LEAD INTOXICATION

S. IURIAN

Ph.D. Candidate, The "Lucian Blaga" University of Sibiu.

Abstract*: Lead is one of the „heavy metals" that can cause intoxications. The author mentions the toxic dose, toxicokinetics and toxicodynamics of organic / inorganic lead, clinical data, treatment and the particularities of lead intoxication and prevention in children.*
Keywords: *child, inorganic / organic lead, lead intoxication.*
Rezumat*. Plumbul este un metal moale şi maleabil care este utilizat în multe procese tehnologice şi intră în compoziţia multor produse, de unde rezultă multitudinea de posibilităţi de intoxicaţie cu plumb. Autorul trece în revistă în lucrarea de faţă sursele de expunere la plumb organic şi anorganic, doza toxică de plumb organic şi anorganic, toxicocinetica şi toxicodinamica, particularităţile intoxicaţiei cu plumb la vârsta pediatrică (copiii sunt predispuşi la intoxicaţia cu plumb), fiziopatologia intoxicaţiei cu plumb, tabloul clinic al intoxicaţiei şi tratamentul intoxicaţiei cu plumb corelat cu măsurile de prevenţie.*
Cuvinte cheie*: copil, plumb organic / anorganic, intoxicaţie.*

Lead is a soft and malleable metal, existing in nature under the form of a mixture of 3 isotopes: Pb^{206}, Pb^{207}, Pb^{208}, which enters in the composition of certain organic and inorganic compounds (tetra-ethyl lead). Regarding the sources of lead exposure, we can mention: lead melting factories, fabrication of batteries, rubber, plastic materials industry, lead products welding, zinc melting factories, lead-based additives, carbons combustion, copper melting factories, pigments fabrication (1).

Occupational exposure and environment. The exposure occurs as a result of soil, water and contaminated food contact. Air lead concentration varies from 7,6 x 10^{-5}μg/m^3 in the areas far from the pollution source up to > 10 μg/m^3 near the melting factories. The surface waters in the Unites States of America contain lead in quantities between 5 and 30 μg/l. The water lead sources are the lead pipes or the lead welding coming from the pipes joining. The reduced value of Ph may increase the lead concentrations in the drinking water. Lead could be found in milk, meat, fish, poultry and cereals. The level of lead in the uncontaminated soil varies between 10 and 30 μg/g. The lead level in the soil around roads may reach values of 2.000 – 10.000 μg/g and near the melting factories, the soil may contain lead up to the value of 60.000 μg/g.

The daily contribution of lead is of 5-15 μg/day for all age categories (1), but it may be higher in children, due to ingestion and their soil contaminated contact and to the respiratory frequency which is higher in children than in adults (8). Parents' occupation may also contribute to the children's lead exposure (the cloths of the miners working in the lead mines represent a source for the lead exposure). Lead based paints and dust remain the major source for the lead exposure in children. At the same time with the paints shrinking, the lead concentration increases in the soil around the building. The tetra-ethyl lead is a very toxic organic compound used in special conditions in oil distilleries with a view to increase the octane rating of gasoline. Its use was largely reduced, so in the Unites States the use of the lead based additives has been forbidden even from 1997. Today, according to statistics, the children in the Unites States are exposed to reduced levels of lead than in the past. Some statistics show that regarding children, the lead prevalence of more than 25 μg/dl decreased from 9,3% in 1970 to 0,5% in 1980 (2,3). In most of the countries, the causes of the lead intoxication in children remain the same.

Toxic dose. The toxic doses may occur after a single exposure or, more probably, after repeated exposures to reduced doses of lead. The ingestion of one single important dose of lead brings about the increased seric levels of lead with serious toxicity or death. After the chronic exposure to lead small doses, the level of lead quantity may vary between 10-15 μg/dl in children.

The lead toxicity even to reduced seric values was mentioned in certain studies. The symptoms and the signs of the lead intoxication appear when the value of lead poisoning is over 40 μg/dl. Lead poisoning of 40-60 μg/dl is associated with neurological disorders.

Lead toxicokinetics and toxicodynamics. At the organism level, the lead is distributed in three main compartments: blood, soft tissues and bones. After the exposure to large quantities of lead, lead poisoning increases rapidly, but it also decreases rapidly. This decrease seems not to be determined only by the lead elimination by urine but also as a result of being

distributed in the organism. At the same time with the lead storage in bones, its release is made very slowly (approximately 10 years).

Thus, the level of lead in blood or tissues is still high even after years of exposure.

