Aluminum, Drinking Water, and Alzheimer's Disease [Project #818]

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BACKGROUND
Aluminum (Al) is the third-most-common element in the earth’s crust and is present in all natural waters. Moreover, Al salts are used extensively as coagulants in drinking water treatment. It is not surprising, then, that measurable Al is present in the distributed water of all drinking water utilities, irrespective of whether Al was used as a coagulant.

The possibility of an association between Al concentration in drinking water and the occurrence of Alzheimer's disease (AD) has long been a topic of research, discussion, and considerable debate.

This report presents a critical review of research conducted to determine if there is a basis for the theory that Al in drinking water plays a part in the pathogenesis of AD.

APPROACH
Six major epidemiologic studies that have addressed the possibility of an association between the concentration of Al in drinking water and the occurrence of AD were reviewed. Also evaluated were the chemistry of Al in drinking water and the likelihood that drinking water Al is a meaningful contributor to the overall body burden.

Epidemiologic Studies
The study of AD is particularly difficult because clinical diagnosis in the early stages of the disease is inexact. Further, the presence of Al in the brains of AD patients and normal individuals may differ, but the preponderance of evidence to date indicates that any observed difference may be artifactual or potentially unimportant in the pathogenesis of AD. There is as yet no evidence of an excessive incidence of AD among persons with very high levels of Al exposure or ingestion.

The role of Al in the pathogenesis of AD should be further elucidated by studies within the basic sciences. Because of the rapid progress in genetics, it may soon be possible to identify more homogeneous subgroups of what is now called AD, and an adequate biological marker to do so may soon be available. But if a case-control or cohort study was mounted now to search for the potentially weak association between Al and AD, it could easily take 5 to 10 years to complete. By that point, basic scientific research may have rendered the question of an association between Al and AD moot. Attempting to address that question with anything less than antemortem biologic markers of exposure and disease occurrence may be unproductive and futile.

If observational studies are undertaken, they should focus on overall Al intake, rather than Al intake from drinking water only. The cohort study design (either historical or prospective) is preferred over ecologic and case-control designs. However, any of these study designs would be quite costly and time consuming, and the risk that they would be superseded by basic science appears to be significant, especially if Al is found to play no role in the pathogenesis of AD.
Aluminum Chemistry, Distribution, and Bioavailability

Al is only sparingly soluble at near-neutral pH; therefore, the Al compounds present in natural water will exist in a variety of insoluble and complexed forms. Al speciation has been well described for natural waters and fairly well described for drinking water. Only a small fraction (<10 percent) of the total Al content exists as free Al or in other monomolecular forms.

Conventional water treatment practices that utilize alum and other coagulants change the distribution of the Al fractions but do not substantially increase the overall Al content of the finished water. The proportion of the Al bound with colloidal and other particulate material is reduced via treatment, and the monomolecular species are proportionally increased. Consequently, the treated water monomolecular content may exceed 50 percent of the total. Because of the particle removal function of conventional treatment, some 40 percent of alum treated waters have a lower total Al concentration than the raw water source.

A review of the chemistry of the human gut relative to Al solubility suggests that Al uptake into the bloodstream may be independent of the form of Al ingestion and possibly even independent of the quantity of Al ingested. The acidic conditions, digestive fluids, mixing, and residence time in the stomach ensure that a major portion of consumed Al will be converted to soluble monomolecular species, regardless of whether the Al was ingested as drinking water particulates, in antacid tablets, or vegetable matter. In this sense, the stomach is the great leveler, converting the bulk of all ingested Al to an equivalent form.

The solubilized Al in the stomach is available for complexation by resident organic acids that may enhance its solubility when the stomach contents are transferred to the small intestine. In the small intestine, the pH shifts to near-neutral conditions, converting noncomplexed Al to insoluble forms that are not available for uptake. Insoluble Al compounds ultimately are excreted from the body in the feces. Citrate, a likely Al-complexing agent, may have an important role in determining blood Al levels. It helps to solubilize Al in the stomach, and an appreciable portion of the alumino-citrate complexes exist as neutral molecules that can pass through the intestinal membranes and provide a vehicle for absorption into the body.

CONCLUSIONS

It is far from clear that Al is the etiologic agent of AD or that drinking water Al contributes substantially to the Al body burden. The results of the six epidemiologic studies have been inconclusive. Three of the studies reported a positive correlation, but the remainder found no meaningful association. Each study can be criticized on a number of points, and each has weaknesses that can be attributed to the peculiar nature of the disease.

The issue of supposed variations in Al bioavailability has been raised to explain dichotomous epidemiologic findings, especially regarding Al exposure via drinking water. Simple solubility and mass flux considerations suggest that the quantity of drinking water Al ingested is unimportant relative to Al uptake to the blood. The authors of this study believe that the hypothesis that drinking water Al is more readily assimilated (bioavailable) than other forms of Al should be rejected, based on issues of solubility and likely chemical transformations that take place in the human gut.