

---

**Original Article**

---

## High Accumulation of Aluminum in Hairs of Infants and Children

Hiroshi Yasuda<sup>1)</sup>, Kazuya Yoshida<sup>1)</sup>, Mitsuru Segawa<sup>1)</sup>, Ryoichi Tokuda<sup>1)</sup>,  
Yuichi Yasuda<sup>2)</sup> and Toyoharu Tsutsui<sup>1)</sup>

<sup>1)</sup> Research Laboratory, La Belle Vie Inc., Tokyo 103-0006, Japan

<sup>2)</sup> Health Science Laboratory, Tokyo 202-0001, Japan

### Abstract

This report demonstrates that infants and children have suffered from high aluminum accumulation, based on the evidence data of 1,720 children. For estimating its body burden, the scalp hair aluminum concentrations were measured with inductively coupled mass spectrometry (ICP-MS). The geometric mean of hair aluminum concentration was 10.4 and 11.1 µg/g (ppm) for boys and 11.8 and 10.5 ppm for girls, in the groups aged 0-3 and 4-9 years, respectively. These levels were high-significantly ( $p < 0.0000$ ) and nearly 3-fold higher than those in the adults (3.8 and 4.0 ppm for male and female). Ten children exhibited higher aluminum levels exceeding 50 ppm, and the highest level observed was 116.8 ppm in a five-year-old boy.

This wide-used metal should be monitored as toxic element risky to the young generation and its adverse effects remain to be clarified.

**Keywords :** Aluminum accumulation ; Toxic metal ; Infants ; Brain development

### Introduction

In the meeting of the Joint FAO/WHO Expert Committee on Food Additives in 2006, the Committee concluded that aluminum compounds have the potential to affect the reproductive system and developing nervous system, and recommended that the provisional tolerable weekly intake (PTWI) for aluminum should be reduced from 7 to 1 mg/kg body weight [1].

Aluminum is known to have a neuro-toxic character as well as lead [2-5], and known as the causative agent that induces dialysis encephalopathy in the patients with renal

failure [6-8]. This element also seems to link with microcytic anaemia, osteo-malacia, and amyotrophic lateral sclerosis or other neurodegenerative diseases [8-14]. However, there is little report on body exposure to aluminum in children and also on its adverse effects on infants. In this study, we surveyed the aluminum concentrations in scalp hair of total 1,720 Japanese children for estimating their body burden, in comparison with those of adults, and demonstrated that the young children aged 0-9 years have suffered from high exposure to this toxic metal.

### Materials and Methods

Scalp hair samples from 1,720 subjects aged 0-15 years (male : 1,276 ; female : 444), from whose parents informed consent was obtained, were examined for mineral analysis, and compared to those of adults aged 21-40 years. The study procedures were approved by the ethical committee of this laboratory.

The hair sample of 75 mg was weighed into 50ml plastic tube, and washed with acetone and then with 0.01% Triton solution, as previously reported [15]. The washed hair sample was mixed in 10 ml of 6.25% tetra methyl ammonium hydroxide (TMAH, Tama Chemical) and 150 µl of an internal standard solution (SPEX Certi Prep.),

---

Address correspondence to :

Hiroshi Yasuda, Ph.D.  
Research Laboratory, La Belle Vie Inc.  
8-4 Nihonbashi-Tomizawacho, Chuo-ku, Tokyo  
103-0006, Japan  
TEL : 03-5614-2711  
FAX : 03-3668-5001.  
E-mail : yasuda@LBV.jp

---

Received : 16 August 2007

Revised : 3 March 2008

Accepted : 4 March 2008

and then dissolved at 75 °C with shaking for 2 hours. After cooling to room temperature and topping up to 15.00 g gravimetric, the obtained solution was used for analysis. The aluminum concentration was measured with inductively coupled plasma mass spectrometry (ICP-MS ; Agilent Technologies) with the internal standard method [15-17]. The inter-daily variation of analysis (C.V) for aluminum of control stocked-solution was estimated to be 6.9 %. The aluminum contents in hair were expressed as  $\mu\text{g/g}$  hair (ppm).

