Risiken erkennen – Gesundheit schützen

No risk of Alzheimer's disease from aluminium in consumer products

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Aluminium is the third most frequent element in the earth's crust and occurs naturally in drinking water and other foods, particularly in fruit and vegetables. For consumers the main uptake route is food. There may be additional exposure from aluminium-containing food-contact articles like kitchen utensils, cans, foils or tubes from which the light metal migrates into the food. Furthermore, aluminium may also be contained in medicinal products to neutralise gastric acid, so-called antacids and in cosmetic products. In roll-on deodorants, for instance, it is used for its antiperspirant action.

The safety of aluminium uptake from food-contact articles and cosmetic products is repeatedly questioned. This applies in particular to its possible involvement in the development of Alzheimer's disease, a form of dementia that may be linked to elevated aluminium concentrations in the cerebral regions affected. This suspicion is based on the fact that high doses of aluminium are neurotoxic and can pass the blood-brain barrier. Against this backdrop the Federal Institute for Risk Assessment (BfR) has assessed estimated aluminium intake from food-contact articles and cosmetics and has come to the following conclusion.

Compared to uptake from food or antacids, aluminium intake from food-contact articles and cosmetic products is low. It is far lower than the intake which is deemed to be safe on the basis of an updated assessment of the Food and Agriculture Organisation and the World Health Organisation (JEFCA, 2006).

So far no causal relationship has been proven scientifically between elevated aluminium uptake from foods including drinking water, medicinal products or cosmetics and Alzheimer's disease. Amyloid deposits in the brain are typical for Alzheimer’s. However, an above-average frequency was not observed either in dialysis patients or in aluminium workers – two groups of individuals who come into contact with aluminium on a larger scale. BfR does not, therefore, see any health risk for consumers from aluminium intake from food-contact articles or cosmetics.

Concerning the increased solubility of aluminium in the presence of acids and salts, BfR recommends that no aluminium-containing pans or bowls should be used for foods like apple puree, rhubarb, tomato puree or salted herring. No aluminium foil should be used in contact with these foods either. This is one way of actively avoiding unnecessary aluminium uptake.

1 Subject matter of the assessment

Aluminium can cross to and be ingested from food in contact with various aluminium-containing articles like cooking utensils, cans, foils and tubes. Cosmetics like roll-on deodorants are another exposure route for aluminium. In recent years the safety of aluminium uptake from the above-mentioned sources has frequently been questioned, particularly in conjunction with the possible development of Alzheimer's disease. This is a form of dementia that mainly affects old people and may be linked to elevated aluminium concentrations in the brain regions affected. A policy statement on aluminium in food-contact articles is contained in the Council of Europe Resolution on Metals and Alloys (2002).

2 Result

The estimated aluminium uptake from both food-contact articles (e.g. aluminium foils, cooking utensils) and cosmetics (antiperspirants) is low compared to uptake from foods containing aluminium naturally or foods manufactured using aluminium-containing additives, and medicinal products like antacids. It is well below the weekly intake of 1 mg/kg body weight which was established by the Joint Expert Committee on Food Additives of the Food and Agriculture Organisation (FAO) and the World Health Organisation (WHO) as the provisional, tolerable intake of aluminium from food (JEFCA, 7 July 2006). Up to now no scientifically secured evidence could be provided of an association between elevated aluminium uptake from food/drinking water, medicinal products (antacids) or cosmetics (antiperspirants) and Alzheimer's disease despite numerous corresponding indications. Nevertheless, for reasons of precautionary health protection, improper use of aluminium-containing food-contact articles should be avoided. These articles should not be allowed to have lengthy contact with moist, acid or salt-containing foods. Aluminium foils should not be used to cover food of this kind on trays or in bowls.

3 Reasons

3.1 Risk assessment

3.1.1 Agent

Aluminium is the third most frequent element in the earth's crust and therefore also occurs as a natural ingredient particularly in foods of plant origin (Schmidt / Grunow, 1991). Many aluminium compounds are not water soluble at neutral pH. Solubility increases at acidic or alkaline pH. Given the low mechanical stability of aluminium, alloys are frequently used (Council of Europe, 2002). Aluminium and its alloys are highly resistant to corrosion. On contact with atmospheric oxygen a thin aluminium oxide film is formed which prevents any further oxidation (surface passivation). Contact with acidic and/or salty foods does, however, destroy the oxide layer and aluminium can then migrate to the food.

