

ALUMINIUM AND THE NUCLEUS OF NERVE CELLS

SIR.—Birchall and Chappell¹ have reviewed in *The Lancet* neurochemical aspects of the interaction of aluminium (Al) with physiological ligands, emphasising the preference of this neurotoxin for association with oxygen donor groups, especially cytosolic phosphates. We would add to their argument the potential for Al to interact with nucleic acid polyphosphates. This is of neurotoxicological interest because Al accumulates within affected neocortical nuclei in Alzheimer disease.²

The cell nucleus, with its phosphate-containing DNA and RNA, has the highest phosphate density—and thus the highest potential Al binding capacity—of any cellular organelle. Neuronal nuclei, with their large size, extensive euchromatisation, the faster digestion kinetics when exposed to nuclease, high transcriptional output, and extensive nuclear pore complex system, are especially susceptible to Al intoxication.

Al interacts strongly with chromatin and DNA and this association has harmful effects on nuclear metabolism. There is preferential binding of Al within the nucleus,²⁻⁵ and associated with raised nuclear Al levels is decreased cell division and DNA synthesis,⁶ and an increase in DNA replication errors and other effects at the chromosomal, DNA, and RNA levels* suggest Al-induced impairment of nucleic acid metabolism—and, ultimately, a deficit in the transmission of genetic information.

The small ionic radius and high positive charge density of Al may favour the translocation of this cation across endothelial, glial, or neuronal membrane barriers.^{4,7-9} Concentrations of phosphate are 2 mmol/l in plasma, 10 mmol/l in the cytosol, and at least 50 mmol/l within the nucleus, so the nucleus provides a high affinity, high capacity sink which traps aluminium.

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ALUMINIUM, HOT WATER TANKS, AND NEUROBIOLOGY

SIR.—Dr Martyn and colleagues (Jan 14, p 59) report a geographical relation between Alzheimer disease and aluminium (Al) in drinking water. Al levels in individual households may depend on the condition of the house's hot water heater. Most glass-lined hot water heaters are made with a "sacrificial" anode rod of an active metal, such as Al or magnesium, which corrodes more easily than the steel tank if there is a chip or crack in the glass lining. The Al anode rod corrodes, through galvanic interaction with the steel of the tank of the hot water heater, and Al ions pass directly into the water supply. The steel wall in the tank is protected from rusting by the mild electric current generated by the corrosion of the Al. When the Al anode in a hot water heater is actively corroding Al

*A fuller list of references in support of these (and other) statements is obtainable from *The Lancet*.

levels higher than those in the local water supply may be released into the household water supply.

Even small amounts of Al compete effectively for Mg binding sites in biological systems. Al³⁺ initiates tubulin polymerisation with an association constant about 10⁷ times that of Mg²⁺, and calcium-ion induced depolymerisation of such Al³⁺ microtubules is greatly inhibited.¹ Mg²⁺ blocks the N-methyl-D-aspartate (NMDA) receptor channel in central nervous system neurons in a voltage-dependent manner^{2,3} and there is thought to be an Mg binding site within the channel pore. The NMDA receptor complex provides a recognition site for the neurotransmitter glutamate that is coupled to a Ca²⁺ selective ion channel.^{4,5} Since Al ions compete so strongly with Mg they may displace Mg ions from the Mg²⁺ binding site within the NMDA channel pore, resulting in disruption of the usual Mg²⁺ block of the NMDA-receptor-coupled ion channels and release of Ca²⁺ into the neuron. Ca²⁺ entry through NMDA-receptor-activated channels is believed to cause striking increases in glutamate-induced cell death.⁶

The neurotoxic effects seen with Al intoxication may be mediated through disruption of Mg²⁺ block of NMDA receptors, resulting in uncontrolled activation of excitatory synapses or cell death from calcium influx. Such uncontrolled activation of excitatory synapses could lead to dementia.⁷ Even small amounts of Al, by strong competition for Mg binding sites, may lead to unrestrained Ca influx at the NMDA receptor, followed by neuronal death and Alzheimer, or other neurodegenerative diseases.

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ALUMINIUM FROM A COFFEE POT

SIR.—Like Dr Martyn and colleagues (Jan 14, p 59) we are concerned about aluminium (Al) (and other substances) in drinking water and with the various ways Al enters our water.

One of us purchased an electrically heated pot for preparing instant coffee or tea ('Rival' model 407011). The salesperson told him that the heating chamber was ceramic but on examination it seemed to be made of Al.

We have compared the Al concentration of water heated in this new pot (A) with that in water from our regular coffee pot (B) ('Mr Coffee' model CM1Z), filtered with 'Mr Coffee' paper filters and unfiltered. Both results were compared with Al concentrations in tap drinking water filtered and unfiltered. Water in pot B is heated to about 88°C.

Duplicate water samples were collected and delivered to the laboratory without telling the technician their origin. Al was measured by atomic absorption, an excellent method for trace elements.¹

Pot A contributed a significant amount of Al to the water. Al concentrations in $\mu\text{g/l}$ (1 $\mu\text{g/l}$ = 0.037 $\mu\text{mol/l}$) were: 22 in plain tap water; 11 in plain tap water run through a filter; 27.5 in tap water heated in pot B, no filter; 21 in tap water heated in pot B, with filter; and 1640 in tap water heated in pot A.