### Statistical Analysis

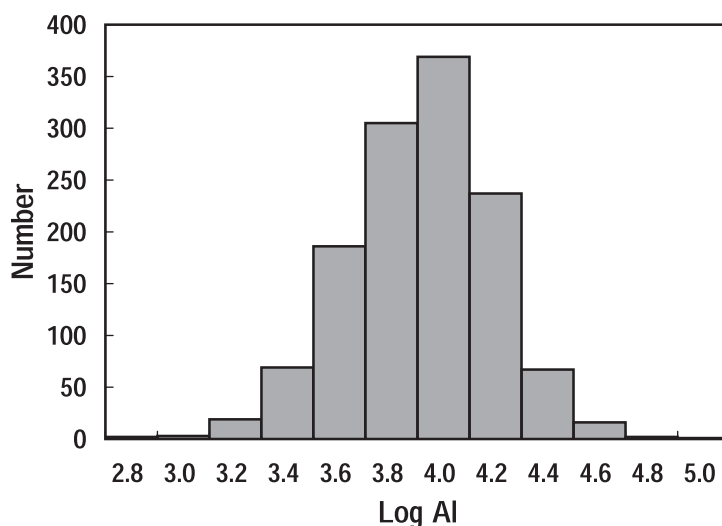
For normalization and further statistical analysis, the values of hair aluminum contents were transformed to the logarithm. An overall difference between the groups was determined by one-way analysis of variance (ANOVA, JMP6), and the differences between groups were estimated using Fisher's LSD test.

### Results

Figure 1 shows the logarithmic distribution of hair aluminum concentrations in male children aged 0-15 years old, in comparison with adults aged 21-40 years old (Fig. 2). The hair aluminum levels were approximately distributed in lognormal manner, and so the geometric rather than arithmetic means were used as representative of hair mineral level. Table 1 shows the geometric mean of hair aluminum levels,  $\pm 1$  geometric standard deviation

(GSD) range, and minimum and maximum values for three age-groups of children, in comparison with the adult group. Compared to the mean levels in adults (3.8 and 4.0 ppm), high-significant ( $p < 0.0000$ ) and nearly 3-fold higher levels, namely 10.4 and 11.1 ppm for boys and 11.8 and 10.5 ppm for girls, were observed in the infants/children groups aged 0-3 and 4-9 years, respectively. Ten children (9 male and 1 female) exhibited higher aluminum levels exceeding 50 ppm, which was the expected toxic level (Table 2). The highest level observed was 116.8 ppm in a five-year-old boy, which was estimated to be over 30-fold higher than mean adult level. Thus, the younger children groups less than 10 years of age were estimated to have significantly higher aluminum accumulation than the low-teenager (10-15 years) group and adult group.

In the lowest age group, the infants of 0-year age tended to exhibit the highest geometric mean value of 15.4 and 13.7 ppm for boys and girls, respectively (Table 3). These results suggest that the aluminum accumulated in mother's body is co-transferred with calcium and magnesium to the fetal, through bone-resorption during pregnancy and breast-feeding. The hair aluminum levels in girls were little different from those in boys, suggesting that there is little gender difference in aluminum accumulation.



**Fig. 1** Logarithmic histogram of hair aluminum levels in male Japanese children.

The histogram of hair aluminum concentrations for 1,276 male children aged 0-15 years is shown in the logarithm. The numbers on the abscissa indicate the logarithms of hair aluminium concentrations. The width and height of each rectangle represents the class interval in the logarithm of hair aluminium level and the corresponding frequency, respectively. This histogram indicates an approximate logarithmic normal distribution with the highest frequency of 369 in the range of 4.0-4.2 logarithms.

