EFFECTS OF LEAD ON HUMAN HEALTH: TOXICOLOGICAL MECHANISMS, CLINICAL CONSEQUENCES, AND PREVENTIVE MEDICINE

Mamanov Jaloliddin
Assistant Professor at the Department of
Ecology and Environmental Protection
Karshi State Technical University
https://doi.org/10.5281/zenodo.20526216

Abstract: The article provides a comprehensive analysis of the pathophysiological mechanisms of lead (Pb) exposure to humans, assesses the clinical consequences of saturnism, and systematizes modern methods of preventive medicine. Based on the analysis of 10 relevant peer-reviewed sources for the period 2018–2026, the molecular mechanisms of lead toxicity are described in detail, including the induction of oxidative stress, blockade of heme synthesis enzymes (ALAD and ferrochelatase), and the phenomenon of ion mimicry with calcium (Ca^{2+}) displacement. Particular attention is paid to irreversible neurotoxicity in children and the risk of endothelial dysfunction and arterial hypertension in adults. The absence of a safe threshold for lead concentration in the blood is proven. Recommendations for environmental monitoring, antioxidant support, and the use of selective chelation therapy (DMSA, $CaNa_2EDTA$) in severe forms of intoxication are formulated.

Key words: lead, heavy metals, saturnism, oxidative stress, neurotoxicity , enzyme inhibition, ion mimicry, blood lead (BLL), chelation therapy, environmental medicine.

Introduction: Lead (Pb) is a heavy metal with high systemic toxicity and bioaccumulation potential . Despite global efforts to reduce its use, lead poisoning remains one of the most pressing environmental and public health problems.

Objective of the work: Comprehensive analysis of the pathophysiological mechanisms of the effects of lead on the human body, assessment of the clinical manifestations of saturnism (lead poisoning) and systematization of modern methods of prevention and therapy based on the analysis of current scientific literature.

Methods: A systematic review and meta-analysis of data from 10 key peer-reviewed publications (2018–2026) indexed in PubMed , Scopus , and Web of Science was conducted. Biochemical, neurological, and cardiovascular markers of toxicity were examined.

Results: Lead was found to induce pronounced oxidative stress, block heme synthesis enzymes (delta-aminolevulinate dehydratase and ferrochelatase), and mimic calcium ions ($Ca2^{+}$), disrupting neurotransmission . A direct correlation was found between blood lead levels (BLL) and decreased cognitive function (IQ) in children, as well as the development of arterial hypertension in adults.

Discussion: There is no safe threshold for lead concentration in the blood. Current protocols call for stricter environmental standards and the implementation of selective chelation therapy at critical levels of intoxication.

1. Introduction

Lead (Pb) is a ubiquitous toxic element, ranking high on the WHO list of hazardous chemicals. During the industrial era, anthropogenic lead emissions into the environment increased dramatically due to the development of metallurgy, the production of lead-containing

paints, batteries, and cables, and the long-term use of tetraethyl lead as an antiknock additive in fuels.

The primary danger of lead lies in its **persistence** (it does not break down in the environment) and **its ability to bioaccumulate** in the tissues of living organisms. Entering the human body through the respiratory tract (inhalation) or the gastrointestinal tract (alimentary route), lead enters the systemic bloodstream and is then distributed among soft tissues (liver, kidneys, brain) and mineralized structures (bones and teeth). Lead can accumulate in the skeleton for decades, representing an internal source of endogenous intoxication, especially during periods of accelerated bone turnover (pregnancy, lactation, osteoporosis).

The relevance of this topic is due to the fact that, according to the latest epidemiological data, even ultra-low concentrations of lead in the blood, previously considered safe (less than 5 mg/ dL), cause irreversible cognitive impairment in children and increase the risk of mortality from cardiovascular diseases in the adult population.

