The Putative Role of Environmental Aluminium in the Development of Chronic Neuropathology in Adults and Children: How Strong is the Evidence and What Could be the Mechanisms Involved?

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This article is exceptionally detailed: 21 pages long citing 231 references.

Adjuvants: A substance that enhances the body's immune response to an antigen.

"In this paper we aim to review the available evidence purporting to establish an association between increased aluminium exposure and an increased risk of developing Alzheimer's disease (AD)."

The objective is to inform readers in the "pathogenesis and pathophysiology of ASD who might not be aware of concerns regarding aluminium in the pathogenesis of conditions other than autistic spectrum disorder (ASD)."

We aim to "highlight accumulating evidence suggesting that aluminium adjuvants [vaccines] can precipitate serious autoimmune or auto-inflammatory pathology in genetically susceptible people which is a growing area of concern."

"We will then move on to consider evidence suggesting an association between the increased use of aluminium salt adjuvants and an increased incidence of ASD."

"The remainder of the paper will focus on mechanisms by which increased exposure to aluminium could be an environmental trigger of ASD in at least some children with a range of abnormalities in the performance of their immune systems."

KEY POINTS FROM THIS ARTICLE:

1) Both autistic spectrum disorder (ASD) and Alzheimer's disease involve a "highly complex and diverse combination of genetic, epigenetic and environmental factors."

- "One such environmental factor implicated as a potential cause in both syndromes is aluminium, as an element or as part of a salt, received, in oral form or as an adjuvant [in vaccines]." **[Key Point]**

2) Aluminium "has the potential to induce pathology via several routes such as provoking dysfunction and/or activation of glial cells which play an indispensable

role in the regulation of central nervous system homeostasis and neurodevelopment."

3) Aluminium also:

- Increases oxidative stress
- Depletes glutathione
- Damages mitochondrial performance and integrity
- Increases the production of proinflammatory cytokines in the brain and peripherally

4) "Significant quantities of aluminium introduced via immunization could produce chronic neuropathology in genetically susceptible children."

5) The prevalence of ASD is increasing, with estimates as low as 1 in 38 children.

- These authors disagree that the increase in the incidence of autism is "an artifact stemming from the development of broader diagnostic categories and increased medical awareness." **[The so-called "diagnostic shift"]**

6) "The concept of ASD as an illness of purely genetic origin has given way to the view that, at the very least, the aetiopathogenesis of ASD involves a highly complex interaction between numerous genes and environmental risk factors."

- "Alterations in the epigenetic landscape and dysregulation of epigenetic mechanisms responsible for gene expression also play a major role in the aetiopathogenesis of these disorders."

- There is evidence that "global DNA hypomethylation in the brain is a driver of altered gene expression in ASD children."

- Studies emphasize the "importance of epigenetic rather than genetic factors in the pathophysiology and pathogenesis of ASD."

7) ASD is not an illness or illnesses exclusively affecting the brain. ASD children have evidence of activated microglia and astrocytes, which are characteristic of many neuroimmune and neurodegenerative diseases, but "there is also copious evidence of abnormalities in the peripheral immune system."

- This includes excessive pro-inflammatory cytokine expression and reduced anti-inflammatory cytokine expression.

- "Genes governing immune and inflammatory responses are upregulated in some children with an ASD."

8) "An unusually potent and/or prolonged immune response allows for the development of macromolecular or tissue damage leading to the formation of damage-associated molecular patterns."

- "Environmental agents putatively associated with an increased risk of developing the ASD phenotype, such as organophosphates, mercury and aluminium, also have the capacity to provoke a prolonged and or exaggerated immune response." **[Key Point]**

- Aluminium salts in adjuvant [vaccines] "exert profound stimulatory effects on innate immune responses."

- There is "evidence of increased aluminium levels in the hair and urine of ASD children compared with unaffected controls."

- "Aluminium adjuvants are becoming a recognized trigger of autoimmune pathology in genetically susceptible individuals."