**Table 1** Hair aluminum levels in Japanese children.**Male Children (N = 1,276)**

Age	No.	Geomean	Range	Minimum	Maximum	P-value
0-3 years	373	10.42	5.61-19.4	1.39	62.0	<0.0000
4-9 years	743	11.07	5.99-20.5	1.34	116.8	<0.0000
10-15 years	160	7.30	3.71-14.4	0.72	43.4	<0.0000
Adults	436	3.76	1.77-7.96			

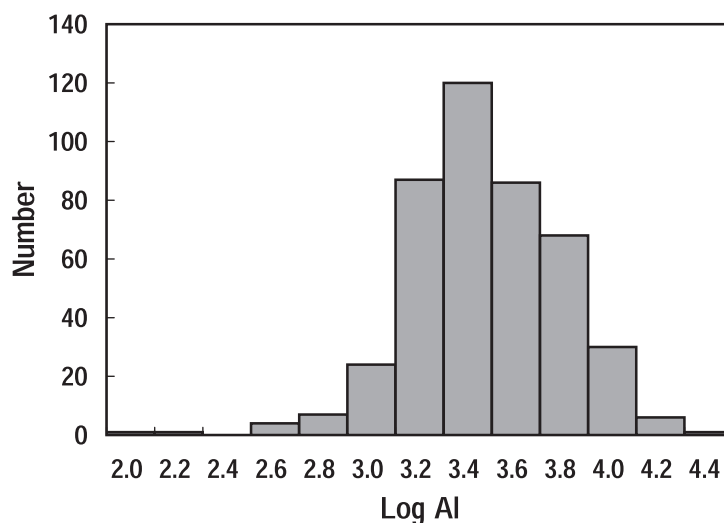
**Female Children (N = 444)**

Age	No.	Geomean	Range	Minimum	Maximum	P-value
0-3 years	129	11.78	6.03-23.0	1.02	46.0	<0.0000
4-9 years	236	10.50	5.35-20.6	0.71	50.9	<0.0000
10-15 years	79	6.33	3.10-12.9	0.91	27.9	<0.0000
Adults	415	4.04	1.93-8.48			

Range:  $\pm 1$  GSD rangeUnit:  $\mu$ g/g (ppm)**Table 2** Appearance rate of individuals with high hair aluminium levels in children.

High Al level	Male		Female	
	Number #	Rate (%)	Number #	Rate (%)
> 37 $\mu$ g/g	22	1.72	9	2.03
> 50 $\mu$ g/g	9	0.71	1	0.23

#: Number of the children with excessively high aluminum levels

37  $\mu$ g/g (ppm): 10-fold higher level of the average in adults.50  $\mu$ g/g (ppm): Toxic level (expected)**Fig. 2** Logarithmic histogram of hair aluminum levels in male Japanese adults.

The histogram of hair aluminum concentrations for 436 male adults aged 21-40 years is shown in the logarithm. The numbers on the abscissa indicate the logarithms of hair aluminium concentrations. The width and height of each rectangle represents the class interval in the logarithm of hair aluminium level and the corresponding frequency, respectively. This histogram indicates an approximate logarithmic normal distribution with the highest frequency of 120 in the range of 3.4-3.6 logarithms.

## Discussion

Hair is a unique kind of tissue containing hair-specific protein "hard keratin" which is rich in cysteine residue capable of binding with heavy metals, and functions to excrete them out of the body. Thus, scarp hair has been accepted as a good marker sample for estimating body

mercury burden, and widely used for monitoring body exposure to this toxic heavy metal among general populations [18-20]. We have been measuring several toxic and essential minerals in the subjects from infant to elderly, in order to assess body toxic metal exposure, mineralome and some relationship between the minerals and

**Table 3** Geometric means of hair aluminum levels in infants.

Age (years)	No.	Geometric Mean	
		Male	Female
0	14	15.4	13.7
1	55	9.8	13.6
2	146	9.6	10.5
3	287	10.8	11.6

Unit:  $\mu$  g/g (ppm)

physical or mental disorder for the last several years [15-17].

Aluminium is the most abundant metal in the earth and one of the most widely used metals in the present society. Therefore, aluminum in the soil is taken by various plants such as cereals, legumes, vegetables and seaweed, and bio-accumulates in the food chain, eventually causing exposure to humans. Aluminum is also taken via consumption of some processed foods, infant formulas, drugs and tobaccos etc [1, 21-24].

