SESSION 9

TRACE ELEMENT AND MINERAL TOXICITY: ASPECTS OF ENVIRONMENTAL, FORENSIC, OCCUPATIONAL AND MEDICAL TOXICOLOGY

THE EFFECT OF CADMIUM TOXICITY ON ANTIOXIDANT DEFENSE SYSTEMS AND TRACE ELEMENTS

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Cadmium stimulates the production of reactive oxygen species (ROS) and causes cell damage. In this study, 30 Wistar albino male rats were included as experimental group and 20 as control group, and they were fed with normal food and tap water for 8 weeks. But, in experimental group water contained 15 ppm cadmium chloride. The blood levels of cadmium (Cd), zinc (Zn) and copper (Cu) and the activities of blood copper-zinc superoxide dismutase (Cu-Zn-SOD) and catalase (CAT) and selenium glutathione peroxide (SeGPx) were determined in experiment and control group. Blood samples from experiment and control groups were drawn using heparinised tubes. The erythrocyte Cu-Zn-SOD and CAT and SeGPx activities were determined spectrophotometrically and levels of Cd, Zn and Cu were determined in whole blood by atomic absorption spectrophotometry. In cadmium administered experiment group, blood Cd levels was found to be significantly higher than the control group ($p < 0.001$). Besides, there was significant increase in red cell Cu-Zn-SOD activities in experiment group ($p < 0.05$). SeGPx activity decreased ($p < 0.05$) and CAT activity ($p < 0.001$) was found increased significantly in experiment group compared to control. In experiment group, significant increase was observed in trace elements. Significant decrease in blood Zn level ($p < 0.001$), an increase in blood copper level ($p < 0.001$) and Cd/Zn ratio ($p < 0.001$) were seen in the experiment group. In conclusion, cadmium is a heavy metal, the toxicity of which increases ROS and influences antioxidant defence system.

ROLE OF MITOCHONDRIAL ELECTRON TRANSPORT CHAIN IN HEAVY METAL-INDUCED TOXICITY: A COMPARISON OF CADMIUM, MERCURY, AND COPPER ON TWO RAT CELL LINES, PC12 AND AS-30D

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To further elucidate role of mitochondrial electron transport chain (ETC) in heavy metal-induced cytotoxicity, we compared action of Cd^{2+}, Hg^{2+} and Cu^{2+} on cell viability, respiratory function, and intracellular reactive oxygen species (ROS) generation of rat neuron-like PC12 cells. The cell viability and protective action of different effectors against the heavy metal-induced cytotoxicity was estimated by spectrophotometric monitoring of the lactate dehydrogenase release from the cells; the cell respiration was determined polarographically and the ROS production was measured spectrofluorometrically using DCFH2-DA as the ROS-sensitive probe. As found, all metals produced, although in a different way, dose- and time-dependent changes in the cell viability, ROS generation and respiratory capacity. In particular, Cd^{2+}, beginning from 10 μM and already at short incubation time (3h), significantly inhibited the CCCP-uncoupled cell respiration, i.e. the respiration with maximal rate limited only by ETC efficiency. Practically its complete inhibition was reached after 3h-incubation with 50 μM Hg^{2+} or 500 μM Cd^{2+}, whereas even after 48h-exposure with 500 μM Cu^{2+} only 50% inhibition of the respiration took place. Against Cd^{2+}-induced ROS-dependent cell injury not only well-known antioxidants, such as N-acetylcysteine, vitamin E, butylhydroxytoluene, TEMPO, mannitol and the mitochondrial permeability transition pore inhibitors — cyclosporine A, bongkrekic acid and Ru-360 were protective but also the mitochondrial ETC effectors — CCCP and stigmatellin (complex III inhibitor). However, all mitochondrial ETC effectors tested did not protect against the Hg^{2+}- and Cu^{2+}-induced cell damage. Importantly, stigmatellin was shown to be one of the strongest protectors against the Cd^{2+}-induced injury of PC12 cells, producing 15—20% increase in the cell viability that is in a good accordance with our data obtained before on AS-30D rat ascites hepatoma cells (Russian Foundation for Basic Research: grants No. 07-04-00722 and 10-04-01050).

