# An Overview about Lead Acetate Possible Neurological Hazards and Antioxidant Roles of Selenium

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**Abstract**

Adults absorb from 5% to 15% of ingested lead and commonly retain less than 5% of the absorbed part. Children absorb about 42% of swallowed lead and retain about 32%of absorbed. Low dietary manganese, zinc, calcium, and iron enhance lead absorption mainly in children. Airborne lead is a minor source of exposure. Lead absorption by the lungs depends mainly on the particle size, form (vaporvs particle), and concentration. About 90% of lead particles in inhaled air are small enough to be retained. Absorption of retained lead through alveoli is effective.Lead can induce in humans a wide range of adverse effects reliant on the dose and duration of exposure. The toxic effects range from enzymes inhibition to the severe pathology induction or death. In children, the central nervous system is the target of lead toxicity, while in adults; chronic nephropathy, peripheral neuropathy and hypertension are worries. Other targets include the immune, gastrointestinal, reproductive, and skeletal systems. It is possible to detect effects on heme biosynthesis by a sensitive biochemical indicator, even when no other effects are detectable.Clinically obvious encephalopathy may occur in children with high lead exposure. Symptoms of lead encephalopathy initiate with lethargy, dizziness, loss of appetite, vomiting and irritability. These manifestations progress to obvious ataxia and decreasing in consciousness level that may progress to coma and death. The pathological findings at autopsy are loss of neuronal cells and an increase in glial cells. Recovery is always accompanied by complications: mental retardation, epilepsy and, in some cases, optic neuropathy and blindness.Selenium is critical to the brain. Irreversible brain injury may occur due to its deficiency.Selenium's beneficial antioxidant capabilities have been demonstrated in numerous studies. Se interacts with seleno enzymes like glutathione peroxidase (GPxs) and seleno amino acids, which have a significant impact on sperm quality and male fertility. Gpx4 shields cell membranes from free radical damage and is primarily present in germ cells. The

proper development of the mid piece during sperm maturation depends on the structural protein Gpx4.

**Keywords:**Lead Acetate, selenium, neurological hazards

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## Introduction

Human used Lead (Pb) for at least 7000 years, because it is widespread and its extraction and using are easy. It is highly flexible and malleable as well as easy to melt. Lead's elemental symbol, Pb, which is an abbreviation to Latin name (plumbum). Lead in lead compounds exists in the divalent form. Lead (Pb) is resistant to erosion and can combine with other metals forming different compounds. Pb 4+ dominates organic lead compounds. Inorganic lead compounds are handed as pigments in dyes, ceramic glazes, and paints. Organic lead compounds were once broadly used as gasoline additives. Lead compounds are used in water pipes, ammunition, batteries, and shields from radiation. Environmental lead comes mostly from human activity. It is listed as a highest toxic substance (1).

Lead-containing paint in houses is a main source of children lead exposure. Main environmental sources of lead for children up to four years is hand-to-mouth transmission of lead-containing paint chips or floors dust (2).

A foremost exposure route for the general population is from water and food (3). Other potent sources of lead exposure are entertaining gunfire, soldering, painting, hand-loading ammunition, glass polishing, jewelry manufacture, ceramic making, and stained glass designing. Herbal medicines could be potential sources of lead exposure (2). More than 55 cases of lead poisoning have been correlated to the ingestion of herbal products contaminated with lead ranging up to 37 mg/g. (4).

Adults absorb from 5% to 15% of ingested lead and commonly retain less than 5% of the absorbed part. Children absorb about 42% of swallowed lead and retain about 32%of absorbed. Low dietary manganese, zinc, calcium, and iron enhance lead absorption mainly in children. Airborne lead is a minor source of exposure. Lead absorption by the lungs depends mainly on the particle size, form (vaporvs particle), and concentration. About 90% of lead particles in inhaled air are small enough to be retained. Absorption of retained lead through alveoli is effective (5).

Only 1% of circulating lead in serum can be distributed to tissues because most of it is bound to haemoglobin in erythrocytes(1).

Lead is firstly distributed to soft tissues as liver and kidney, and then it is redistributed to the hair and skeleton. Lead half-life in the blood is 30 days. With a half-life of about 20 years, lead

in bones increases with age from 70% in childhood to 95% in adulthood.Endogenous lead exposure can arise from bones, which can release up to 50% of lead to blood. There may be an increase in bone lead release in adults with accumulated exposure and in women due to bone loss during pregnancy, lactation, and menopause, and from osteoporosis (5).

