BioMetals 1996, 9, 385–392

Aluminum in Saudi children

Iman Al-Saleh & Neptune Shinwari

Biological & Medical Research Department, King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia

Received 15 December 1995; accepted for publication 30 April 1996

Aluminum was determined in serum samples obtained from 533 Saudi female pupils aged 6–8 years who attended primary public school in Riyadh City, Capital of Saudi Arabia. The aluminum mean value was 23.21 ± 15.25 $\mu g\ l^{-1}$ in the range of 5.98–206.93 $\mu g\ l^{-1}$. Serum aluminum levels of pupils attending the Northern school area were higher than levels found in pupils from other school areas (Southern, Eastern and Central). Renal variables had no correlation with serum aluminum. On the other hand, a significant positive correlation was found between serum aluminium above 49.2 $\mu g\ l^{-1}$ and urea ($r = 0.6$, $P < 0.002$). Although 53% of the screened schools had aluminum in water above the European Union (EU) acceptable limit of 50 $\mu g\ l^{-1}$, there were no differences in aluminum in water between the four different school areas in Riyadh. Factors such as drinking water, diet and the use of aluminum utensils may have contributed to this result. As there is a bulk of literature which highlights the adverse developmental effects of aluminum on children and infants, it would be advantageous to establish regular aluminum monitoring.

Keywords: aluminum, drinking water, pupils, renal failure

Introduction

Aluminum is the third most abundant element in the Earth's crust, and all living organisms are environmentally and constantly exposed to this ubiquitous element. Aluminum in Western diets, excluding the contribution from aluminum-containing food additives, ranges from 2–3 mg day^{-1} (Greger 1985). However, an FDA study (Pennington & Gunderson 1987) reported that the daily aluminum intake may be even higher ranging from 9–14 mg Al(III) day^{-1}. When aluminum-based antacids are used, the intake becomes higher, up to 5g day^{-1} (Lione 1983).

Aluminum is used widely in the manufacture of various construction materials, insulated cables and wiring, packaging materials, and processing equipment. Various aluminum oxides are used as abrasives and refractories in different industrial operations. The metal and its compounds are also used in paper, glass and textile industries, and certain aluminum salts are used as food additives and as pharmaceuticals such as antacids and buffered analgesics (MAFF 1993).

Aluminum in the diet is derived from both natural and anthropogenic sources. Most foods, especially grains and vegetables, contain small amounts of naturally derived aluminum. In plant-based foods, the natural aluminum content is a reflection of aluminum levels in the soil and water in contact with the plants and the ability of the plants to absorb and retain aluminum (Pennington 1987). Certain plants, including tea, herbs and some leafy vegetables, absorb more aluminum than others (MAFF 1993). Aluminum concentrations in foods of animal origin reflect aluminum levels in animal 'food/fodder' and drinking water, the extent of absorption from the gut following ingestion and the ability of specific tissues to concentrate aluminum (Pennington 1987). The aluminum content of foods may be increased by the use of aluminum-containing food additives. Aluminum may also enter food adventitiously from aluminum cookware, utensils and packaging materials, and during food processing (Pennington 1987, Nagey & Jobst 1994). Aluminum is a natural

Address for correspondence: I. Al-Saleh, Biological & Medical Research Department (MBC#03), King Faisal Specialist Hospital & Research Centre, PO Box 3354, Riyadh 11211, Saudi Arabia. Tel: (+966) 1 442 7860; Fax: (+966) 1 442 7858.

constituent of both ground waters and surface waters (Wills & Savory 1989). Higher aluminum concentrations are generally found in waters draining acid-rain sensitive areas where the lack of soil and the acidic bedrock facilitate the mobilization of aluminum from the soil and underlying rock into the run-off surface waters. The aluminum content of drinking water may also be increased by the use of aluminum salts as flocculants during water purification. Aluminum salts, particularly aluminum sulfate, are used to remove organic materials present in surface waters that might affect the color or the taste of the finished product or reduce the efficiency of disinfection of water.

Over the past 30 years, there has been considerable research into the relationship between aluminum and several neurodegenerative diseases, notably Alzheimer's disease. Some epidemiological studies, including that by Martyn *et al.* (1989), have suggested an association between aluminum in the water supply and Alzheimer's disease. The finding is difficult to interpret since the daily intake of aluminum from water is much lower than that from food. One suggestion is that aluminum in water may be more readily absorbed from the gut than aluminum in food.

Concern has also been expressed over elevated levels of aluminum in infant formulae. This concern has arisen largely because of the suggestion (Hewitt *et al.* 1987) that the absorption of aluminum from the gut may be higher in infants than in adults and that the retention of aluminum could be increased due to inefficient renal clearance by the immature kidneys.

