Blood Aluminum Levels in a Psychiatric Outpatient Population.

High Aluminum Levels Related to Memory Loss.

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Introduction

Aluminum is the most abundant metal and the third most abundant element in nature. Combined with oxygen and silicon it occurs as feldspar. KASJ308, mica, KISi04, and Kaolin, H2AI2SJ208H20. Although aluminum salts have been used for various purposes since ancient times the free metal was not isolated until 1827 when Wohler reduced aluminum chloride with potassium. Commercial utilization of free aluminum was not feasible until the development of the electrolytic refining process of Hall in 1886. Since that time the use of aluminum has increased at a phenomenal rate and with it, man's exposure.

It has generally been felt in the past that aluminum is well tolerated and generally harmless. Experiments which have attempted to demonstrate that aluminum is an essential element in man have been unsuccessful. Lifetime studies in rats by Schroeder and Mitchener (1975) have demonstrated that 5 ppm of Al in drinking water was innocuous as measured by median life span, longevity, incidence of tumors, glucose, uric acid and cholesterol levels.

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Recently, however, a number of studies have shown that under certain circumstances aluminum may not be innocuous. Alfrey et al. (1976) have reported on a progressive fatal encephalopathy syndrome which appears to be associated with high tissue aluminum levels and is observed in patients on chronic hemodialysis. Aluminum containing phosphate binding gels are usually employed in these patients to control serum phosphorus levels.

It has been generally assumed that aluminum salts are poorly absorbed and that nearly all of them are excreted in the feces. Recently Kaehny et al. (1977) have demonstrated that in normal human subjects measurable amounts of aluminum are absorbed and urinary excretion is markedly increased on ingestion of various aluminum salts. This finding has been confirmed by Recker et al. (1977) who have presented evidence that urinary excretion of Al is markedly increased upon ingestion of aluminum carbonate. These authors also present evidence for bone deposition. Bone aluminum was elevated in dialysis patients and in a single osteoporotic patient who had ingested aluminum antacids for 25 years.

Gorsky et al. (1979) have carried out metabolic balance studies on subjects who were taking aluminum containing antacids. When such antacids were taken a positive aluminum balance was observed indicating a pos-

sible tissue storage of aluminum.

Kushelevsky et al. (1976) have shown a specific uptake of aluminum by liver cell nuclei and DNA. Aluminum uptake by liver is believed responsible for an induced experimental porphyria in the rat.

Table 1 lists a number of environmental sources of aluminum. From this list the ubiquitous nature of aluminum in the environment is self evident.

Signs of dementia and motor impairment were found in an aluminum flake powder worker. A number of studies have shown that high concentrations of aluminum are toxic to the nervous system. Aluminum salts injected into the brain or cisterna magna of rabbits produce neurofibrillary tangles similar to those seen in human presenile dementia or Alzheimer's disease (Wisniewski and Terry, 1970).

The present study is concerned with the blood aluminum levels found in some four hundred psychiatric outpatients. The relationship of symptomatology and age to aluminum levels will be examined.

Methods

Aluminum was determined with a Perkin-Elmer 503 Atomic Absorption Spectrophotometer equipped with an HGA 2000 graphite furnace, an HGA ramp accessory, and a deuterium background corrector. Experimental parameters were as listed in Table 2.

Sample preparation consisted of diluting a 1 ml blood sample in half with a solution of five percent Triton-X 100 containing 100 units sodium heparin per ml. Blood and Triton-X solution were thoroughly mixed and stored in polyethylene tubes that had been washed in 0.4 percent EDTA and rinsed with deionized water.

Initially blood had been collected and stored in vacutainers. Examination of these original samples indicated that aluminum was leached from the glass during storage. Figure 1 presents aluminum levels for blood samples stored over a period of six months. Aluminum levels in these samples increased significantly depending upon the length of storage. The collection of samples in vacutainers was, therefore, abandoned and storage in polyethylene tubes was adopted.

The assay proved to be linear over the range of 0 -100 ppb and recoveries were of the order of 100 percent.

