The effect of exposure to aluminium on concentrations of essential metals in serum of foundry workers

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Abstract

The concentrations of aluminium (Al) in serum and urine of 33 volunteers exposed to inhalation of Al_2O_3 dust at a concentration in the air of less than 1 mg Al/m^3 were measured. These were compared with results from 20 normal subjects not exposed. The concentrations of copper (Cu), zinc (Zn), and total iron (Fe) in serum were also measured. The Al concentration in serum was significantly raised in the subjects exposed to dust, but Al concentrations in urine showed no significant difference from controls. This suggests a possible change in distribution of metals in the body tissues due to the presence of Al, with incomplete excretion of Al in the urine. This redistribution was selective, as the serum concentrations of Cu were conclusively decreased whereas the serum concentrations of Zn were conclusively increased. The serum concentration of Fe did not change significantly.

Until recently aluminium (Al) was regarded as poorly absorbed and biologically inert in man, but there is now convincing evidence that it accumulates in patients with impaired renal function, mainly due to contamination of dialysis fluids with Al, as well as by absorption of Al through the gut from Al containing phosphate binders used medicinally by these patients. In these subjects, Al exerts neurological toxicity (dementia) due to accumulation of Al in brain tissue.¹ Increased concentrations of Al in the brain have also been found in patients suffering from Alzheimer's disease.² Animal experiments have placed the neurotoxic effects of Al beyond doubt.³

Although occupational exposure to Al and its compounds is common, relatively few monitoring studies have been performed.

One case of dementia and pulmonary fibrosis in an Al powder production worker was described by

McLaughlin *et al* as long ago as 1962.⁴ Previous and recent studies on Al toxicity in industry have been confined to pulmonary function in Al smelters^{5,6} and epidemiological studies of mortality in Al reduction plant workers.^{7,8}

One study by Longstreth *et al*,⁹ however, investigated three patients with a progressive neurological disorder, all of whom had worked for over 12 years in the same potroom of an Al smelting plant. The authors concluded that "it is theoretically possible that long term low level exposure to Al could lead to neurotoxicity." Studies investigating the actual concentrations of Al in biological fluids of occupationally exposed subjects are sparse,^{10,11} due mainly to the analytical difficulties in analysing for Al. This is partly because of its ubiquity so that contamination is difficult to avoid. Also, conflicting normal concentrations are reported.

We know that the route of absorption as well as the type of compound plays a paramount part in determining the toxicity of metals. The interaction of the toxic metal with essential trace elements is important in understanding its toxicity. The few published investigations of the interaction of Al with trace metals in man are concerned only with patients undergoing haemodialysis¹² or dietary Al intake of healthy subjects.¹³ Little information exists about the interaction of Al with essential elements other than calcium and phosphate.¹⁴

In this communication we report the effect of exposure to Al on concentrations of essential metals in foundry workers. We measured concentrations of Al in serum and urine. Iron (Fe), copper (Cu), and zinc (Zn) in the serum were also measured as well as lead (Pb) and cadmium (Cd) concentrations in whole blood. The Al exposed workers were compared with non-exposed subjects.

Materials and methods

Thirty three volunteers from the workers in two different foundries, who were exposed to aluminium dust and fumes, were investigated. They consisted of smelters, low and high pressure die casting operators, fettlers, and sand casters. All gave informed consent to the taking of their blood for this survey. A group of 20 normal, non-exposed subjects' was used for com-

Table 1 Operating parameters for furnace atomic absorption spectrophotometry

Step	Pb			Cd			Cu		
	Temp (°C)	Time (s)	Argon (l/min)	Temp (°C)	Time (s)	Argon (l/min)	Temp (°C)	Time (s)	Argon (l/min)
1	75	2.0	3.0	75	2.0	3.0	50	10.0	3.0
2	95	15.0	3.0	95	15.0	3.0	80	10.0	3.0
3	140	10.0	3.0	140	10.0	3.0	100	5.0	3.0
4	300	8.0	3.0	180	20.0	0.5*	120	5.0	3.0
5	450	7.0	0.5*	350	20.0	0.5*	150	10.0	3.0
6	480	10.0	0.5*	450	60.0	3.0	600	10.0	3.0
7	480	5.0	3.0	450	1.0	0.0	600	5.0	0.5
8	480	1.0	0.0	1800†	1.1	0.0	2600†	1.0	0.5
9	2600†	1.1	0.0	1800†	2.0	0.0	2600†	1.5	0.5
10	2600†	1.0	0.0	1800	2.0	3.0	2600	1.0	3.0
11	2600	2.0	3.0						
Integration time (s)		1.0			1.0			0.5	
Wavelength (nm)		283.3			228.8			324.8	
Slit (nm)		0.5			0.5			0.5	
Lamp current (mA)		5.0			4.0			4.0	

*Air replaces argon as carrier gas. †Read command: on. Mode: peak height. Background correction: on.

parison. The mean exposure time for the exposed workers ranged between one and 17 years with a median value of seven years.

Environmental Al at different work stations was measured with personal filters over a period of eight hours. Concentrations found were 0.17 mg/m³ for smelters, 0.027 mg/m³ for operators, and 0.58 mg/m³ for fettlers—that is, well below the 10 mg/m³ threshold limit value time weighted average proposed by the American Conference of Governmental Industrial Hygienists.¹⁵

Blood was collected in Venoject heparinised tubes (Terumo Corp., Tokyo, Japan) for Pb and Cd determinations. Blood for determination of Cu, Fe, Zn, and Al concentrations in serum was collected into Sterilin tubes (Sterilab Services Catalogue No 144AS), which were found to be free of trace metals.

Syringes used were metal free B-D (sterile, disposable from Becton, Dickinson and Company, Rutherford, NY, USA). Urine was collected into acid washed polystyrene specimen bottles. Precautions were taken to avoid contamination during collection. Blood samples were stored at 4°C until analysed. The serum samples were analysed immediately for Al and then stored at -20°C until analysed for the other metals. Specific gravity of urine was determined on the day of collection and the samples stored at -20°C until analysed.

INSTRUMENTATION

A Varian model AA-975 atomic absorption spectrophotometer equipped with a GTA-95 furnace and autosampler as well as an HP-85 desktop computer was used. Deuterium background correction was applied in all cases. The purge gas was argon and in the case of blood for Pb and Cd, air was introduced during the charring stage to help to oxidise the matrix.

PROCEDURE

In all cases micromethods by flameless atomic absorption spectrophotometry were used and standard graphs were prepared by the method of additions to overcome matrix interferences in biological specimens. Extreme care was taken to avoid and eliminate all possible contamination.

Blood for Pb and Cd determination was diluted 10-fold with 0.1% Triton X and 5 µl aliquots were taken for the determinations. A tungsten coated tube was used as previously described.¹⁶ Table 1 gives the heating programmes for the graphite furnace.

The determination of Cu and total Fe concentrations in serum was modified from our methodology previously described for the Perkin-Elmer 603 AAS^{17,18} with adjustments of the heating parameters adapted to the Varian instrument (table 1). Table 1 also shows the parameters for determination of Zn concentrations in serum.

Determination of Al concentrations in serum was performed according to the method of Röllin *et al*¹⁹ (10-fold dilution with 0.1 N HNO₃) on the day of collection to prevent contamination due to storage.²⁰ Urine samples were diluted fivefold with 0.1 N HNO₃ and Al was determined by the method of addition. Specific gravity of urine was measured using a refractometer.

STATISTICAL METHODS

Student's *t* test was used. Differences were considered statistically significant when *p* < 0.05. Criteria were according to Miller.²¹

Results

Table 2 shows the statistical differences between normal and industrially exposed subjects.

Because Zn concentrations were significantly raised in exposed subjects, personal filters were also