9) "Chronic or cumulative exposure to aluminium reflected by increased levels in cerebrospinal fluid and serum may be one environmental factor in the pathogenesis and pathophysiology of MS, Parkinson's disease (PD) and AD."

- "Increased aluminium exposure increased the risk of developing AD by 71%."

10) Many children with ASD manifest oxidative stress mitochondrial dysfunction.

11) The metal aluminium is the third most frequently occurring element in the Earth's crust. It has a preferred oxidation state of +3.

12) "Several authors have reported a strong positive correlation between the level of aluminium in drinking water and the incidence of AD throughout the world including the United Kingdom, Canada, Norway and France."

- Studies using more sensitive techniques have detected aluminium in the brains of AD patients within plaques and elsewhere at "significantly higher levels than in age- and sex-matched unaffected controls."

13) "Aluminium administered orally or via injection significantly decreased reduced glutathione levels."

14) "Aluminium is a potential causative agent in certain types of breast cancer cells as well as in primary invasive breast cancers and ductal carcinoma in situ."

15) Aluminium concentration is far higher in the posterior cerebral artery, which supplies the hippocampus. [memory area]

- "There is little doubt that the weight of evidence implicating aluminium in the causation of AD in at least some patients is increasing."

16) There is "an accumulating body of evidence suggesting that that aluminium in adjuvant form [vaccine] may provoke systematic and symptomatic autoimmune conditions in genetically susceptible individuals." **[Important]**

17) "Evidence demonstrating the development of chronic autoimmune or auto-inflammatory conditions following environmental exposure to aluminium salts, and indeed other adjuvants, is increasingly becoming a cause for concern." **[Key Point]**

18) "Adjuvants were once thought to pose little or no independent threat as drivers of pathology. Unfortunately, studies of animal models and humans have demonstrated the ability of some of them to induce autoimmunity and immune-mediated diseases."

19) "Children living in countries with the highest prevalence of ASD appear to have the greatest exposure to vaccine based aluminium."

- "The increase in exposure to aluminium adjuvants displayed a significant positive correlation with the increased prevalence of ASD in the USA recorded over the last 20 years."

20) "Aluminium adjuvants, and indeed vaccination per se, can cause serious long-term pathology in people with a certain genetic vulnerability."

21) "Vaccines may accelerate or precipitate the transition between subclinical and overt symptomatic autoimmune conditions within the first 30 days post-immunization, particularly in those aged under 50 years."

22) There is a "positive association between a personal and family history of autoimmune diseases and the development of several different autoimmune diseases post-vaccination." **[Important]**

23) "There is considerable evidence that vaccines, or more likely vaccine adjuvants, may precipitate specific autoimmune sequelae in genetically or epigenetically vulnerable people."

24) "Chronic aluminium exposure exerts profound detrimental effects on cellular anti-oxidant defenses leading to significantly reduced cellular levels of glutathione transferase, glutathione peroxidase, catalase, superoxide dismutase and reduced glutathione (GSH)."

- Aluminium ingestion decreases GSH levels in humans.

- Aluminium-induced depletion of GSH increases intestinal inflammation and intestinal barrier permeability.
  [leaky gut, autoimmune responses, systemic inflammation]

- Aluminium ingestion increases oxidative stress and mitochondrial dysfunction.

25) "Exposure to aluminium ions leads to a significant decrease in the activity of cytochrome C oxidase." **[Important for laser therapy]**

26) Aluminium ions bind to the phosphate groups of ATP and "impair energy homeostasis."

27) Aluminium exposure leads to a state of chronic mitochondrial under-performance rather than cellular death. **[Important]**

28) Aluminium exposure can induce significant metabolic changes in astrocytes.

29) Aluminium induces significant alterations to glutamate recycling leading to increased intracellular levels of glutamine. **[excitotoxicity]**

- This may "impair neurodevelopment as astrocytes play an important role in the development of the brain by regulating processes involved in synaptic transmission, neuronal migration, synaptogenesis and maybe even myelination."

