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## Review Article

# Neurotoxicity caused by lead present in food and environment: A review

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## Abstract

A problem we are facing more and more often has caught our attention. Neurotoxicity is caused by lead contamination of the environment and food chain. The purpose of this review is to present the harmful effects of lead on human health. In the long term, lead accumulated in the body can cause cognitive, motor, and behavioral changes. According to recent studies, lead is a real danger for children because it affects the development of the nervous system even in small amounts. This review also focused on suggesting a powerful antioxidant, vitamin C in the diet. Studies have shown that it has a possible neuroprotective role, being kept in high concentrations in the brain.

## Abbreviations

PB: Lead; LOD: Values below the Limit of Detection; LLOQ: Values below the Lower Limit Of Quantitation; SD: Standard Deviation; LCRs: Lifetime Cancer Risks; SNC: The Central Nervous System; SVCT2: Sodium Vitamin C Co-Transporters; RDA: The Recommended Dietary Allowance; UL: The Tolerable Upper Intake Level

## Introduction

In recent years we have been experiencing the presence of lead in the environment, but also in food. Following studies and analyzes, the chronically accumulated lead from the environment and food causes neurotoxicity and oxidative stress [1-20].

Toxic metals, most commonly lead, are prevalent in both the environment and are often found in the food supply chain. An example would be their presence in the game meat. It is generally caused by environmental pollution and hunting techniques (ammunition for hunting), and the consumption of these contaminated by-products has shown an adverse effect on the health of consumers [4].

Several researchers in this field have said that hunting offers, in addition to regulating the populations of animals and food for families in mountain areas, hunting families in particular. We do not know the course of the wild animal, the diet, or the way of life. For this reason, thorough expertise is required, guided by specialists in the field of food safety [2-19].

The greatest risk comes from the use of lead bullets, as these bullets tend to fragment and disperse in harvested game animals, which causes a wide distribution of lead in carcasses [19].

Contamination of soil and water and exposure of wild and domestic animals to lead is a global problem. They pose a significant risk to organisms and ecosystems [2].

Some recent studies have identified that urban chickens and their eggs are subject to high levels of Pb. However, few studies have attempted to measure all potential routes of exposure (e.g. soil, water, feed) for trace element exposures. One study addresses and demonstrates that contaminated soil in the urban garden poses the greatest potential risk for chickens in the yard in terms of exposure to Pb. Study data show that soil



Pb concentrations are an appropriate indicator for estimating blood Pb in poultry and also their eggs; Soil Pb concentrations should be below 117 mg kg<sup>-1</sup> to keep egg Pb concentrations below 100 mg kg<sup>-1</sup>, a concentration above which there is an increased risk to consumers [25].

Another study that caught our attention aimed to assess the potential risks associated with the presence of heavy metals in children’s food [10] [Tables 1–3].

**Lead and neurotoxicity**

Lead (Pb) is a heavy, toxic metal that is found naturally in the Earth’s crust. Lead is found in all parts of the environment, mainly from human activities such as mining, production, and burning of fossil fuels. Lead does not degrade in the environment, remaining strongly absorbed by the soil [22].

The body bioaccumulates lead which causes serious health problems. It is toxic, teratogenic (affects the development of an embryo or fetus), and carcinogenic. The daily intake of lead from all sources is about 0,1 mg. the human body stores on average 120 mg of lead in the bones [17].

Lead (Pb) is a toxic metal whose widespread use has led to widespread environmental contamination and health problems around the world [24].

Lead binds to cellular components, such as structural proteins, enzymes, and nucleic acids, which interfere with the functioning of plants, animals, and humans [21].

The ionic mechanism of lead toxicity causes significant changes in various biological processes, such as cellular adhesion, intra-, and intercellular signaling, protein folding, maturation, apoptosis, ionic transport, regulation of enzymes, and release of neurotransmitters. Lead can replace calcium even in the picomolar concentration, affecting protein kinase C, which regulates neural excitation and memory storage [8–23].

Many of the neurotoxic effects of lead appear to be related to the ability of lead to mimic or, in some cases, inhibit the action of calcium as a regulator of cellular function. At the neural level, lead exposure alters the release of chemical mediators from the presynaptic nerve endings. Spontaneous release is improved and evoked release is inhibited. The first may be due to the activation of kinase proteins in nerve endings, and the second to the blockage of tension-dependent calcium channels. This disruption of neural activity can, in turn, alter the development processes of synapse formation and result in neurodegenerative diseases [3–6].

The most severe neurological effect of lead exposure is encephalopathy, a response to very high doses of lead that results in the development of irritability, headaches, mental weakness and attention difficulties, memory loss, tremors, and hallucinations within a few weeks of exposure. Symptoms worsen sharply to paralysis, convulsions, delirium, coma, or death. Children may develop lead encephalopathy at lower doses of lead than adults. Postmortem pathological findings include edema, capillary disturbance, glia proliferation, and diffuse anoxic lesions [18].

The development of the central nervous system is susceptible to lead toxicity. In critical moments of development, lead can have a disorganized influence with long-lasting effects that can continue into adolescence and beyond. Long-term effects of lead can cause cognitive and motor disorders, with behavioral changes. The particular vulnerability of the immature nervous system to lead poisoning is probably due to the fact that at this stage of development the establishment of appropriate neural networks is dependent on synaptic activity, which in turn could be altered by lead [9–16].

**Vitamin C, a strong antioxidant**

Following studies, vitamin C used in the diet would have a possible neuroprotective role in fighting lead toxicity. Even if

**Table 1:** Pb Concentrations (µg kg<sup>-1</sup>) in Baby Food Samples by Ingredient Category.

Heavy metals	Ingredient Category	No. of Samples	Detection Frequency n %	Concentration (µg kg <sup>-1</sup> )				
				Minimum	Mean	Median	Maximum	Error ±SD <sup>b</sup>
Pb	Leguminous	9	2(22)	1.5	2.3	1.5	5.0	1.5
	Grain	9	9(100)	5.0	9.7	5.0	20.0	7.0
	Root Vegetable	9	8(88)	1.5	15.8	5.0	48.0	15.6
	Fruit	9	3(33)	1.5	2.7	1.5	5.0	1.8

Note: Values below the lower limit of quantitation (LLOQ) were replaced with ½ the LLOQ (10(µg kg<sup>-1</sup>), 5 (µg kg<sup>-1</sup>))

<sup>a</sup>Values below the limit of detection (LOD) were replaced with ½ the LOD (3(µg kg<sup>-1</sup>), 1.5 (µg kg<sup>-1</sup>)).

<sup>b</sup>SD = Standard Deviation.

Source: [10]

**Table 2:** Lifetime Cancer Risks (LCRs) for Children Ages <1 to <3 Years Consuming Baby Foods Containing Pb.

Heavy metals	Ingredient Category	Mean	Median	Max
Pb	Fruit	8.87E-09	4.99E-09	1.66E-08
	Grain	1.96E-08	1.01E-08	4.06E-08
	Leguminous Vegetable	2.08E-09	1.37E-09	4.57E-09
	Root Vegetable	1.76E-08	5.56E-09	5.34E-08
ILCR from Pb		4.82E-08	2.21E-08	1.15E-07
Total ILCR		3.75E-05	5.12E-05	5.54E-05

Note: CRs >10<sup>-6</sup> are shaded in grey. LCRs using the mean, median, and max sample concentrations are provided in the table.

Source: [10]

**Table 3:** The maximum level of lead allowed in the food according to the European Commission, Food Safety.

Food	Maximum levels mg kg <sup>-1</sup> wet weight
Unprocessed milk, heat-treated milk, and milk intended for the manufacture of milk products	0,020
Beef, sheep, pork, poultry	0,10
Livestock, sheep, pigs, and birds.	0,50
Fillet fish muscles	0,30
Legumes, cereals, and dried legumes	0,20
Fruit	0,10
Fruit juices	0,050

Source: https://food.ec.europa.eu/safety/chemical-safety/contaminants/catalogue/lead\_en [7]



we have an antioxidant system, the body tends to bioaccumulate constantly, and as the number of toxic substances increases, the antioxidant system can no longer cope. An important pillar is VC which plays a significant role in eliminating ROS and/or inhibiting free radical production. Vitamin C is a promising agent for providing protection against toxicity induced by co-existing chemicals in the environment and food [13,14].

Metabolic processes reuse vitamin C from its oxidized form (dehydroascorbic acid), present inside cells. The concentration of ascorbic acid is higher in the neurons of the central nervous system (CNS) in mammals. In the CNS, intracellular ascorbate performs important functions, including antioxidant protection, myelin formation, synaptic potentiation, and protection against glutamate toxicity. SVCT2 maintains the content of neural ascorbate in the CNS, with studies demonstrating the neuroprotective role for neurodegenerative diseases such as Alzheimer's, Parkinson's, and Huntington's disease. Ascorbate supplements decrease the size of the heart attack in ischemia-reperfusion lesions and protect neurons from oxidative damage, which is a vital food antioxidant [15].

Vitamin C is maintained at high concentrations in the brain and neurons. Homeostatic mechanisms keep the brain and neuronal ascorbate concentrations within very strict limits [11].

Another role of vitamin C is to stimulate the immune system, hence its use in the treatment and prevention of infections. Vitamin C enhances the mobility of leukocytes, inhibits their autooxidation, and simultaneously enhances the level of serum immunoglobulins and the formation of antibodies. Vitamin C is also a protector of the body against anaphylactic shocks [5].

### Recommended quantitie

**RDA:** The recommended dietary dose for young people 19 years of age and older is 90 mg per day. Women and men 75 mg. for pregnancy and lactation, the amount increases to 85 mg, 120 mg per day. Smoking lowers the level of vitamin C in the body, so an additional dose of 35 mg is recommended [12].

**UL:** The tolerable upper intake level is the maximum daily intake unlikely to cause harmful effects on health. The UL for vitamin C is 2000 mg per day. A higher amount can promote gastrointestinal distress and diarrhea. Only in specific scenarios, such as under medical supervision or in controlled clinical trials, larger amounts are sometimes used [12] [Table 4].

### Conclusion

We concluded that the amount of lead in both the environment and food increases from day to day, and we are prone to neurodegeneration caused by it. The main pawns in their fight are food specialists and environmental specialists who track the traceability of products and draw an alarm signal if necessary. One possible protective role would be vitamin C, which is a powerful antioxidant. Vitamin C is involved in the production of certain neurotransmitters, in the metabolism of glucose, collagen, and folic acid, and in the neutralization of

**Table 4:** Vitamin C content in food.

The product	mg Vit C per 100 g	The product	mg Vit C per 100 g
Rose hips	400	Celery	10
Cabbage	180	Cucumbers	10
Peppers	160	Spinach	80
Blueberries	160	Melon	40
Lemon	50	Liver	35
Cauliflower	45	Milk	1-2

Source: [26].

free radicals and nitrosamines, in immunological reactions. Further investigation is needed into other treatments that could be combined with vitamin C in the diet and that would help combat lead-induced neurodegenerative processes.

### Discussion

From future research perspectives, we have thought of possible treatment with vitamin C and another effective antioxidant (further investigation is needed) in a leaded diet. Food culture among the population can save millions of lives from day to day.

### Conflict of Interest

The authors declare no conflict of interest.

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