Biological indicators of exposure to total and respirable aluminium dust fractions in a primary aluminium smelter

Halina B Röllin, Penelope Theodorou, Anthony C Cantrell

Abstract

***Objectives*—The study attempts to define biological indicators of aluminium uptake and excretion in workers exposed to airborne aluminium compounds in a primary aluminium smelter. Also, this study defines the total and respirable aluminium dust fractions in two different potrooms, and correlates their concentrations with biological indicators in this group of workers.**

***Methods*—Air was sampled at defined work sites. Non-destructive and conventional techniques were used to find total and respirable aluminium content of the dust. Blood and urine was collected from 84 volunteers employed at various work stations throughout the smelter and from two different cohorts of controls matched for sex, age, and socioeconomic status. Aluminium in serum samples and urine specimens was measured by flameless atomic absorption with a PE 4100 ZL spectrometer.**

***Results*—The correlation of aluminium concentrations in serum and urine samples with the degree of exposure was assessed for three arbitrary exposure categories; low (0·036 mg Al/m^3), medium (0·35 mg Al/m^3) and high (1·47 mg Al/m^3) as found in different areas of the smelter. At medium and high exposure, the ratio of respirable to total aluminium in the dust samples varied significantly. At high exposure, serum aluminium, although significantly raised, was still within the normal range of an unexposed population. The workers with low exposure excreted aluminium in urine at levels significantly higher than the controls, but still within the normal range of the population. However, potroom workers with medium and high exposure had significantly higher urinary aluminium than the normal range.**

***Conclusions*—It is concluded that only urinary aluminium constitutes a practical index of occupational exposure at or above 0·35 mg Al/m^3, and that the respirable fraction of the dust may play a major role in the biological response to exposure to aluminium in a smelter environment.**

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National Centre for Occupational Health, P O Box 4788, Johannesburg 2000, South Africa
H B Röllin
P Theodorou
A C Cantrell

Department of Community Health, University of the Witwatersrand, Johannesburg, South Africa
A C Cantrell

Correspondence to:
Dr H B Röllin, National Centre for Occupational Health, P O Box 4788, Johannesburg 2000, South Africa.

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Aluminium and its compounds obviously comprise a large part of the numerous air contaminants present in a primary aluminium smelter. With global primary production of aluminium expected to rise above 20 million tonnes annually, chronic occupational exposure by the inhalation of aluminium dust and fumes is a common problem.

The bioavailability of aluminium in biological systems is influenced by the route of exposure. Other factors such as species, age, sex, renal function, nutritional state, and concentration of the specific aluminium compound also affect bioavailability. This has been shown by numerous experimental studies.[1–3] These studies, however, deal mostly with exposure routes other than those found in primary aluminium production, where the main exposure is by inhalation. The kinetics of aluminium uptake by this route are not well understood. The question of whether aluminium is absorbed directly across the epithelium of the upper respiratory tract and the lungs, and how much of the inhaled aluminium is ingested in the process, remains unanswered.[4]

Adequate biological indicators of aluminium uptake, retention, and excretion are yet to be developed fully, although increases in serum and urinary aluminium concentrations have been reported. These may reflect both body burden and current exposure. It has been suggested that urinary excretion is the better indicator of exposure, reflecting mainly current intake by either ingestion or inhalation. This conclusion is drawn from studies of short exposures in healthy people with no previous exposure to aluminium.[5–7]

Occupational exposure to aluminium dust and fumes by inhalation increases serum and urinary aluminium concentrations.[8 9] Although some researchers report that the increase in urinary aluminium is proportionally greater than changes in concentrations in serum samples, very few studies correlate these indicators with the actual occupational exposure to aluminium.[10–12] On the other hand, renal clearance depends on the exposure route and studies indicate that apparent fractional clearance of aluminium varies between people, and increases with urine production.[13–15] In contrast, long term exposure is said to lead to a modest increase in serum aluminium concentrations.[16] In animal experiments in our laboratory, we noted that changes in concentrations of serum samples were cyclic and, when high, were only just significantly greater than the controls.[17] This reduces the usefulness of serum sample

concentrations as an indicator of exposure. Also, occupational exposure by inhalation may result in the slow dissolution of particles trapped in the respiratory tract. This could affect the dynamics of the system as a long term source of aluminium.[18 19]

The current study was undertaken to characterise the occupational exposure to airborne aluminium, taking into account the total and respiratory fractions and their aluminium content. Air samples were collected in a primary aluminium smelter at different localities. Workers from these stations provided specimens for the measurement of aluminium concentrations in serum and urine samples, so that their biological responses could be measured, and appropriate indicators of exposure identified.