Aluminum, both as a metal and as an 'Al^{3+} ion' (Klaassen *et al.* 1986, Cotton & Wilkinson 1988) was long considered a harmless element; on the contrary, nowadays, it is a well recognized neurotoxic agent promoting considerable morbidity and mortality (Boegman & Bates 1984, Nicolini *et al.* 1991). In spite of this awareness, the basic mechanisms for Al(III) toxicity are yet to be fully understood. Several recent reviews deal with the relevance of Al(III) speciation and the toxic properties of the metal (Martin 1991, Corain *et al.* 1992a,b). Chronic aluminum poisoning is a well-known causative factor in osteomalacia, dialysis encephalopathy and microcythemia in patients with renal failure (Parsons *et al.* 1971, Alfery 1991). Besides, Al(III) has been proposed as a risk factor in the etiology of Alzheimer's disease (Crapper McLachlan 1986).

This study was undertaken during visits to 33 girls' primary public schools in Riyadh City to investigate the possible effect of lead exposure in female Saudi school children, as measured by blood lead concentration, on their performance in tests of neuropsychological ability and on their academic achievement. In Saudi Arabia, the addition of sodium aluminate solution to the drinking water, the wide use of aluminum utensils and the lack of information on the level of aluminum in the serum of Saudi children had led us to use those samples for the present study. We also investigated the possible influence of elevated serum aluminum concentrations on renal parameters.

Materials and methods

Study population

Subjects used in this study were identified and selected from a previous epidemiological cross-sectional study of a subpopulation of the Kingdom of Saudi Arabia, specifically Saudi female children aged 6–8 years attending first and second grade primary public schools in Riyadh City, in which the relationships between blood lead concentrations and neuropsychological test and academic achievements were studied. In order to ensure a representative sample, stratification was conducted with respect to geographic or socioeconomic distribution using a systematic sampling technique. Thirty three schools were selected. Details of the study were reported elsewhere (personal communication).

Analytical methods

Blood samples were collected by venipuncture into red-top Vacutainer tubes (Becton Dickinson, Rutherford, NJ) and allowed to clot for 20 min at room temperature. Then the tube was centrifuged for 10 min at 2000 r.p.m. at 4°C. The serum was transferred to disposable glass tubes, all found to be aluminum free, and kept frozen until analyzed. Aluminum concentrations in serum samples were determined by a Varian AA-40 atomic absorption spectrophotometer with an aluminum hollow cathode lamp, coupled to a GTA 96 electrothermal atomizer and a programmable sample dispenser (Varian Techtron, Milgrave, Victoria, Australia). The optimized heating program followed was that described by the instrument manufacturer (McKenzie 1988). Quadruplicate determinations were made on all samples. If the range of the quadruplicates exceeded 10% of the mean, further replicates were performed. Serum samples were diluted 4-fold with 0.2% Triton X-100 (Aldrich Chemical Company Inc., USA) in 0.1 M 'selectipur' = nitric acid (Merck, Darmstadt, Germany). Calibration standards were prepared using an automatic standard addition procedure recommended by the manufacturer (McKenzie 1988). Additions were prepared from a single standard 0.015 $\mu g\ l^{-1}$ Al solution (Fischer Scientific Company, Fair Lawn, NJ) and Triton X-100 as a diluent. Additions of 0, 2.5, 5.0 and 10 $\mu g\ l^{-1}$ were used. Total injection volume was 24 μl. The results were interpreted by using linear least-squares program. External quality assessment (EQA) scheme specimens (Robins Institute, University of Surrey, UK) were incorporated to measure and maintain accuracy and reproducibility of the procedure (Taylor & Briggs 1986). Serum samples were sent to the Pathology Laboratory, King Faisal Specialist Hospital, for the analysis of calcium, total protein, urea, creatinine, sodium, chloride, potassium and glucose using a Hitachi 717 analyzer (Boehringer-Mannheim, Japan). Hematological parameters were determined with an automated Coulter Counter (Coulter Electronics).

Running water samples were collected from two drinking water coolers in each of the selected schools and stored in 50 polyethylene bottles previously washed in nitric acid. One school did not have water facilities. Out of the other 32 schools, five had one water cooler. Therefore, the total number of tested water samples was 59. Only high use water coolers were selected. The water was acidified with 50% (v/v) 'selectipur' nitric acid (Merck, Darmstadt, Germany) to bring the pH to less than 2, as acidification minimized the adsorption of metals into the walls of the container. Analyses of water were performed by inductively coupled plasma spectrometry. The instrumentation consisted of a Unicam, ICP-701 (ATI-Unicam, Cambridge, UK). Details of the analytical procedures have been reported previously (Al-Saleh, 1996).

Statistics

Aluminum was considered as the dependent variable whereas the others were independent variables. Parametric statistical analyses such as one-way analysis of variance (ANOVA), Scheffe's test (Scheffe 1959) for multiple comparisons and correlation analyses were used to analyze the data. The analysis of the data was accomplished with the Statgraphics programs (Statgraphics 1992). A confidence level of 95% was chosen to evaluate the calculated P value. However, for the multiple comparison statistical analysis, a 99% confidence level was applied.

