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Do Metals in the Human Environment Pose a Threat? A Review of the Available Literature

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ABSTRACT

Introduction and purpose: The impact of aluminum on human life is significant. Scientists have been studying the presence of aluminum in our environment for many years. This research is particularly important given that we live in a world dominated by aluminum, where its diverse applications can expose humanity to this metal from numerous sources. Long-term exposure to aluminum in humans has been connected to changes in behavior, as well as in brain structure and neurochemical processes. The aim of this article is to analyze the current state of knowledge on whether aluminum has a negative impact on human health and the body.

Summary: Depending on the dose of aluminum, the following scientific studies suggest that aluminum may impact human health, and regularly exceeding the permissible intake of aluminum throughout life is undesirable, as it leads to an increased risk of health impairment. Therefore, information is available on ways to reduce overall exposure to aluminum.

Materials and Evidence: A literature review was conducted using the PubMed database.

Keywords: aluminum, metal, toxicity, neurodegeneration

INTRODUCTION

Aluminum is one of the most commonly encountered metals in our daily lives. It is a widely known fact that it is not essential for humans and, moreover, can be toxic. Increasing attention is being paid to the exposure to aluminum present in vaccines, cosmetics, and food. We are unable to determine what dose of aluminum is toxic to us [1, 2, 3].

The kidneys act as the body's primary filter, undertaking the challenging task of eliminating aluminum. Thus, it is crucial for this metal to be removed from the body as quickly as possible. The accumulation of aluminum in the kidneys can lead to various disorders, such as dementia, osteomalacia, or microcytic anemia. Some aluminum is expelled from the body through bile, but the main elimination pathway is via the kidneys [4].

It has been proven that aluminum influences the development of breast cancer and affects human fertility. Interestingly, antiperspirants play a particular role here, as they may increase the risk of this cancer by causing aluminum to accumulate in the breasts [5, 6].

PARENTAL NUTRITION

Aluminum, which is one of the components of parenteral nutrition (PN), can pose a serious risk to many patients, such as newborns, premature infants, and those with impaired kidney function [7, 8, 9].

Natural defense systems in our bodies keep us from ingesting this metal. The lungs, skin, and gastrointestinal tract play a special role in minimizing exposure to aluminum, which has led to the belief that aluminum toxicity is unlikely. Aluminum that enters the systemic circulation binds to proteins and is then eliminated from the body via the kidneys. However, if aluminum is consumed in extremely large amounts, the body's ability to eliminate it in the stool may be impaired. This can increase the absorption of aluminum into the bloodstream, which can increase the risk of toxicity to the body [7].

In those receiving parenteral nutrition, the risk of aluminum accumulation is significantly increased, and this is due to the fact that the gastrointestinal tract is bypassed during intravenous administration, the gastrointestinal tract reduces the absorption of aluminum to less than 1%. Aluminum can accumulate in various tissues such as bone, liver, brain, kidneys, which can lead to serious conditions such as encephalopathy, neurotoxicity, metabolic bone disease and anemia [7, 8, 9].

Aluminum has been shown to negatively affect bone structure, causing phosphate deficiency. In addition, aluminum contamination discrupt calcium absorption in bones and interferes with osteoblast growth and activity. Aluminum partially affects bone remodeling, accumulates in the parathyroid glands, which inhibits the secretion of parathyroid hormone. Patients who are exposed to aluminum through parenteral nutrition tend to have lower levels of parathyroid hormone in their blood compared to those receiving PN with minimal or no aluminum [7].

Infants, especially premature infants, are particularly susceptible to aluminum toxicity due to their immature urinary system and high demand for calcium and phosphates, which support bone mineralization. These minerals come from parenteral nutrition components such as calcium gluconate and phosphate salts, and they are among the contaminants of aluminum. Studies have shown that exposure to aluminum from PN can significantly exceed recommended doses; moreover, premature infants can receive doses of aluminum many times higher than the 5 μg/kg/day considered safe by the U.S. Food and Drug Administration (FDA). It has been proven that excessive exposure to aluminum can cause long-term delays in neurological development, as shown in research in which high concentrations of aluminum in PN led to cognitive deficits in children. Despite FDA regulations requiring labeling of aluminum content in PN products, current PN formulations still contain significant amounts of aluminum, making it difficult for healthcare workers to reduce aluminum exposure. Although changes have been made to reduce aluminum contamination, such as product packaging and improved manufacturing, aluminum remains a problem in parenteral nutrition, particularly in the treatment of pediatric patients [7, 8, 9].