Materials and methods

FILTERS

Sampling of total airborne particulate material was performed with strategic samplers positioned at breathing height. Personal sampling might well have been more appropriate, but was not used as workers were grouped into job related cohorts for comparison. Dust samples were collected on 37 mm diameter cellulose acetate membrane filters with a pore size of 0·8 μm (Millipore AAWP 03700) in two separate potrooms, the carbon plant, the cast house, anode rodding, the boiler shop, the chemical laboratory, and the stores. These samples were subjected to gravimetric, non-destructive, and chemical analysis. Once the concentrations of aluminium in the air of various work stations had been measured, further samples were collected at a later stage from each of the two potrooms. These were the main areas of interest to this study, being the sites of highest exposure. Total dust was measured with the National Institute of Occupational Safety and Health (NIOSH) 0500 method and the respirable fraction was estimated with the NIOSH 0600 method. Average pump air flow rate during collection was 1·9 l/min and the total volume of the air sampled ranged from 0·38 to 0·76 m^3 depending on the concentration of dust present.

To characterise the dust by scanning electron microscopy, airborne samples were collected for 5–10 minutes on 37 mm diameter cellulose acetate filters precoated with 250 Å gold.

EXPOSED SUBJECTS

In total, 84 volunteers from various work stations throughout the smelter, and exposed to varying concentrations of aluminium dust and fumes, were investigated. The sections represented included potrooms, carbon plant, cast house, anode rodding, boiler shop, chemical laboratory, and stores. All volunteers gave informed consent to donate blood and urine for the survey. Volunteers known to be using medication containing aluminium were excluded from the study.

CONTROL SUBJECTS

Two cohorts of control subjects were used, none of whom had ever worked in the aluminium industry. Cohort 1 (20 serum and 28 urine specimens) consisted of subjects from the same geographical region, but residing in an area 50 km from the smelter. Cohort 2 (28 serum and 31 urine specimens) was drawn from a different geographical region. Both cohorts were matched to the exposed group for sex, age, and socioeconomic status.

Table 1 shows details relating to age and years of exposure of all the subjects under study.

COLLECTION OF BLOOD AND URINE

Biological fluids were obtained from subjects in the non-fasting state. To minimise the possibility of sample contamination, workers were instructed to report for the collection before the start of the shift, wearing their street clothes. Collection took place in the smelter's medical station under dust free conditions.

Polystyrene collection vessels for both blood (Sterilin 144AS) and urine (Sterilin 145SA) were acid soaked overnight in 50% HNO_3 and rinsed repeatedly with metal free Millipore water (resistivity > 16 MΩ.cm) and left to dry in a class-100 laminar flow cabinet. All containers tested were found to be aluminium free.

Blood for measurement of aluminium was collected into acid washed Sterilin tubes with 10 ml syringes (metal free, sterile, disposable from Becton, Dickinson, Rutherford, NY) and 20 gauge needles.

Blood was left to clot and centrifuged. The resulting serum samples were transferred to acid washed Sterilin tubes with disposable polyethylene Pasteur pipettes. Specimens were frozen immediately and stored at −20°C in accordance with accepted procedures.[20 21]

Volunteers were instructed to collect midstream urine. After collection the specific gravity of urine was measured, the urine frozen, and kept at −20°C until analysed.

All specimens were handled in a laminar flow cabinet.

INSTRUMENTATION: DUST ANALYSIS

A Varian model AA-975 atomic absorption spectrophotometer equipped with a GTA-95 furnace and autosampler was used for measurement of aluminium on the filters. Also, a Spectroflame P-ICP emission spectrophotometer was used to validate the results.