Results

Descriptive statistics, sample size, means, standard deviations, and the ranges for the measured variables, aluminum, hemoglobin (Hb), hematocrit (Hct), red blood cells (RBC), white blood cells (WBC), mean corpuscular cell volume (MCV), mean corpuscular hematocrit (MCH), mean corpuscular hematocrit concentration (MCHC), glucose, urea, creatinine, sodium, calcium, potassium, chloride, total protein, age, weight (WT) and height (HT) are provided in Table 1.

The cumulative distribution plot of aluminum concentrations in the screened pupils ($n = 533$) did not follow a Gaussian distribution but was positively skewed (5.283) as shown in Figure 1. Therefore, all aluminum measurements were subjected to log transformation to obtain approximate normality of their distribution as shown in Figure 2. Frequency tabulation of the aluminum data revealed that 76.4% of the screened pupils had aluminum concentrations less than or equal to 26.6 $\mu g\ l^{-1}$, 19.3% had 26.6–49.2 $\mu g\ l^{-1}$ and 4.3% had greater than 49.2 $\mu g\ l^{-1}$ (Table 2). Looking at the distribution of each class interval showed that both aluminum class intervals of 0–26.6 and 26.6–49.2 $\mu g\ l^{-1}$ did follow a normal distribution (Figures 3 and 4) with a skewness of 0.1 and 0.4, respectively. On the other hand, the skewness of aluminum class interval greater than 49.2 $\mu g\ l^{-1}$ is 2.87.

In Saudi Arabia, pupils attend schools that locate within the same area of their residence. To ascertain whether the location of schools had any influence on aluminum data, screened schools were grouped according to their location in relation to the main highways in Riyadh. There are five major highways dividing the city into five areas: (1) Northern Circle Highway, (2) Southern Circle

Table 1. Descriptive statistics of data

Variable	n	Mean	SD	Range
Aluminum ($\mu g\ dl^{-1}$)	533	23.21	15.252	5.984–206.934
Age (months)	515	93.708	10.827	70.87–142.90
Weight (kg)	517	22.831	5.342	13.2–56.5
Height (cm)	519	121.688	6.649	101–153
WBC	532	7.368	2.03	3.5–16.8
RBC	533	4.881	0.420	0.09–6.29
Hb ($g\ l^{-1}$)	533	127.891	9.572	63–153
Hct	533	0.38	0.026	0.209–0.453
MCV (fl)	533	77.77	5.453	52–96.8
MCH (pg)	533	26.249	2.202	15.8 33.8
MCHC ($g\ l^{-1}$)	533	336.925	8.754	302–399
Glucose ($mmol\ l^{-1}$)	533	5.402	1.099	3.1–10.7
Urea BUN ($mmol\ l^{-1}$)	533	3.77	0.915	1.6–7.1
Creatinine ($\mu mol\ l^{-1}$)	533	45.328	5.698	32–70
Sodium ($meq\ l^{-1}$)	533	140.824	2.425	115–148
Potassium ($meq\ l^{-1}$)	533	4.396	0.433	3.3–6.5
Chloride ($meq\ l^{-1}$)	533	102.672	2.638	86–110
Calcium ($mmol\ l^{-1}$)	533	2.432	0.107	1.59–2.85
Total protein ($g\ l^{-1}$)	533	73.816	3.897	49–86

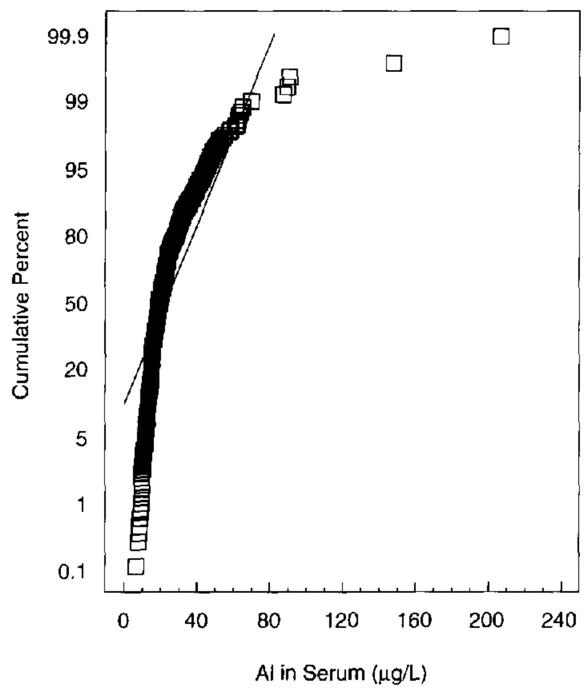

Figure 1. Cumulative frequency distribution plot of aluminum.

