# TRACE ELEMENTS TOXICITY: INCREASED RISK OF INTOXICATION IN CHILDREN

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**Abstract**

Increased concentration of trace elements is especially hazard for child's population health. One of the critical periods with manifested genetic influence is early prenatal ones. Aim of present work was determination of trace elements content in the brain and lung tissues of the newborns and 26-28-week fetuses whom mothers for their pregnancy had lived in the big industrial sites and clearing up possible negative aftereffects for posterity health. In the autopsy material trace elements presence was measured by atomic absorption method.

Investigation has been found out in 50% samples of the brain and lung tissues of the newborns lead accumulation had taken place in the concentration in 10-time higher than normal parameters. The most considerable level of the toxicant was in the lung. It was correct for zinc. In the lung tissue cobalt and nickel concentrations exceeded normal ones in 3-15-time. In studied simples iron and copper levels decreasing was shown. However some tests of the lung tissue contained increased quantity of copper. Thus, in the child's organism microelements imbalance has been shown. The role of the trace elements in normal development and pathogenesis or prenatal pathology of this posterity is emphasized.

**Introduction**

One of first places among chemical contamination factors of environment is occupied by salts of transitional metals (d-elements, trace elements, heavy metals, microelements) described by wide spectrum of negative influence on human organism. Significance of heavy metals as industrial pollutants grew up in consequence of their wide inculcation in many branches of industry and transport (use of ethyl petrol), that brings about phenomenon, when the supplementary peoples groups are exposed by influence of these elements.

Microelements are chemical elements contained in little quantity in organism tissues. From influence degree on human organism the microelements separate on:

- essential: iron, copper, zinc, manganese, chrome, selenium, molybdenum, iodine, cobalt;
- conventional essential: bor, bromine, fluorine, lithium, nickel, silicon, vanadium;
- toxic: aluminum, cadmium, lead, mercury, beryllium, barium, bismuth;
- potentially toxic: thallium, gold, indium, rubidium, silver, titan, uranium, strontium, zirconium (1).

Even essential microelements become toxic, if their content exceeds the physiological normal concentrations.

Connecting with organism proteins the heavy metals easy penetrate over protective barriers, acquire properties of haptenes, disturb the cells co-operation in immune reaction, are antagonists $Ca^{2+}$ in the cell, significant influence on activity of much enzymatic systems, state of cell membranes. Ability of some kations of bivalent metals to change penetrability of cell membranes for account of electrostatic interactions with its albumin and phospholipids components can be attended with changes of mitochondria membrane and violation of mitochondria breathing speed.

Increased microelements concentrations are especially danger for health of children's population. Structural-functional peculiarities of children's organism stipulate raised organs sensitiveness to action of harmful factors, peculiarly in critic periods of development. Immaturity of enzymatic systems and excretory systems, sharp raising masses of fatty and osseous tissues during growth process bring about depositing xenobiotics in child's organism (2), including heavy metals. One of such critic periods, in which genetic dominance display, is early prenatal ones, peculiarly the $1^{st}$ trimester of pregnancy, when laying and forming of organs takes place.

European researchers established that for pregnant women living in zone of high contamination risk of birth of children with diverse pathologies rises on 33% in comparison with women above-ground on more environmentally friendly territories: for their posterity a risk of cognitive defects connected with partial deformation of cerebrum with consequent development of damages of spinal brain, heart-diseases, anomalies of main blood vessels increases considerably (3)/.

Aim of represented work is determination of concentration of some microelements in tissues of cerebrum and lungs new-born and also 26-28-week fetuses, whose mothers lived during pregnancy time in large industrial center for exposure of possible negative consequences on posterity health.

**Methods**

Determination of microelements content - Cu, Zn, Fe, Co, Ni, Pb – was realized in the autopsy material: tissues of cerebrum and lungs of the new-born and 26-28- week fetuses. Speedy after extraction material for analysis was frozen immediately and kept at t=10$^{O}$C.

Mineralization of biological material was realized by samples ashing. At t=150-200$^{O}$C pressure in the tubes rose in dependence on samples composition and used reagents to 10-15 atmosphere and higher. At such temperature parameters and pressure use of strong oxidants allows to realize ashing of majority of biological samples types. In got mineralizes content of microelements was measured by atomically-absorption method.

