



## Letter to the Editor

## Aluminium in brain tissue in autism



## 1. Introduction

The discovery of aluminum (Al) in quantities unexpectedly high in brain tissue in five patients with autism spectrum disorder [1] has immediately imposed to us the question: from where has this aluminum come? We live in what one leading researcher on the chemistry of aluminum has called "the Aluminum Age" [2] and concerns about the toxicity of ingested Al were expressed over hundred years ago [3] long before it became as widely used as it is today. Al is the third most abundant element in the earth's crust and occurs naturally in the environment, foodstuffs, and drinking water [4]. It is also used in: processed foods, materials and articles such as, Al-containing food packaging, Al foils, cooking utensils and baking trays. It has long been assumed that dietary Al is the main risk source of exposure to biologically available Al. Under physiologic conditions intestinal absorption of aluminum is impossible since biometals (Fe, Cu, Zn, Mn, Mo, Cr) and toxic metals (Pb, Hg, Ni, Cd,) are absorbed exclusively in their 2<sup>+</sup> state. Aluminum as a trivalent under physiologic conditions cannot be absorbed. Trivalent Al can be absorbed through the intestinal mucosa only in the cases of mucosal damage (infection, inflammation, intoxication as was the case in 1988 in England [5]). The **Camelford water pollution incident** [5] involved the accidental contamination of the drinking water supply to the town of Camelford, Cornwall, in July 1988, when twenty tonnes of aluminium sulphate was inadvertently added to the water supply, raising the concentration to 3000 times the admissible level. If present in the intestinal lumen while the mucosa is damaged, or is ingested in toxic quantities, Al<sup>3+</sup> is absorbed probably by simple diffusion. It has been suggested that acid digestion in the stomach would solubilise most of the ingested aluminum compounds. In acidic aqueous solutions with pH < 5 the aluminum ion exists mainly as Al<sup>3+</sup>, e.g. hydrated Al<sup>3+</sup> [Al(H<sub>2</sub>O)<sub>6</sub>]<sup>3+</sup>. By passing from the stomach to the intestines the increase in pH results in the formation of complexes of aluminum with hydroxide and finally the formation of insoluble aluminum hydroxide at neutral pH. Therefore as the pH is neutralized in the duodenum the aluminum ion is gradually converted to aluminum hydroxide and the majority is then expected to precipitate in the intestine with subsequent fecal excretion, leaving only a minor fraction available for potential absorption. In conclusion, independently of the pH value Al in its compounds always retains its trivalent state. Divalent aluminum does exist. It has been detected in the gas phase after explosion of aluminized grenades in the upper atmosphere and in stellar absorption spectra [6]. Usually humans live very far from these events and spaces. Aluminum can be potentially absorbed through the skin essentially if it is shaved or irritated by application of skin care creams, rejuvenation creams, sprays against unpleasant smells and sweats and after shave lotions that contain aluminum [7]. However, the use of these cosmetic products in newborns, infants, and children is not common. Al can be also absorbed across the lung or olfactory epithelia by persons working in workplaces where Al

welding is carried out during electrolysis in Al production or in the processing industries (e.g., foundries, powder production). There are thus clearly different routes of Al exposure and what must be emphasized is that these are not necessarily equivalent with regard to the amount delivered per unit of time and more importantly with regard to the age at which the person is exposed to Al. The younger age carries greater probability for toxic effects. Although it is commonly assumed that children obtain much more Al from diet than from vaccination [8], this notion contradicts basic toxicological principles. The route of exposure that bypasses the protective barriers of the gastrointestinal tract and/or the skin will likely require a lower dose to produce a toxic outcome [2]. In the case of Al only approximately 0.25% of dietary Al is absorbed into systemic circulation [9]. Much of the Al that enterally enters the human body is typically rapidly removed by the kidneys [10]. In contrast, Al hydroxide (the most common adjuvant form) injected intramuscularly may be absorbed at nearly 100% efficiency over time [11]. More importantly, wherever the anatomical place of vaccine application is, adjuvant Al enters into the circulation where it binds to transferrin. This adjuvant Al bound to transferrin, has a unique capacity to cross the blood-brain and blood-cerebrospinal fluid barriers, access the brain where it is deposited probably for the whole life [12] since adjuvant Al is poorly excreted [13]. Today we live in an era of aluminum. Aluminum is all around us. Therefore, one can rightly ask the question: were Mold et al. [1] aware in their research that there was no contamination with external aluminum during the acquisition of brain tissue and the procedure for determining the amount of aluminum in it? The same question can be posed to all other former researchers and to their research on the basis of which a "Handbook on the Toxicology of Metals" has been written [14].