The kidney is the main excretion route of absorbed lead. Lead renal excretion is always through glomerular filtration with some renal tubular resorption. Fecal excretion thru biliary tract accounts for one-third of total absorbed lead excretion (1).

Lead can induce in humans a wide range of adverse effects reliant on the dose and duration of exposure. The toxic effects range from enzymes inhibition to the severe pathology induction or death. In children, the central nervous system is the target of lead toxicity, while in adults; chronic nephropathy, peripheral neuropathy and hypertension are worries. Other targets include the immune, gastrointestinal, reproductive, and skeletal systems. It is possible to detect effects on heme biosynthesis by a sensitive biochemical indicator, even when no other effects are detectable (5).

In adults, cumulative occupational exposures can affect neurobehavioral measures.Peripheral neuropathy is a usual symptom of adult lead toxicity. Over half a century ago, house painters and other workers exposed to excessive lead exposure suffered from foot drop and wrist drop. Peripheral neuropathy is characterized by segmental demyelination and maybe axonal degeneration. An electrophysiological measurement of nerve conduction velocity is used to assess motor nerve dysfunction (5).

Clinically obvious encephalopathy may occur in children with high lead exposure. Symptoms of lead encephalopathy initiate with lethargy, dizziness, loss of appetite, vomiting and irritability. These manifestations progress to obvious ataxia and decreasing in consciousness level that may progress to coma and death. The pathological findings at autopsy are loss of neuronal cells and an increase in glial cells. Recovery is always accompanied by complications: mental retardation, epilepsy and, in some cases, optic neuropathy and blindness (6).

Multiple gastrointestinal symptoms as cramping, nausea, constipation, vomiting and abdominal pain, all these symptoms known as lead colic(1). Both male and female animals have shown gametotoxic effects due to lead exposure. The hypothalamic-pituitary-gonadal axis may also be disrupted by lead(5).

Hematologic effects of lead range from increased urinary porphyrins, coproporphyrins, δ-aminolevulinic acid (ALA), and zinc protoporphyrin to anemia. Microcytic and hypochromic anemia occurs only in very marked cases of lead toxicity and is as in iron deficiency. (1).

Acute lead nephrotoxicity represents as proximal tubular dysfunction and can be inverted by chelating agents' treatment. Chronic lead nephrotoxicity represents as interstitial fibrosis,

advanced nephron loss, azotemia, and renal failure **(5)**.Lead nephrotoxicity harms the synthesis of heme-containing enzymes in the kidney, like heme-containing hydroxylase involved in vitamin D metabolism resulting in bone effects **(1)**. Hyperuricemia with gout occurs commonly in the lead nephropathy. Lead nephropathy can be a source of hypertension **(7)**. There is confirmation of a connecting relationship between hypertension and lead exposure **(7; 1)**.

Lead has a very long half-life in bone, containing over 90% of the adult body lead. It affects bone by interfering with homeostatic and metabolic mechanisms, such as calcitonin, parathyroid hormone, vitamin D and other hormones that affect calcium metabolism. Bone calcium substitutes with lead **(5)**.

Recently, studies have strongly backed up the association between lead exposure and an increased risk of cancer. Inorganic lead compounds were reclassified as perhaps carcinogenic to humans **(1)**. Organic lead compounds are not classifiable as carcinogenic to humans **(8)**.

**Selenium**

Selenium (**Se**) is a chemical element with atomic weight 78.96 and atomic number 34. In 1818, the Swedish chemist JonsJakob Berzelius discovered elemental form of selenium when had been asked by Swedish sulphuric acid manufacturer to look at a reddish deposit that keep on the floors of his lead chamber during sulfuric acid production. It was named selenium as the Greek goddess of the moon "Selene". It is chemically related to sulphur and tellurium. Selenium position in the periodic table confirm that it belongs to metalloids that are neither metal nor non-metal but share the properties of both **(9)**.

Elemental selenium is hexagonal, crystalline in shape, metallic grey in colour. Many selenium forms occur according to the elements they combined with resulting in variable shapes and colours as sodium biselenite, which is white to greyish pink granular powder **(10)**.

