Abstract for talk: Aluminum as a neurotoxin: the evidence from cell culture, *in vivo*, and human studies

Most age-related neurological disorders appear to arise due to environmental toxins acting against still unknown genetic susceptibility factors. Determining which of the immense numbers of potential toxins and genes might be responsible is a daunting task but one made potentially manageable by the study of unique disease clusters. For Lou Gehrig's disease (ALS) there are two such clusters. The first was identified on the Western Pacific island of Guam in the late 1940s by American neuroepidemiologists. The second is the ALS cohort within the multisystem disorder termed Gulf War Syndrome. For both, a range of potential toxins have been proposed. On Guam, epidemiological analysis pointed to consumption of the seeds of the cycad palm. In vivo studies in male outbred mice fed washed cycad seeds as part of diet showed a range of behavioural abnormalities and neuronal cell losses in different regions of the central nervous system. The range of outcomes resembled the spectrum of the disease on Guam. Aluminum in the soil had also been postulated to be related to the disease and aluminum neurotoxicity in various circumstances has been well documented. In neuronal and other cell culture preparations, aluminum salts such as the hydroxide as well as aluminum chloride cause the loss of cells. Mice exposed to aluminum chloride in water showed a range of motor and cognitive behavioural deficits. Mice injected with the adjuvant aluminum hydroxide showed motor behaviour deficits and motor neuron loss in motor cortex and lumbar spinal cord and a range of cognitive disorders. Morin staining for aluminum showed that motor neurons in the aluminum treatment group were labeled. Motor neurons also showed the presence of abnormally phosphorylated tau protein, the latter a hall mark of Alzherimer's disease and ALS-PDC. In addition to inducing outcomes similar to age-related neurological disorders, aluminum may contribute to early developmental disorders in humans. A comparison of autism spectrum disorder incidence since the early 1990s and the aluminum content in the Center for Disease Control and Prevention's recommended vaccine schedule shows a high level of correlation. Overall, the data presented suggest that substances such as aluminum can be highly neurotoxic at different stages of life. Presumptions of vaccine safety for aluminum or other adjuvants based on incomplete data should be reevaluated by adequately powered, controlled, and longitudinal studies involving multiple time points and animals of both sexes.

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