

# Does antiperspirant use increase the risk of aluminium-related disease, including Alzheimer's disease?

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**Aluminium salts are the major constituent of many widely used antiperspirant products. The use of such antiperspirants has been linked with the systemic accumulation of aluminium and an increased risk of Alzheimer's disease. But can the frequent use of aluminium-based antiperspirants lead to the accumulation of toxic levels of aluminium? And are there measures that we can take to reduce such accumulation without reducing the effectiveness of antiperspirants?**

Aluminium is a ubiquitous, though paradoxically non-essential, metal that is used by man in a burgeoning and diverse number of applications. Despite the fact that it is known to be toxic and has been implicated in Alzheimer's disease<sup>1</sup>, it is widely used as an antiperspirant. But are we, in our vanity, being almost as foolish as the Elizabethans who used arsenic as a cosmetic? In this article I critically examine the contention that aluminium in antiperspirants has implications for human health. I also make a number of suggestions as to how aluminium might be used both safely and effectively in future antiperspirant products.

## Routes of entry into the body

### *Inhalation and ingestion*

The research implicating antiperspirants in disease<sup>2,3</sup> has assumed that the aluminium in these products will be absorbed into the body. However, the only site for which the evidence of aluminium uptake in humans is unequivocal is the gut<sup>4</sup>. Antiperspirant aluminium can enter the gut when the antiperspirant is applied as a spray, some of which might inadvertently be inhaled via the mouth or nose (Fig. 1). Aluminium entering the lung and nasal-olfactory pathway in this manner will be diverted into the gut via the mucociliary pathway (Fig. 1), but does this mucus-bound aluminium make a significant contribution to the 6–20 mg of aluminium present in the normal diet? I think this is unlikely; if aluminium in antiperspirants is a factor in human disease it is probable that either alternative sites of absorption or novel non-systemic target sites will be involved<sup>5</sup>.

The mucociliary clearance of aluminium from two such alternative sites, the lung and olfactory-nasal pathway, takes hours to days to complete, and during this time aluminium will dissolve

in and diffuse throughout the mucus lining. For example, aluminium administered to rats as an aerosol was internalized by the epithelial cells of the lung and precipitated with phosphate in lysosomes<sup>6</sup>. Aluminium will also be bound by membrane phospholipids<sup>7</sup> with concomitant effects upon the rheology of these lipids<sup>8</sup>. These interactions will alter the barrier properties of the membrane and promote the paracellular absorption of aluminium<sup>9</sup>. The fate of aluminium entering the body through these mechanisms is unknown. However, the absorption of metals via the nasal-olfactory pathway<sup>10</sup> might have important implications for diseases of the central nervous system because this route offers direct access to the brain (Fig. 1)<sup>11,12</sup>. Clearly, the frequent inhalation of aluminium aerosols will increase the body burden and, more worryingly, the brain burden of aluminium.

### *Transdermal uptake*

The skin, to which antiperspirant is applied, supports the highest local concentrations of aluminium. Although much research has been undertaken into the antiperspirant properties of a number of aluminium salts<sup>13</sup>, very little of this work has focused upon the transdermal uptake of aluminium. We do know that keratin is the main sink for topically applied aluminium salts. Much of the keratin-bound aluminium would be expected to be lost from the body surface with shed skin (Fig. 1). The antiperspirant activity of aluminium requires either the precipitation of protein plugs in the sweat duct or a direct action of aluminium on the stimulation of the sweat gland<sup>14</sup>. Neither of these mechanisms requires the transdermal absorption or intracellular accumulation of aluminium. Further research into the mechanism of action of aluminium-based antiperspirants would help to clarify this anomaly. Recent experiments