Table 2. Frequency distribution of aluminum in the screened pupils

Class intervals of aluminum data (µg l^{-1})	n	%
0–26.6	407	76.4
26.6–49.2	103	19.3
49.2–207.4	23	4.3
Total	533	

Highway, (3) Eastern Circle Highway, (4) Western Circle Highway and (5) Central (represented by Khurais Highway). Screened schools that are located above the Khurais Highway were designated as Northern area schools, screened schools located to the east of the Eastern Circle Highway were designated as the Eastern area schools. Schools located to the south of the Southern Circle Highway were designated as the Southern area schools. No schools were found to the west of the Western Circle Highway. The Central area schools were encircled by the five above-mentioned highways.

One-way analysis of variance provided evidence for statistically significant differences among the different locations ($F = 18.85$; d.f. between groups = 3; d.f. within groups = 529; $P = 0$). This analysis is only valid if the variances are equal. Bartlett's test

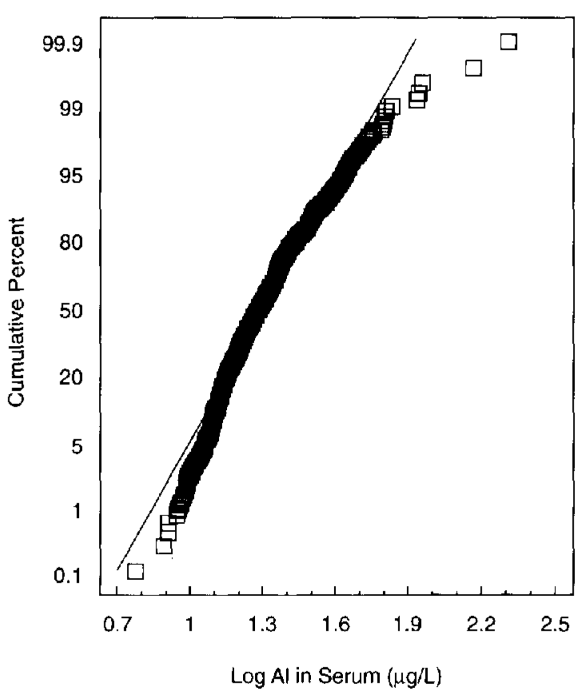

Figure 2. Cumulative frequency distribution plot of log-transformed aluminum.

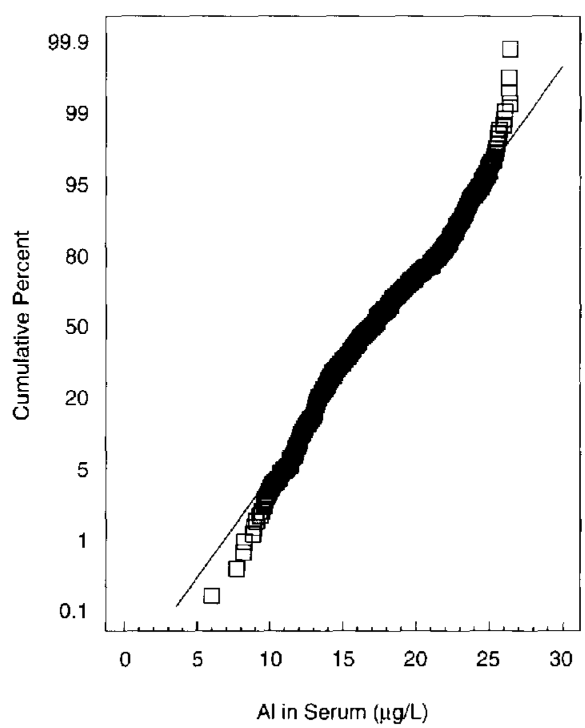

Figure 3. Cumulative frequency distribution plot for aluminum data less than or equal to 26.6 µg l^{-1}.

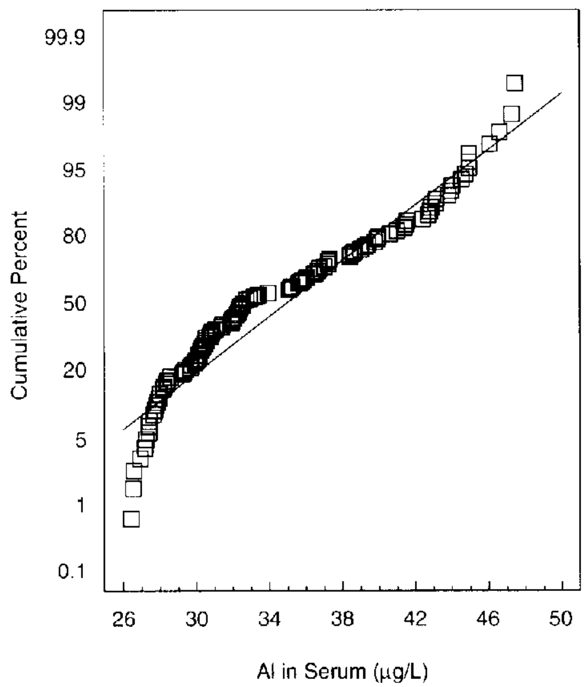

Figure 4. Cumulative frequency distribution plot for aluminum data greater than 26.6 μg l^{-1} and less than or equal to 49.2 μg l^{-1}.

