Exposure to aluminium

# Exposure to aluminium and the subsequent development of a disorder with features of Alzheimer's disease

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Increased efforts towards surveillance of people exposed to aluminium in Camelford is necessary to correctly identify the relationship of the exposure to increasing risks of the development of Alzheimer's disease.

The paper by Exley and Esiri[1] ***(see p 877)*** reports a most unusual case, namely, a 58-year-old woman with a rapidly progressive, fatal dementing illness, who, at autopsy, shows dramatic β-amyloid deposition of cerebral cortical and leptomeningeal blood vessels, modest numbers of neurofibrillary tangles and Lewy bodies, and evidence of very high aluminium content in affected brain regions. Of particular interest is that she was among the 20 000 people who were accidentally exposed, in July 1988, to exceedingly high concentrations of aluminium in their water supply in the so-called ''Camelford incident''. This is the first autopsy-documented case of Alzheimer's disease-like neurodegeneration in a victim of this incident.

This case raises the question of whether the relatively short but massive exposure to aluminium in the water supply played a part in the development of subsequent neurological illness in this woman. The association of aluminium and Alzheimer's disease has a long and rather controversial history. In 1965, Terry and Pena[2] and Klatzo *et al*[3] reported the experimental induction of neurofilamentous changes in rabbits after direct exposure of the brain to aluminium salts. These findings led to the work of Crapper-McLachlan and coworkers,[4] who found increased aluminium content in the brain tissues of patients with Alzheimer's disease, particularly in brain regions containing many neurofibrillary tangles. Subsequently, we and others documented increased aluminium content in the neurofibrillary tangle-bearing neurones of Alzheimer's disease and of amyotrophic lateral sclerosis or parkinsonism–dementia complex of Guam (see for extended review and references, Perl and Moalem[5]). The environmental source of the excess aluminium is, however, unclear and the element's possible role in the pathogenesis of Alzheimer's disease remains controversial, to say the least. Over the years, a particular problem has been the lack of convincing epidemiological data to support the hypothesis that exposure to aluminium increases the risk for the development of Alzheimer's disease. Aluminium is widespread in the environment, much of it in insoluble, non-bioavailable forms, thus making it difficult to obtain valid aluminium exposure histories.

In recent years, immense progress has been made in identifying and characterising genetic factors for the development of Alzheimer's disease. Yet, clearly, the interplay of genetic and environmental factors (plus the constant feature of increasing age) underlies the development of most cases of this disorder. Despite great progress being made on the genetic front, we still know little about the relevant modifying environmental factors. It is impossible to identify such factors on the basis of a single case. If additional similar cases, however, were to appear among the 20 000 people exposed, then the implications of this incident would become extremely important. Only time will tell. It should be noted that this brief exposure occurred almost 15 years before the onset of the disease, suggesting that the phenomenon of latency between this environmental exposure and the onset of clinically apparent features could have taken place.

As viable strategies for the prevention of Alzheimer's disease will likely stem, in part, from modification or avoidance of relevant environmental factors, the importance of this paucity of knowledge is clear. As the authors point out, aluminium binds tightly to proteins and in vitro models have shown the element's capacity to induce stable cross-linked, β-pleated sheet configurational changes. In past years, many hastily rejected the possible role of aluminium in the aetiology or pathogenesis of Alzheimer's disease and this issue has never been resolved properly. Can this report signal renewed interest in the potential involvement of aluminium in the development of Alzheimer's disease? At the very least, increased efforts towards surveillance of people exposed in Camelford is certainly warranted.

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