The group studied consisted of 147 male subjects with a mean age of 43.6 ±19.7 years with a range of 18 - 91 years and 255 female subjects with a mean age of 48.7 ± 16.7 years with a range of 3 - 92 years. The group was heterogeneous with regard to their psychiatric problems.

Memory loss was noted when either the patient complained of failing memory or a close relative reported that the patient's memory was failing. Memory loss was not tested.

Results and Discussion

Figure 2 is a histogram of the distribution of blood aluminum levels in the group of four hundred psychiatric outpatients. Comparison is made between the aluminum levels in patients less than fifty years old and those fifty and over. There appears to be a tendency for the aluminum level to be higher in the older group. This may indicate that aluminum does accumulate with age; possibly in cases where kidney function is no longer optimal.

Table 3 presents aluminum levels for various age groups in male and female subjects younger than fifty years of age. There is a tendency for blood aluminum levels to be higher in female subjects when compared to males. However, the differences are not sufficient to reach statistical significance.

Table 4 presents some of the factors examined for relevance to aluminum levels. Among these factors were depression, memory loss, blood histamine, serum copper and urinary kryptopyrrole levels. Mean blood aluminum levels were not different in depressed and non-depressed subjects or in low and high histamine subjects. Only in the presence of memory loss was there a tendency for the aluminum level to be elevated. The mean level for 120 subjects who suffered from some memory loss was 39.4 ± 24.7 ppb as compared to 272 subjects who had no memory loss who had a mean blood aluminum level of 31.3 ±

16.2. A t test on these data showed the difference in Al was significant at the .001 level.

Table 5 presents blood aluminum levels on an initial visit to the Center and on a subsequent visit. Eighty-two percent showed a decrease in their blood aluminum levels when put on a nutritional therapeutic regime. The difference between the initial blood aluminum level and a subsequent visit level was significant at the one percent level. The therapeutic regime consisted of supplementation with zinc, manganese and magnesium.

The relationship of aluminum to memory impairment has been demonstrated with an animal model. Crapper and Dalton (1973) have demonstrated alterations in short term retention, conditioned avoidance response acquisition and motivation in cats following neurofibrillary degeneration induced by aluminum chloride. In cases of senile or presenile dementia, referred to as Alzheimer's disease, Sourander and Sjogren (1970) distinguished three stages in the development of this condition. Initially, memory disturbances, spatial disorientation and lack of spontaneity occur. Secondly, focal neurological signs such as dysphasia occur some times associated with motor disturbances. Finally, complete dementia occurs often with seizures.

Ball (1976) has shown that neuro tangle formation in the hippocampus in normal subjects increases slightly with age; however, in cases with clinically significant dementia between 6 and 40 times more tangles are found than in sections from age matched controls. In normal subjects there is a direct correlation with age, particularly in the sixth to ninth decades of life. Ball also found that in the case of subjects with senile dementia, there was a tendency for an increasing percentage of neurofibrillar tangles to be found in the posterior hippocampus.

The role of the hippocampus in memory has been studied by a number of investigators, Scoville and Milner (1957); Victor et al. (1961). The anterior portion of the hippocampus seems to be involved in instant recall and recent memory while Penfield and Mathieson (1974) have recently proposed a hypothesis that the posterior hypothalmus may be involved in access to diencephalic longterm memory.

Aluminum levels have been measured in the brain of patients with Alzheimer's disease by Trapp et al. (1978). Considerable variation in aluminum levels in adjacent brain areas was found but a trend to high Al levels in brains from Alzheimer patients was noted. Since in Alzheimer's disease one prominent feature is the loss of brain and neuronal mass, the high Al tissue levels may be more apparent than real. Although the etiological role of Al in Alzheimer's disease is open to question there is little doubt that aluminum is neurotoxic and that it can produce neurofibrillary pathology. This has been demonstrated in cats and rabbits by intrathecal injection of aluminum phosphate by Wisniewski (1970). The results of the present study indicate that blood aluminum levels appear to become elevated with ageing, and elevated blood aluminum levels are possibly associated with memory impairment.

TABLE 1

Environmental sources of aluminum

1-Aluminum pots and pans
2-Aluminum cans, aluminum foil packaging
3-Water supplies-aluminum flocculating agents employed in purification
4-Hot water supplies-cathodic corrosion prevention using aluminum cores
5-Food supply
a) Baking powders
b) Spices
c) Food additives-sodium aluminum phosphate emulsifier in cheese-aluminum calcium silicate-anticaking agent added to salt-potassium aluminum bleaching agent
6-Pharmaceutical preparations
a) Antacids-magaldrate
b) Bufferin
c) Aluminum hydroxide gels
7-Antiperspirants-deodorants
8-Air born contamination from:
a) Air conditioner corrosion
b) Clay dust

TABLE 2

	Operating Parameter for AAS
Wave Length	309.2
Slit	4 (0.7 mm)
D_2	On
Argon Gas	3
Flow	On
Gas interrupt	15ma
Lamp	
Furnace Dry	100° 60 sec.

Char 100° ----------->1700° (90 sec ramp) 1700° 30 sec.
Atom. 2700° 8 sec.

Sample injected 25 λ

TABLE 3

MEAN ALUMINUM LEVELS IN VARIOUS AGE GROUPS

Age Group	Males	n 12	Females	n 11
10-19	Alppb 36.3 ±28.8		Alppb 27.9 ±11.2	
20-29	28.4 ±15.0	37	37.1 ±21.9	36
30-39	25.7 ±11.6	12	28.1 ±15.6	38
40-49	27.6 ±10.2	14	34.1 ±19.8	42
50-59	35.1 ±21.5	29	38.3 ±19.5	62
60-69	36.5 ±19.6	26	34.1 ±14.4	51
70-79	40.6 ±36.1	14	39.1 ±23.8	25

TABLE 4

ALUMINUM LEVELS (ppbl IN VARIOUS DIAGNOSTIC CATEGORIES

		n	*±S
Histamine	<40	201	34 4±19 0
40 -70		160	34.0±20.0
>70		57	34.0±19.4
KP	<20	155	34.0±20.9
>20		255	33.6±18.5
107			31.6±17.1
		193	36.5±19.5
High Cu ♂ ♀ Low Cu ♀ ♀ ♂		98	31.9±22.4
Depression present		214	34.6±20.4
Depression absent		184	32.8±18.6
Memory loss present		120	39.4±24.7
Memory loss absent		273	31.3±16.2