KIDNEYS

Exposure to aluminum, especially in patients with chronic kidney disease, can lead to poisoning and even to dangerous nephrotoxic effects. The kidneys play an important role in the elimination of aluminum by excreting it in the urine. However, patients with impaired kidney function, especially dialysis patients, have a reduced ability to remove aluminum from the body, which leads to its accumulation in tissues such as the brain and bones [10, 11]. Moreover, high concentrations of aluminum in dialysis fluids have been shown to contribute to bone and neurological disorders in patients undergoing dialysis over the years. Preventive measures, including monitoring aluminum exposure and limiting the consumption of aluminum-containing medications, play a crucial role in controlling aluminum toxicity in various populations [11].

Renal excretion of aluminum is a complex process involving both glomerular filtration and tubular reabsorption, with most aluminum bound to transferrin and therefore not filtered by the kidneys [4]. Studies have shown that aluminum is only partially filterable, most often in combination with low molecular weight compounds such as citrate. In the case of increased exposure to aluminum, for example in medications or food additives such as sodium aluminum phosphate (SALP), its bioavailability has been shown to increase significantly, highlighting the fact that aluminum filtration is dose dependent [10].

COSMETICS

Aluminum compounds are commonly found in cosmetic products such as antiperspirants. Their mechanism of action is to block sweat pores by creating so-called gel plugs. Recently, concerns have been raised about their potential impact on human health. Researchers are drawing attention to the interaction between aluminum salts and biomolecules in sweat, leading to their precipitation in the sweat ducts. This mechanism effectively inhibits sweating but also raises questions about how aluminum is absorbed through the skin and what potential negative effects may be associated with it. Prolonged exposure to aluminum, especially in high concentrations, may be associated with neurotoxicity, which may consequently lead to neurological diseases such as Alzheimer's disease, but the evidence for this remains ambiguous. Due to the fact that many consumers of the cosmetics market are opting for safer alternatives, studies have been conducted on plant extracts and other biodegradable compounds that may be an equally effective form of replacement compared to those based on aluminum [12].

The doses of aluminum in cosmetics and toothpaste determined by the US Food and Drug Administration (FDA) and the European Scientific Committee on Consumer Safety (SCCS) are considered safe, however, this does not change the fact that our skin is exposed to ingredients contained in cosmetics often used repeatedly, affecting the functioning of our body. The safety of aluminum in cosmetics has been discussed, but it is believed that it may have neurotoxic or carcinogenic effects. Scientific studies show that aluminum can enter the brain, but due to the small amount of information on the exact mechanism of absorption through the skin, we are not sure whether it is through the cosmetics used that it can cause neurological diseases such as autism [1].

Type of product	Maximum Concentration
Non-spray deodorants	6,25%
Spray deodorants	10,6%
Toothpaste	2,65%
Lipstick	14%

Table 1. Safe concentrations of aluminum created by the Scientific Committee on Consumer Safety of The European Union [13].

FOOD

Aluminum is a metal that can also be found in food, which is why it can be a serious public health problem. What we don't really realize is that by consuming food, we are exposing ourselves to the accumulation of aluminum in the body and having toxic effects, especially on the nervous and skeletal systems. Aluminum can enter the human diet through three routes: first, when aluminum is naturally found in food products, second, when there are contaminations with aluminum-based food additives, and third, which results from leaching from cookware and aluminum packaging, such as aluminum foil [14].

Once ingested, aluminum has a low gastrointestinal absorption rate—typically around 0.1–0.3%—but this is sufficient to allow gradual accumulation in tissues over time, particularly in bones, the liver, kidneys, and brain. The body's primary means of aluminum excretion is through the kidneys, making individuals with renal impairment, as well as infants and young children with immature renal systems, more vulnerable to aluminum's toxic effects. For instance, studies of infant and toddler diets have shown that those reliant on formula, especially soy-based or hypoallergenic options, may experience aluminum exposures that exceed the European Food Safety Authority's (EFSA) tolerable weekly intake (TWI) of 1 mg/kg body weight. This level was established to mitigate risks related to cumulative toxicity in vulnerable populations [15, 16].

The Joint Expert Committee on Food Additives of the Food and Agriculture Organization/World Health Organization (JECFA) has developed recommendations for a temporary tolerable weekly intake (PTWI) of aluminum at a level of 1 mg/kg body weight. A study was conducted on the leaching of aluminum from aluminum foil, in which its effect on food stored in it was observed. It was determined that the transfer of aluminum to food is influenced by a number of factors, such as time, temperature of heating, composition of the food, and chemical interactions that play an indispensable role in this. In summary, they concluded that consumers do not have to worry about eating food prepared in aluminum foil, so a few years later WHO JECFA changed the PTWI of 1 mg/kg body weight to 2 mg/kg body weight. However, it should be noted that high temperature and longer contact time with aluminum foil can increase the level of aluminum, which has an adverse effect on the functioning of our body. These results underscore how much more research we need to do, given the imprecision in some studies [14, 17].

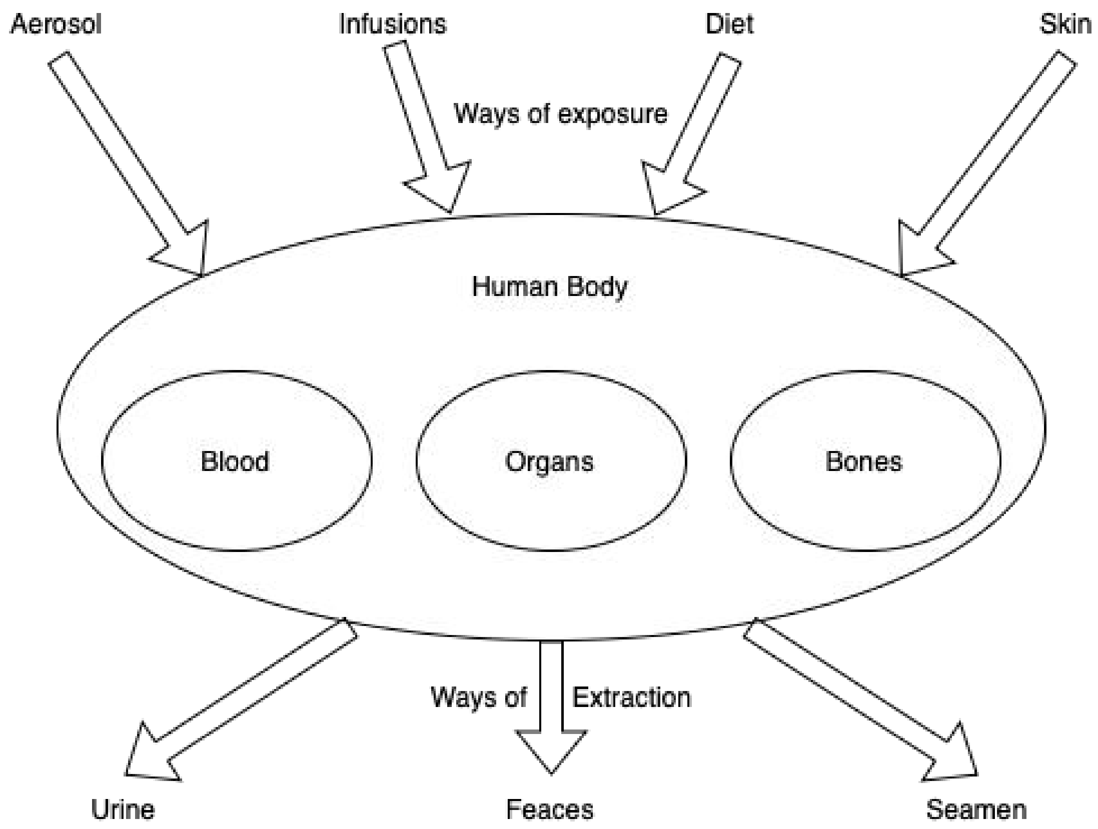
ALZHEIMER

Aluminum and its associated neurotoxicity are increasingly being addressed in research on neurodegenerative diseases, particularly Alzheimer's disease. Aluminum has been found to promote the formation of beta-amyloid plaques and hyperphosphorylation of tau protein, which are the genesis of this disease. This metal contributes to oxidative stress by producing reactive oxygen species (ROS), thus disrupting the functioning of mitochondria and the homeostasis of essential metals: iron, zinc, and copper, which play a key role in the functioning of neurons [18]. In particular in iron, where aluminum affects its metabolism, leading to an increase in redox-active iron, which increases oxidative stress and neuronal damage [19]. Moreover, scientists have also shown that aluminum activates microglia, the so-called immune cells of the brain, which leads to chronic inflammation, which intensifies neurodegenerative processes. Epidemiological studies have shown increased levels of aluminum in the brains of Alzheimer's patients, particularly in areas associated with memory and cognition, such as the hippocampus and cerebral cortex [20].

Accumulation of this compound correlates with neuronal loss and cognitive impairment, supporting the notion that aluminum acts as a risk factor for Alzheimer's disease.

Animal studies have shown that chronic exposure to aluminum causes behavioral and cognitive deficits similar to those seen in Alzheimer's disease, supporting the neurotoxic role of aluminum [21].

Figure 1. Pathways of aluminum absorption and excretion in the human body [21].



To further understand the link between aluminum and AD, researchers have developed therapeutic interventions, such as metal chelation therapy, to reduce aluminum concentrations in the brain. Chelators such as deferoxamine have shown satisfactory results in experimental models, reducing oxidative damage and improving cognitive function. Unfortunately, more large clinical trials are needed to refine the process to determine the effectiveness of such treatments in patients with AD [19].

BREASTS

Aluminum in the context of breast cancer development is still a topic of much debate, scientists continue to conduct research and focus on the role of aluminum in this difficult topic. Several studies indicate that aluminum, commonly found in antiperspirants and personal care products, can accumulate in breast tissue and thus contribute to carcinogenesis [5, 16, 22].

Aluminum is described as a metalloestrogen, metals that mimic estrogen activity by binding to estrogen receptors and altering gene expression. This mechanism is important because prolonged exposure to estrogen is a well-known risk factor for breast cancer [5].

Studies have been conducted on the relationship between aluminum accumulation in breast cancer patients and healthy patients. Some of them indicate higher aluminum concentrations in breast tissues in cancer patients compared to healthy individuals. The changes particularly concern the upper outer quadrant of the breast, which is the area closest to the armpit area, where antiperspirants are used [5,22].

In addition, it has been found that the concentration of aluminum in aspiration fluid from the nipple is significantly increased in women with breast cancer, which further confirms the fact that aluminum accumulates in the tissues of the mammary gland. Studies on aluminum confirm that it can cause DNA damage, oxidative stress, and genomic instability in breast cells. At physiologically relevant concentrations, aluminum has been shown to cause double-stranded DNA breaks, a critical step in carcinogenesis [22].

Aluminum has also been observed to disrupt cell cycle regulation, promote uncontrolled proliferation, and increase resistance to apoptosis, a hallmark of malignant transformation [5]. Despite these data, some reviews caution that confounding factors such as genetic predisposition and general exposure to many environmental pollutants make it difficult to establish a direct causal relationship between aluminum and breast cancer [16].

In addition, the lack of long-term studies limits conclusions about aluminum's involvement in breast carcinogenesis. However, the evidence that aluminum accumulates in breast tissue and has the potential to act as a pro-carcinogen should not be underestimated, and the need for precautionary measures, including limiting the use of personal care products containing aluminum and, as scientists emphasize, conducting further large-scale studies to clarify its effect on breast cancer risk [5, 6, 22].

SPERMA

Studies have shown that aluminum can have a negative effect on sperm. The mechanisms that can lead to sperm damage include: oxidative stress, inflammation, and disruption of cell signaling pathways. As a result of these mechanisms, aluminum can cause: a significant reduction in sperm count, motility, viability, and acrosome connection, all of which are important for fertility. The most important mechanism that exerts a toxic effect is through the creation of reactive oxygen species. Oxygen radicals then interact with the sperm cell membrane, which causes structural damage to the cell membrane, reduced fluidity, and disruption of cellular processes that occur in the sperm, such as enzyme activity and ion transport [6,23].