**Results**

Besides causes, bringing about accumulation of heavy metals in organism of adult population (living in large industrial centers, living in cities nearby contamination sources, use of products and drinking-water contamined pollutants, low social-economic status, smoking), for children's population the supplementary risk factors are typical: possibility of hands contamination by dust containing the microelements and receipt of heavy metals over mouth; inhalation of over ground air layers on streets, which most saturated by heavy oxides of exhaust motor transport gases; dietary peculiarities, iron and calcium imbalance in the organism. Taking into account combination of age physiological and behavior peculiarities the children of early age are by cohort of highest risk because developing nervous system is more sensible to toxic action of heavy metals; their digestive tract because of immaturity protective mechanisms, not clever to prevent to absorption of these metals in blood and inlaying organs; in them lightly dyspepsia and related to its imbalance of essential and toxic microelements become.

**Lead** is one of most toxic and dangerous heavy metals. In environment this toxic matter is extraordinarily spread and included in lists of primary contaminating substances by much international organizations such as World health organization (WHO), UNO Program on environment protection, European economic commission. There are worked up national program directed to lowering of surround contamination by lead and limitation of its negative influence on children's population health in much world countries (USA, Germany, Denmark, Australia, Mexico, Russia and other) (4)

Ecologically conditioned, comparatively low and early deferring safe lead levels in soil, water and food products of mass consumption actually are by cause of some mental, physical and psychophysiologocal violations, lowering of synthesis intensity of hem, anaemias development, rise of threshold of auditory perception and lowering of vitamin D level in blood. Special attention is spared to neurotoxical disorder development, influencing mainly on cognitive functions preserved even after lowering of lead level in blood in children that raises risk of mental and physical development violation in growing up generation. Straight tie between accumulation of lead in child organism and lowering of intellectual coefficient (IQ), capacity for attention concentration, to orientation and to involving, violation of speech and neuromotor functions is defined ( 4).

Statistic reliable connection between postnatal lead level in blood in limits 0,48- 1,20 mcMole per liter (100-249 mcg/l) and raised hyperactivity, absent-mindedness, low tolerance to disorders and tendency to violations development similar with associating with raised timidity, departure from social reality and loss of interest to girding is established (5).

Risk of mental undevelopment and other lesion attached to accumulation in child organism of lead can grow under dominance of other factors pre- and neonatal periods. Individual sensitiveness to damaging lead action having presumably genetic base has also great significance. Dominance of lead becomes stronger attached to presence of other ecological toxical and medical factors, in particular, raised pollutants level in the surround, diverse chronic diseases and alimentary disorders.

On our data accumulation of lead in tissues of the cerebrum and the lungs new-born in concentrations exceeded normal parameters in ten time has been found out in 50% cases (table 1). Peculiarly high level of the toxicant was marked in the lung tissue. In accordance with estimate lead concentration scale in blood reflecting a lead accumulation degree in organism, defeating risk and measures of medical, sanitary-hygienic and ecological services an inspected contingent belong to III-IV groups, when a child needs medical and ecological control, perhaps, pharmacological correction with use of sorptive therapy or application of chelates agents that is confirmed by data that almost 44% children in large cities can have the problems in conduct and teaching caused by lead influence (6). Lead is known to break normal course of much metabolic processes under its influence starts in prenatal period, for example, myotoxical lead affects when the skeletal muscles are main object for display of element toxicity (7).

Table

Content of the microelements in tissues of cerebrum and lungs of the children

| | Cerebrum, mg per kg of weight | | Lungs, mg per kg of weight | |
|---|---|---|---|---|
| | Control | Experiment | Control | Experiment |
| Cu | 2,20 - 4,60 | 0,13 - 1,70 | 1,1 | 0,66 - 3,07 |
| Zn | 8 - 15 | 9,88 - 27,73 | 6,5 | 18,77 - 50,62 |
| Fe | 50 -80 | 15,63 - 45,32 | 170 | 39,22 - 174,60 |
| Ni | 0,1 | - | - | 0,45 - 1,00 |
| Co | - | - | 0,30 | 0,87 - 4,71 |
| Pb | 0,34 | 0 - 4,18 | 0,34 | 0 - 7,64 |

Danger of low lead concentrations is based on two arguments: a) even «soft» metal ions dominance clever considerably to bring capacity down for adaptation, that impairment of life quality, at least, in subjects with limited adaptive resources; b) the early «soft» affects can be signs of primary changes in functioning of nervous system accelerating after lead accumulation in the organism (8).