TABLE 5

AL LEVELS (ppb): INITIAL AND SECOND VISIT

n=66

Initial visit	Second Visit
"X 48.3	30.8
S ± 18.3	± 16.2

t=5.85

P=<.01

82 % showed a decrease in Al level

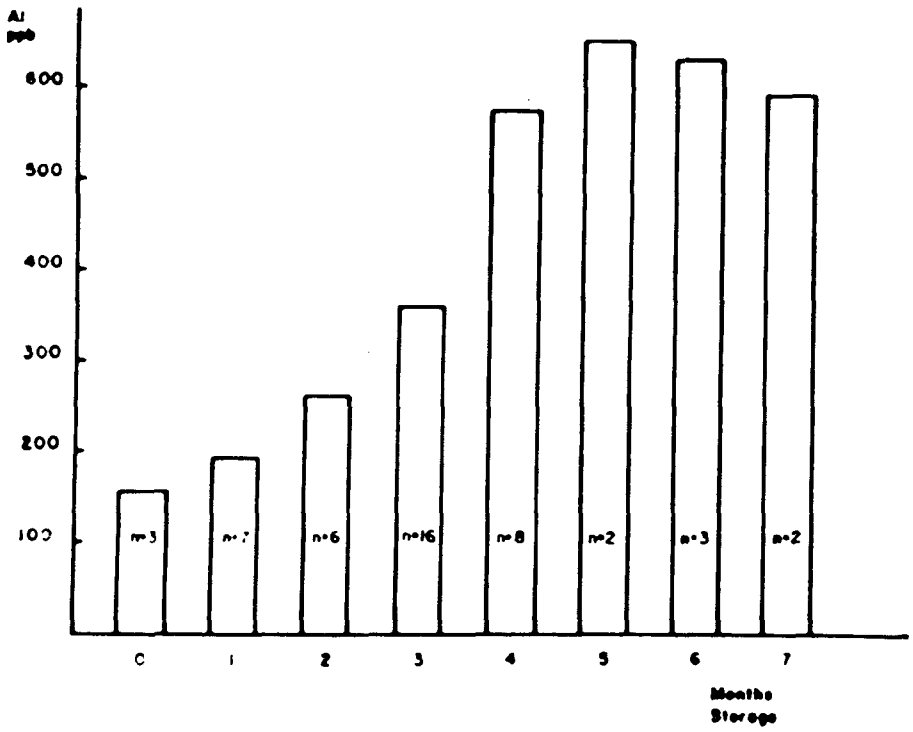

FIGURE 1 – Effect of Blood storage in vacutainers on Blood Aluminum Levels

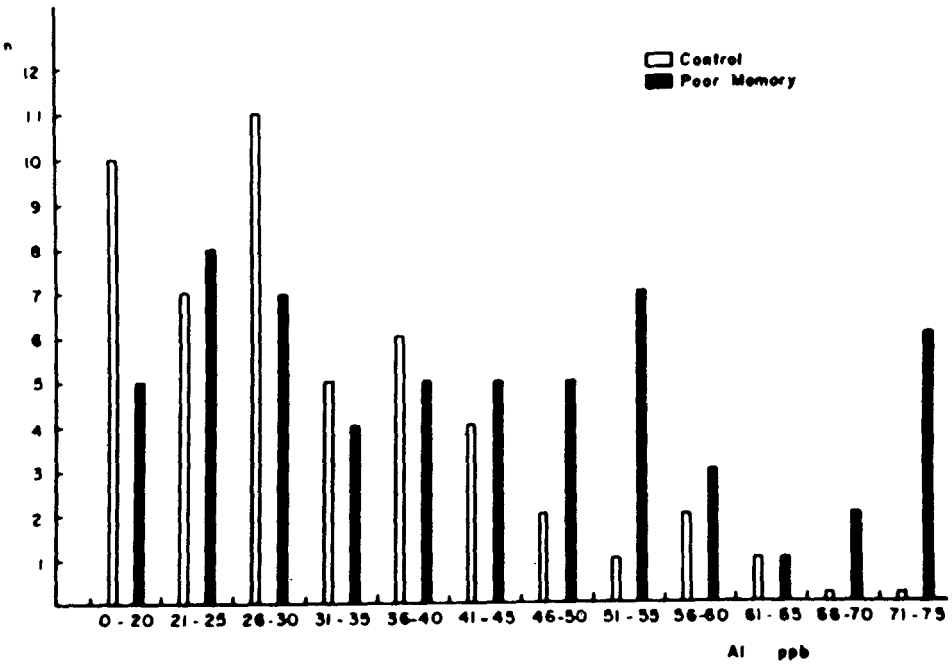

FIGURE 2 - Frequency distribution histograms of control and poor memory groups with regard to Blood Aluminum levels.

Summary

Aluminum levels in whole blood were studied in some four hundred psychiatric outpatients. The relationship of symptomatology and age to aluminum levels was examined. Aluminum levels were found to be higher in older individuals indicating that aluminum may accumulate in the course of time. Mean blood aluminum levels were not found to differ in depressed and non-depressed subjects or in low and high histamine individuals. Subjects reporting memory loss had a significantly higher mean blood aluminum level. The mean aluminum level for 120 individuals suffering from memory loss was 39.4 ppb as compared to 272 individuals without memory loss whose mean was 31.3 ppb. The relationship of aluminum to memory is discussed. Blood aluminum levels can be lowered with supplements of zinc, manganese and magnesium.

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