FEATURES OF DIAGNOSTICS OF ACUTE POISONINGS WITH THALLIUM COMPOUNDS

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The Tl content in earth crust is high enough ($3x10^{-4}$%), however, because of dispersion of an element, acute poisonings with thallium happen rather seldom and are much less investigated, than intoxications by other heavy metals. For diagnostics of thallotoxicoses use measurement of content Tl in human biomediums (in blood, urine, hair), however the question on what levels to consider as medium-population norm, has no clear answer. Even more it concerns toxicological norm that is to a threshold of acute and chronic action. How much informatively direct definition of Tl in biomediums? On the one hand, it doesn't have reasonable alternative. On the other hand, as practice shows, even in case of a heavy poisoning not always it is possible to diagnose a metallotoxicosis. So, in July 2009 to our toxicological laboratory have been delivered samples of whole blood and hair of patient Z, who has arrived in hospital with heavy metals poisoning signs. Samples have been investigated by an atomic emission spectroscopy method, thus has not been revealed HM levels menacing to health, including Tl. Doctors insisted on the diagnosis and in a week biomediums of the patient (blood, hair and this time urine) have been delivered to laboratory again. Repeated research has shown that at normal contents in blood and in hair Tl level in urine has been exceeded in hundreds times — 1044.5μg/l. The subsequent researches have confirmed noted fact: at the highest concentration Tl in urine its levels in blood and hair were in the limits diagnosed as harmless. It is known, that the period of a semiexcretion of Tl is from 2 to 4 days. There is a reason to assume that its content in blood already in a day after an exposition decreases to usual levels. Thus, quantitative determination of Tl in blood is expedient only during rather narrow time interval directly after an acute poisoning. Tl determination in hair can be useful only in case of a chronic intoxication when exposition time is comparable with time of regrowth of hair. For diagnostics of an acute poisoning by Tl its only quantitative determination in urine suits.

O-ACETYLSERINE(THIO)LYASE (OASTL) A PROMINENT ENZYME IN THE HEAVY METALS RESPONSES IN *SCORPIURUM CIRCINATUM*

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The toxic effects of heavy metals in plants are related to the inhibition of enzyme activity and oxidative damage into the cell. Most metal ions present in the shoots and roots of plants are bound to low molecular mass ligands or to proteins. The major types of S-containing ligands potentially involved in metal binding are metallothioneins, phytochelatins, and glutathione (GSH), all derived from cysteine. Cysteine biosynthesis in the plant cell proceeds via a two-step reaction: in the first step the amino acid serine is activated by acetyl-CoA to form O-acetylserine (OAS), through serine acetyltransferase (SAT) enzyme. In a second step O-acetylserine(thio)lyase (OASTL) enzyme inserts sulphide into OAS to form the amino acid cysteine. *Scorpiurum circinatum* (Brid.) Fleisch. & Loeske is a widespread epiphytic moss in Mediterranean areas. Moss gametophytes were collected from Botanical Garden of Naples and cultured in vitro in Mohr modified medium with concentrations of 10^{-5} and 10^{-4} M of Cd, Pb, Zn and Cu for 24 h. After metal treatment the samples were prepared for TEM observations or for assays of O-acetylserine(thio)lyase (OASTL) enzyme. TEM observation showed that heavy metals caused ultrastructural alterations of vacuolar system and thilacoidal organisation. In *S.circinatum*, OASTL activity seems strongly correlated with the ability to hyperaccumulate heavy metals like Cd, Cu and Pb. Through the various metals tested, Cu and Pb at very low concentration (10^{-5}M) effected OASTL activity more than to that observed in moss, Cd-treated where OASTL activity enhances at higher concentration (10^{-4}). Increased cysteine synthesis associated with heavy metals, appears to be a necessary response for biosynthesis of GSH and the other ligands involved in metal binding. The authors suggest the use of OASTL enzymatic assay in *Scorpiurum circinatum* as one of the used bioindicators of some heavy metals.

METALLOTHIONEINS FROM YEASTS TO MAMMALS: PROTEINS STILL IN SEARCH FOR A FUNCTION

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Metallothioneins (MTs) are low molecular weight proteins characterized by a high cysteine (Cys) content and a high affinity for metals, such as Zn, Cu and Cd. Despite MTs were discovered 5 decades ago the true function of MTs is still elusive. Some authors believe that MTs are multifunctional proteins whose duties range from essential metal buffering, non essential metal detoxification, free radicals scavenging to signal transduction. Here we will discuss the diversity of MTs and their link with some pathologies which are of relevance in medicine, e.g. cancer, diabetes and neurodegenerative processes. An overview of MT sequences along different *Phyla* evidences a lack of homology, e.g. in the yeast *Saccharomyces cerevisiae*, the isoform Crs5 containing 19 Cys was more similar to MTs of higher eukaryotes than the isoform Cup1 with 12 Cys. Cup1 may encapsulate up to 8 Cu (I) digonally and trigonally coordinated with a stable Cu4S6 cluster. Also in the fruit flee *Drosophyla melanogaster* MT is related to Cu metabolism whereas in the Roman snail *Helix pomatia* a CdMT and a CuMT were present. In the sea urchin *Strongylocentrotus purpuratus* the main characteristic was the inversion of the two clusters. Most data are related to mammals MTs which consist of four subfamilies designated MT1 — MT4. MT-3 is expressed predominantly in brain and MT-4 in differentiating stratified squamous epithelial cells. In wild animals MTs are studied mostly for their ecotoxicological significance whereas in humans, pets and animal models they are studied for medical application. Increased levels of MTmRNAs and the related MT isoforms have been reported in various human cancers while *MTI* and *MTII* genes are downregulated in other tumors. MT is increased in cells surrounding Alzheimer's plaques and is connected with Parkinson disease. It has been postulated that in prions the conversion of PrPC to PrPSc may deregulate Zn homeostasis mediated by MT.

ENHANCED APPROACHES OF METABOLIC PATHWAYS OF Mn- AND Fe SPECIES IN SPRAGUE-DAWLEY RATS EXPOSED TO MnCl2·4H2O (I.V./I.T.)