Chronic intoxication of rat kids by lead (lead acetate in food for all period of intrauterine development and two weeks of postnatal period) caused essential mechanisms violations of long-term potentiation in hypocamp that is phenomena lain in memory base and depends on receipt of $Ca^{2+}$ into hypocamp neurocytes. In its turn, attached to brain trunk pathology disorders of vitally important functions become, such as breathing and cardiac activity owing to violation of nervous impulse transfer speed over synapses. Lead easy penetrates over hematoencephalic barrier and in new-born mammals it's twice as more intensive than in adults. Lead accumulating in nervous tissue practically doesn't abandon its even after lowering of microelement level in the blood.

**Iron** is necessary element for normal development and functioning of basic organs and organism systems and cerebrum too. The iron ions take part in oxidizing phosphorylation, synthesis and degradation of neurotransmitters, oxidizing metabolism. This is important part of myelin. Deficiency of iron is cause of violations of motor functions, capacities for teaching, behavior reactions. Change in redistribution of iron on regional, cultural and molecular levels can be reason of pathogenesis of central nervous system diseases, aging, neurodegenerative illnesses, dissipated sclerosis, traumatic brain damages, AIDS-infection (9).

In experienced samples (as in tissue of the cerebrum, so the lungs) lowering of iron level (table) is revealed. Straight dependence between maintenance of microelement in the brain and the light is observed. Interest to study of microelements homeostasis attached to chronic pulmonary unspecific diseases is conditioned by researches results, in obedience to which the metals (Cu and Fe) regulate intensity of free radical processes, are modulators of second mediators (cyclic nucleotides and $Ca^{2+}$), control secretor activity of lung fat cells light, state of local defense of breathing organs and bronchial conductivity. It's can be supposed that the disorder of metal-ligand homeostasis is very important in pathogenesis of lung diseases.

**Zinc** backs up integral structure and function of biomembranes. Majority of the metalenzymes is zinc-containing. Stability constants of complexes of toxic metals with bioligands are above zinc complexes, therefore ones is easy forces out by these metals from co-ordinating conjugates that is followed with zinc deficit in the tissues. Zinc maintenance (changes attached to action of diverse factors) likeness in different kind cells allows to consider these changes to signs of unspecific adaptive syndrome of cultural system.

One of determining antioxidative properties of metalthioneines is expelling of zinc under oxidation of metal-thiolate clusters. These ions, presumably, inhibit lipid peroxidation interfering with iron ions, which are activators of freely-radical processes, to associate with oxidation sites or edges out them from there (10). Zinc goes into superoxiddismutase active center as one of major components of antioxidative system catalyzing dismutation of superoxidative radicals and that the very prevents pathogenic action of active oxygen forms. Determination of zinc level in experienced samples indicates on raised its maintenance: zinc accumulation is the highest in the lungs (table 1). Metal accumulation in tissues can bring about imbalance of bivalent cautions and that over cyclic nucleotides system affects on state of bronchial wall receptor apparatus being instrumental in change of reactivity of bronchial tree, conduces to infection persistence in respiratory tract and to prolonged course of inflammatory process in the lungs.

Six **copper** atoms as two positively charged ions go into ceruloplasmin molecule composition participated in guaranteeing of some processes of cultural metabolism, maintenance of functional activity of reticuloendothelial and immune systems, possessed by anti inflammatory properties. As antioxidant it partakes immediate of neutralization of free radicals making in organism, peroxide conjugates, aromatic amines, histamine. Ceruloplasm improvements lipid peroxidation under action of

diverse external factors, for example ionizing irradiation, and toxic matters, salts of heavy metals also. It partakes of transport and interchange of iron, neutralizing oxidizing-restoration ions properties of bivalent iron. Intracellular copper deficit, probably, is one of factors, limitative antiradical activity of superoxiddismutase having copper ions in catalytic center structure of cytosole fraction. Observed copper maintenance lowering in the cerebrum and lungs indicates on violations possibility in antioxidative defense system and can begin by starting mechanism of pathological processes development. Depression of intracellular radical defense, in its turn, brings about free radical processes intensification, oxidative-antioxidative imbalance as one of the causes forming bronchoobstructive syndrome (11).

However, some samples of lung tissue contain raised concentration of copper. Mechanism of pathogenic action of high copper concentrations is related to oppression of oxidizing enzymes activity and cells death owing to hypoxia. The cells of central nervous system are peculiarly sensible, and also immunecompetent cells because of its high require of oxygen.

Decreasing of intracellular concentration of copper and iron and rising of zinc level reinforce atherosclerotic changes in the organism.