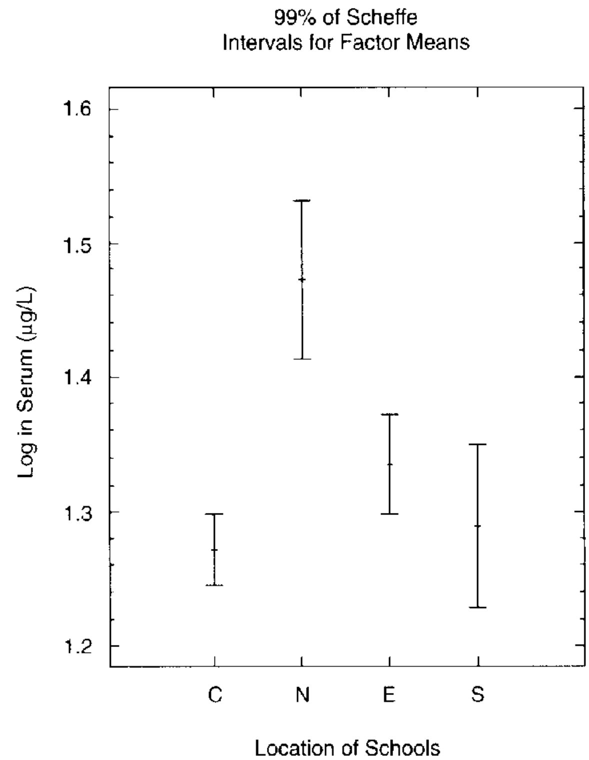

Figure 5. Aluminum concentrations in serum according to location of schools.

was used to ascertain the validity of this assumption. The test showed that the variances were equal ($P > 0.001$). However, this test did not indicate which groups were different. To answer this, multiple comparisons, as evaluated by Scheffe's *F*-test (Scheffe 1959), were applied to log-transformed aluminum data. At the 99% confidence level, the results of this method showed that no significant differences were found between aluminum concentrations from schools located in the Central, Eastern and Southern areas (Group A, Table 3). Schools in the Northern areas were significantly different from those in other areas (Group B) and the highest aluminum concentrations were found in schools located in the Northern part of Riyadh (Figure 5).

We also examined the correlation between log aluminum data and the renal parameters such as

Table 3. Multiple range analysis test

School location	No.	Mean log aluminium concentration (μg l^{-1})	Grouping A	Grouping B
Central	271	1.272	*	
Southern	54	1.289	*	
Eastern	152	1.336	*	
Northern	56	1.473		*

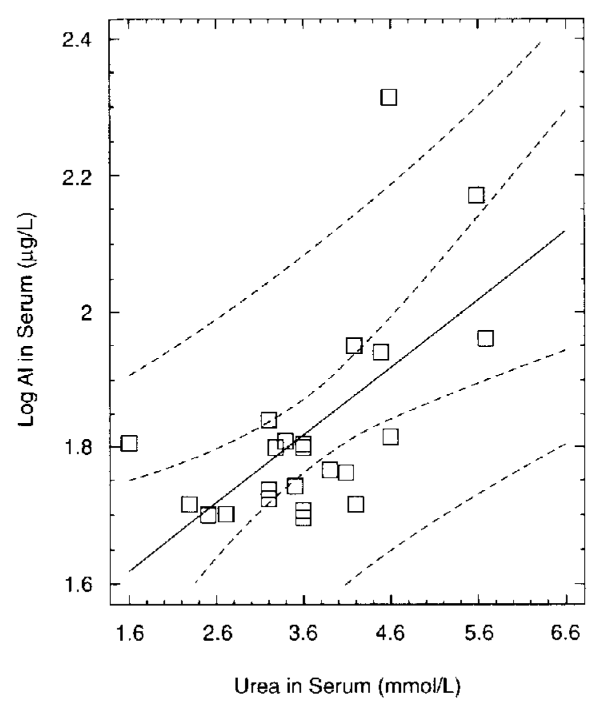

Figure 6. Relationship between aluminum concentrations above 49.2 μg l^{-1} and urea in serum.