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Chronic Mn exposure leads to Mn accumulation in the basal ganglia, damaged neurons and finally to Mn dependent Parkinsonism, called «manganism». However, the exact mechanism, how Mn can enter the brain without using the transferrin-receptor mediated transport, is still unknown. Excessive Mn load causes an overload of the native Mn transporters (transferrin, albumin). Thus, excess inorganic Mn and low molecular mass (LMM) Mn species (above all Mn-citrate) apparently cross the blood-brain barrier unimpeded and accumulate in the brain. Fe depletion is discussed to facilitate manganism as Fe is the main competitor in Mn species formation. This paper reports about Mn- and Fe species in unexposed and exposed Sprague-dawley rats (single i.v. injection or i.t. instillation of up to 1 mg Mn per kg body weight, 4 d incubation). The comparison of Mn species from unexposed/exposed rats helps to understand Mn species homeostasis. N_{2liq} (homogenization, storage) and inert Ar gas (extraction) were used for sample preparation. Size exclusion chromatography coupled on-line to inductively coupled plasma — dynamic reaction cell - mass spectrometry (SEC-ICP-DRC-MS) was used for speciation analysis of labile Mn- and Fe species, whilst capillary electrophoresis (CE) — ICP-DRC-MS represents the second analytical approach with superior separation potential. The results showed significant higher Mn levels in the sera, brain-, kidney- and muscle tissue of exposed animals with high molecular mass (HMM) organic Mn species at 80—160 kDa (e.g. transferrin) and probably harmful LMM Mn species in serum (600 Da), brain (0.7—4 kDa) and kidney (0.7—4 kDa). These findings may be discussed due to a chemical equilibrium between Mn species. The relevance of metallothionein in Mn homeostasis has to be discussed. To date, the specific transport mechanism of LMM Mn species into the brain is unknown. Our results suggest that excess ionic Mn and formation of Mn-citrate facilitates neuronal Mn accumulation.

RELATION OF MIDKINE AND HYPOXIA INDUCIBLE FACTOR-1 WITH CADMIUM EXPOSURE IN HUMAN HEPATOCYTE CELL LINE IN NORMOXIC AND HYPOXIC CONDITIONS

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AIM AND BACKGROUND: Cadmium (Cd) is well known toxic heavy metal, as a pollutant of air and water and an increasing public health concern. Inhalation of Cd fumes or dust is the primary cause of Cd exposure. Cd accumulates in the human body especially in liver and kidney. It is shown that Cd blocks DNA binding of hypoxia inducible factor-1α (HIF-1α) and its activation under hypoxia, and suppresses erythropoietin production in hypoxic Hep3B cells. Midkine (MK) is a retinoic acid-responsive, heparin binding growth factor that promotes cell growth, cell migration and inflammation. On pulmonary vascular remodelling study suggested that HIF-1α enhances the transcription of MK viaacting on HIF-1α regulatory elements located in the MK gene promoter. The present study was focused to evaluate the HIF-1α mRNA expression levels in Hep3B cell line in Cd toxicity model and its relationship with midkine level in normoxia and hypoxia. METHODS: Cell proliferation measured by MTT in different doses (0.5—50 μM) at the 2-24-48th hours. MK levels were measured by ELISA and HIF-1 α mRNA expressions were analyzed by RT-PCR. RESULTS: We found decreased cell number by dose and time dependent manner in Cd treated groups in both conditions. Cd induces MK secretion at lower doses whereas it depresses it at higher doses. Hypoxia decreased MK secretion in both hypoxia and normoxia ($p < 0.01$). Cd toxicity inhibits HIF-1α expression in Hep3B cells ($p < 0.05$). CONCLUSION: Our results showed that HIF-1α expression inhibited by Cd application in Hep3B cells. Midkine expression is not correlated with HIF-1α expression in hepatocytes. Further studies might be explanatory for evaluation of role of HIF-1α expression and midkine under normal and hypoxic conditions.