Fe			Zn			Al		
Temp (°C)	Time (s)	Argon (l/min)	Temp (°C)	Time (s)	Argon (l/min)	Temp (°C)	Time (s)	Argon (l/min)
50	10-0	3-0	75	5-0	3-0	50	10-0	3-0
80	10-0	3-0	90	60-0	3-0	80	10-0	3-0
100	5-0	3-0	120	10-0	3-0	100	5-0	3-0
120	5-0	3-0	150	5-0	3-0	120	5-0	3-0
150	10-0	3-0	400	10-0	3-0	150	10-0	3-0
600	10-0	3-0	400	10-0	3-0	1000	10-0	3-0
600	5-0	3-0	400	5-0	0-7	1000	5-0	0-0
2400†	1-1	0-5	1900†	1-0	0-7	2500†	1-0	0-0
2400†	1-0	0-5	1900†	2-0	0-7	2500†	1-5	0-0
2400	2-0	3-0	1900	1-0	3-0	2500	1-0	3-0
	1-0			1-0			1-0	
	248-3			213-9			309-3	
	0-5			1-0			0-5	
	5-0			5-0			5-0	

analysed for Zn content and contained no Zn. Serum Al concentrations for control subjects ranged between 0.25 and 2.26 µg/dl with mean 1.13 (SD 0.55) µg/dl. Urinary Al concentrations ranged between 7.86–17.19 µg/l, mean 12.90 (SD 3.35) µg/l. Mean concentrations for Cu were 145 µg/dl, for Zn 89 µg/dl, and for total serum Fe 177 µg/dl, which are within accepted normal values.

Values reported for Al in serum and urine vary widely between different authors.²² Dietary, geographical, methodological, or even seasonal differences can influence the result.²³ This makes it difficult to compare our results with other published values.

The mean concentrations for Pb and Cd in blood of exposed subjects were 12.63 µg/dl and 0.126 µg/dl respectively. These concentrations of Pb and Cd in blood were within the normal reported ranges.^{24,25} This fact excludes the possibility of Pb or Cd having an effect on the concentrations of the measured essential metals, which could lead to false conclusions about the effects of Al. A significant increase in the concentrations of Al in serum was found in the exposed subjects compared with normal values ($p < 0.05$) but no significant difference was found ($p > 0.1$) for urine.

The concentrations of serum Cu were lower in exposed subjects ($p \leq 0.001$) and the concentration of serum Zn higher ($p \leq 0.001$) compared with

normal values. No significant difference in concentration of total serum Fe was found between normal and exposed groups. We did not find statistical differences in concentrations of any of those metals between different sites of exposure.

Discussion

It is evident from our study that even low Al exposure has an effect on concentrations of two major essential elements—namely, Cu and Zn. The Al concentrations measured in the air of these factories were well below threshold limit values and the increase in concentrations of Al in serum were only just significant ($p < 0.05$). Also, the urinary excretion of Al was not increased at these concentrations suggesting that it is not excreted readily and probably accumulates in other organs first.

Kavalchik *et al*²⁶ suggest that plasma may have a limited ability for Al binding. Excess of Al may then be translocated to other tissue stores making it unavailable for excretion.

To be able to explain why minute amounts of Al can exert unquestionable neurotoxic effects, the mode of its absorption and the mechanism by which it is transported within the physiological environment must be investigated. Birchall *et al*²⁷ suggest that the strong binding of Al by adjacent phosphate groups on inositol and slow ligand exchange charac-

Table 2 Comparison of concentrations of metals in normal and industrially exposed subjects

Sample	Normal subjects (n = 20)	Exposed subjects (n = 33)	p Value*
Serum Al (µg/dl)	1.13 (0.55)	1.60 (0.88)	<0.05
Urine Al (µg/l)	12.90 (3.35)	18.93 (15.38)	>0.1
Serum Cu (µg/dl)	144.90 (38.47)	99.27 (15.37)	≤0.001
Serum Zn (µg/dl)	88.68 (15.11)	127.63 (29.14)	≤0.001
Serum Fe (µg/dl)	177.20 (48.40)	147.41 (51.98)	>0.1

Results are expressed as mean (SD).

*Two tailed Student's *t* test.

teristics of Al would be expected to have a profound effect on the function of the phosphatidylinositol derived second messenger system.

The findings by Altman *et al*²⁸ show that low Al concentrations inhibit haemoglobin synthesis. Interaction of a toxic metal with essential elements plays a major part in its toxicity. If the molecular site on an enzyme normally occupied by the essential metal is usurped by a toxic metal, toxic effects will be seen.

We found that Al influences serum concentrations of Cu and Zn in workers exposed to less than 1 mg/m³ aluminium dust. It will be of interest to find out what changes occur in other soft tissues and bone at similar levels of exposure. This requires a controlled animal experiment at low concentrations of Al exposure and this is in progress.

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