In 1976, Crapper et al. [25] found that an average aluminum concentration in a normal brain was  $1.9 \pm 0.7 \mu\text{g/g}$  dry weight. McDermott et al. [26,27] reported a mean aluminum concentration of  $2.5 \pm 0.3 \mu\text{g/g}$  dry weight for non-neurologic control brain and significantly higher  $15.9 \mu\text{g/g}$  for the patients died with dialysis encephalopathy. Alfrey et al. [28] published  $2.2 \pm 1.3 \mu\text{g/g}$  dry weight for brain, with  $3.3 \pm 2.9 \mu\text{g/g}$  for spleen and  $4.0 \pm 1.3 \mu\text{g/g}$  for liver. Howard [29] reported that the normal concentrations of serum aluminum in children ranged from 3-21  $\mu\text{g/L}$  (mean 9.5  $\mu\text{g/L}$ ) while higher aluminum concentrations were found in hyperactive children (range 9-30  $\mu\text{g/L}$ , mean 16.6  $\mu\text{g/L}$ ) and those with learning disorders (range 8-34  $\mu\text{g/L}$ , mean 17.1  $\mu\text{g/L}$ ). Recently, Yasuda et al. [16] reported that a sub-group of autistic children has subjected to higher aluminium burden : the individuals with high aluminium levels exceeding 30  $\mu\text{g/g}$  (ppm) were estimated 2.8 %.

In the present study, the average aluminum level in scalp hair for Japanese adults was estimated to be about 4  $\mu\text{g/g}$  (4 ppm) (Table 1). This value of the hair aluminum level was close to the aluminum content in normal, healthy human liver, and higher than that in the brain tissue, reported by Alfrey et al. [28]. These results indicate that scalp hair is a good marker sample for estimating body aluminum burden.

The most noted finding in this study is that smaller children aged 0-9 years have suffered from higher aluminum accumulation : the average value of 10-11 ppm was nearly 3-fold higher than that of adults. More higher and

toxic levels over 50 ppm were observed in the ten individuals out of 1,720 children, with the highest value of an extraordinary 116.8 ppm (Table 1). High aluminium levels in children were reported in a sub-group of individuals with autistic disorders, who have suffered from a global mineral deficiency [16].

The Joint FAO/WHO Expert Committee on Food Additives noted that the PTWI for aluminum is likely to be exceeded to a large extent in some population groups, particularly in infants fed on soy-based formula and children regularly consuming foods that include aluminum-containing additives [1]. Some processed foods such as processed cheese, biscuits, bread, muffins, baking powder, are reported to have a very high aluminum contents. Some medical applications of aluminum such as aluminum antacids, phosphate-binders and buffered anti-febrile/analgesics, namely aluminum-buffered aspirin, may also lead to higher exposure.

The high accumulation of aluminum in infants aged less than 1 year-old (Table 3) indicates that they are under the circumstance of high exposure to this toxic element, perhaps through foods/drinks such as breast milk, infant formulas and weaning foods. Compared to human breast milk containing 5-20  $\mu\text{g}$  aluminum per litre, the aluminum concentrations were reported to be 10- to 20-fold higher in cow's milk-based formulas and 100-fold higher in soy-based formulas [23]. Thus, compared to breast milk-fed children, the intake of dietary aluminum can be higher in the children feeding on infant formulas and weaning foods [11, 21, 23].

Yumoto et al. [30] reported that aluminium ( $^{26}\text{Al}$ ) injected to lactating rats is taken up through maternal milk into the brain of suckling rats and its considerable amounts remained in the brain tissues throughout their lifetime. Bishop et al. [13] reported that in preterm infants receiving prolonged intravenous-feeding solutions contaminated with aluminium, increasing aluminium exposure was associated with impaired neurological development. The association of increased brain-aluminium concentration with neurological disorder was reported in

the study on the patients died with dialysis encephalopathy [27].

Another major origin of aluminum accumulation in children is probably through the cigarette smoking by their parents, in particular by their mothers, because of high aluminum content in tobaccos and the accumulation property of aluminum to bone [24, 31, 32]. The finding of the highest geometric mean level observed in 0-year children (Table 3) suggests the possibility that the aluminum accumulated in mother's bone, through the bone-resorption during pregnancy and lactation, is co-transferred to foetal body, with calcium, magnesium and other essential trace elements.