Several forms of organic selenium exist as seleno-methionine and seleno-cysteine. Seleno-methionine is synthesized by plants and frequently used as a supplement. Seleno-cysteine represents the protein-genic amino acid and selenium applies its biological effects mostly thru seleno-cysteine containing proteins. Selenate (Na2SeO4), Selenite (Na2SeO3), and methyl-seleninic acid represent inorganic forms of selenium **(11)**.

Sodium biselenite ($Na_2SeO_3$) is absorbed from the gastrointestinal tract. The primary absorptive site is duodenum. The jejunum and ileum share in its absorption **(12)**.

Inorganic selenium (selenate or selenite) is very well absorbed but less reserved in the body than organic selenium forms like seleno-methionine and seleno-cysteine **(13)**. **Thomson (14)** added that, organic selenium is absorbed with 50% -90 % efficacy.

Water-soluble selenium compounds and selenium containing plasma proteins are rapidly distributed. Selenium is kept in the tissues in variable density: 30% in the liver, 30% in muscles, 15% in the kidney, 10% in the plasma and the remaining all over other organs. Free selenium concentrations are highest in the pituitary gland and renal cortex then in the adrenals, testes, thyroid gland, ovaries, spleen, liver, and cerebral cortex. Selenium is secreted in human milk. The mature milk contains 20 ug/L, falling to 15 ug/L at 3-6 months while colostrum contains the double.Selenium chemical form affects its bioavailability. In general, organic forms are more bioavailable than the inorganic compounds **(15)**.

The fate of selenium has one of three: (a) combination into selenoproteins mainly selenoprotein P (the principal selenoprotein in plasma), selenoenzymes like glutathione peroxidases, thioredoxin reductase and type 1-iodothyronine deiodinase (b) combination into nonspecific plasma proteins like albumin or globulins (c) in liver, methylation into nontoxic metabolites (**16**).

The selenium half-life in the human body has been valued to be about 100 days. Three routes of selenium excretion are in urine, feces, and expired air. Urine is the main route of selenium excretion. The proportion of se excreted in this way depends on the level of intake in the diet **(9).**

The major source of selenium is plant foods in most countries **.** Within the common cereal crops, wheat is the most efficient selenium accumulator (wheat > rice > maize > barley > oats). wheat is also the most significant source of dietary Se for human **(17)**.

Selenium in dietary products most frequently co-occurs with proteins, hence selenium content is typically higher in foods with higher protein contents. Meat, seafood, and grains are some of these products. Selenium levels and fat content are inversely associated in dairy products. Selenium is present in limited quantity in fruits and vegetables. Their high-water content and low protein content are to reason for this. Brazil nuts and mushrooms both contain extremely high levels of selenium. Also reported to contain high levels of selenium are plants belonging to the Brassica genus, such as broccoli, cabbage, and cauliflower. A rich source of selenium includes garlic and onions, which lower the chance of developing cancer. **(18)**.

WHO has recommended consuming 50–55 µg of selenium per day for humans. Se deficiency occurs when Se dietary intake is less than 40 µg /day and chronic toxicity occurs when dietary intake exceeds 400 µg **/day (19)**.

The glass industry uses selenium. Its photoelectric and semiconducting characteristics are widely used in electronics. To compensate for selenium deficiency, selenium fertilizers and nutritional supplements are utilized. Fungicides and antidandruff shampoos both include selenium sulphide.

The "amorphous selenium detector" in mammographic equipment is a new use for selenium **(20)**.

Several important roles are played by selenium in the thyroid, including converting thyroxine to its active precursor triiodothyronine by the selenium-dependent iodothyronine deiodinases. Additionally, numerous studies have demonstrated that selenium supplementation, in the form of sodium selenite or selenomethionine, at doses of 80 or 200 μg per day, is useful in treating Hashimoto's thyroiditis, the most prevalent kind of autoimmune thyroid disease. Moreover, selenium helps in treating Graves' disease, an autoimmune hyperthyroidism **(21)**.

Selenium is critical to the brain. Irreversible brain injury may occur due to its deficiency. Selenoprotein P (SEPP1) binds to a member of the lipoprotein-receptor family (apolipoprotein E receptor 2) to deliver selenium to brain. Spasticity, atypical movement patterns, and spontaneous seizures appear in mice that are unable to synthesise SEPP1. Selenium may play a role in seizures, coordination, Parkinson's disease, and cognitive loss, according to studies on humans. Children and adults who had epileptic seizures as well as children who had febrile seizures, their serum selenium level is noticeably low. Moreover, selenoprotein P (SEPP1) plays a key role in neuroprotection by prolonging neuronal survival and inhibiting apoptosis. Human research shows that selenium status is related to the risk of dementia and Alzheimer's disease **(22)**.

