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Commentary

A vexing Commentary on the important issue of aluminium and Alzheimer' disease

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The Commentary by Zatta [9] on our recent publication [4] is error strewn and interwoven with unsubstantiated claims which can only serve to blur the edges not only of the research published in our paper but also the general question of the role of aluminium in Alzheimer's disease [2]. It is perhaps surprising that someone who has built his scientific reputation on the investigation of the putative role of aluminium in AD should now present such a prejudiced view.

The essence of Zatta's piece is immediately clear from its title. The use of the term '*Vexata Questio*' implies that putting aluminium and AD together is to act in a *malicious*, *irritating* and even *trivial* manner. He is imploring the reader as to why he/she should have to waste his/her time considering aluminium and AD and not least because of new data [4] which he believes leaves more to the imagination than to the scientific method. His major unsubstantiated criticism is 'modestly' reiterated at the end of the Commentary and concerns the scientific method and statistical analyses. The research in our paper has been peer-reviewed and it is unfortunate that Zatta's Commentary includes unsubstantiated opinions on its validity, opinions which can only serve to seed doubt in the scientific rigour of our findings. Another criticism with which he sought to reject our research was that the mineral water in question would include other constituents which could be responsible for the observed reduction in the body burden of aluminium. When challenged to explain this allusion he now reports in his Commentary that the 8.0 mg/L magnesium in Volvic could be responsible for the observed changes in the excretion of aluminium through an unsupported mechanism which he calls 'the domino effect'. We have trawled through the literature on both animal and human studies to try to find one example of how drinking water containing 8.0 mg/L magnesium influenced the urinary excretion of aluminium. There are no data to support any such effects and presumably Zatta's lack of any reference to such shows that he is aware of this. This does not, of course, prevent him from making this statement and using it along with his unsubstantiated criticisms of our scientific method as basis to reject our research.

Zatta now turns his attentions to the general subject areas of aluminium, silicon and AD. I found his manner to be condescending and his reference to JD Birchall FRS ill-informed and unnecessary. He also gives the impression that he is unaware that what he calls 'the old story' has moved on and, as exemplified by our JAD paper, continues to this day, relying only upon sound science for its substance (see, http://www.keele.ac.uk/depts/ch/groups/aluminium/publications.htm).

However, Zatta's understanding of the bioinorganic chemistry of silicon is very much an 'old story'. It has been acknowledged for at least the last twenty years that there are no Si-C, Si-N, Si-O-C . . . etc. bonds in any form of life on Earth [8], though we are still looking for these up to this day, and therefore Zatta's allusion to silicon being 'usually bonded to glycoproteins' is to say the least, ill-informed. The reference to the silicon concentration of blood is similarly out-dated, the lowest

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value for healthy individuals (over 74 years of age) being closer to 216 μg/L, more than twice the 'normal' value quoted by Zatta [1]. A brief attempt is made by Zatta to suggest that drinking a mineral water which is rich in silicic acid could lead to the formation of what he calls 'silicon dioxide' stones. Silicon dioxide is 'sand' and is the same term used by the authors of the one reference which Zatta cites to support this claim. Those of us who work on biological silicification are aware of the deposition of hydrated amorphous silica in the body, for example, with bone, though these deposits are associated with neither an increased absorption of silicic acid nor are they implicated in the aetiology of any known disease. As someone who understands the bioinorganic chemistry of silicic acid I am completely clear in my mind that it is perfectly safe, at least from the point of view of the silicic acid content, to drink potable waters containing significantly under-saturated concentrations of silicic acid.

Zatta then admits to applying a broad brush to the subject of aluminium and its putative role in Alzheimer's disease and proceeds to wheel out all of the old arguments as to why aluminium could not be involved in the disease. These are the favourite smokescreens of the international aluminium industry and are, to use Zatta's title phrase, indeed '*Vexata Questio*' and all have been addressed *ad nauseum* in the scientific literature. Zatta is not correct in the facts he uses to summarise the poisoning in 1988 of the Camelford water supply with aluminium sulphate. He begins by suggesting that large numbers of scientists have investigated the incident (in almost twenty years there has been almost no investigation of the health effects of this incident on the Camelford population) and continues by questioning the conclusions drawn by Professor MM Esiri (a world reknowned neuropathologist) concerning a recent neuropathological examination of the brain of a Camelford resident [3]. He then selectively quotes from Professor DP Perl's Commentary of the report of the findings to suggest that Professor Perl did not believe that the aluminium and the neuropathology were linked in this case [6].

Zatta's Commentary is festooned with selective citations of scientific literature, for example, choosing to completely ignore recent epidemiological data, as cited in our paper, which does link the silicon content of potable waters with the incidence of AD [5,7]. Similarly he dismisses without any foundation clearly substantiated aspects of scientific method applied in our research, for example, considering that our use of 'spot' urine samples being a major criticism of our methods. He takes neither account of the data which we included to validate their use nor the large number of scientific publications which totally justify their use in the context of our study. Of course, Zatta does not provide any reference to support his criticism.

Zatta's conclusions are simply a summary of the errors and prejudices contained within his Commentary. Many are his personal opinions and have neither need for nor regard to the scientific literature. Others are bemusing such as his reference to the presence of silicon in the brains of silicon-supplemented rats. Is there a point to this reference? Some are frustrating such as his continued assertion that silicic acid in potable waters has not been linked to the indicence of AD! Finally we are presented with his 'magnesium hypothesis' for AD therapy. This is published without any reference to the scientific literature and without having undergone any form of peer review, unlike, of course, our paper in JAD [4].

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