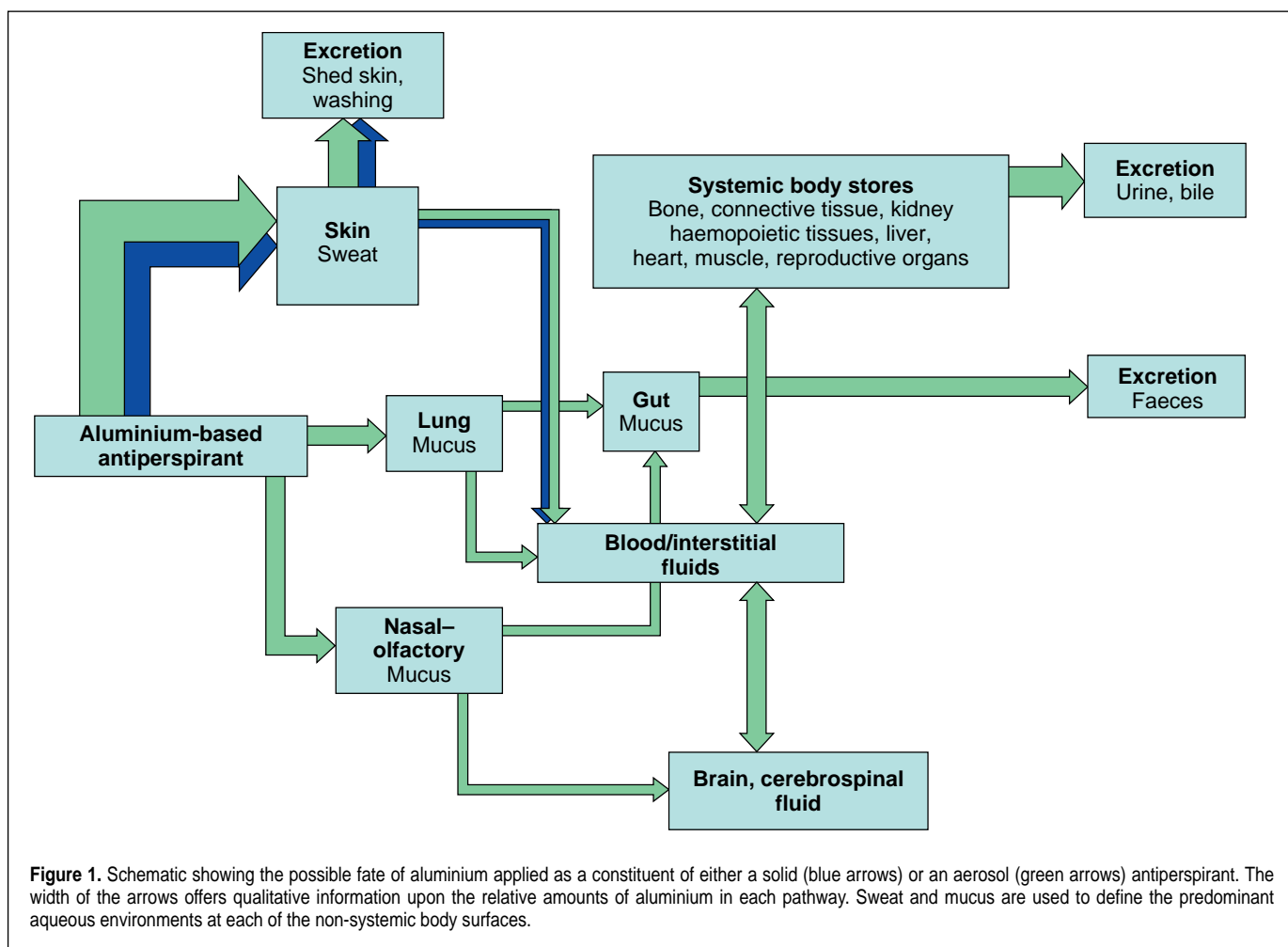
with shaved adult mice, naked mouse pups and excised skin patches taken from adult mice have shown unequivocally that mouse skin was not a barrier to the absorption of a topically applied aluminium salt<sup>3,15</sup>. More pertinently, the transdermal uptake of aluminium resulted in the preferential accumulation of aluminium in the hippocampus of the mouse brain. At first sight these results appear to support the earlier research linking aluminium in antiperspirants to Alzheimer's disease<sup>2</sup>. However, mouse skin lacks functional sweat glands, making the mouse an inappropriate model for the study of aluminium chemistry at the human skin surface.

## Non-systemic target sites

Antiperspirant aluminium might have implications for human health through interactions at non-systemic target sites. The effect of such interactions might, but need not, involve the subsequent transport of aluminium to a systemic site, such as the brain. For example, mucin, the main component of mucus, is a potential non-systemic target site. Aluminium can influence the rheological properties of this ubiquitous and highly conserved biopolymer<sup>16</sup> with implications for a number of diseases such as asthma, cystic fibrosis and disorders of the gastrointestinal tract. Small peptides are also likely ligands for aluminium. Binding often alters the conformation of the peptides<sup>17</sup> with subsequent effects upon their solution chemistry and biological function. One such class of peptides might be the antibiotic peptides prevalent in skin and other epithelia<sup>18,19</sup>.