BIOCHEMICAL MECHANISMS OF DEVELOPMENT OF CADMIUM-NITRITE INTOXICATION IN CONDITIONS OF EXPERIMENT

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The problem of chemical pollution of the environment and xenobiotics influence on the human health has been focus of modern medical and biologic sciences. The most common pollutants are heavy metals compounds nitrates and nitrites. The problem of soil and waters pollution is of current interest not only for Ukraine. According to WHO's data most of the world's population live on the territories exposed to harmful chemical compounds causing the development of ecological pathologies. Therefore, the investigation of essential and toxic chemical elements level in the sources of drinking water of the Precarpathian region was the first stage of our research. Obtained results have shown that water of different geographic zones of the Precarpathian region is characterized by low contents of the essential micronutrients, namely chrome, copper, and iron. Besides, high level of cadmium has been detected in waters of the flat zone were it was 2.5 times as high as admissible concentrations. Investigating the level of nitrates we have recorded the increase of nitrates contents in drinking water of the flat zone versus the mountain one. These results have become the ground for experimental investigations of biochemical mechanisms underlying the harmful effect of these xenobiotics. Blood cells, liver, kidneys, and bone tissue are major target organs for nitrites and cadmium. Erythrocytes are one of the first body cells to react with xenobiotics and to play important role in homeostasis maintenance; investigation of the structural-and-functional state of these cells is of immediate interest. Obtained by us results have shown that both in conditions of cadmium intoxication and in combined action of cadmium and nitrites the disturbance of ligand haemoglobin forms is observed. We have also recorded decrease by 68% of haemoglobin level and quadruplication of methaemoglobin, twofold increase of sulfhaemoglobin, and increase by 32% of dyshaemoglobins. These changes of haemoglobin ligands were accompanied by the decrease of oxygen blood volume, hypoxia development, and oxidative stress. In such conditions the investigation of energy metabolism state in experimental animals is very important. We performed the investigation of metabolites of energy metabolism and activity of Na^+, K^+-activating Mg^{2+}-dependant ATPase determining to a great extent the

effectiveness of oxidative phosphorylation processes. Analysis of the obtained data has shown that at early periods of intoxication activation of anaerobic glucose oxidation occurs. It is accompanied by the increase of lactate/pyruvate correlation to 117 (20 in healthy animals) and the simultaneous decrease of activity of Na^+, K^+, Mg^{2+}-ATPase. Besides, the concentration of magnesium in animals' blood was threefold. These results show the disturbance of the experimental animals power supply being very important for all organs and tissues functioning. The next stage of our research was the investigation of metabolic processes in the bone tissue. Obtained results show the disturbance of potassium-phosphorous metabolism accompanied by the decrease of level of general calcium in blood plasma by 27%, ionized calcium — by 12% with the simultaneous increase of non-organic phosphate by 25% at late period of intoxication. The investigation of macro- and micronutrients contents in femoral bones of the affected animals has shown the increase of magnesium level by 19.5% on the background of the decrease of calcium by 13.8%, zinc — by 45% comparing with intact animals. Analysis of theses elements level in jaw bones has shown that contents of calcium was twice as low, the contents of magnesium was 2.5 times and magnesium 3 times as high on the 28th day of intoxication. Thus, performed investigation has made it possible to establish that cadmium-nitrite intoxication is accompanied by the disturbance of mineral contents of the bone tissue, the development of hypoxia and hypopower state in the experimental animal's organism.

ASSESSMENT OF EXPOSURE TO TOXIC/POTENTIALLY TOXIC ELEMENTS IN WOMEN OF FERTILE AGE WITH DIFFERENT NUTRITIONAL STATUS IN ONE SELECTED DISTRICT OF MOSCOW USING NUCLEAR AND RELATED ANALYTICAL TECHNIQUES

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The impact of chronic heavy metal exposure on nutritional status has been controversial. Relatively few studies have been conducted to assess the risk of undernourishment from exposure to toxic elements at low levels, taking into account potential confounding factors. The overall objective of our case-control study is to fill in this gap based on examination of a cohort of Moscow women aged 20—45 years. The hospital-based case-control study was performed in two districts of Moscow with different levels of heavy metal pollution. Detailed lifestyle, occupational and health status data were collected from 30 «undernourished» women-cases (BMI <18.5 kg/m^2) and 30 «normal» women-controls (BMI: 18.5—24.0 kg/m^2) based on their body mass index. Controls were frequency-matched to cases on age, smoking, residential area, educational level, marital status, and income. Eligible cases and controls were selected among women attending local (district) outpatients clinics, without clinically significant chronic and infection diseases, mental disorders, and history of malignancy during the last 5 years. The list of determined elements includes: Na, Cl, K, Sc, Cr, Fe, Co, Zn, As, Se, Br, Rb, Cd, Sb, I, Au, Hg, and Pb. Some of these elements are either known to be toxic or potentially toxic at higher concentrations, and the rest ones could be useful for general characterization of blood of examined patients. Environmental assessment was based on the levels of Pb, Sb, and Co in blood samples using neutron activation analysis and atomic absorption spectrometry. Multiple logistic regression analysis was applied with adjustment for confounders. Overall mean Pb, Sb and Co levels in blood of women were 14.6, 5.3, and 9.5 μg/l, which can be considered as low levels. Cases and controls differed significantly in mean concentration levels of Pb (16.8 vs 12.3 μg/l), Sb (4.7 vs 2.5 μg/l), and Co (10.9 vs 8.2 μg/l). Multiple logistic regression analysis showed that Sb exposure was significantly and negatively associated with the risk of undernourishment (Odds Ratio=1.56, and 95% Confidence Interval: 1.08—2.25; $p < 0.02$). The risk was less apparent for Pb (OR=1.09; and 95% CI: 0.98—1.21; $p < 0.12$); and for Co (OR=1.24; and 95% CI: 0.85—1.79; $p < 0.23$). Approximately 34% of the variance in BMI can be attributed to these exposures, to the concentrations of Fe in blood and to the type of residential area. The findings from this study suggest that chronic exposure to low levels of Sb, Co and Pb may slightly increase the risk of undernourishment in women.