3.1.2 Hazard potential

In human beings absorption of aluminium from the gastrointestinal tract is normally low. It amounts to maximum 1% and in the case of high intakes (>1 g aluminium) can fall to 0.01%. In the presence of specific anions like citrate, malate or ascorbate (e.g. from fruit juices) oral absorption may be higher. Mean blood levels are given as 7 µg/l. Aluminium is mainly excreted via kidneys. At an intake of 5-125 mg Al/day no accumulation of aluminium was observed in healthy men (EU SCMPMD, 1999). So far BfR has only had access to limited data on the dermal uptake of aluminium, e.g. from cosmetics (see Exposure). The estimated uptake from skin (dermal absorption) is 0.01% (Yokel / McNamara, 2001). Exley *et al.* (1996) drew attention to uncertainties concerning the involvement of different uptake routes in overall aluminium intake.

In the case of dietary intake aluminium has low acute toxicity. Interactions with phosphate and calcium metabolism have been demonstrated in human beings and in animal experiments. At high doses of aluminium chloride (355 ppm), there was reduced phosphate retention in mice. At 0.1% and 0.2% aluminium chloride in feed, functional or neurochemical changes were observed. At high doses embryotoxic effects occurred in reproduction toxicological studies, too. But no teratogenic effects (deformities) were observed (Schmidt / Grunow, 1991).

After administration of antacids (>1,000 mg Al/person/day) disruptions to phosphate and calcium status have been reported in human beings. There was demineralisation of bones and reduction in bone strength (Schmidt / Grunow, 1991). Elevated, toxicologically relevant aluminium blood levels were found in dialysis patients as a consequence of high concentrations in dialysis water and/or therapeutic administration of aluminium hydroxide. The toxic effects of aluminium manifested themselves in these patients as symptoms of dialysis encephalopathy. This is characterised by vitamin D-resistant osteomalacia, anaemia and brain damage. There are numerous indications that aluminium can pass the blood-brain barrier although the transport mechanism is still unclear (Exley *et al.*, 1996).

Alzheimer's disease has also been linked to the neurotoxic effect of aluminium. Various epidemiological studies, which attempted to prove an association between aluminium uptake from drinking water and onset of the disease, failed to provide any scientific evidence because of the lack of dose-response relationships and other methodological shortcomings (Schmidt / Grunow, 1991). Pathological amyloid deposits in the brain are assumed to be the cause of Alzheimer's disease. They are seemingly caused by conversion of membrane protein as a consequence of the destruction of nerve cells or nerve cell membranes which increase with age. As the neuropathological changes in Alzheimer's disease vary considerably from those of dialysis patients, it is rather unlikely that aluminium triggers the disease. The World Health Organisation (WHO) (IPCS 1997), therefore, came to the conclusion that aluminium is not the cause of Alzheimer's disease. In the pharmacological standard literature, too, and in publications on antacid tolerance, there are no reports that the administration of these medicinal products contributes to the onset of Alzheimer's disease.

A possible association between aluminium intake and neurodegenerative diseases is discussed in various, more recent epidemiological studies and animal experiments. In one study by Walton (2006) brain tissue from six individuals, who suffered from Alzheimer’s, and from six control persons who had died at a mean age of 82.5 and 78.8 years respectively, was examined histopathologically. The author suspects that aluminium must be seen as a possible causal factor in the pathogenesis of Alzheimer’s disease. However, this study does not provide clear evidence of a causal association. The author discusses the possibility that aluminium accumulation in certain brain tissue structures is the consequence but not the cause of pathological changes.