A part of high accumulation of aluminum in infants is likely explained by their high intestinal absorption rate and low ability of renal excretion activity. When immature or reduced kidney function occurs in infants, aluminum from cow's milk- or soy-based formulas is accumulated and stored thereafter. Freundlich et al. [21] reported that in two infants with severe kidney failure, the absorption and retention of aluminum from a cow's milk-based formula resulted in clinical toxicity. Thus, infants are at increased risk of taking high amount of aluminum and retaining absorbed aluminum in their bodies.

Aluminum exhibited the highest levels in infants and young children, a characteristic profile similar to lead and cadmium but different from mercury and arsenic [15]. Therefore, infants and children must be considered and cared as a high-risk group for adverse effects caused by aluminum. It is important to well understand about the unique characters and biological actions of aluminum and to reconsider its risk [3, 10, 33]. We need to study further surveying the aluminum accumulation levels among general populations.

In the present study of a total of 1,720 Japanese children aged 0 to 15 years, we were able to demonstrate that infants and children have suffered from high exposure to aluminum. This report also demonstrates that aluminum is an element that has a character of high accumulation in infants and children. This wide-used metal should be monitored as risky element to the young generation and its adverse effects remain to be clarified.

#### Acknowledgements

The authors thank Earle T. Okumura for valuable discussions.

#### References

- 1) JOINT FAO/WHO EXPERT COMMITTEE ON

FOOD ADDITIVES : Summary and conclusions of sixty-seventh meeting (Rome, 20-29 June 2006). <http://www.who.int/ipcs/food/jecfa/summaries/en/index.html>

- 2) Yokel RA : The toxicology of aluminium in the brain : a review. *Neurotoxicol* 21 : 813-828, 2000.
- 3) Becaria A, Campbell A, Bondy SC : Aluminum as a toxicant. *Toxico Ind Health* 18 : 309-320, 2002.
- 4) Canfield RL, Henderson CR, Cory-Slechta DA, Cox C, Jusko TA, Lanphear BP : Intellectual impairment in children with blood lead concentrations below 10µg per decilitre. *N Engl J Med* 348 : 1517-1526, 2003.
- 5) Sanna E, Liguori A, Palmas L, Soro MR, Floris G : Blood and hair lead levels in boys and girls living in two Sardinian towns at different risks of lead pollution. *Ecotoxicol Environ Saf* 55 : 293-299, 2003.
- 6) Alfrey AC, LeGendre GR, Kaehny WD : The dialysis encephalopathy syndrome. Possible aluminium intoxication. *N Engl J Med* 294 : 184-188, 1976.
- 7) McDermott JR, Smith AI, Ward MK et al : Brain aluminium concentration in dialysis encephalopathy. *Lancet* I : 901-904, 1978.
- 8) Wills MR, Savory J : Aluminium poisoning : Dialysis encephalopathy, osteomalacia, and anaemia. *Lancet* : 29-34, 1983.
- 9) Kawahara M : Effects of aluminum on the nervous system and its possible link with neurodegenerative diseases. *J Alzheimer Dis* 8 : 171-182, 2005.
- 10) Cooke K, Gould MH : The health effects of aluminium - A review. *J Roy Soc Health* 111 : 163-168, 1991.
- 11) American Academy of Pediatrics, Committee on Nutrition : Aluminium toxicity in infants and children. *Pediatrics* 97 : 413-416, 1996.
- 12) Zatta P, Lucchini R, van Rensburg SJ, Taylor A : The role of metals in neurodegenerative processes : aluminium, manganese, and zinc. *Brain Res Bull* 62 : 15-28, 2003.
- 13) Bishop NJ, Morley R, Day JP, Lucas A : Aluminium neurotoxicity in preterm infants receiving intravenous-feeding solutions. *N Eng J Med* 336 : 1557-1561, 1997.
- 14) Friesen MS, Pursell RA, Gair RD : Aluminium toxicity following IV use of oral methadone solution. *Clin Toxicol (Phila)* 44 : 307-314, 2006.
- 15) Yasuda H, Yonashiro T, Yoshida K, Ishii T, Tsutsui T : High toxic metal levels in scalp hair of infants