The tetra-ethyl lead is a colourless, oleaginous, aromatic and sweetish liquid which produces vapours at normal temperatures. This substance is used for the increase of the octane rating. The toxic enters the organism by breathing, (vapours inhalation), cutaneously or digestively (in the case of voluntary or accidental intoxication).

Absorption. Lead is easily absorbed through lungs. The particles with the diameter smaller than 5 μm reach even the alveoli where they are absorbed and the particles with larger sizes are retained by the mucous of the respiratory tract from where, by swallowing, they reach the digestive system. Orally, lead is absorbed in proportion of 20-30%, but children usually absorb up to 50% of the ingested lead (children are predisposed to lead intoxication). In exchange, the organic compounds with lead are transdermally absorbed. After absorption, the tetra-ethyl lead is rapidly diffused in the organism humours, fixing itself in brain, liver, muscles and adipose tissue.

Release. In adults, lead is released from kidneys in a quantity of 30 μg/day, but at the same time with the lead accumulation in a larger quantity in organism, the release may reach the value of 200μg/day.

The renal release is due to the glomerular filtration and to the tubular epithelial cells exfoliation where lead is accumulated. Lead is also released digestively (through the bile). The organic lead is rapidly eliminated through urine and faeces under organic and inorganic shape.

Physiopathology. The absorption of the ingested lead is influenced by the size of the particles. Lead is related to erythrocytes and is distributed in different bone tissues, teeth, liver, lungs, kidneys, brain and spleen. Lead actions as a "warehouse", protecting other organs. Within the context of certain affections which mobilize the lead (fractures), its toxicity may be validated.

Lead contributes to the malfunction of many enzymatic systems in the organism (1), with affinity on the sulphydryl groups and it is toxic for the calcium and zinc dependent enzymatic systems. Thus, lead inhibits the delta-ALA activity of the citoplasmatic dehydrate, of the coprogen-oxidase and of ferochelatase, enzyme which intervenes in the hem synthesis. The lead interference with ALA dehydrate is dose dependent; thus, the enzymatic inhibition starts when the level of lead poisoning reaches the value of 10-20 μg/dl and is completed on the value of the lead seric level of 70-90 μg/dl. Ferochelatase is an enzyme which determines the transfer of ferrum from ferritin in protoporphyrin for the hem formation. The inhibition of ferochelatase will induce the increase of the urinary excretion of coproporphyrin and of the level of coproporphyrin in the red cells. The hem synthesis is important not only for the synthesis of haemoglobin, but of the cytocromes as well, which play an important part in the oxidative metabolism. Also, lead blocks the transcriptions factors for RNA, joining itself at the level of cysteine's loci. It also interferes with the ability of calcium of inducing the exocytose of the neurotransmitters and with the protein-kinase C calcium dependent (enzyme which intervenes in the cell increase, learning and memory). Lead stores enzymes with the role in the cells integrity, as well as the renal hydrolysis which converts the 25 hydroxy-colecalciferol to 1,25 dihydroxy-colecalciferol. Lead also aims at the axons of the motor neurons with axonal degenerescence and segmentary demyelinisation. Studies have proved that the reduction of the nervous conducting speed in the motor fibres of the ulnar nerve may constitute a marker for the sub-clinical neurotoxicity of the lead (6).

Organic lead toxicity. Tetraethyl lead is metabolized at lead triethyl which actions directly on the cerebral energetic metabolism by the inhibition of glycolysis and synthesis of ATP. Degenerative and hemorrhagic injuries are thus produced in cortex, thalamus, hypothalamus and white substance.

Clinical picture. Anamnesis is important as it reveals the exposure history of the lead. The most common consequences of the lead intoxication are: sleepiness, irritability, nausea, staturo-ponderal hypotrophy; children chronically exposed to reduced levels of lead do not present suggestive signs and symptoms.

Effects on the central nervous system (4, 6). The acute lead exposure determines encephalopathy. Ataxy, the alteration of the sensory system and convulsions were reported in children with the level of lead poisoning over 100 μg/dl. The effects of the chronic secondary lead exposure may be less evident. The inverse-proportionally relation between the dental lead concentration and the scholar performances was proved (this effect was maintained for a period of 11 years, according to a research). The elimination of the lead deposits from the bones may contribute to injuries on the central nervous system, late after the exposure, when the mobilisation of these deposits is possible within the context of pregnancy, nursery or osteoporosis.

Haematological effects. Anemia occurs as a result of the alteration of the haemoglobin production and of changes taking place at the level of the cell membrane of erythrocytes. The level of haemoglobin may be maintained within the normal limits despite the medium-severe intoxication. The increase of the haemoglobin concentration takes place when the lead intoxication is stopped. Regarding the lead intoxication, the normochromic, normocyte anemia occurs, which is characterised by the presence of erythrocytary basophilic granulations (upon the examination of the peripheral blood smear). The severe anemia may also occur in the case of the associated haemolysis, haemolysis explained by the secondary lead exposure erythrocytary membranopathy.