This study was carried out in the framework of the IAEA Co-ordinated Research Programme (CRP) on exposure to toxic and potentially toxic elements in women of childbearing age in developing countries (Research Contract No. 13249/R0).

SELENIUM AND LIPID PROFILE IN A HOSPITAL BASED WORKING POPULATION

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OBJECTIVE: Selenium is an essential trace element that is part of antioxidant enzymes. The aim of this study was to assess the association between serum selenium and lipid profile in a volunteer employee population of the Hospital Clinico San Carlos in Madrid. MATERIAL AND METHODS: 70 subjects (14 men and 56 women) participated in the study. Dependent variable: serum selenium. Independent variables: cholesterol, HDL, colesterol/HDL, LDL and triglycerides in serum. The subjects were divided into: Group I: Selenium < 70 μg/L and Group II: Selenium ≥ 70 μg/L. The concentration of selenium in serum was measured by electrothermal atomic absorption spectrometry with Zeeman background correction on a Perkin-Elmer AAnalyst 800 spectrometer. The cholesterol, HDL and triglycerides were analyzed using an Olympus AU5430 Olympus autosampler. LDL and the cholesterol/HDL quotient were calculated. The SPSS 15.0 statistical package was used to process the data. RESULTS: Selenium (μg/L): mean = 81.24 (SD = 10.87). Cholesterol (mg/dL): mean = 212.74 (SD = 34.33). HDL (mg/dL): mean = 65.79 (SD = 15.34). Cholesterol/HDL: mean = 3.36 (SD = 0.76). LDL (mg/dL): mean = 130.63 (SD = 29.03). Triglycerides (mg/dL): mean = 73.50 (IQR = 53.75—99.50). A statistically significant correlation ($p < 0.001$) was observed between selenium and serum cholesterol ($r = 0.452$) and between selenium and LDL ($r = 0.475$, $p < 0.001$). The comparison of means shows a statistically significant difference ($p < 0.05$) in cholesterol between group I (192.92) and group II (216.84) and in LDL ($p = 0{,}007$) between group I (109.27) and group II (134.75). CONCLUSIONS: The results suggest that when subjects have normal-high selenium concentrations (70—120 μg/L) they present an atherogenic lipid profile. More studies will be necessary in order to confirm these findings in the Spanish population, with a suboptimal intake of selenium due to low soil content of selenium, as well as to be able to establish possible causality.

BLOOD LEAD AND CADMIUM LEVELS IN A SIX HOSPITAL EMPLOYEE POPULATION. PESA STUDY 2009

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BACKGROUND: Exposure to lead and cadmium is a public health problem due to the broad exposure to these toxic substances among the general population. The objective of this study is to determine blood lead and cadmium concentrations in a hospital employee population from six different cities in Spain, and to identify associated factors. MATERIAL AND METHODS: A cross-sectional study was carried out on 951 subjects (231 men and 720 women). We studied the following variables (PESA QUESTIONNAIRE®): socio-demographics, daily habits, occupational exposure, housing characteristics, exposure to traffic, use of kitchen utensils and exposure during leisure time. Blood lead and cadmium concentration were determined by electrothermal atomic absorption spectrometry with Zeeman background correction on a Perkin-Elmer AAnalyst 800 spectrometer. The statistical package SPSS 15.0 was used for data analysis. RESULTS: Mean overall blood lead and cadmium concentrations were 1.6 μg/dL (IQR: 0.9—2.7) and 0.2 μg/L (IQR: 0.1—0.4). Mean lead in post-menopausal women was higher (2.6 μg/dL) than in pre-menopausal women (1.1 μg/dL) ($p < 0.001$). Mean lead in men was higher (2.0 μg/dL) than in women (1.5 μg/dL) ($p < 0.001$) and mean lead in users of earthenware pots was higher (2.1 μg/dL) than in non-users (1.5 μg/dL) ($p = 0.020$). After setting a predictive logistic regression model, we observed that age, menopause, housing age, and cooking in earthenware pots were independent factors associated with blood lead concentrations above 2 μg/dL. Mean cadmium concentrations in subjects who smoke (0.70 μg/L) were higher than in non-smokers (0.13 μg/L) ($p < 0.001$). CONCLUSIONS: Lead and cadmium blood levels have shown a substantial decline, compared with data from previous studies in Spain. As no safe threshold for lead and cadmium has yet been identified, biomonitoring of these toxic heavy metals in the general population, especially among the vulnerable groups, is required.

