Evidence of aluminium accumulation in aluminium welders

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Abstract

Using atomic absorption spectrometry the aluminium concentrations in blood and urine and in two iliac bone biopsies obtained from welders with long term exposure to fumes containing aluminium were measured. The urinary excretion of two workers who had welded for 20 and 21 years varied between 107 and 351 μg Al/l, more than 10 times the concentration found in persons without occupational exposure. Urinary aluminium excretion remained high many years after stopping exposure. Blood and bone aluminium concentrations (4–53 μg Al/l and 18–29 μg Al/g respectively) were also raised but not to the same extent as urine excretion. It is concluded that long term exposure to aluminium by inhalation gives rise to accumulation of aluminium in the body and skeleton of healthy persons, and that the elimination of retained aluminium is very slow, in the order of several years.

Aluminium is an abundant metal comprising about 8% of the earth's crust. Despite this, the concentration of aluminium in water, foodstuffs, and biological media is usually low.[1] For many years aluminium was considered innocuous and virtually not absorbed from the gastrointestinal tract.

As a consequence of improved analytical facilities, it has been possible during the past decades to obtain accurate data on the concentration of aluminium in human media such as blood and urine. In 1976 Alfrey et al[2] showed that aluminium accumulates in patients

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on haemodialysis and may give rise to a severe and sometimes fatal encephalopathy. Patients with severe chronic renal failure cannot eliminate aluminium through the urine and are therefore prone to accumulate the metal and suffer from aluminium toxicity.[3 4] The skeletons of patients on haemodialysis may also become affected from accumulation of aluminium; a typical bone disease, aluminium osteomalacia, was described in the late 1970s.[5 6] These early observations of the systemic toxicity of aluminium in uraemic patients gave rise to considerable interest, and have been described in a vast number of publications during the past decade (see review by de Broe and Coburn[7]).

It is now well established that the most important source of aluminium exposure in patients on haemodialysis before 1976 was the dialysis fluid, but important additional exposure may also take place through the use of phosphate binders containing aluminium.[8] Toxicity from aluminium also occurs in other organs of patients with chronic renal failure. Microcytic anaemia, joint pain, repeated severe infections, and liver dysfunction have been reported to occur as a result of retention of aluminium.[9] Nowadays, the aluminium concentration in dialysis water is thoroughly monitored in most dialysis wards and should be kept below 10 μg Al/l.[7] The use of drugs containing aluminium has been minimised. Furthermore, it is possible to treat aluminium encephalopathy and osteomalacia by repeated injections of desferoxamin, an aluminium chelating drug, given in conjunction with dialysis.[10 11]

Despite the improved knowledge about exposure routes and the occurrence of aluminium toxicity the metal presents an insidious threat to all patients with chronic renal failure.[12]

Aluminium is also of concern for people without renal failure. Increased concentrations of aluminium have repeatedly been found in samples of brain tissue obtained from patients with Alzheimer's disease.[13] A causal relation has been proposed, although this has not yet been conclusively shown.[14]

Exposure to aluminium may also pose an occupational hazard. Deposition of stamped aluminium powder and dust in the lungs may give rise to pulmonary fibrosis. Symptoms of obstructive lung disease have been reported from workers at aluminium production plants.[15] Appreciably raised concentrations of aluminium have been recorded in blood

Figure 1   Aluminium concentration in urine obtained from 23 welders after a period (16–37 days) without exposure. Filled dots represent the two men who provided bone biopsies.

and urine samples obtained from aluminium welders and workers engaged in the production of aluminium powder when compared with non-exposed persons.[15 16] It is not known to what extent aluminium may cause systemic toxicity in exposed workers without renal failure, but one case report indicates that encephalopathy may indeed occur after heavy exposure to stamped aluminium powder.[17]

In 1984 we studied 23 welders who had welded aluminium for 0·3 to 21 years.[18] The urinary excretion of aluminium among these welders was related to the number of years of exposure to aluminium (fig 1). To diminish the effect from current exposure to aluminium the urine samples were collected after a period of vacation without any exposure (16–37 days). Two of the long term exposed welders volunteered for iliac bone biopsies and further measurements of aluminium in blood and urine.

In this report we provided further evidence that long term exposure to aluminium by inhalation gives rise to accumulation of aluminium in the body of healthy persons, and that the elimination of aluminium is very slow.