Table 1 Study subjects

			Years of exposure	*Age*
Subjects	*n*	*Sex*	*Mean (SD, range)*	*Mean (SD, range)*
Controls	48	M	— —	42·7 (11·0, 21 – 64)
Exposed:				
Low	33	M	12·8 (5·4, 2 – 23)	41·5 (9·8, 26 – 59)
Medium	12	M	7·3 (3·1, 2 – 11)	36·9 (5·4, 30 – 45)
High	39	M	13·1 (5·5, 4 – 23)	40·3 (8·8, 28 – 65)

Controls were matched for socioeconomic status.

INSTRUMENTION: NON-DESTRUCTIVE ANALYSIS

Energy dispersive *x* ray (Spectro XLAB analyser) was used to measure the aluminium content on filters before dissolving them for atomic absorption analysis or inductively coupled plasma emission (ICP) analysis.

Scanning electron microscopy (JOEL JSM 255) was used to characterise the dust.

BIOLOGICAL FLUIDS

For the measurement of aluminium in serum and urine we used a Perkin-Elmer Model 4100ZL spectrometer with Zeeman effect background correction equipped with transversely heated graphite atomiser (THGA). Table 2 shows the instrument settings and furnace programmes for the Model 4100ZL.

PROCEDURES

All the reagents used were Analar grade and reagent blanks were applied routinely in all analytical procedures. Millipore water (> 16 MΩ.cm resistivity) was used for all dilutions. All prepared reagents were stored in aluminium free plastic bottles.

CHEMICAL ANALYSIS OF ENVIRONMENTAL FILTERS

After non-destructive analysis, filters were dissolved in concentrated HNO_3 in platinum crucibles for flameless atomic absorption spectroscopy. For ICP analysis, the filters were placed in teflon bombs, hydrofluoric and nitric acid were added, and the samples were digested in a microwave oven.

SERUM ALUMINIUM

Serum was diluted 3x with 5·46 mM $Mg(NO_3)_2$ in 0·1% Triton X-100 with the AS-70 autosampler on the spectrophotometer. A total of 9 µl of diluted sample was injected in triplicate into the graphite tube and the concentration derived directly from the linear calibration.

A calibration curve was constructed by the method of addition and was found to be linear up to 40 µg/l.

URINARY ALUMINIUM

Urine samples were diluted 5x with 5N HNO_3 to keep salts in solution. A calibration curve was constructed by the method of addition, and was found to be linear up to 200 µg/l. The specific gravity of urine was measured with a refractometer and the aluminium concentration for each urine specimen was corrected for a specific gravity of 1·020.

QUALITY CONTROL

Accuracy of analysis was assessed by including quality control samples from Nycomed Seronorm trace elements (Oslo, Norway, batch 108) with each batch analysed, both for serum and urine samples.

Also, European Pharmacopoeia Commission BRP human albumin was analysed periodically.

STATISTICAL METHODS

The ANOVA test was used for normally distributed data. The Kruskal-Wallis test (Mann-Whitney or Wilcoxon two sample test) was used for non-parametric data.

Table 2 Instrument settings and furnace variables

Instrument:	*Perkin Elmer 4100ZL with transverse heated graphite atomiser*				
Conditions:					
Wavelength (nm)	*309·3*				
Low slit (nm)	*0·7*				
Lamp current (mA)	*10*				
Integration mode	*Peak area, Rollover Absorbance-s: 0·85*				
Integration time (s)	*5*				
Sample volume (µL)	*15*				
Standard gas	*Argon*				
Furnace variables:	*Step*	*Temperature °C*	*Ramp s*	*Hold s*	*Internal flow ml/min*
Drying	1	50	5	5	250
	2	80	3	2	250
	3	100	5	5	250
	4	130	10	25	250
	5	150	5	10	250
	6	400	30	20	50
Ashing	7	1300	10	25	250
	8	1400	1	5	250
Atomisation	9	2300	0	5	0
Cleanout	10	2500	1	4	250
	11	20	1	5	250

Characteristic mass = 16 – 28 pg/0·0044 Absorbance-s

Results

AIRBORNE ALUMINIUM

Scanning electron microscopy with energy dispersive microprobe analysis showed that most of the dust particles collected were aluminium compounds. No other metals were detectable in significant amounts. No quartz or asbestos particles were encountered during the study. These data will be published elsewhere.