STUDY OF BIOCONCENTRATION AND VARIATIONS IN HEMATOLOGICAL PARAMETERS IN TILAPIA *(OREOCHROMIS NILOTICUS)* FED WITH DIET CONTAMINATED WITH METHYLMERCURY

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Aquaculture is a production system that is experiencing one of the fastest growths worldwide, specially in developing countries. Brazil contributes with 10% of the production of Latin America. The culture of tilapia *(Oreochromis niloticus)* is developing quickly and is one of the most important among the aquaculture activities in tropical and sub-tropical countries. Mercury contamination in fish can have several consequences, such as: inhibition of metabolic processes, low fecundity, decrease in survival rate and alterations in cell defence capacity. Fish can incorporate mercury by direct contact with contaminated water, by branchial breathing and by absorption through the digestive tract and in most aquatic organisms methylmercury is accumulated more efficiently than inorganic mercury. In the present paper, the bioconcentration of methylmercury in organs, as well the variations in haematological parameters were studied in tilapia fish *(Oreochromis niloticus)* fed with diet contaminated with methylmercury. The diets were prepared by spraying the fish feed with methylmercury chloride solutions of two different concentrations. Two groups of fish were fed with contaminated diets (Hg concentration 1 = 1.03 ± 0.15 μg g^{-1} and Hg concentration 2 = 8.27 ± 1.25 μg g^{-1}) and one group was fed with diet not contaminated with methylmercury (control group).The experiment was conducted for a period of forty two days, and periodically the haematological parameters of the fish were analyzed, as well as the hepato and splenossomatic relations and the bioaccumulation of Hg in muscle, liver, kidney, spleen and brain. Methylmercury was determined as Hg by CV AAS. Methylmercury was bioaccumulated mainly in the kidney and liver and the accumulation rank was: liver > kidney > brain > muscle > spleen. As to the haematological parameters, it was found for instance that the leucocytes and lymphocytes presented a significant mean decrease after forty two days of experiment, for both concentrations of methylmercury, as compared to controls.

ENVIRONMENTAL SILVER POPULATION EXPOSURE, OVEREXPOSURE, AND TOXICITY

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OBJECTIVE: Silver is a non-essential member of the body elementome that may induce human poisoning in high doses, i.e., the medical disease condition known as *«argyrosis»*. Silver has strong antibacterial properties and has been used in many home and medical appliances now available at the market. However, and except for the occupational setting, the data on environmental population silver exposure and possible health effects of overexposure and toxicity are scarce and inconclusive. The aim of this study was to investigate the level of hair silver in a random segment of the occupationally non-exposed population. METHODS: The study was conducted by strict adherence to the Declaration of Helsinki principles on human subject research, and approved by the appropriate ethic committee. Hair was collected from 87 men and 126 women (n = 213), and analyzed for its Ag content by the ICP-MS at the CBM, Moscow. RESULTS: The observed median concentration of silver in the hair was 0.065 μg/g Ag. Considering the pattern of frequency distribution of silver in the hair, tentative limits were proposed for the normal silver in the hair of up to 0.650 μg/g Ag, an increased silver exposure to be from 0.650 to 1.900 μg/g Ag, and a silver toxicity due to internal contamination following oral ingestion if its concentration in the hair exceeded 1.900 μg/g Ag. CONCLUSION: When assessing the body silver status after oral ingestion hair has an advantage over the blood, since hair accumulates grossly more silver than blood due to its high sulphur content and unidirectional growth what makes it a «memory tissue», whereas the silver in the blood dynamically equilibrate between and within the different biochemical compartments of the body all the time.

CHEMICAL ELEMENTS CONTENT IN DIFFERENT BRAIN STRUCTURES IN CADMIUM AND ETHANOL TREATED RATS

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Effect of simultaneous cadmium, ethanol influence on metabolism of chemical elements in different structures of brain (hippocampus, cerebellum, white substance, cortex) was studied on experimental model. Male Wistar rats (n = 30) of 2 months old were divided in 3 groups. Group 1 consumed 15% ethanol and water. Group 2 also consumed 15% ethanol, but additionally took cadmium sulphate with diet in dosage 47.1 mg/day per animal. Group 3 was a control, consumed usual diet and water. The experiment continued 8 weeks. After this period animals were decapitated, brain structures were sampled and subjected to multielement ICP-AES/ICP-MS analysis in ANO CBM, Moscow, Russia. It was found that ethanol mostly influenced brain cortex, where significant increase of Mg, Na, As, Cr, Cu, Fe, Li, Mn, Se, V, Zn, Cd was detected. The ethanol/cadmium combined administration mostly affected cerebellum and white substance. In cerebellum an increase of K, Co, Fe, Si, V, Zn, B, Cd, Al content was found; in white substance — an increase of As, Co, Cr, Fe, Mn, V, Cd; in cortex — an increase of Co, Fe, B, Cd, Al. In hippocampus, the changes were differently directed: content of As, Cr, Se, V, Cd became increased while content of Mg, P, Si, Sn became decreased. Thus, different brain structures were found to possess selective accumulation of certain chemical elements.

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SYSTEM ANALYSES OF HAIR ELEMENTAL PROFILE IN STUDENTS OF SURGUT STATE PEDAGOGICAL UNIVERSITY

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OBJECTIVES: ICP-MS and ISP-OES methods inspection of 106 hair' tests in students of Surgut State Pedagogical University was lead. Obtained data estimated from a position of the traditional stochastic approach and methods of identification of parameters attractors in multivariate phase space of conditions. METHODS: Content of chemical elements in hair was determined in 106 students of Surgut State Pedagogical University 17—20 years old. RESULTS: High occurrence of complex disturbances in elemental status was found, namely a decreased content of selenium: essential trace elements in hair (in males — 0.47 ± 0.02 ppm, in females — 0.03 ± 0.04, $p < 0.001$) and increased levels of other ones: iron (in males — 40.9 ± 6.9, in females — 25.2 ± 3.5, $p < 0.05$), magnesium (in males — 467.8 ± 6.9 ppm, in females — 1855.8 ± 173.8, $p < 0.001$). Distinct sex-dependent differences in content of some chemical elements in hair were established: higher levels of iron, sodium and phosphorus in males and higher calcium, magnesium and copper in females. Levels of some toxic elements in males (cadmium, lead) were found to be permanently higher as compared with average data from Russia. Comparative group have the different parameters of attractors in multivariate phase space of conditions.

ELEMENTOME OF *HIRUDO MEDICINALIS*

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Leech is a sole representative of the fauna in the state register of medical products of the Russian Federation. *Hirudo medicinalis* is the only one from 400 known kinds of leech which is resolved to medical application. By this time more than 100 biologically active substances were allocated from the secret of a *Hirudo medicinalis*. These substances have organic nature and possess anticoagulant action in particular. In literature there is almost no information on biogenic and trace elements which could render therapeutic effect, being presented in organism of *Hirudo medicinalis* in ionic form as a part of biologically active coordination compounds. In the report results of research of the nature and content s- p- and d-elements in *Hirudo medicinalis* and prognostication of mechanisms of their biological activity are informed. *Hirudo medicinalis* which were realised by the International Centre of Medical Leech (Moscow) were analyzed by ISP-MS, ELAN DRC II. Initial stage included: devitalisation of analyzed object by freezing, subsequent drying to constant weight at 105°C, microwave mineralization with a mix of concentrated nitric acid and peroxide hydrogen in closed systems. According to the standard classification results of analysis have been grouped as follows: macroelements ($\omega > 10^{-2}\%$) — Na > P > K > Mg > Fe > Cl > Br; microelements ($10^{-5}\% < \omega < 10^{-2}\%$) — Si > Zn > Cu > Cr > Ag > Ni > Ca > Al > Sr > Mn > Se > Pb > Mo > As > B > V > Rb > Li > Zr > Sn > Co > I; ultramicroelements ($\omega < 10^{-5}\%$) — Sb > Be > Ba > Ce > La > Eu > Y > Nb > Ge > Au > Tb > Bi > Hf > Ta > Tl > Ho > U > Ir > Os > Th > W. Not only essential and conditional essential elements have entered into a group of microelements, but also trace elements such as Ag, Al, Pb, As, B, Rb, Li, Zr, Sn. Their content considerably exceeds norm for human's blood plasma that assumes possible participation in biogene processes in the organism of the patient. The received results confirm the theory of academician V.I.Vernadsky about participation of all known elements in equilibrium processes of biological systems.

ASSESSMENT OF TRACE METAL CONTAMINATION OF ANKARA WATERCOURSE AND DRINKING WATER SPRINGS IN AYAŞ

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In this study the dissolved concentrations of five trace elements, i.e. lead, copper, zinc, cadmium and cobalt were determined both in drinking water samples collected from various natural water springs in Ayaş and in water samples collected from five locations of Ankara watercourse in which water is polluted by the discharge of municipal and industrial wastewaters. Concentrations of metals in the water samples were determined by flame atomic absorption spectrometry and varied between water samples and between sampling sites. The range of zinc concentration determined for drinking water samples was 0.091—0.112 mg/L. The concentrations of the remaining four metals were under the limit of determination. Overall, the quality of water samples taken from the water springs in Ayaş was first quality based on zinc content. It was found that Zn was 0.075—0.119, Cu 0.051—0.60 and Cd 0.06 mg/L in water samples taken from Ankara watercourse. The water quality of Ankara Watercourse was second quality for Cu content.

DEPLETED URANIUM IN HAIR BY ISOTOPE RATIO QUADRUPOLE INDUCTIVELY COUPLED PLASMA MASS SPECTROMETRY

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Depleted uranium (DU) is a by-product of the enrichment process of the uranium isotope employed in the production of fuel for nuclear reactors. DU has been used for military purposes in the last years' conflicts because of its high density, great availability and low cost. Although the radioactivity of DU is weak (lower than that of natural U), the presence of depleted uranium in the environment and its possible transfer to humans are matters of concern because DU poses both radiological and chemical risks to human health. Human biological fluids, like urine and blood were mostly sampled to ascertain the level of uranium and assess a possible exposure. As an alternative, human hair can be considered a good indicator for monitoring purposes for its ability of accumulating a number of chemical elements. Specimens of human hair are easy to obtain with several advantages in transportation, handling and analysis. The measurement of the isotopic composition and the low level of DU in hair require the employment of a very sensitive and precise analytical technique. Furthermore, the content of DU can be masked by the presence of a background level of NU. In this study, a method to determine DU in hair by Isotope Ratio ICP-MS was developed. The method was in-house validated at three different levels of DU concentration (50, 500 and 1000 ng/l) according to common standards guidelines. A number of validation parameters was considered and evaluated, namely, working concentration range, specificity/selectivity, trueness through recovery, within-laboratory reproducibility and stability. The limit of quantification of the method for DU in hair was 7.21 μg/kg with within-laboratory reproducibility, in terms of variation coefficient, of 16.8%, 6.1% and 5.5% for the three levels of concentration, respectively. Finally, a novel analytical approach was undertaken by using specificity studies to distinguish DU contamination in hair containing different background levels of NU.