The aim of this study is to study in detail the molecular, biochemical and systemic mechanisms of lead toxicity, classify the clinical syndromes caused by it and identify the most effective intervention strategies based on a systematic analysis of 10 fundamental and modern scientific papers.

2. Research methods : To achieve this objective, a methodological approach based on the principles of a systematic review was used. **Ten key scientific studies** (including monographs, meta-analyses, and randomized cohort studies) from recent years were selected as the empirical base .

Analysis steps: Data screening: Primary search in PubMed and Google Scholar databases using keywords : lead toxicity , plumbism , oxidative stress , neurotoxicity , heavy metals .

Data extraction: Extraction of specific biochemical parameters (enzyme inhibition, free radical levels) and systemic pathologies (endothelial dysfunction, neurodegeneration).

Synthesis: Comparison of results from independent authors to form a unified pathogenetic picture.

3. Results: Analysis of the collected material allowed us to classify the negative impact of lead on the human body at three main levels: molecular-cellular, systemic-organ, and population.

3.1. Molecular-biochemical mechanisms of toxicity: The central mechanism of the toxic effect of lead is its ability to bind to sulfhydryl (-SH), amino and carboxyl groups of proteins, which leads to the inactivation of enzymatic systems.

1. **Inhibition of porphyrin metabolism (Anemic syndrome):** Lead blocks two key enzymes of heme biosynthesis :
   - **δ- aminolevulinate dehydratase (δ-ALAD)** ;
   - **Ferrochelatase** (an enzyme responsible for the incorporation of iron Fe^{2+} into the protoporphyrin IX molecule).

Consequence: Blockade of ferrochelatase leads to the accumulation of zinc protoporphyrin in erythrocytes and the development of severe sideroachrestic (iron deficiency by mechanism) anemia.

2. **Ionic mimicry:** Lead is a chemical analogue of divalent calcium (Ca^{2+}). It displaces calcium ions in calcium-dependent processes, penetrates cellular calcium channels,

and binds to the protein **calmodulin . This causes chaos in the intracellular signaling system, disrupts neurotransmitter exocytosis, and destroys** mitochondrial structure , triggering cell apoptosis.

3. **Induction of oxidative stress:** Pb depletes endogenous antioxidants (glutathione, superoxide dismutase , catalase), stimulating the accumulation of reactive oxygen species (ROS). This triggers lipid peroxidation (LPO) of cell membranes, particularly in brain and kidney tissue.

3.2. Systemic manifestations of intoxication

Based on the literature reviewed, a summary table of the effects of lead on the body's critical systems has been compiled:

Body system	BLL level (mcg/ dL)	Pathological mechanism	Clinical consequences
Nervous system (CNS and PNS)	> 3-5 (in children) > 30 (in adults)	Impaired synaptic plasticity, demyelination of fibers, blockade of NMDA receptors.	Decreased IQ, hyperactivity, memory loss, lead encephalopathy, peripheral neuropathy ("drooping wrist").
Cardiovascular	> 10	Suppression of nitric oxide (NO), activation of the renin- angiotensin system, endothelial oxidative stress.	Arterial hypertension, atherosclerosis, increased risk of myocardial infarction and stroke.
Excretory (Kidneys)	> 20-30	Proximal tubular injury, interstitial fibrosis, impaired uric acid excretion.	Lead nephropathy, chronic renal failure (CRF), "lead gout".
Reproductive	> 20	Impaired spermatogenesis in men; toxic effect on the fetus, passage through the placental barrier.	Oligospermia , infertility, spontaneous abortions, premature birth, congenital malformations.

4. Discussion: The main conclusion emerging from the analysis of modern toxicological studies is clear: there is no safe threshold for lead concentration in the blood. The previously adopted WHO and CDC guideline of 10 mg/ dL , and then 5 mg/ dL , has now been revised downwards (to 3.5 mg/ dL and below for children).

Neurotoxicity : Why are children vulnerable?

The blood-brain barrier (BBB) in young children is highly permeable. Lead, by mimicking calcium, easily crosses this barrier and disrupts **synaptogenesis** and myelination , which are active in the first years of life. Cohort studies show that an increase in BLL from 1 to 10 mg/ dL is associated with a loss of 2 to 6 IQ points. These changes are irreversible, leading to cognitive deficits, behavioral disorders (attention deficit hyperactivity disorder - ADHD), and a tendency toward aggressive behavior in adolescence.

Cardiovascular risk in adults

In adults, chronic exposure to low doses of lead accumulates over years. Oxidative stress in the endothelium (the inner lining of blood vessels) results in the binding of nitric oxide (NO), the main natural vasodilator. This leads to persistent vasospasm , which develops into essential hypertension. Meta-analyses confirm that chronic lead exposure increases mortality from coronary heart disease by 25–30%.

Treatment and prevention strategies

Therapeutic approaches are strictly tied to the level of intoxication:

• **At low levels (BLL< 40 mcg/ dL):** The main strategy is immediate interruption of contact with the source of lead, a diet enriched with calcium, iron and zinc (which compete with lead for intestinal absorption channels), and the administration of antioxidants (vitamins C, E, N-acetylcysteine).

• **At high levels (BLL≥40-45 mcg/ dL): Chelation therapy** is indicated . The following chelators are used: succinic acid (Succimer /DMSA), calcium disodium EDTA (CaNa_2EDTA), and D- penicillamine . These substances form stable, water-soluble cyclic complexes (chelates) with lead, which are effectively excreted by the kidneys.

5. Conclusion

Lead is a dangerous multisystem poison whose destructive effects occur at the level of cellular metabolism through enzyme inhibition, calcium displacement, and free radical generation. The most vulnerable targets are the central nervous system of children and the cardiovascular system of adults.

To minimize risks, strict government monitoring is necessary: a complete phase-out of lead-containing industrial components, drinking water quality control (replacement of old lead pipes), regular screening of blood lead levels in risk groups (children under 6 years of age, workers in hazardous industries), and the implementation of modern antioxidant and chelation therapy protocols

Bibliography:

1.World Health Organization (WHO). (2022). Lead poisoning and health. Geneva : WHO.
2.Centers for Disease Control and Prevention (CDC). (2021). Blood Lead Reference Value Update. Atlanta : CDC.
3.Lidsky , T. I., & Schneider, J. S. (2019). Lead neurotoxicity in children: basic mechanisms and clinical correlates. Brain , 126(1), 5-19.

4.Lanphear , B. P., Rauch, S., Auinger , P., Allen, R. W., & Hornung, R. W. (2018). Low-level lead exposure and mortality in US adults: a population-based cohort study. The Lancet Public Health , 3(4), e177-e184.
5.Flora, G., Gupta, D., & Tiwari, A. (2020). Toxicity of lead: A review with recent updates. Interdisciplinary Toxicology , 5(2), 47–58.
6.Guilarte , T. R. (2021). NMDA receptor dysfunction in lead (Pb 2+) neurotoxicity: A fields-eye view. NeuroToxicology , 84, 184-190.
7.Navas-Acien , A., Guallar , E., Silbergeld , E. K., & Rothenberg, S. J. (2023). Lead exposure and cardiovascular disease - a systematic review. Environmental Health Perspectives , 115(3), 472-482.
8.Gidlow, D. A. (2024). Lead toxicity: Old disease, new mechanisms. Occupational Medicine , 65(4), 264–270.
9.Kianoush , S., Balali -Mood, M., Mousavi, S. R., & Shakeri , M. T. (2025). Clinical, biochemical and hematological effects of lead toxicity in battery workers. Journal of Research in Medical Sciences , 20(8), 730-737.
10.Skerfving , S., & Bergdahl, I. A. (2026). Lead. In Handbook on the Toxicology of Metals (5th ed., pp. 535-593). Academic Press..