It was important to ensure that the method used to find aluminium on the filters was giving an accurate reflection of the material collected. For this reason we selected different methods for both dissolving and analysing the dust samples as described under methods. It was reassuring to find that the two methods gave similar results with a correlation coefficient of $R = 0{\cdot}9977$ for the samples collected in the same areas of exposure. The conclusion to be drawn is that a valid estimation of the amount of aluminium present had been obtained. When expressed as Al_2O_3, this accounted for between 16% and 33% of total dry material on the filters. The concentrations of Fe, Pb, Cu, and Zn as detected by both methods were negligible in terms of sample mass and the residue comprised other unidentified particles.

The airborne concentrations of aluminium found at the various work sites differed considerably, and were grouped into three arbitrary exposure categories; low (carbon plant, cast house, anode rodding, boiler shop, chemical laboratory, and stores), medium (potroom 1), and high (potroom 2). Table 3 shows the concentrations of airborne aluminium in these three categories. The concentrations found were all well below the generally accepted threshold limit value (TLV) of 10 mg/m^3.[22] Other elements present were in the form of traces of Fe, Pb, Cu, and Zn as detected by graphite furnace atomic absorption spectroscopy, ICP, and energy dispersive *x* ray analysis. However, these were at such low concentrations as not to be considered toxic.

Results obtained from the graphite furnace

Table 3 Airborne aluminium by workstation

Area	Total aluminium (Al mg/m³) Mean	(SD, range)
Low exposure: Anode rodding Cast house Carbon plant Boiler shop Lab and stores	0·036	(0·035, 0·002 – 0·13)
Medium exposure: Potroom 1	0·35	(0·15, 0·20 – 0·57)
High exposure: Potroom 2	1·47	(0·20, 1·25 – 1·66)

Traces of Fe, Pb, Cd, Zn were also detected by graphite furnace atomic absorption spectroscopy.

atomic absorption spectroscopy and ICP studies were very similar but non-destructive energy dispersive *x* ray analysis gave higher results with urban particulate calibration. Subsequent calculations are based on the graphite furnace atomic absorption spectroscopy and ICP results.

From the results obtained, it became apparent that the main areas of interest in the smelter are potrooms 1 and 2. Here the concentrations of airborne aluminium found could be expected to result in a measurable biological response.

The levels of total dust during the second dust collection (to measure the respirable fraction) were somewhat lower than at the initial collection but still within acceptable limits. The total and respirable aluminium dust fractions in both potrooms differed considerably (fig 1). The respirable fraction as a percentage of the total was 52% in potroom 1 and 87% in potroom 2.

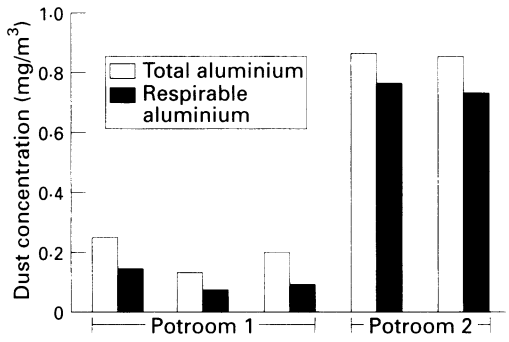

Figure 1 Total and respirable fraction of airborne aluminium dust at sites in potrooms 1 and 2.

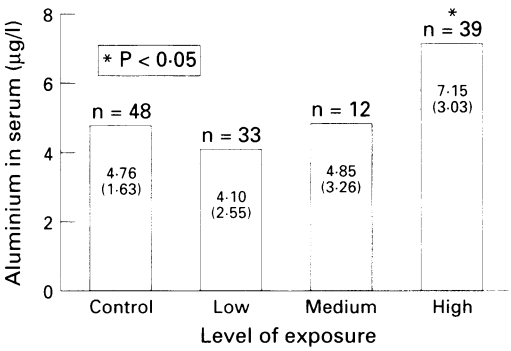

Figure 2 Effect of level of exposure on the concentration of aluminium in serum samples.