30) Aluminium can activate microglia neuroimmunological responses.

- "There is now overwhelming evidence demonstrating that microglia play an indispensable role in the development of the brain by regulating processes such as synaptic pruning, synaptic plasticity, synaptogenesis, neuronal development and other vital processes in neurogenesis." **[Important]**

- Activated microglia upregulate cyclooxygenase-2 (COX-2) with the resultant production of prostaglandin E2. **[an omega-3 connection]**

31) Aluminium clearly could provoke chronic pathology in "children with an abnormal immune system and a predisposition to autoimmunity."

32) "There is ample evidence demonstrating that chronic immune system activation and systemic inflammation can lead to the development of chronic neuro-inflammation." **[The purpose of aluminium adjuvants is to enhance immune system activation]**

33) "The concept of microglial priming could change the frame of reference from a consideration of a single inoculation containing aluminium adjuvant to a cumulative effect caused by a vaccination schedule in which successive immune insults over a short period could provoke chronic pathology either directly, by provoking microglial activity, or more indirectly by provoking macromolecular damage which could eventually reach a threshold capable of provoking chronic pathology." **[Key Point]**

34) "There is good evidence to suggest that immunization may accelerate or precipitate the transition between subclinical and overt symptomatic autoimmune

conditions within the first 30 days post-immunization, particularly in those younger than 50 years of age."

35) "Aluminium exposure is associated with the production of pro-inflammatory cytokines and chemokines and with the development of chronic oxidative stress, mitochondrial dysfunction and glial activation or dysfunction; these changes in turn are associated with ASD."

36) "Aluminium has no known beneficial physiological action in the human body and some genetic polymorphisms predispose to a greater susceptibility to its adverse effects." **[Important]**

- "A strong case can be made for avoiding unnecessary exposure to environmental sources of aluminium salts, especially on the part of children, pregnant mothers and women of childbearing age who may become pregnant."

    •• "Aluminium cookware may be replaced by safer alternatives."

    •• "Aluminium-containing antiperspirants, potentially implicated in the rise of cases of breast cancer particularly affecting the upper outer quadrant of the mammary gland, may be replaced by non-aluminium versions."

    •• Antacids with aluminium should not be consumed.

37) "It is recommended that the use of aluminium salts in immunizations should be discontinued and that adults should take steps to minimize their exposure to environmental aluminium." **[Key Point]**

38) "It would seem prudent to try to find an alternative to aluminium adjuvants [in vaccines] as soon as possible and phase out their use." **[Important]**

- "The avoidance of immunizations which do not contain aluminium salts as adjuvants has wider political and financial implications."

COMMENTS FROM DAN MURPHY

We have reviewed a number of articles also suggesting that aluminum exposure, including aluminium in vaccines, is an important risk factor in the development of autism spectrum disorder, including:

<u>Article Review #38-13</u>
Empirical Data Confirm Autism Symptoms Related to Aluminum and Acetaminophen Exposure

Article Review #04-14
Aluminum Induced Immunoexcitotoxicity in Neurodevelopmental and Neurodegenerative Disorders [This article quantified the aluminum exposure from pediatric vaccines, and it is not trivial].

Article Review #41-17
Subcutaneous Injections of Aluminum at Vaccine Adjuvant Levels Activate Innate Immune Genes in Mouse Brain that are Homologous with Biomarkers of Autism

Article Review #21-18
Aluminum in Brain Tissue in Autism

We have also reviewed studies suggesting that the harm from aluminum can be reduced if the child has sufficient levels of glutathione. We have also reviewed studies suggesting that giving a child acetaminophen (Tylenol and many other products) may result in a meaningful depletion of one's glutathione levels, increasing the risk of autism spectrum disorder.

As a convenience, the US Centers For Disease Control (CDC) vaccine ingredients page is attached with all aluminum highlighted: