miners, and the test for trend was highly significant ($F[1,594] = 17·2$, $p = 0·0001$).

Exposure duration correlated well with underground time for exposed miners, and underground time was negatively associated with cognitive test performance in both exposure groups. However, with adjustment for exposure duration, the effect of underground mining time on cognitive test results was not significant (β-coefficient = 0·001 [SE 0·001]).

Discussion

Do the adjusted differences in cognitive test performance between the groups reflect an effect of exposure to McIntyre powder, and to what extent may these findings be interpreted as evidence of aluminium neurotoxicity? The first point to note is that the sampling strategy and methods of assessment did not permit separation of exposure status from ores mined, separation of age and year of first exposure from duration of exposure, or investigation of ages at onset, progression or rate of cognitive decline. These factors limit our ability to generalise from the findings, and to define the disease process(es) that may be operative. However, the exposure data were abstracted from an existing data file, further information on exposure was not sought from the participants, and the study was conducted within a cohort not defined on the bases of clinical diagnoses or symptoms. The subjects and interviewers were blind to the specific hypothesis regarding the relation between exposure to the aluminium agent and performance on selected cognitive state examinations.

The differences between the exposed and unexposed miners on cognitive function measures were robust, consistently in the direction of disadvantage for exposed miners, and persisted with adjustment for factors that influenced the effect measure. Differences between exposure groups were observed across all three screening measures, which reflects an increased risk for non-specific cognitive deficits among exposed miners. The gradation in this effect with increasing duration of exposure opportunity was maintained with adjustment for factors likely to influence the effect estimates.

Self and proxy reported medical conditions did not indicate an excess of diagnosed neurological disorder. Whether this was due to missed diagnoses or to the fact that specific conditions (eg, dementia of Alzheimer type) may be an extreme and atypical manifestation of aluminium intoxication, or to some other factor, are critical questions to be addressed in follow-up studies of this cohort.

The measures of individual exposure in this study were based on reported exposure status as recorded at each of the annual chest clinic examinations. Although this method of measuring exposure was considered likely to result in a conservative bias, biological indices of aluminium uptake and retention were not available. Markers of aluminium body burden in this population, and aluminium concentration in brain tissues specifically, would be of particular value in view of uncertainties about the bioavailability of aluminium compounds.

Information on the uptake and metabolism of aluminium compounds in man is limited. Normal total body aluminium has been calculated to be in the range of 30 to 45 mg, with skin, lungs, and gastrointestinal tract accepted as "natural barriers" to uptake.[25,26] Aluminium that is absorbed was thought to be efficiently excreted, mainly through the kidney;[23] however, aluminium has been reported to accumulate in brain tissues with age.[24]

Evidence that aluminium can be transported to the brain via the nasal-olfactory pathways[25] suggests that it is possible for respirable aluminium dusts to circumvent certain natural barriers to uptake. Moreover, recent population studies have also shown a positive relation between aluminium concentration in drinking water and regional rates for dementia syndromes.[26-28] This accumulation of evidence raises important questions about factors that govern the bioavailability and neurotoxicity of aluminium, and the implications of chronic, low-dose exposure to aluminium compounds.

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Impact of active immunisation against enteritis necroticans in Papua New Guinea

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Enteritis necroticans, known locally as pigbel, has been a major cause of illness and death among children in the highlands of Papua New Guinea. After a successful trial of active immunisation against the beta toxin of the causative organism, *Clostridium perfringens* type C, immunisation of children was begun in 1980. The effects of the immunisation programme on pigbel admissions in 3 of the 5 major highland hospitals were assessed. In each of the centres studied the proportion of admissions due to enteritis necroticans dropped significantly after immunisation was introduced ($p < 0.001$) and hospital admissions for pigbel in 1984–86, when immunisation was well established, were less than one fifth of previous figures.

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Introduction

Enteritis necroticans—a necrotising enteritis caused by *Clostridium perfringens* type C[1]—occurs in many parts of the developing world, but only in the highlands of Papua New Guinea, where it is called pigbel, has the disease been a major and persistent health problem.[2] Pigbel has been second only to respiratory infections as a cause of childhood death after the first year of life in highland hospitals,[3] although it rarely affects infants under the age of 1 year. A controlled trial of a *Clostridium perfringens* beta toxoid vaccine showed protection against pigbel for over 2 years.[4] After this trial, an immunisation programme was introduced in 1980 by the Papua New Guinea health services, in which pigbel vaccine (Wellcome, Beckenham, UK) was given to children at 2, 4, and 6 months of age and, initially, to older children who attended clinics and schools.

Although health services staff have noted a reduction in pigbel morbidity and mortality, and attributed this to the effects of immunisation,[5] a detailed evaluation of the immunisation programme has not been reported. We describe the impact of immunisation on pigbel admissions in 3 of the 5 highland provincial hospitals—major centres where pigbel has been common and where hospital data are reasonably accessible and reliable. Medical services are organised around district health centres and provincial hospitals; in heavily populated areas most patients with severe pigbel reach the provincial hospitals, so that the hospital-based data provide a reasonable indication of the overall incidence of severe pigbel in the community.

Subjects and methods

Hospital diagnostic records were obtained from discharge and surgical records of Mendi, Mount Hagen, and Goroka Hospitals. Mendi Hospital serves the Southern Highlands Province (population 235 000), Mount Hagen Hospital the Western Highlands Province (population 264 000), and Goroka Hospital the Eastern Highlands Province (population 275 000). All diagnoses of pigbel, enteritis necroticans, necrotising enteritis, small-bowel gangrene, and acute jejunitis were recorded as pigbel. Data for all admissions were available from Mendi and Mount Hagen, but only those for the children's ward from Goroka because of known omissions in the adult records. Records of vaccine use were obtained from the provincial maternal and child health services.

Data were collected for the years 1976 to 1987, when complete annual records were available. The number and age distribution of cases and the cumulative total of second doses of vaccine were recorded. As two doses of vaccine are required to produce circulating antibody in a naive individual,[6] the number of children who have received two doses of vaccine indicates the immunised population. To compensate for changes in use of hospital services, the proportion of pigbel cases per thousand admissions was calculated for each year of the study.

Results of the 3 years before widespread immunisation (1978–80) were compared with those for 1984–86, when vaccination was well established. Logistic regression was used to model the proportions as a function of year and centre and 95% confidence intervals (CI) were determined by standard methods.[7]

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