Table 4. Aluminum concentrations in water and serum samples collected from schools in Riyadh

School area	No. of pupils	Mean serum aluminum ± SD ($\mu g\ l^{-1}$)	Mean water aluminum ± SD ($\mu g\ l^{-1}$)	No. of water samples
Northern	56	31.858 ± 12.069 (13.129 – 64.319) (n = 4)[a]	38.0537 ± 30.845 (0.1 – 68.933) (n = 4)	7
Southern	54	20.384 ± 6.215 (9.683 – 37.4) (n = 4)	49.792 ± 17.175 (26.289 – 75.978) (n = 4)	8
Eastern	152	24.409 ± 17.973 (8.194 – 206.934) (n = 10)	45.427 ± 21.935 (0 – 85.778) (n = 10)	19
Central	271	21.313 ± 14.796 (5.984 – 148.334) (n = 15)	52.914 ± 32.597 (0 – 106.8) (n = 7)	25
Total	533	23.209 ± 15.252 (5.984 – 206.934) (n = 33)	48.183 ± 27.295 (0 – 106.8) (n = 32)	59

[a]n, number of screened schools.

creatinine, glucose, calcium, potassium, chloride, sodium and urea for all the pupils ($n = 533$). No correlation was found between aluminum data and the renal variables. Attempts were made to examine the correlation between a subgroup with aluminum concentrations greater than 49.2 $\mu g\ l^{-1}$ ($n = 23$) and the renal parameters. There was a significant positive correlation between aluminum and urea ($r = 0.62$, $P = 0.0016$) as shown in Figure 6.

The results for aluminum in drinking water in the screened schools are listed in Table 4, together with the aluminum in serum taken from pupils attending the same schools. Using simple linear regression analysis, no significant relationship was found between aluminum in water and serum. No significant differences were found in the concentrations of aluminum in water between the four different areas in Riyadh.

Discussion

In this study, the aluminum data distribution in the screened pupils suggests the existence of three mixed populations. This raised an important question – whether this is related to the existence of three different types of aluminum exposure or due to other factors? Two cut-off points of 26.6 and 49.2 $\mu g\ l^{-1}$ were found where the three populations separate. This revealed that 76.4% of the pupils have aluminum levels below 26.6 $\mu g\ l^{-1}$, which represents the first population within the studied subjects (reference population). Subjects with aluminum above 26.6 $\mu g\ l^{-1}$ and below 49.2 $\mu g\ l^{-1}$ (19.3% of the entire studied subjects) and in the range of 26.62–47.89 $\mu g\ l^{-1}$ are considered as the second population within the screened pupils. The third group represents the highly exposed pupils with aluminum levels above 49.2 $\mu g\ l^{-1}$, which represents 4.3% of the screened population and in the range of 49.7–206.93 $\mu g\ l^{-1}$. Despite the lack of any comparative study, it is reassuring that the reported serum aluminum concentrations in the screened pupils are high since current studies suggest that the plasma aluminum concentration is less than 10 $\mu g\ l^{-1}$ in healthy individuals (Alfery 1986). The normal body burden of aluminum is quite small, the body absorbs only 15 μg (<1%) of the 3–5 mg of aluminum ingested daily (Alfery 1984). Renal excretion keeps the body burden below 30–40 mg and the plasma level approximately 6 $\mu g\ l^{-1}$ (Alfery 1983, 1984). Although the available data suggest that serum aluminum levels greater than 100 $\mu g\ l^{-1}$ are clearly associated with an increased risk of developing aluminum toxicity in children (Trompeter *et al.* 1986). Under ordinary conditions in healthy people, the kidney appears to be able to excrete all of the absorbed aluminum. Many cases of aluminum toxicity have been described in patients with renal failure (Griswold *et al.* 1983, Andreoli *et al.* 1984, Salusky *et al.* 1984, Sedman *et al.* 1984a,b, Chazan *et al.* 1988). However, Kaehny *et al.* 1977 demonstrated elevated plasma aluminum levels in normal adults when they consumed a variety of antacid-containing aluminum (ACA) in large doses. Although serum aluminum levels in our screened pupils were markedly elevated, no sign of aluminum toxicity has been seen. This was confirmed by the absence of a relationship between serum aluminum in the screened pupils and the measured renal parameters. On the other hand, a signifiant positive relationship between serum aluminum concentrations greater than 49.2 $\mu g\ l^{-1}$ and serum urea was noted. However, the serum concentration of urea rises with impaired renal function. Other factors not connected with renal function or urine excretion can influence serum urea such as the degree of protein catabolism, whether produced by a high protein diet or by hypersection or injection of adrenal steroids that results in the mobilization of protein for energy purposes (Kaplan *et al.* 1988). However, aluminum toxicity over time may still occur.

