

## Brief Assessment of Aluminum Exposure and Endocrine Disruption

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The brain is a main target of aluminum exposure and effect[1] where it induces neurodegeneration[2-4]. At high levels, aluminum has been demonstrated to inhibit prenatal and postnatal neurodevelopment in humans and animals[5-11]. Aluminum has been shown to target and accumulate in the hippocampus, the primary area of the brain associated with memory formation[12-14]. Aluminum exposure in human populations has been associated with deficits in cognitive function[15]. Aluminum neurotoxicity in children manifests symptoms of verbal impairment and regression[16]. Although the relationship between aluminum exposure and associated disease such as Alzheimer's disease[13, 17-23], amyotrophic lateral sclerosis[24], and Parkinson's disease[24, 25] remains to be fully elucidated, the specific toxicology of aluminum exposure on the endocrine system has been firmly established[26-31]. Aluminum deposits in the pituitary, parathyroid, and adrenals[32] and has been demonstrated to interfere with parathyroid hormone secretion[33-36], insulin like growth factor and T3 levels[37], and the reproductive system[28, 29, 31, 38].

It is thought that inflammation resulting from aluminum exposure may induce learning and memory deficits[39]. Certainly, targeted effects on the endocrine system may affect immune-modulation and produce a pro-inflammatory cascade that responds to targeted aluminum deposition in the hippocampus with resultant neurotoxicity.

Aluminum-containing adjuvants are used in certain vaccines to promote an immune response. The vaccines that contain aluminum adjuvants are: DTP (diphtheria-tetanus-pertussis

vaccine), DTaP (diphtheria-tetanus-acellular pertussis vaccine), some but not all Hib (Haemophilus influenzae type b) conjugate vaccines, Pneumococcal conjugate vaccine, Hepatitis B vaccines, all combination DTaP, Tdap, Hib, or Hepatitis B vaccines, Hepatitis A vaccines, Human Papillomavirus vaccine, Anthrax vaccine and Rabies vaccine.

There is demonstrated variability in aluminum neurotoxicity across species and age groups [40]. Therefore, it is likely variability in disease response to aluminum exposure exists within the human population. This variability may be due to variable elimination rates (kidney function, GI function), dietary intake, genetic predisposition, and previous exposure levels. Vaccine injections with aluminum bypass the usual biological barriers to absorption and thus confer maximal dose exposure. This bolus of aluminum (each vaccine may contain up to 850 ug of aluminum) may target specific regions of the brain and endocrine system, and in concert with the expected immune reaction, instigate a cascade of events leading to inflammation, neurotoxicity, and disease. There is no known physiological role for aluminum within the body and therefore it can be considered as only a deleterious influence[1]. As background levels of environmental aluminum exposure rise over time throughout the world, additional sourced of aluminum exposure should be eliminated, especially in vulnerable populations such as pregnant mothers, infants, and the elderly.

## **Background Information**

Exposure and absorption: Aluminum is the most abundant metal in the earth's crust and due to acid rain, this neurotoxic element has dramatically increased in biological ecosystems with demonstrated lethal effects on fish and plant species [40]. Human exposure is primarily through food, water, and pharmaceuticals, with an average human intake of 1-10 mg. The total body burden in healthy human subjects is 30-50 mg[1]. In urban areas, atmospheric aluminum is associated with particulate matter and generally ranges from 0.5-180  $\mu\text{g}/\text{m}^3$ [1]. There is a relatively high rate of absorption of atmospheric mercury through the lungs (3%) and directly via the olfactory pathway[41]. Aluminum is transferred from soil to food supplies when the food is grown in acidic condition ( $\text{pH} < 5$ ). Aluminum is poorly absorbed through digestion, with only 0.1% absorbed, although this rate of absorption can increase with impaired kidney function, gastrointestinal disorders, and is dependent on other dietary intake. In the plasma, aluminum competitively binds to transferrin, an iron-transport protein and is ultimately removed from the blood by the kidneys and excreted in urine.

Biological Targets: The lung, bone, and central nervous system are the primary targets of aluminum deposition and effect. There is wide variation in aluminum toxicity across different species and increases with age of exposure[1]. The normal concentration in the mammalian brain is 1-2  $\mu\text{g}/\text{g}$ . In aluminum sensitive species, concentrations of aluminum above 4  $\mu\text{g}/\text{g}$  induce clinical and pathological symptoms.

Symptoms of Exposure: Acute aluminum exposure results in learning and memory deficits, poor motor function, tremor, weakness and ataxia [40]. Exposure is associated with neurofibrillary tangles (NFT), tau proteins, and decreased DNA synthesis. Aluminum exposure interferes with

glucose metabolism, ATPase, calcium channels, cytoskeletal proteins, genomic interference, and oxidative stress[1].

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