Exley and Esiri (2006) report on the occurrence of an elevated aluminium content in pathologically changed brain tissue in a woman who showed symptoms of a neurodegenerative disease one year before. Fifteen years earlier the woman had been exposed for a few weeks to a high aluminium concentration in drinking water (in the range of 100-600 mg/l). The authors stressed that no conclusions can be drawn from this individual case about the hazard potential of aluminium. For this, more of the approximately 20,000 exposed individuals would have to be examined in comparison to non-exposed individuals.

In a study by Kaneko *et al.*, mice were given an aluminium chloride solution or a solution of an aluminium-maltolate complex as an intraperitoneal injection (equivalent to a dose of approximately 1 mg/kg body weight) over a period of 60 days. The memory capacity of the animals was then determined using a behaviour test and the aluminium content in the brain was measured. In the study impairment of memory capacity correlated with an elevated aluminium level in the brain. This study can contribute to describing the hazard potential of aluminium. A risk to humans resulting from oral aluminium intake cannot, however, be deduced from this study because a relatively high dose of aluminium was directly injected into the animals’ abdomen.

Even if aluminium and other metals like iron and copper do not probably play any causal role in the onset of Alzheimer's disease, they could be involved as cofactors in the formation of critical neuropathological lesions. At the present time, many experimental studies are being conducted in order to clarify the possible mechanisms of action of these metals which could be involved in the aging brain in the formation of reactive oxygen species (Perl and Moalem, 2006), in the triggering of inflammatory processes (Becaria *et al.,* 2006; Campbell 2006) or inhibition of the breakdown of amyloid peptides (Sparks *et al.,* 2006; Sakamoto *et al.;* Banks *et al.,* 2006).

The Joint Expert Committee on Food Additives (JEFCA) of the Food and Agriculture Organisation (FAO) and WHO and the Scientific Committee on Food (SCF) of the European Commission established a provisional tolerable weekly intake (PTWI) of 7 mg/kg body weight for total dietary aluminium intake, including aluminium salts in food additives in 1989 (JECFA, 1989). In 1991 SCF set a TDI of 1 mg/kg body weight for aluminium from food-contact materials and articles. Based on the conventional conversion factors (1 kg aluminium-containing food/person of 60 kg body weight/day) an overall level of 60 mg Al/kg food would, therefore, be tolerable. JEFCA established in 2006 an updated PTWI of 1 mg/kg body weight for the total dietary intake of aluminium (JEFCA, 7 July 2006). The Committee came to the conclusion that lower doses of aluminium than the doses taken as the basis for the establishment of the earlier PTWI value can already impair reproduction and the developing nervous system.

3.1.3 Exposure

Several exposure routes must be taken into account for aluminium. For the general population food is the most important intake route. Besides fresh foods like vegetables (0.3-26 mg/kg) and fruit (0.5-14 mg/kg), tea and spices may also be major sources of intake because of their high aluminium contents. Foods that are produced using aluminium-containing additives (e.g. confectionery, bakery goods) may also lead to an elevated intake. Additional dietary burden may arise from aluminium-containing packaging and aluminium-containing cooking utensils. Aluminium-containing food packaging (e.g. lid foils of plastic beakers, beverage cans) are frequently coated which means that no significant migration of aluminium is to be expected (Schmidt / Grunow, 1991). An additional intake of maximum 3.5 mg Al/person/day has been estimated from food prepared, heated or stored in aluminium pots and pans (Greger, 1985). For the migration of aluminium from food-contact articles after cooking, freezing and defrosting various foods, values of <0.4-7.1 mg/kg food are indicated with a maximum single value of 57 mg/kg for tomato sauce. The former Federal Institute for Consumer Health Protection and Veterinary Medicine (BgVV) pointed out in its expert opinion on the use of aluminium foil for grilling that, even under the worst conditions, consumption of mackerel fillets with a spice mixture (200 g fish) grilled in foil would only use up a small part of the intake amount covered by the TDI for aluminium (2.5 %) (BgVV, 2000), equivalent to approximately 18% of the current PTWI value.