Groups such as the American Water Works Association, the US Environmental Protection Agency, and the World Health Organisation have suggested a water quality goal of about 50 $\mu\text{g/l}$ (or

less) of aluminium for drinking water, but it is important to be aware of how the water is processed before it is consumed. The water heated in pot A contained over thirty times the recommended water quality limit.

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INTERNATIONAL PROSTITUTES AND TRANSMISSION OF HIV

SIR,—In 1985, when commercially available kits permitted the routine testing for HIV in Dominica, one of the first seropositive individuals identified was a 30-year-old woman. She had been sent back to Dominica from a neighbouring island because of HIV seropositivity. She was not an intravenous drug user but had been practising prostitution outside her country of birth. At that time few seropositive women had been identified in Dominica,¹ and even in 1986 the prevalence of HIV seropositivity was found to be only 1.55% in prostitutes in Santo Domingo.²

Over the past three years, other women have come to the laboratory for serological testing after spending months to years as prostitutes in other countries. Some of them came voluntarily while others were referred by foreign health services for further counselling due to HIV seropositivity. Doctors at local hospitals have also sent blood samples from women whose profession included prostitution and travel. Because this group of individuals in Dominica represents a greater source of HIV transmission than local prostitutes, we have classified them as international prostitutes.

In our studies blood samples were tested for antibody to HIV by ELISA (Abbott and Ortho kits) with confirmation by western blot or indirect immunofluorescence.³

By the end of November, 1988, 80 women tested in our laboratory had been classified as international prostitutes (table). Most of them were aged 20-32 years, though some were over 40.

AGE DISTRIBUTION OF HIV SERPOSITIVITY IN INTERNATIONAL PROSTITUTES

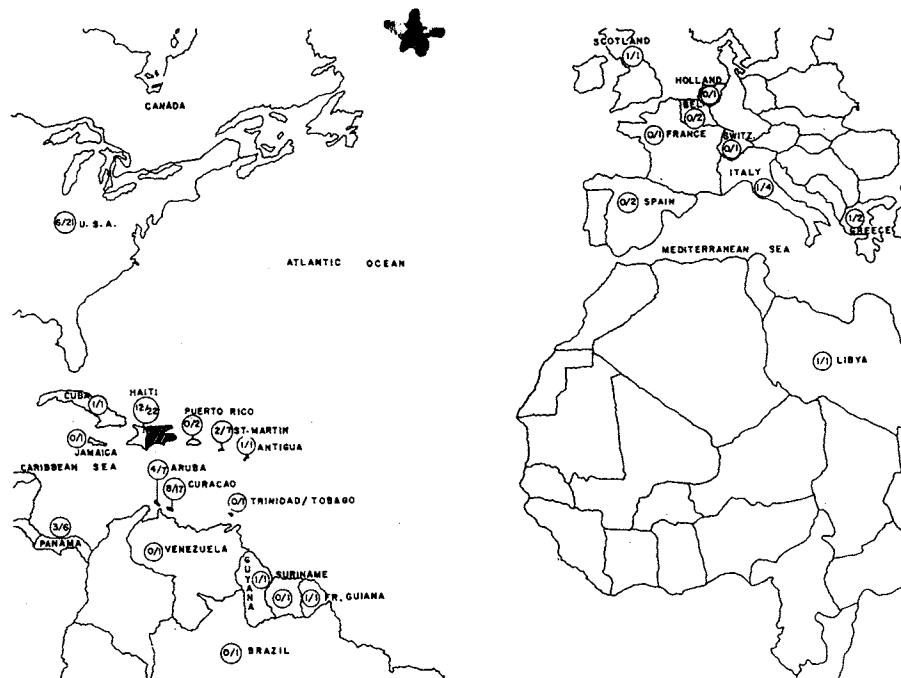
Age	Seropositive
20-24	9/21
25-28	5/13
29-32	9/16
33-36	3/11
37-40	2/7
> 40	4/6
Unknown	6/6
Total	38/80 (49%)

These women had been prostitutes in twenty-seven countries (figure), most of them visiting only one place. One woman, however, reported liaisons in six countries. The level of seropositivity in this group of women (49%) was considerably higher than that of the general population in 1988 (1%) and higher than that in homosexuals (about 10%) in Dominica. Moreover, since many of the international prostitutes never come in to be treated, the true prevalence of infection in this group remains unknown.

For the 65 international prostitutes for whom complete epidemiological data are available, heterosexual transmission remains the most probable means of infection with HIV. Only 6 reported blood transfusions, and 2 of these were HIV positive. 1 out of 4 who admitted to the use of intravenous drugs was found to be seropositive, while 2 other seropositive women out of 11 had clients who used intravenous drugs. Of the 21 women who reported a venereal disease, 7 were HIV antibody positive.

The international prostitutes apart, 12 other young women in Dominica have recently asked for an HIV antibody test to obtain documents for travel. They have the same age distribution as the international prostitutes and are basically from the same socio-economic background. Although they have been promised work as hostesses or waitresses or in factories in the nearby islands or abroad, it is clear that their jobs will also include prostitution. All were seronegative—not surprisingly, in view of the low level of HIV seropositivity in 289 local Dominican prostitutes (2%).⁴

Dominican women, it seems, travel to many areas of the Caribbean, Europe, and the Middle East. In view of the low



Countries visited by international prostitutes.

Dominican Republic is shown by shading. Number of seropositives and numbers visiting a country indicated in circle associated with country named.

A 20ml, 100x20A.