

Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Aluminum

Evidence Summary

There is no consistent or compelling evidence to associate aluminum with increased Alzheimer's disease or breast cancer, but to be safe, limiting excessive exposure may be a good idea.

Brain health risk: No associations between aluminum exposure and dementia risk have been found except a few studies linking higher aluminum content in drinking water and increased dementia risk.

Risk for aging and related health conditions: Observational studies probing the link between aluminum and breast cancer or other diseases have been inconclusive. Limiting excessive exposure may be recommended.

Safety concerns: No studies have proven that aluminum is completely safe for brain health or for the rest of the body. Dietary exposure may exceed provisional tolerable weekly intake depending on age, medications, and diet.

What is it? Aluminum is an element abundantly present in the earth, and therefore, occurs naturally in our drinking water and the food we eat. Aluminum is also used in some medications and cosmetics. Some studies have shown a link between brain levels of aluminum and Alzheimer's disease [1]. Since the association was observed, there have been many studies looking into whether aluminum from food/drinks, pots/pans, antiperspirants, and antacids increases the risk for Alzheimer's. Aluminum can come in many forms and its toxicity depends on the levels of trivalent aluminum (Al^{+3}), which can react with water to produce aluminum superoxides, which in turn can deplete mitochondrial iron and promote generation of reactive oxygen species [2]. Al^{+3} -induced formation of reactive oxygen species can lead to oxidative damage and apoptosis.

Brain health risk: No associations between aluminum exposure and dementia risk have been found except a few studies linking higher aluminum content in drinking water and increased dementia risk.

Types of evidence:

- 6 meta-analyses or systematic reviews based on numerous observational studies
- 1 meta-analysis comparing aluminum levels in Alzheimer's patients versus controls
- 1 randomized crossover trial testing the effects of acute exposure to aluminum
- 1 open-label trial testing the effects of silicon-rich mineral water on aluminum excretion and cognition in Alzheimer's patients and controls
- 5 reviews
- Numerous laboratory studies

Human research to suggest aluminum exposure can increase risk of cognitive decline or Alzheimer's disease/dementia:

Aluminum in drinking water. POTENTIAL RISK. Several meta-analyses and systematic reviews have examined aluminum from different sources such as drinking water [3; 4; 5]. The pooled OR among those who drank water containing aluminum at or higher than 0.1 mg/L is 1.95 (95% CI, 1.47–2.59) compared to those who drank water containing less than 0.1 mg/L. The only high quality study was a prospective cohort study of almost 4,000 older adults in southwest France (the PAQUID study; [6]), which found that levels of aluminum consumption in drinking water in excess of 0.1 mg/d were associated with a doubling of dementia risk and a 3-fold increase in Alzheimer's risk [7]. Of the remaining 13 moderate quality studies, 6 found an association between higher aluminum levels in drinking water and increased dementia risk [8; 9; 10; 11; 12], 4 found no association [13; 14; 15], and 1 found a protective effect of higher soil aluminum levels [16]. It is worth noting that other elements present in drinking water, such as



fluoride, copper, zinc, or iron could also have an effect on cognitive impairment and modify any aluminum toxicity [17].

Antacid use: NO HARM. A 2015 meta-analysis of 7 case-control studies and 2 cohort studies (total of 6,310 subjects) reported that regular antacid use was not associated with Alzheimer's disease [18]. In the case-control studies, the odds ratio was 1.0 (95% CI, 0.8-1.2), and in the cohort studies the relative risk was 0.8 (95% CI, 0.4-1.8). There was also no association with Alzheimer's when limiting the studies to over 6 or 12 months of regular use (OR=1.1 and 1.0, respectively). However, longer follow-up may be needed to definitively exclude the association between antacid use and dementia risk.

Occupational exposure to aluminum: NO HARM. A 2015 meta-analysis of 3 retrospective case-control studies including 1,056 subjects reported that occupational aluminum dust exposure was not associated with Alzheimer's (OR=1.00; 95% CI, 0.59-1.68) [19]. However, a role for aluminum cannot be definitively excluded without further prospective studies with precise ascertainment of aluminum exposure. In a 2016 meta-analysis including 4 studies, the relationship between aluminum exposure and dementia was mixed due to the studies being small with low statistical power [3].

Acute aluminum: In a randomized crossover trial of 38 people with (n=8) or without dementia (10 aged, 20 young), acute ingestion of an aluminum gel (Amphojel) did not result in significant differences in cognitive test scores [20]. This study suggested that a single dose of aluminum resulting in serum aluminum levels between 50-150 µg/L does not produce negative effects on cognition.