Materials and methods
Urine and blood samples were obtained on several occasions from two men who had been engaged in aluminium welding for 20 years or more. Urine was collected into 500 ml polythene bottles with lids of the same material. Bottles and lids had been carefully cleaned, soaked in 5% RBS 25 solution for at least five hours, soaked in 1% ethylenediaminetetra-acetate solution overnight, and carefully rinsed with ion free water to prevent contamination. Blood samples were collected into tubes cleaned in the same way as the urine bottles. In the laboratory a small portion of the urine was taken for determination of creatinine using a photometric reaction rate analyser (LKB 8600). To

the remaining urine 1·5% of 9 M sulphuric acid was added and the samples were stored at 20°C until analysed. Urine and blood were diluted 1:4 or more and analysed by electrothermal atomic absorption spectrometry (ETAAS). The standard deviation was 1·35 µg/l at an aluminium concentration of 40 µg/l and the coefficient of variation was 3·3%. More details regarding the analytical methods for measuring aluminium in blood and urine are given elsewhere.[16 18]

Iliac bone biopsies were obtained from two of the workers using a modified Bordier needle as described by Norris et al.[19] Double labelling of the bone with tetracycline, which enables fluorescence microscopy to assess bone formation, was done by oral administration of 600 mg diemethylchlortetracycline (Ledermycin) during three days, on two occasions, before taking the bone specimens. The bone biopsies (5 mm in diameter) from the workers were taken at the Huddinge hospital in the same way as from renal patients from whom it is considered important to get a morphological diagnosis. Two samples were taken from each subject: one was fixed in absolute ethanol and submitted to Dr Feemont (University of Manchester, UK) for morphological examination and the other, in an aluminium free test tube, was sent for aluminium analysis. The project was approved by the local ethical committee at Huddinge hospital.

Before analysis the bone biopsies were rinsed briefly in purified water, wiped with analytical filter paper, and dried overnight at 110°C. Subsequently the dried bone samples underwent wet acid digestion using analytical grade nitric acid (Merck) purified at our laboratory by sub-boiling distillation in a quartz still (Hans Kuerner D-8200 Rosenheim, Germany) to avoid any possibility of contamination. About 1 ml of 9·5 M nitric acid was added to each 100 mg of bone. The liquid sample of digested bone was diluted and analysed using the standard addition method. The analyses were performed by ETAAS using a Perkin-Elmer Zeeman/3030 system comprising a microcomputer controlled HGA-600 graphite furnace, AC-Zeeman magnet, closed HGA cooling system, and an AS-60 autosampler. The autosampler was programmed to dispense 20 µl of the solution followed by 20 µl of 5 M ammonia matrix modifier to avoid sputtering and attack from nitric acid on the graphite tubes. Blanks were run in each series. The detection limit was 0·1 µg Al/g with a 100 mg sample of dried bone and the coefficient of variation was 4%.

Results
Worker BI, born 1936, welded aluminium mainly with the metal inert gas (MIG) welding technique between 1964 and 1984. Measurement of air concentrations was performed during one week in 1982. The mean of his eight hour time weighted averages at that
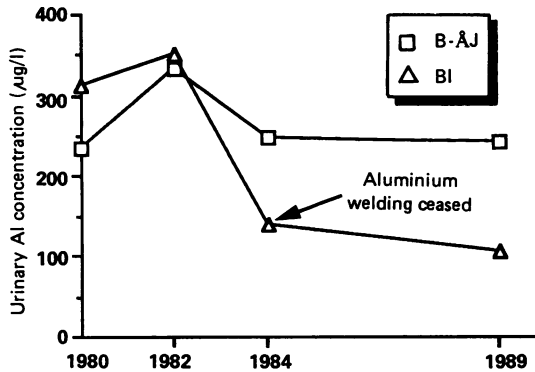
Figure 2   Urinary concentration of aluminium in two aluminium welders.

time was 8·9 mg Al/m³. He became a foreman in 1984 and has since encountered only minimal exposure to aluminium. Worker B-Å J, born 1942, welded aluminium with the MIG technique as well as the tungsten inert gas (TIG) welding technique between 1963 and 1984. In 1982 his mean eight hour time weighted average exposure to aluminium was 3·0 mg Al/m³. Since 1984 he has only worked with TIG welding in aluminium, which generates considerably lower exposure compared with MIG welding. Neither of the men had previously taken extensive quantities of antacids containing aluminium, and since 1982 had used no drugs containing aluminium. Serum creatinine, urea, and albumin concentrations were normal for both men in 1982 and 1985.

Figure 2 shows the urinary concentration of aluminium at four different points in time from 1980 to 1989. The urinary excretion of aluminium remained high for a long period after stopping exposure. Aluminium concentration in blood was also raised (4·0 to 16 µg Al/l for B-Å J and 7·0 to 53 µg Al/l for BI) though to a lesser extent. The concentrations of aluminium in bone were 29 µg Al/g for B-Å J and 18 µg Al/g dry weight for BI. The bone morphology was normal for B-Å J whereas moderate osteopenia was noted for BI. Stains for aluminium were negative in both biopsies.