Renal effects. A research made in our country regarding children with ages between 3 and 6 years old

having the level of lead poisoning of 34 μg/dl, proved the direct proportioned relation between the level of lead poisoning and the urinary level of N-acetyl-β-glucosamine.

Organic lead intoxication. As the result of the contact with tetraethyl lead, after a period of some hours, three clinical forms of intoxication may occur:

- Easy form, manifested by agitated sleep, headaches, anorexia, metallic taste, sialosis, profuse sweats, bradicardy, arterial hypotension, hyperreflectivity, trembling;
- The medium form of intoxication in terms of severity is clinically validated by the exaggeration of the osteo-tendinous reflexes, equilibrium and walking disorders, delirium, hallucinations, confusion, temporal-spatial disorientation, trembling and muscle fasciculations;
- The severe form presents subintrant convulsions, coma and death. Within the easy and medium forms, the symptoms are remitted in a few days, and regarding the severe forms, in 3-4 weeks.

Diagnostic tests. The measurement of the seric level of lead represents the key of the diagnosis. Lead poisoning reflects the impregnation produced weeks before the laboratory examination. The determined plumburia reflects more accurate the impregnation of the vascular and parenchimatous sector, as it allows the elimination of the lead form the body. Its mobilisation is made by the administration of the Ca-EDTA chelator followed by the dosage from the 24 hour urine (or for the period of 6 hours in the case of the short test). The fluorometric dosage of erythrocytary protoporphirins represents a relatively accurate test for the identification of the lead intoxication and, at the same time it is a precocious test. The increase of the erythrocytary protoporphirins is also encountered in the feriprive anemias, as well as in the erythropoietic protoporphyria. The dosage of the delta-ALA urinary acid is a less sensitive test. Coproporphirin is also high in urine. The routine examinations may reveal the decrease of the haemoglobin level, but the severe anemia is rarely encountered. The presence of the basophilic granulations of the peripheral blood smear was rarely described. The increase having been stopped, the osteodense epiphysary lines (described in lead intoxication) are not developed any longer. In the Unites States, the Centre for Disease Control and Prevention (7) recommends the screening method for all children, using the monitorization of lead poisoning as the standard diagnosis method. Regarding the organic lead intoxication, a high level of plumburia can be noticed in opposition with the reduced lead poisoning level. The urinary coproporphirins and the delta-ALA have normal values and there are no erythrocytary anomalies.

Treatment. First stage regarding therapy consists in the identification of the lead source, of other persons who may be exposed and exposure ending. The involvement of the local medical authorities is essential for the confirmation of the exposure source and for the identification of the risk factors.

The affected individuals will not resume their activity until the risk of exposure is eliminated.

Decontamination. The acute lead exposure is more frequent in children than in adults. The ingestion of a lead-made object may induce toxicity in a few days and the gastro-intestinal decontamination is necessary if lead can be seen as a result of the abdominal radiography.

The evacuation by clyster or the endoscopically removal helps to the elimination of the ingested object. The environment decontamination is very important, especially if children are involved. The children‘s separation from the contamination source is a priority.

Antidotes (1,5). For a lead poisoning level under 25 μg/dl, the therapeutic guides do not recommend the therapy with chelating agents. A lead poisoning level of 25-45 μg/dl does not oblige the chelation therapy initiation but the oral chelation therapy is necessary when the seric level does not decrease in spite of the measures taken. Regarding the lead poisoning level of more then 45-70 μg/dl Succimer po therapy is recommended and those who present encephalopathy or with lead poisoning level of more than70 μg/dl require the intra venous therapy with Dimercaprol and EDTA. The Dimercaprol therapy is initiated every four hours. Subsequently, the EDTA therapy is added in continuous perfusion. The combined therapy will last 5 days. For the intoxication with tetraethyl lead, there is no specific antidote. The chelating agents are not efficient (as against the inorganic lead intoxication). Thus, the therapy is only symptomatic. Regarding the contact with teguments it is necessary to wash the skin with soap and water and in case of ingestion, the lavage with sodium sulphate 1% is recommended. The state of convulsive illness requires the administration of cerebral anti-convulsive and depletives

Supportive therapy (5). Certain measures of diet have been suggested: regular timetable for meals, the correction of iron deficit, the increase of calcium, phosphorous and vitamin C consumption.

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