- and children. *Biomed Res Trace Elem* 16 : 39-45, 2005.
- 16) Yasuda H, Yonashiro T, Yoshida K, Ishii T, Tsutsui T : Mineral imbalance in children with autistic disorders. *Biomed Res Trace Elem* 16 : 285-292, 2005.
  - 17) Yasuda H, Yonashiro T, Yoshida K, Ishii T, Tsutsui T : Relationship between body mass index and minerals in male Japanese adults. *Biomed Res Trace Elem* 17 : 316-321, 2006.
  - 18) Suzuki T, Hongo T, Yoshinaga J, Imai H, Nakazawa M, Matsuo N, Akagi H : The hair-organ relationship in mercury concentration in contemporary Japanese. *Arch Environ Health* 48 : 221-229, 1993.
  - 19) Yasutake A, Matsumoto M, Yamaguchi M, Hachiya N : Current hair mercury levels in Japanese for estimation of methylmercury exposure. *J Health Sci* 50 : 120-125, 2004.
  - 20) Harada M, Nakachi S, Cheu T, Hamada H, Ono Y, Tsuda T, Yanagida K, Kizaki T, Ohno H : Monitoring of mercury pollution in Tanzania : relation between head hair mercury and health. *Sci Total Environ* 227 : 249-256, 1999.
  - 21) Freundlich M, Zilleruelo G, Abitbol C, Strauss J, Faugere MC, Mallunche HH : Infant formula as a cause of aluminium toxicity in neonatal uraemia. *Lancet* II : 527-529, 1985.
  - 22) Bishop N, McGraw MD, Ward N : Aluminium in infant formulas. *Lancet* I : 555, 1989.
  - 23) Fernandez-Lorenzo JR, Cocho JA, Rey-Goldar ML, Couce M, Fraga JM : Aluminum contents of human milk, Cow's milk, and infant formulas. *J Pediatr Gastroentero Nutr* 28 : 270-275, 1999.
  - 24) Exley C, Begum A, Woolley MP, Bloor RN : Aluminium in tobacco and cannabis and smoking-related disease. *Am J Med* 119 : 276.e9-11, 2006.
  - 25) Crapper DR, Krishnan KC, Dalton AJ : Aluminium neurofibrillary degeneration and Alzheimer's disease. *Brain* 99 : 67-80, 1976.
  - 26) McDermott JR, Smith AI, Iqbal K, Wisnieski HM : Brain aluminium in aging and Alzheimer's disease. *Neurology* 29 : 809-814, 1979.
  - 27) McDermott JR, Smith AI, Ward MK, Parkinson IS, Kerr DN : Brain-aluminium concentration in dialysis encephalopathy. *Lancet* I : 901-904, 1978.
  - 28) Alfrey AC, Hegg A, Craswell P : Metabolism and toxicity of aluminium in renal failure. *Am J Clin Nutr* 33 : 1509-1516, 1980.
  - 29) Howard JMH : Clinical import of small increases in serum aluminium. *Clin Chem* 30 : 1722-1723, 1984.
  - 30) Yumoto S, Nagai H, Kobayashi K, Tamate A, Kakimi S, Matsuzaki H : <sup>26</sup>Al incorporation into the brain of suckling rats through maternal milk. *J Inorg Biochem* 97 : 155-160, 2003.
  - 31) Mutti A, Corradi M, Goldni M, Vettori MV, Bernard A, Apostori P : Exhaled metallic elements and serum pneumoproteins in a symptomatic smokers and patients with COPD or asthma. *Chest* 129 : 1288-1297, 2006.
  - 32) Hellstrom HO, Mjoberg B, Mallmin H, Michaelsson K : The aluminium content of bone increases with age, but is not higher in hip fracture cases with and without dementia compared to controls. *Osteoporos Int* 16 : 1982-1988, 2005.
  - 33) Golub MS, Domingo JL : What we know and what we need to know about developmental aluminum toxicity. *J Toxicol Environ Health* 48 : 585-597, 1996.