Selenium is crucial for immunity, according to in-vitro and animal research. supplementation with selenium has significant immunostimulant effects, such as increasing the activity of natural killer cells and the multiplication of activated T cells. Early studies indicate that patients with allergic asthma may benefit from high selenium status or selenium supplementation, and this is consistent with the conception that selenium supplementation may promote the differentiation of CD4+ T cells into T-helper-1 (Th1) and T-helper-2 (Th2) effector cells **(23)**.

**Hefnawy and Tórtora-Pérez, (24)** stated that Se shortage impacts.

T cell and IgG blood levels, which affects the severity and frequency of current diseases in animal populations. Additionally, it has a negative impact on the activity and shortens the life of lymphocytes, macrophages, and neutrophils.

Se has a critical role in maintaining redox balance inside cells, and its anti-inflammatory and antioxidant activity is credited to its role in immunity. Consequently, Se, is of importance in viral infections, and it can play an important role in assisting corona virus disease 2019. Moreover, Se is necessary for seriously ill patients, and its deficiency is related to severity and mortality rate of corona virus **(25)**.

In people with hepatitis B or C infection, selenium also seems to prevent the illness from developing into liver cancer. Selenium appears to be an essential vitamin for those with HIV. It effectively prevents HIV replication in vitro **(21)**.

Around 80 years ago, researchers in a province of northwest China made the initial discovery of a chronic selenium deficiency. Patients had a cardiomyopathy that was fast progressing and causing severe fibrosis and degenerative alterations. This condition is now known as Keshan disease after a province in China. In the cardiovascular system, selenium is useful. Selenium consumption and status are associated with several health outcomes, particularly cardiomyopathy, myocardial ischemia/infarction, and reperfusion injury. A biomarker for coronary heart disease is selenium. Patients undergoing heart surgery must take supplements containing selenium (26).

Selenium's beneficial antioxidant capabilities have been demonstrated in numerous studies. Se interacts with seleno enzymes like glutathione peroxidase (GPxs) and seleno amino acids, which have a significant impact on sperm quality and male fertility. Gpx4 shields cell membranes from free radical damage and is primarily present in germ cells. The proper development of the mid piece during sperm maturation depends on the structural protein Gpx4 (27).

Women who miscarried in the first trimester had significantly lower selenium levels than women who did not miscarry. Preeclampsia has been associated with selenium intake and status (21).

Glutathione peroxidase (GPx) and thioredoxin reductase are two examples of selenium-dependent enzymes. Selenium is a key component in the catalytic sites of both enzymes. Selenium has been shown to lower the production of ROS, protect cells against glutamate toxicity, oxidative stress, and inflammatory cytokines, and eventually prevent cell death brought on by these conditions (28).

selenium Administration significantly improved neurotoxicity and hepatotoxicity-induced by acrylamide. Also, selenium decreased Bax/Bcl-2 ratio and caspase 3 levels in brain and liver tissues. selenium can inhibit many detrimental mechanisms induced by cerebral ischemia/reperfusion (29).

Numerous searches have shown that Se supplementation significantly decrease Malondialdehyde (MDA) levels and increase Glutathione and total antioxidant capacity (TAC) levels. Intragastric administration of glycine nano-selenium decreased neurobehavioral defects by reducing oxidative stress in rat brain (30).

Se protects neurons from amyloid beta-induced toxicity, proposing a neuroprotective role for Se in prevention of neurodegenerative conditions (22). Simultaneous treatment with sodium selenite saves glutamate-induced cell death by reduction of superoxide production, preventing intrinsic cell death pathway, blocking mitochondrial fission, and containing mitochondrial autophagy. It is established that the Se protective effects against glutamate cytotoxicity is related with saving mitochondrial integrity and dynamic balance (27).

Selenium has been shown to protect against methyl mercury toxicity in experimental studies, but epidemiological studies have been insufficient to support this claim (31) but epidemiological

studies have been insufficient to support its protective effect with Pb. Therefore, the aim of the present study is to evaluate the effect of lead in different doses in the rats' cerebral and cerebellar structure and to clarify possible protective role of selenium in the amelioration of this damage by investigate its potential effects on oxidative and apoptotic markers by histopathological and biochemical methods.

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