The **cobalt** ions initiate development of oxidizing stress, by important link of which is manifestation of chain lipid peroxidation and lowering of restored glutationum and macroergs levels in the cells. Atherogenic cobalt action with cholesterol redistribution between atherogenic extra low density lipoproteins and antiatherogenic high density lipoproteins attracts special attention. The cobalt ions cause considerable rise trygliserides in the blood serum and liver cytosole that testifies transfer of interchange of matters with carbohydrate type into fatty ones. A cobalt influences to erythropoiesis changing phospholipid composition in blood serum (12). Cobalt affects cultural metabolism: conjugation of cobalt with thiol groups leads to SH-containing enzymes inactivation; forcing out of iron from hem-containing albumen takes place; superoxid perox-complexes with cobalt are formed. All of these phenomena bring about violation of intracellular equilibrium between free-radical processes and antioxidative defense system. The cobalt ions act to lysosomal membranes injury and that will initiate a going out lysosomal enzymes into cytosole and breaking up biological macromolecules with consequent development of pathological changes.

In examined lung tissue cobalt level exceeds normal maintenance in 3-15 times and that is negative prognostic factor of chronic unspecific pulmonary diseases development. Cobalt ions not displayed in the cerebrum samples.

**Nickel** participates in lipid interchange of cultural membranes heightening its penetrability and facilitating fat cell degranulation and also bringing immunelogical reactivity down. The element is strong carcinogen, clever to slow fibril epithelium cilia motions. Nickel was not displayed in the cerebrum, however, its level was high in the lungs (table ).

**Conclusions**

Thus, the got results indicate on microelements imbalance in organism tissues developing in prenatal period that is negative prognostic health violation factor in the descendants. Multifactor analysis of microelements level violations influence on state parameters of cultural membranes, endocrine, immune systems, a calculation of cumulative properties of heavy metals allow to consider these children by sensitive, hyperactive group in population with raised risk for health in ecologically inauspicious environment conditions.

**References**

1. Agget P.J. Physiology and metabolism of essential trace elements: an outline //Clin.Endocrinol.Metabol.- **Vol.14, №3.** - P.513-543. (1985).

2. Lukyanova O.M., Povoroznuk V.V., Antipkin Y.G. et all. Physical development and structurally-functional figure of osseous tissue in children residing in the zone of radiation control //Pediatric, obstetrics and gynecology.- **№2**. - P.10-17. (2000).

3. Chemical Landfills and Birth Defect Risks // CRI/ICEIT Newsletter. - **Vol.8**, **№4**.- P.5. (1998).

4. Rosanov V.A. Lead Neurotoxicity in children's age: epidemiological, clinical and neurochemical aspects // Ukrainian. Med. J.- **XLI**, **№5**. - P.9-17. (2000).

5. Lead Exposure and Behavioral Problems in Children /CRI/ICEIT Newsletter.- **Vol.8**, **№3**.- P.5. (1998).

6. Snakin V.V. Contamination of biosphere by lead: // J. Medicine and industrial ecology. - **№5**. - P.21-27. (1999).

7. Myotoxic Effects of Chronic Low Level Lead Exposure // CRI/ICEIT Newsletter. - **Vol.9**, **№ 2**. - P. 4. (1998).

8. Impairment of the Central Nervous System Resulting from Occupational Exposure to Lead // CRI/ICEIT Newsletter. - **Vol.8**, **№3**. - P.3. (1998).
9. Zozula Y.P., Mychaylic O.M., Chernenko. A.P. et all. Metabolism Peculiarities of non-heme iron attached to experimental glial brain swellings of the rats // J. Academy of medical sciences of Ukraine- **Vol.7, №1.** - P.3-21. (2001).
10. Grygorova N.V. Dominance of extreme factors on maintenance of zinc in granulocytes of blood and pancreas islets // Questions of bioindication and ecology. - **Vol.5**, **№1**. – P.120-125. (2000).
11. Phedoseev T.B., Emanuel V.L., Gycharev S.S et all. Microelements role in pathogenesis and clinic of bronchial asthma // Clinical medicine. - **№12.** - P.44-48. (1989).
12. Kaliman P.A., Zagayko A.L., Shalamov R.V. et all. Maintenance and composition of lipoproteins of blood and liver of the rats and some indexes of oxidizing stress attached to introduction of cobalt chloride// Ukr..Biochem. J.- **Vol.69**, **№5-6**. - P.138-148. (1997).