Human research to suggest aluminum exposure can increase risk in patients with Alzheimer's disease/dementia:

In the RCT described above that tested acute ingestion of an aluminum gel, Alzheimer's patients were not more vulnerable to the acute effects of aluminum compared to controls, though the study was small and tested only a single dose (resulting in serum levels between 50-150 µg/L).

A meta-analysis of 34 studies reported that in Alzheimer's disease patients compared to controls, aluminum levels are higher in the brain, serum, and cerebral spinal fluid [1]. Some epidemiological studies suggested that silica could be protective against aluminum-induced damage, because it reduces oral absorption of aluminum and enhances aluminum excretion [17]. In an open-label trial, drinking silicon-rich mineral water (up to 1L/day) for 12 weeks facilitated excretion of aluminum in the urine in both Alzheimer's disease patients and controls (caregivers or spouses)[21]. No effects were seen on

excretion of other metals such as iron and copper. Of the 15 Alzheimer's patients included in this trial, cognitive scores declined in 7, improved in 3, and were unchanged in 5. Of 14 controls, cognitive scores declined in 3, improved in 2, and were unchanged in 9. The data is limited and cannot probe whether these changes in aluminum excretion or cognitive scores translate to improvement in cognitive symptoms in Alzheimer's patients.

Mechanisms of action of how aluminum exposure might increase risk of cognitive decline:

Aluminum can cross the blood-brain-barrier and accumulate in the brain [22; 23]. Aside from Al^{+3} -induced oxidative damage [2], there are several other possible mechanisms of aluminum neurotoxicity. In rats, an aluminum-rich diet (1.6 mg/kg/day, equivalent to the high end of human dietary aluminum intake) induces memory deterioration, accumulation of aluminum in neurons, oxidative damage, 41% reduction in PP2A activity (enzyme that dephosphorylates tau), and increased hyperphosphorylated tau [24]. Aluminum also alters $A\beta$ processing and increases $A\beta$ production, aggregation, and levels of toxic oligomeric forms [25; 26]. In addition, *in vitro* studies have shown that $A\beta$ -aluminum complexes disrupt intraneuronal calcium homeostasis and mitochondrial respiration [27].

APOE4 interactions: It is unknown whether aluminum affects APOE4 carriers differently from non-carriers. In a randomized crossover trial testing the acute effects of an aluminum gel (Amphojel), there was no association between APOE4 genotype and aluminum absorption [20].

Risk for aging and related health conditions: Observational studies probing the link between aluminum and breast cancer or other diseases have been inconclusive. Limiting excessive exposure may be recommended.

Types of evidence:

- 2 systematic reviews, one based on 469 observational studies and another based on 2 observational studies for breast cancer risk
- 1 observational study not included in the systematic review
- 3 reviews
- Numerous laboratory studies

Breast Cancer: INCONCLUSIVE. A systematic review including 2 case-control studies reported no increased risk of breast cancer with antiperspirant use; however, this analysis was based on an insufficient number of studies and the findings may not be reliable [28]. The first study examined 813

breast cancer patients and 793 controls and reported that the risk for breast cancer did not significantly increase with antiperspirant use (OR = 0.9) or deodorant use (OR = 1.2)[29]. Although aluminum may be more readily absorbed via small nicks or abrasions caused by shaving, breast cancer risk was not increased in antiperspirant/deodorant users who shaved with a razor blade, or with application of products within 1 hour of shaving (for antiperspirant, OR = 0.9; for deodorant, OR = 1.2). The second study was smaller and found that 51.8% of breast cancer patients (n=54) and 82.0% of patients visiting the hospital for other reasons (n=50) used antiperspirants, and therefore this study did not find an increased breast cancer risk with the use of antiperspirants [30].

However, in a population of breast cancer patients, those who used antiperspirant products more frequently and for longer (starting use at an earlier age) on a shaved underarm tended to be diagnosed with breast cancer at an earlier age [31]. Preclinical studies suggest that exposure to aluminum can increase migratory and invasive properties of human breast cancer cells [32]. Aluminum has also been shown to cause DNA double-strand breaks in human breast epithelial cells [33]. *In vitro* and *in vivo* studies have also shown that aluminum is a “metalloestrogen” and can bind to estrogen receptors [34]. Although aluminum has not been shown to definitively cause risk for breast cancer, it has not been demonstrated to be perfectly safe.

Safety concerns: No studies have proven that aluminum is completely safe for brain health or for the rest of the body. Dietary exposure may exceed provisional tolerable weekly intake depending on age, medications, and diet.