In the paper of Mold et al. [1] the strangest and most intriguing fact is that the highest concentrations of aluminum were measured in the youngest person. The boy was only 15 years old (case A4). Generally accepted claim that dietary aluminum is the main source of exposure to aluminum, inevitably raises the question: how is it possible that in the course of only 15 years of life, this boy "absorbed" such amount of aluminum and deposited it in his brain? On the other hand the boy in that age probably did not use creams containing aluminum, anti-perspirant sprays, nor shaved. He also could not have been present in 1988 in Camelford, Cornwall (UK). At the age of 15 he could not be a worker in the aluminum industry where he would be exposed to aluminum dust and fumes. Even less it was likely that this boy lived near the place where aluminized grenades exploded! We also do not believe that the boy was a cosmonaut and he travelled in interstellar spaces where divalent aluminum is located. In the work of Mold et al. [1] the year of birth of persons shown in the work is not indicated. We can only assume that the 15-year-old boy was born around the year 2000.

Given all of the above under normal, usual, physiological conditions the most important, the most regular and most predictable even by the law legislated access of aluminum into the human body is through

vaccines. According to the vaccination schedule which was established in 2000 in the USA, by the age of 18 months, approximately 4425 µg of aluminum is parenterally delivered into the human body through vaccines [15]. After 2005 with the introducing of new vaccines, the quantity of adjuvant Al has increased up to 4925 µg [15].

Aluminum neurotoxicity has been shown in experiments on mice [16]. Aluminum toxicity has been shown even in one clinical study in which 182 infants were treated with intravenous injections of nutritional formula that contained different quantities of aluminum [17] but received significantly less aluminum than the infants receiving aluminum via vaccines. Recently it was shown that another metal i.e. mercury is also neurotoxic for children even in much less quantities in comparison with aluminum [18]. Toxic effects of Al can be assigned to its physical and chemical properties. Owing to its 3<sup>+</sup> charge Al attracts negatively charged ions and electrons but because it cannot transition to other oxidation states besides 3<sup>+</sup>, Al is not a direct component in any redox reactions but may participate indirectly in Fenton reactions. Moreover, the small ionic radius and the high charge of Al<sup>3+</sup> are its important properties by which this metal can exert its toxic activity. The Al ion (0.054 nm) is roughly the same size as the ferric (Fe<sup>3+</sup>) ion (0.065 nm) and much smaller than magnesium (Mg; 0.072 nm) and calcium (Ca) ions (0.100 nm). Thus, in biological systems, Al can effectively replace these essential biometals in many enzymatic reactions [19,20].

## 2. Conclusion

Aluminum is undoubtedly neurotoxic. The main the most important "physiological" way to reach the human body is via vaccines in the form of a trivalent adjuvant. But on the other hand, vaccines have saved humanity from many deadly infectious diseases. So-called cost-benefit is in absolute overdose in favor of vaccination. **One should never think about abolishing vaccination**, but rather to work on finding ways to reduce the toxicity of adjuvant aluminum and if possible to completely eliminate it.