Aluminum-induced oxidative stress has been shown to decrease mitochondrial membrane potential (MMP), a marker of cellular energy production, which is essential for sperm motility. By lowering MMP, aluminum compromises the cell's bioenergetic state, leading to reduced sperm motility and viability. Further, there is also an increase in the level of malondialdehyde (MDA), which is a byproduct of lipid peroxidation, the concentration of this compound, which is formed under the influence of aluminum radicals, indicates sperm damage. In addition to damage directly in the membrane, there is a disruption in the functioning of ion channels, which enable capacitation and acrosomal reactions, as a result of destabilization of their function, successful fertilization of the egg may not occur [23].

Studies have shown that aluminum affects the hormonal balance of the body, its action has an impact on the reduction of the secretion of reproductive hormones such as testosterone, luteinizing hormone and follicle-stimulating hormone. These hormones affect spermatogenesis, and their reduced level can reduce the quality of sperm. In addition, aluminum promotes the release of pro-inflammatory factors including: cytokines, TNF-α, IL-6, tests have shown that these compounds are harmful to sperm, which can also affect their quality. Looking at all these aspects, one can come to the conclusion that in order to prevent male infertility, the level of aluminum that enters the body should be controlled [6,23].

VACCINATIONS

Aluminum-based substances have been used as an adjuvant component in vaccines for many years to enhance the immune response, but there is still some debate about their potential toxicity. These adjuvants, such as aluminum hydroxide (AlOH) and aluminum phosphate ($AlPO_4$), act to stimulate the immune system by promoting antigen presentation and then inducing a stronger immune response. However, concerns have been raised over the years about their persistence in the body and long-term side effects. Namely, bioaccumulation and their slow clearance from the body are the main concerns with aluminum-related vaccines. Scientific studies describe that aluminum adjuvants can accumulate at the injection site and also remain there, where they are phagocytosed by immune cells such as macrophages.

Some of these cells can transport aluminum particles to lymph nodes and distant organs, and animal studies have shown that aluminum can persist in tissues for months or even years after vaccination [24].

Some sources suggest that aluminum adjuvants may contribute to conditions such as macrophage fasciitis and adjuvant-induced autoimmune/autoinflammatory syndrome (ASIA).

Unfortunately, a definitive causal relationship between aluminum adjuvants and these conditions has not been established.[25] Furthermore, the evidence on the neurotoxicity of aluminum in vaccines and related research findings is conflicting, so further steps are needed to fully understand their long-term effects.[24] Current evidence suggests that aluminum toxicity in vaccines is low, but further research is needed to ensure vaccine safety and maintain public confidence [25,26].

SUMMARY

The primary sources of aluminum exposure in the human body are through the digestive and respiratory systems, while its excretion occurs via the urinary system. From the literature presented, we can conclude that aluminum may influence the development of certain diseases as well as the proper functioning of the human body. However, the development of these diseases occurs in cases of very high aluminum exposure. After analyzing the cited literature, it can be concluded that excessive exposure to aluminum may contribute to some diseases. For this reason, direct exposure to aluminum should be controlled, and appropriate standards should be established.

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Author's contribution

Conceptualization: Weronika Goliat, Konrad Haraziński; methodology: Oliwia Sysło, Izabela Jastrzębska; software: Nikola Rubik; check: Maksym Gmur; formal analysis: Michał Gajewski; investigation: Barbara Sławińska; resources: Zuzanna Błecha; data curation: Izabela Jastrzębska; writing – rough preparation: Nikola Rubik, Maksym Gmur; writing – review and editing: Weronika Goliat, Konrad Haraziński, Oliwia Sysło; visualization: Michał Gajewski; supervision: Nicole Maryniak; project administration: Weronika Goliat; receiving funding: Not applicable

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Data Availability Statement

As a review paper, our work does not present new data or analyses. Therefore, there are no specific databases or data availability to report. The information and findings presented in this review are based on previously published studies, which can be accessed through their resective sourses as cited in the reference section.

Conflicts of Interest Statement

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