## The chemistry of aluminium in living systems

The chemistry of aluminium at the gut, lung, nasal-olfactory pathway and skin will determine the exposure and subsequent biological



availability of aluminium at these sites<sup>5</sup>. Thus, in humans the solution chemistry of aluminium in secretions such as sweat and mucus will be of fundamental importance. Aluminium reacts in biological systems through the  $Al^{3+}_{(aq)}$  cation. Reactions with other charged monomeric forms of aluminium are both thermodynamically and kinetically unfavourable. Therefore, the role of aluminium speciation can be adequately considered as the mechanism whereby  $Al^{3+}_{(aq)}$  is delivered to a target site where its coordination might elicit some biological response. The many different forms of aluminium – for example, complexes with citrate or phosphate – determine both the fate of  $Al^{3+}$  (its target site) and the rate at which it will be delivered to this site. In this way, different ligands might alter the toxicity of aluminium. However, in almost all examples, it is the  $Al^{3+}$  cation and not the complex that initiates the response. There are examples of aluminium chemistry that appear to contradict this definition: for example, hexokinase is inhibited by  $Al-ATP^{20}$ . However, in such cases the ligand, in this case

ATP, should be considered as the target site and not the substrate with which the metal complex interacts.

### Reducing the risk of aluminium toxicity

It is with this chemistry in mind that the constitution of antiperspirant formulations and their role in determining the biological availability of aluminium at body surfaces should be considered. Aerosol formulations present the major challenge because they impact upon secondary surfaces such as those of the nose and lung. At best the antiperspirant formulation should help to promote the mucociliary clearance of aluminium. This could be achieved through the introduction of suitable ligands into the formulation. These would reduce the number of interactions of aluminium that, in turn, lead to its association with membrane surfaces, its internalization and its subsequent systemic accumulation. These new constituents could also act at the surface of the skin to promote the rapid delivery of aluminium to

its site of action and to maintain a concentration gradient to replenish such sites over extended time periods. One as yet untested approach might be to replace chlorhydrate aluminium salts with hydroxyaluminosilicates. Hydroxyaluminosilicates combine a potentially antiperspirant hydroxide phase with significantly reduced biological availability<sup>21,22</sup>. The exact nature of the changes in formulation required to achieve an effective and safe aluminium-based antiperspirant cannot be ascertained without a greater understanding of the mechanism of antiperspirant activity. There is little evidence in the published literature that antiperspirants have been formulated to optimize the activity of  $Al^{3+}$ , their active ingredient. There is a similar paucity of information concerning possible biotransformation reactions that might convert a reservoir of inert aluminium at the skin surface to a neutral, lipid-soluble complex capable of being accumulated systemically. This is not such a remote possibility when one considers how long-lived antiperspirant applications can be and the likelihood of the emergence of microbial

## The outstanding questions

- Does antiperspirant aluminium gain direct access to the brain via the nasal-olfactory pathway?
- Is human skin an effective barrier to the transdermal absorption of antiperspirant aluminium?
- What are the roles of non-systemic target sites (eg. mucin or antibiotic peptides) in mediating both the systemic absorption and the non-systemic toxicity of antiperspirant aluminium?
- Does the use of a solid as opposed to an aerosol antiperspirant reduce any risk of aluminium-related disease?
- Should antiperspirant formulations be changed to take account of the health risk posed by aluminium?

populations at their sites of application. Clearly, as the frequent use of aluminium-based antiperspirants has been linked to a higher incidence of Alzheimer's disease<sup>2</sup>, manufacturers of these products cannot afford to be complacent.

## Monitoring aluminium uptake

The evidence linking aluminium in antiperspirants to human disease is both scarce and equivocal but the paucity of research in this area reveals that little consideration has been given to our exposure to aluminium from these products. It would be straightforward to find out whether aluminium from an antiperspirant can be accumulated systemically, using the tracer <sup>26</sup>Al. The inclusion of trace amounts of this isotope in an antiperspirant formulation would allow the systemic absorption of aluminium in someone using the antiperspirant to be monitored by identifying the excretion of this isotope in the urine. Experiments designed to discriminate between absorption from the use of either the hard or the aerosol formulations would be especially useful.

## Concluding remarks

Neither the potential for systemic toxicity<sup>1</sup> nor the possibility that antiperspirant aluminium might exert an effect through a non-systemic target site should be ignored. Aluminium salts are extremely effective antiperspirants. A thorough knowledge of the mechanisms underlying their efficacy should ensure their safe and effective use in the future.

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