Types of evidence:

- 1 systematic review based on 469 observational studies
- 1 pharmacokinetic analysis of aluminum from vaccines and diet in infants
- 2 reviews
- 1 case study of hyperaluminemia
- Numerous laboratory studies

Antiperspirants: Aluminum salts in antiperspirants dissolve into the moisture on the skin’s surface and forms a temporary plug within the sweat duct that stops the flow of sweat to the skin’s surface. A study in 2 healthy volunteers showed that a single underarm application of aluminum chlorohydrate (active antiperspirant agent) resulted in absorption of only 0.012%, suggesting that topical aluminum chlorohydrate does not significantly contribute to levels of aluminum in the body [35]. Although much

of aluminum is eliminated by the renal system, sweat is one of the routes for aluminum excretion in humans, and therefore, blocking that route may lead to an increase in aluminum levels in the body [36].

There has been a case study of a woman with bone pain and fatigue who was diagnosed with hyperaluminemia—the study concluded that the source of aluminum was from 1 g of aluminum chlorohydrate-containing antiperspirant cream applied every morning for 4 years on regularly shaved skin [37]. In this 43 year-old patient, aluminum levels in the plasma were 3.88 $\mu\text{M/L}$ (normal values are < 0.37 $\mu\text{M/L}$), but fell back to the normal range after discontinuing antiperspirant use for 8 months. Her symptoms resolved concurrently.

Medications: Antacids (35-208 mg/dose) and anti-ulceratives (35-1450 mg/dose) contain the highest levels of aluminum in medications [38], though alternatives exist that do not contain aluminum (e.g., Rolaids, Tums). The systematic review based on 469 observational studies noted that the extensive scientific literature on the adverse health effects of aluminum points to the need for refinement of the provisional tolerable weekly intake (PTWI) and a reduction of aluminum contamination in parenteral nutrition formulations [2]. An updated analysis of aluminum pharmacokinetics in infants reported that vaccines with aluminum adjuvant continue to be extremely low risk to infants [39].

Sources and dosing: The use of aluminum cookware or utensils has not been shown to lead to increased risks for dementia or other age-related diseases. However, aluminum is also present in some medications (e.g., antacids), drinking water, some foods (e.g., pancake and waffle mixes), vaccines, and antiperspirants, which together may lead to higher exposure levels than what is deemed safe. Dietary exposure to aluminum in the US is typically no greater than the 1 mg/kg/week provisional tolerable weekly intake (PTWI), but may be exceeded depending on the age, medication intake, and dietary patterns of the individual [2].

Drinking water: Based on the [2016 NYC Drinking Water Quality Report](#), the concentration of aluminum ranged from 6-57 $\mu\text{g/L}$ (mean=20 $\mu\text{g/L}$). NYC continues to have some of the cleanest drinking water of any city in the world. Although one might expect water purifiers or filters to remove aluminum, [an analysis carried out by the Natural News Forensic Food Lab](#) reported that some popular filters such as Brita and Pur *increased* levels of aluminum by 33.9% (Brita) and 46.8% (Pur). Based on their analysis, the water filter that performed the best in removing toxic heavy metals was [ZeroWater](#); this filter removed 100% of aluminum and over 99% of all other toxic metals tested (copper, arsenic, strontium, cadmium, cesium, mercury, lead, and uranium). However, this analysis investigated the

filters' ability to remove heavy metals and not their ability to remove chlorine, pesticides, herbicides, BPA, or other chemical compounds.

Antacids: Some antacids contain high levels of aluminum as aluminum hydroxide is often used as an active ingredient to reduce acidity of the stomach. The list of antacids that contain aluminum hydroxide, or a combination of aluminum hydroxide and magnesium hydroxide can be found on [MedlinePlus](#) [40; 41]. Rolaids and Tums are two antacids that do not contain aluminum hydroxide; their active ingredient is calcium carbonate.

Research underway: Although the association between aluminum and Alzheimer's disease is based on a few observational studies and do not prove causation, no studies have proven that aluminum is completely safe for brain health or for the body (e.g., cancer). Results of available studies suggest the need for further analysis of the effects of aluminum on potential risks for dementia, cancers, and other toxicities. However, these analyses will be confounded by other elements/compounds that will be present in drinking water, foods, and medications. Preliminary studies suggest that silicon-rich drinking water increased aluminum excretion [21], but no clinical trials are planned to test if silicon or other agents known to reduce aluminum levels in the body is therapeutic or preventative. (Silicon supplements may possibly be effective for osteoporosis but there is insufficient evidence for improving heart disease, Alzheimer's disease, sprains and strain, digestion problems, or hair loss [42]. Excess silicon intake may cause kidney stones.)

Search terms:

Pubmed, Google: aluminum

- + cognitive, + Alzheimer's, + dementia, + dementia risk, + meta-analysis, + systematic review, + APOE4, + toxicity, + anti-persiprant, + cancer

Clinicaltrials.gov: aluminum

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