To achieve this goal, we suggest:

- 1 All aluminum containing vaccines must be postponed until the time when the child's brain shows sufficient physiological maturation. That would be the day when the child loses its last primitive reflex, corresponding the age of 6–7 months, ideally, after 12 months. By this age most of so-called synaptic pruning is completed and consequently the child's brain is probably less vulnerable to the deleterious effects of aluminum, in comparison with the brain vulnerability to the toxins given immediately after birth when the newborns on their first day of life are injected with 0.25 mg of Al<sup>3+</sup> through the application of hepatitis B vaccine. The younger the time age of exposition to Al, carries the greater harm for Al toxicity and brain damage. This is in accordance with a recent review in which it has been calculated and shown, that the levels of aluminum suggested by the currently used limits place infants at risk of acute, repeated and possibly chronic exposures of toxic levels of aluminum in modern vaccine schedules [21]. Therefore, it has been suggested that vaccination in neonates and low birth-weight infants has to be re-assessed in the sense of aluminum dosage reduction in vaccines, according to the birth-weights. The main obstacle to this proposal is the unknown effect of this proposed reduction on the final antigenicity of the vaccine [21].
- 2 It is necessary to totally eliminate the metal(s) in all vaccines (especially aluminum and mercury), whether in children or in adults; it very much matters to be clear and totally intransigent, on this point. Complete elimination of vaccine aluminum neurotoxicity could be achieved by its replacement with some other element, or compound. Squalene could also be used to replace Al. In a recent review [22] it was reported that calcium phosphate could be as effective adjuvant as aluminum salts, with the following advantages:

Calcium phosphate is present in the general monographic on human vaccines of the European Pharmacopoeia 8.0; calcium phosphate is classified as safe and biocompatible by the US FDA; calcium phosphate is a natural compound of the human body, thus suggesting its good tolerance for individuals; adsorption capability of calcium phosphate is equivalent to aluminum adjuvants depending on preparation mode, considered antigens, and particle size; calcium phosphate booster antigenicity is potentially better than with aluminum adjuvants [22].

Calcium phosphate was used in France until the mid-1980s mainly for the diphtheria-pertussis-tetanus vaccine group without any mention of adverse reactions by physicians. Until the early-1970s it was also successfully used in the pentavalent human vaccination (smallpox, yellow fever, measles, BCG, and tetanus) and also without any reported adverse reaction [23].

With all of this in mind it is very mysterious and curious that in the 1980s, vaccines manufacturers opted for replacing calcium phosphate, which was used as adjuvant for human vaccines with Al as preferred adjuvant. Since then most of the clinical experience has been gathered with the use of Al as vaccines adjuvant while calcium phosphate was only marginally investigated [24]. **From the other side we do not insist but to our knowledge, we would like to suggest that zinc could be the element of choice to replace aluminum** for the following reasons: 1. Both metals, Zn and Al are amphoteric; 2. Zinc is necessary for normal human life (zinc human body burden is between 200 and 300 mg); and finally; 3. so far, no zinc overload related disease has been described. In animal experiments zinc toxicity has been shown but normally and fortunately, humans do not live in "experimental" conditions, in which experimental animals are exposed to excessive, toxic quantities of various substances, including zinc. There are no literature data so far on the use of zinc as adjuvant. Therefore, vaccinologists and immunologists must start as soon as possible with the experiments with zinc compounds (hydroxide, sulphate or phosphate) as adjuvant. If it turns out after the experiment that zinc compound(s) have successfully replaced Al compounds as adjuvants, the amount of zinc that would be administered by vaccine in children up to 18 months of age would be about 5.000 µg (= 5 mg), which is absolutely far beyond the domain of experimental Zn toxicity.

Naturally many scientists will not be in agreement with our arguments on the potential role of zinc in future vaccines. The fact is that we presently possess no critical perspective for zinc to be the substitution for Al, as well. Both of these statements should not at all be the arguments against our proposal for the experiments with zinc as adjuvant to find out whether zinc and its compounds could offer advantages over aluminum.

## Conflict of interest statement

The authors declare no conflict of interest.

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