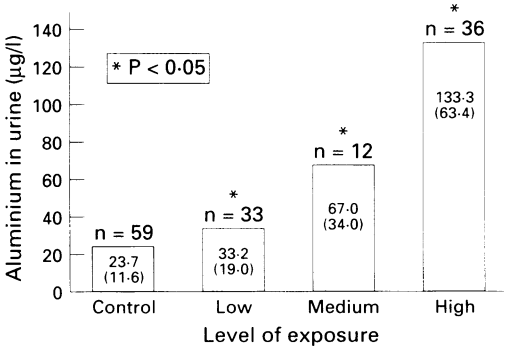

Figure 3 Effect of level of exposure on the concentration of aluminium in urine samples.

BIOLOGICAL INDICATORS

Serum aluminium

Figure 2 shows the comparison of the aluminium concentrations in serum samples for all the categories of exposure (controls and low, medium, and high) and their significance.

The mean serum aluminium for both control groups was 4·76 µg/l.

There was no significant difference in results for controls between two different geographical regions.

No significant differences were found between controls and subjects exposed to low (serum aluminium 4·10 µg/l) and medium (serum aluminium 4·85 µg/l) dust concentrations.

However, a highly significant difference ($P = 0·000054$) was found between the high exposure and control groups. The average concentration of aluminium in serum samples of the exposed group was 7·15 µg/l.

Urinary aluminium

Figure 3 compares the urinary measurements (corrected for specific gravity) for workers in three different exposure categories and the controls. All three exposed groups are significantly higher than the controls. They are also significantly different form each other. The concentrations of urinary aluminium increased with the level of exposure. At low exposure, concentrations were 33·2 µg/l; at medium exposure, 67·0 µg/l; and at high exposure, 133·3 µg/l. The controls had a mean value of 23·7 µg/l.

Discussion

All workers from the various work stations in the primary smelter were exposed to aluminium dust at well below the current TLV as set by the American Conference of Governmental Industrial Hygienists (ACGIH).[22] The mean exposure in potroom 2 (rated as high exposure in this study) was only 1·47 mg Al/m³ for the total dust fraction. This concentration is 1/30th of the ACGIH TLV.

The total dust samples from the smelter contained mainly aluminium with negligible amounts of other metals. These trace metals are unlikely to have any biological effect.

Duration of exposure for all smelter workers in the study is very similar, with the mean of 13 years for the low and high exposure groups, and seven years for the medium exposure group. All groups, including controls, were of similar age (mean 40 years).

A significant increase in serum aluminium concentrations over controls was found in the high exposure group only. However, these concentrations were still within the range of normally encountered values and cannot be used as an indicator of exposure.[23] All other groups had serum concentrations almost identical to controls.

These slight changes in serum aluminium concentrations were, however, accompanied by significant increases in urinary aluminium concentrations which were definitely dose related. This confirms the findings of other recent studies.[9 15] However, this response can only be considered to be a practical index of exposure if the airborne concentration of aluminium is above 0·35 mgAl/m^3 of total dust. This confirms our previous findings in a study of foundry workers where exposures to low concentrations of aluminium were not accompanied by significant increases in urinary aluminium concentrations.[11]

From the current study it seems that the levels of respirable dust encountered in both potrooms may play a significant part in the actual biological response to exposures to aluminium in the smelter environment.

The potrooms differed considerably from each other, not only in the concentration of total aluminium in the air, but also in the concentration of the respirable dust fraction. In potroom 2, 87% of aluminium present was in the respirable form. The biological response was significant both for serum and urinary aluminium concentrations at this level of exposure.

It is well documented that above 50 years of age, there is a decrease in kidney function.[24] When we examined the data for the workers in potroom 2, and took age into account, we did not find any significant differences for subjects under and over 50 years of age for either serum or urinary aluminium.

In interpreting the biological response to aluminium exposure, we suggest that not only total aluminium, but also the respirable fraction, should be monitored and measured in the workplace air.

It could be argued that this and similar studies are flawed in that the subjects have worked for considerable periods in the smelter environment. In many cases exposure started long before the toxicokinetics of aluminium were considered to be of any significance. Cumulative exposures are not easy to estimate.

For this reason, there is an urgent need for baseline studies on new workers entering the potroom environment for the first time. Only then will it be possible to determine at what stage of cumulative exposure a biological response becomes evident. We are fortunate to be in the position to have initiated such a study in a new aluminium smelter presently in the final stages of construction, and will report on our findings in due course.

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