Our results suggest that high serum aluminum levels are associated with the location of the school. The serum aluminum concentrations of pupils who attended the Northern area schools were higher than those from other areas. This could be attributed to dietary factors since the Northern area of Riyadh City represents the highest socioeconomic status. In the Central, Eastern and Southern area schools, the serum aluminum concentrations were not different. On the other hand, no significant differences were found in water aluminum among the four different locations. Surprisingly, the concentrations of aluminum in the tested drinking water from 32 schools were higher than the European Union guideline level (EEC 1981). In this study, 53% of the tested water samples had an aluminum content higher than the EU guideline limit (50 $\mu g\ l^{-1}$). In Saudi Arabia, sodium aluminate solution (25%) is added to water as a flocculating agent in the purification of municipal water supplies. This should be a matter of public health since previous studies (Flaten 1987, Martyn *et al.* 1989) have postulated that aluminum in drinking water is one of the etiological agents of a number of dementia diseases, including Alzheimer's disease. Usually, aluminum in drinking water comes from the treatment process. This has led many countries to discontinue the use of aluminum salts in water treatment. It was found that the risk of Alzheimer's disease was 1.5 times higher in the population of England and Wales living in districts where the mean aluminum concentration in the drinking water exceeded 110 $\mu g\ l^{-1}$ than in districts where aluminum concentrations were less than 10 $\mu g\ l^{-1}$ (Martyn *et al.* 1989). In subjects with normal renal function, high concentrations of aluminum in drinking water (80 $\mu g\ l^{-1}$) have been related to an elevated incidence of Alzheimer's disease (Giordano & Costantini 1993). The lack of relationship between aluminum in water and serum in this study should not be constructed as meaning that aluminum in water has no contribution on the elevation of aluminum in serum since the sample size of water samples was small.

In conclusion, this study showed that the concentration of aluminum in drinking water exceeds the guideline values that were set by the EU (EEC 1981). Guideline values were set according to the assumption of a daily consumption of 2 l by a person weighing 60 kg. Such an assumption may be not applicable for this study for the following reasons. First, water intake is likely to vary with climate, e.g. at temperatures above 25°C there is a sharp rise in fluid intake to meet the demands of increased sweat rate. This study was conducted during May–June when the temperature is usually around 35°C. Second, children consume more fluid per unit weight than adults (WHO 1993). Therefore, children who attend these schools are at a high risk from exposure to metals. It is very important to investigate the cause with a view to taking remedial action.

In addition to drinking water, other factors such as diet might have an influence on aluminum concentrations. The normal dietary source of aluminum is food and water to which aluminum has been added or in which there is naturally a high content (Sorensen *et al.* 1974, Pennington 1987). However, it has been stated that 'the inappropriate choice of foods, methods of food preparation and non-prescription drugs can readily increase the daily intake of aluminum to several thousand milligrams each day' (Lione 1983). Also, one could anticipate that since aluminum is permitted as an external coloring agent for cake decoration and on sugar-coated flour confectionery such as chewing gums, chocolate, sweets, etc. (MAFF 1993), such items of confectionary are likely to be potential hazards of special importance because of the extent to which children consume them.

Although the data in this study are not representative of the general population, they reveal a need to monitor and reduce aluminum in the environment of Saudi Arabia.

References

Alfery AC. 1983 Aluminum. *Adv Clin Chem* **23**, 69–91.

Alfery AC. 1984 Aluminum intoxication, editorial. *N Engl J Med* **310**, 1113–1115.

Alfery AC. 1986 Aluminum metabolism. *Kidney Int* **29 (Suppl 18)**, S8–S11.

Alfery AC. 1991 Aluminum intoxication recognition and treatment. In: Nicolini M, Zatta PF, Corain B, eds. *Aluminum in Chemistry, Biology and Medicine. A Series of Advances*, Vol. 1. Verona: Cortina; 73–84.

Al-Saleh I. 1996 Trace elements in drinking water coolers collected from primary schools, Riyadh, Saudi Arabia. *Sci Total Environ* **181**, 215–221.

Andreoli SP, Bergstein JM, Sherrard DJ. 1984 Aluminum intoxication from aluminum-containing phosphate binders in children with azotemia not undergoing dialysis. *N Engl J Med* **310**, 1079–1084.

Boegman RJ, Bates LA. 1984 Neurotoxicity of aluminum. *Can J Physiol Pharmacol* **62**, 1010–1014.

Chazan JA, Blonsky SL, Abuelo JG, Pezzullo JC. 1988 Increased body aluminum: an independent risk factor in patients undergoing long term hemodialysis? *Arch Intern Med* **48**, 1817–1820.

Corain B, Tapparo A, Abdiqafar A, Sheikh-Osman, Bombi G. 1992a The solution state of aluminum (III) as relevant to experimental toxicology: recent data and new perspectives. *Coord Chem Rev* **112**, 19–32.

Corain B, Nicolini M, Zatta P. 1992b Aspects of the bioinorganic chemistry of aluminum (III) relevant to the metal toxicity. *Coord Chem Rev* **112**, 33 45.

Cotton AF, Wilkinson G. 1988 *Advanced Inorganic Chemistry*. New York: Wiley.

Crapper McLachlan DR. 1988 Aluminum and Alzheimer's disease. *Neurobiol Aging* **7**, 525–532.

EEC. 1981 Official Journal of the European Communities Council directive of 15 July 1980 relating to the quality of water intended for human consumption. 80/778/EEC. No. L229/11.

Flaten TP. 1987 Geographical associations between aluminum in drinking water and dementia, Parkinson's disease and amyotrophic lateral sclerosis in Norway. *Trace Elem Med* **4**, 179–180.