Discussion

Figure 1 provides evidence for accumulation of aluminium in the body as a result of long term occupational exposure from aluminium welding, an observation suggesting that retained aluminium has a long biological half life. The urinary excretion of two workers who had welded for 20 years or more varied between 107 and 351 µg Al/l. This is more than 10 times the concentration found in urine from non-occupationally exposed normal subjects (< 10 µg Al/l). Urinary aluminium concentration remained

high many years after exposure had stopped (fig 2) providing further evidence of a long biological half life. The aluminium concentrations in bone from two workers (18–29 µg Al/g) were raised as compared with those reported by Ellis *et al* for patients without renal disorders (average 7·6 µg Al/g),[20] but were in the lower range of those found in biopsies from renal patients (average 15·1, range 1·5–113·4 µg Al/g). We have analysed aluminium in bone biopsies obtained from 19 patients on dialysis and from four controls without renal disease. Bone aluminium concentrations in the dialysis group ranged from 12 to 100 µg Al/g and increased significantly with the number of years of renal failure. In controls bone aluminium ranged from 0·6 to 5 µg Al/g (Elinder *et al*, unpublished observations). Similar results were reported by Alfrey *et al*.[21]

It is possible to make a rough estimate of the biological half life of aluminium in persons without renal impairment if the following assumptions are made: (1) urine is the only route for aluminium elimination, an assumption supported by the linear relation between bone aluminium concentration and number of years of renal failure as well as animal experiments[1]; (2) about 40% of the body burden of aluminium is stored in the skeleton[22]; (3) aluminium is evenly distributed in the skeleton. The two welders eliminated about 200 µg Al/day (96–146 µg Al/g creatinine × 1·6 g/day) in urine at the time when the bone samples were taken. The body burden of aluminium in these men is likely to be about 300 mg (18–29 mg Al/kg in bone × (1/0·40)) × 5 kg, which is the normal dry weight of bone tissue in adult men.[23] Thus daily urinary elimination of aluminium is about 0·06% of the estimated body burden, which corresponds to a biological half life of about three years.

Volunteers exposed to welding fume containing aluminium for one day excreted 0·1–0·3% of the calculated inhaled dose within a few days. The short term half life for aluminium was estimated to be about eight hours.[24] The half life for aluminium in welders exposed for six months has been calculated to be four days.[25] Among welders exposed for more than 10 years the half life has been estimated to be considerably longer, in the order of years.[18] These results suggest that shortly after exposure to aluminium a rapid elimination of loosely bound aluminium takes place (short half life) followed by a slow release of aluminium firmly bound in tissues and organs such as the skeleton (long half life).

That aluminium may be stored in the bone of healthy persons after a short period of exposure has recently been reported.[26] Two persons who accidentally drank water contaminated with aluminium had positive aluminium staining lines in bone biopsies. Positive aluminium staining is obtained at concentrations of aluminium exceeding about 50 µg Al/g, but as the exposure had been relatively short the overall

aluminium content in bone was in the normal range.[26] The aluminium stains in the two bone samples we obtained were negative. This is not surprising as the workers had exposure that continued for years and the concentration of aluminium in their bone samples was less than 50 μg Al/g.

To what extent does aluminium accumulation in welders comprise a health risk? The men we examined were clearly not demented—on the contrary they were proud, skilled, and active workers. One may correctly argue that if any of the aluminium exposed workers had serious health impairments they would be neither able to work nor to take part in this study. We may therefore have examined a healthy subgroup. A recent observation on different groups of welders by Sjögren et al[27] is somewhat worrying. Using a validated questionnaire, neuropsychiatric symptoms were assessed in welders exposed to iron and to different, possibly neurotoxic, metals (aluminium, manganese, lead). Welders with long term exposure to aluminium had significantly more neuropsychiatric symptoms than those who had shorter periods of aluminium exposure, or those welding in iron.[27] Likewise Rifat et al[28] reported that Canadian miners who between 1944 and 1979 had been submitted to prophylaxis against silicotic lung disease by repeated inhalations of finely ground aluminium powder performed less well in cognitive function tests compared with miners not given any prophylaxis. Retention of aluminium may have an aetiological role in these two observations.[27][28]

Furthermore, it has been found that patients on haemodialysis, with relatively low serum concentrations of aluminium, and no overt signs of aluminium toxicity, have lowered psychomotor test scores when compared with normal subjects and that the test results improved after treatment with desferoxamin.[12] This suggests that aluminium encephalopathy is merely the tip of an iceberg and that many more patients may suffer from more subtle symptoms of aluminium neurotoxicity.

In conclusion, this report shows that persons with normal renal function retain a significant proportion of absorbed aluminium. After long term exposure, aluminium is stored in the skeleton and eliminated very slowly. Findings from other studies suggest that accumulated aluminium may cause neurotoxic effects.

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