However, there are reports of high levels of migration from aluminium containers and foil to acidic foods like rhubarb (41.8 mg/kg), sauerkraut (16.4 mg/kg) and tomatoes (64.8 mg/kg) (Schmidt / Grunow, 1991). With regard to average dietary aluminium uptake, data are available from JECFA (1989) of 2-6 mg/day for children and 6-14 mg/day for adults. IPCS (1997) indicates a range of 2.5-13 mg/day for adults. The contribution of drinking water in daily aluminium intake is relatively low: 0.2-0.4 mg. Uptake from the air is maximum 0.04 mg/day (IPCS, 1997).

Up to 5,000 mg Al/person/day are ingested from aluminium-containing medicinal products (aluminium hydroxide, aluminium-containing phosphate binders) like antacids.

In studies on transdermal uptake of water soluble aluminium chloride in mice, the maximum penetration rate was 24.6 ng/cm^2. If one takes this value as the basis for estimating exposure to aluminium in deodorants, then this leads to an intake of 7.5 µg per application for an application area of 300 cm^2. From more recent studies in human beings it is known that 3.6 µg are absorbed in the armpit after the single application of 0.4 ml of a 21 % aluminium chlorohydrate solution (Flarend *et al.* 2001).

3.1.4 Risk characterisation

Overall, the evaluation of epidemiological drinking water studies does not confirm any causal relationship between aluminium contents in water and the onset of Alzheimer's disease or cognitive dysfunctions in old age (IPCS, 1997). In the case of clinically exposed patients with dialysis encephalopathy, >100 µg/l were given as the critical aluminium concentrations in blood (Schmidt / Grunow, 1991). Hence, they are more than 10 times higher than the blood levels in the general population (see above). The neurofibrillary deposits (degenerative fibrils) - typical for Alzheimer's disease – were not observed more frequently in the dialysis patients exposed to high levels of aluminium (Candy *et al.*, 1992) or in the aluminium workers (JECFA, 1989) than in non-exposed individuals. Regarding the use of aluminium-containing food additives, SCF is also of the opinion that there is no clear association between aluminium intake and Alzheimer's disease. It established a TDI of 1 mg/kg body weight for aluminium uptake from all sources (SCF1991). The current PTWI of 1 mg/kg body weight for the total intake of aluminium leads to a tolerable intake of 60 mg/person/week or 8.6 mg/person/day. Compared with this value the daily aluminium intake levels from food contact articles (3.5 mg) and deodorants (7 µg) are to be considered safe. If acid-containing or salt-containing foods are cooked or stored for longer periods in aluminium pots or come into contact with aluminium foil, the aluminium migrations to the food are, however, so high that repeated weekly consumption of foods of this kind can lead to an exceeding of the PTWI. The regular consumption of foods with aluminium-containing additives could also lead to major exceedings of the PTWI value by some groups in the population – in particular children (JECFA, 2006).

At the 53rd meeting of the Cosmetics Committee, aluminium chloride in cosmetics and a possible association with cases of Alzheimer's disease were discussed. The backdrop to this were the publications by Graves *et al.* (1990) and Anane *et al.* (1995). The epidemiological study by Graves is based on telephone interviews with relatives of Alzheimer patients. A reliable diagnosis was only available for some of the patients and the authors came to the conclusion that their study did not support a correlation between aluminium exposure and the disease.

4 Measures/action framework

Although a causal relationship between elevated aluminium intake and the onset of Alzheimer's disease cannot be scientifically proved, incorrect use of aluminium-containing food-contact articles leading to the unwanted migration of aluminium to food should be avoided for reasons of precautionary health protection. In order to keep aluminium intake as low as possible, aluminium cooking utensils and bowls should not be allowed to come into contact over longer periods with foods with a high acidic or salt content like apple puree, rhubarb, tomato puree, sauerkraut, salted mackerel or salted gherkins etc. Nor should aluminium foil be used, for instance, to cover the above-mentioned foods on trays or in bowls. At the beginning of the

1990s the Association of the Aluminium-processing Industry voluntarily undertook to place corresponding information on the packaging of aluminium foil to be used in private households (Schmidt / Grunow, 1991). In its Resolution on Metals and Alloys the Council of Europe also recommends placing appropriate information for consumers on the packaging of aluminium foil to be used in private households (2002). BfR considers that information of this kind is required for the guidance of consumers.

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