Giordano R, Costantini S. 1993 Some aspects related to the presence of aluminum in waters. *Ann Ist Super Sanita* **29**, 305 311.

Greger JL. 1985 Aluminium content of the American diet. *Food Technol* **39**, 73–80.

Griswold WR, Reznik V, Mendoza SA, Trauner D, Alfery AC. 1983 Accumulation of aluminum in a nondialized uremic child receiving aluminum hydroxide. *Pediatrics* **71**, 56–58.

Hewitt CD, O'Hara M, Day JP, Bishop N. 1987 Exposure of infants to aluminum from milk formulae and intravenous fluids. In: Bratter P, Schramel P, eds. *Trace Element–Analytical Chemistry in Medicine and Biology*, Vol. 4. Berlin: Walter de Gruyter; 481.

Kaehny WD, Hegg AP, Alfery AC. 1977 Gastrointestinal absorption of aluminum from aluminum-containing antacids. *N Engl J Med* **296**, 1389–1390.

Kaplan A, Szabo LL, Opheim KE. 1988 *Clinical Chemistry: Interpretation and Techniques*, 3rd edn. Philadelphia: Lea and Febiger; 112–144.

Klaassen CD, Amdur MO, Doull J. 1986 *Toxicology*, 3rd edn. New York: MacMillan.

Lione A. 1983 The prophylactic reduction of aluminum intake. *Food Chem Toxicol* **21**, 103–109.

Martin RB. 1991 Aluminum in biological systems. In: Nicolini M, Zatta PF, Corain B, eds. *Aluminum in Chemistry, Biology and Medicine. A Series of Advances*, Vol. 1. Verona: Cortina; 3.

Martyn CN, Barker DJP, Osmond C, Harris EC, Edwardson JA, Lacey RF. 1989 Geographical relationship between Alzheimer's disease and the Al in drinking water. *Lancet* **i**, 59–62.

McKenzie T. 1988 Analytical data for the GTA-96. In: Rothery E. ed. *Analytical Methods for Graphite Tube Atomizer*. Milgrave, Victoria, Australia: Varian Tectron; 113.

Ministry of Agricultural, Fisheries and Food (MAFF). 1993 *Aluminum in Food*. The thirty-nine report of the Steering Group on Chemical Aspects of Food Surveillance. Food Surveillance Paper 39. HMSO, London.

Nagey E, Jobst K. 1994 Aluminum dissolved from kitchen utensils. *Bull Environ Contam Toxicol* **52**, 396–399.

Nicolini M, Zatta PF, Corain B. 1991 *Aluminum in Chemistry, Biology, and Medicine*. Verona: Cortina.

Parsons V, Davies C, Goode C, Ogg C, Siddiqui J. 1971 Aluminum in bone from patients with chronic renal failure. *Br Med J* **4**, 273–275.

Pennington JAT. 1987 Aluminum content of foods and diets. *Food Addit Contam* **5**, 161–232.

Pennington JAT, Gunderson EL. 1987 A history of the food and drug administration's total diet study 1961 to 1967. *J Ass Anal Chem* **70**, 772 782.

Salusky IB, Coburn JW, Paunier L, Sherrard DJ, Fine RN. 1984 Role of aluminum hydroxide in raising serum aluminum levels in children undergoing continuous ambulatory peritoneal dialysis. *J Pediatr* **105**, 717–720.

Scheffe H. 1959 The multivariate analysis. In: *The Analysis of Variance*. New York: Wiley; 163–190.

Sedman AB, Miller NL, Warady DA, Lum GM, Alfery AC. 1984a Aluminum loading in children with chronic renal failure. *Kidney Int* **26**, 201–204.

Sedman AB, Wilkening GN, Warady DA, Lum GM, Alfery AC. 1984b Encephalopathy in childhood secondary to aluminum toxicity. *J Pediatr* **105**, 836–838.

Sorensen JRJ, Campbell IR, Tepper LB, Lingg RD. 1974 Aluminum in the environment and human health. *Environ Health Perspect* **8**, 3–95.

Statgraphics software. 1992 Statistical graphics system by statistical graphics corporation. A PLUS*WARE software product, STSC, Inc.

Taylor A, Briggs RJ. 1986 An external quality assessment scheme for trace elements in biological fluids. *Journal of Analytical Atomic Spectrometry* **1**, 391–395.

Trompeter RS, Polonsky MS, Andreoli SA, *et al.* 1986 Neurologic complications of renal failure. *Am J Kidney Dis* **7**, 318–323.

Wills MR, Savory J. 1989 Aluminum and chronic renal failure: sources, absorption, transport and toxicity. *Crit Rev Clin Lab Sci* **27**, 59–107.

World Health Organization (WHO). 1993 *Guidelines for Drinking-Water Quality*, 2nd edn, Vol. 1. Recommendations. Geneva: WHO.