EFFECT OF INHALATION EXPOSURE OF SILICON DIOXIDE ON RESPIRATORY AND BIOCHEMICAL VARIABLES IN RATS

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Human Exposure to silica is of great occupational concern. Occupational exposure to silica dust has been increasing the possible risk of varieties of pathologies, from acute lung inflammation to silicosis, in addition to autoimmune disorders and lung cancer. The present study has carried out to know the effect of repeated exposure of silica on various respiratory and biochemical parameters. Male Albino rats (200—250 g) were exposed to silicon dioxide via whole body inhalation exposure at a dose of 200 mg/m^3, 6 hrs/day, 5 days/week for 4 weeks and the control animals were exposed to fresh air for the same duration. Our finding revealed that inhalation exposure of silica caused increase in respiratory frequency and altered other respiratory parameters. The inhalation of silica caused the elevation of blood biochemical variables such as angiotensin converting enzyme, lactate dehydrogenase, alkaline phosphatase and serum transaminases. A slight elevation was also found in lipid peroxidation,protein contents, while a significant fall was observed in the activities of catalase in the exposed animals as compare to control.

THERAPEUTIC EFFECT OF NAC AND GSH ON LEAD INDUCED ALTERATION IN RATS

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Lead commonly used in industrialized countries, adversely affects human physiological and biochemical functions. Oxidative stress and neurotoxicity has been postulated as one of the mechanism for lead toxicity. Hence, in assessing the protective effect of reduced glutathione (GSH) and NAC on lead toxicity, the therapeutic efficacy of NAC and GSH was studied in the present study, their ability to restore alter haematopoietic hepatic, renal, brain and other biochemical variables indicative of oxidative stress in male albino rats were also investigated. Lead acetate (50 mg/kg, *i.p.*, for 3 days) was administered to induce lead toxicity in rats. Chelating agents NAC (50 mg/kg, p.o.) and GSH (1 mg/kg, *i.p.*) were given for three days 24h after the toxicant administration and animals were sacrificed 24 hours after the last treatment. An increase in the activities of AST, ALT, uric acid, urea, cholesterol, triglyceride in serum, while a decrease in haemoglobin content, was noted. Significant rise in malonaldehyde level whereas slightly change in GSH level. Treatment provided significant recovery in restoring the altered lead sensitive biochemical indices like blood δ-aminolevulinic acid dehydratase (ALAD), δ-aminolevulinic acid (ALA) and decreasing lead concentration in blood and soft tissues. Treatment with chelating agent NAC and GSH ameliorate lead toxicity, however NAC was found to be more effective in combating free radical induced injury.

MODULATION OF HEAVY METAL-INDUCED DYSFUNCTION OF RAT LIVER MITOCHONDRIA BY SUBSTANCES AFFECTING THE PERMEABILITY TRANSITION OR RESPIRATORY CHAIN COMPLEXES

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Cadmium, mercury and copper are very toxic environmental pollutants that exert their toxic effects as cations by targeting mitochondria. To further underscore molecular mechanism(s) underlying the heavy metal-induced mitochondrial dysfunction we continued to compare action of Cd^{2+}, Hg^{2+} and Cu^{2+} using a simple and convenient *in vitro* model, namely isolated rat liver mitochondria incubated in assay media of different ionic content and energized by respiratory substrates, glutamate plus malate for complex I, succinate plus rotenone for complex II, and ascorbate plus tetramethylphenylenediamine for complex IV. With the help of various selective electrodes, fluorescent probes, isotope and spectrophotofluorometric techniques, significant differences were found in the modulating action of various substances affecting the activity of these respiratory chain complexes or permeability transition pore effectors on the mitochondrial functions disturbed by the heavy metals, including clear-cut substrate specificity of many effects of these cations. Sequence of events manifested in the mitochondrial dysfunction produced by the metals under test was elucidated. The involvement of the respiratory chain and the mitochondrial Ca^{2+} uniporter in the mitochondrial membrane permeabilization induced by the heavy metal ions is discussed.

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THE PROBLEM OF TIME IN THE TRACE ELEMENTS TOXICOLOGY

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The factor of time is the basic one in the trace elements toxicology. It is manifesting in cumulative properties of their toxic action, and also plays the dominant role in such fundamental relations as «dose — time» and «time — effect». But many aspects of the problem of time in modern toxicology of metals remain insufficiently studied. Therefore the purpose of this work was the complex estimation of the factor of time role in metalopathies development. The influence of typical heavy metals (Cd, Hg, Pb) in doses 0,1—1,0 μmol/l on cell morphology, functions and metabolism was studied both in the experiments *in vivo* on white mice, rats at acute, subacute and subchronic exposition and in vitro on the rat thin intestine segments, rat, rabbit and sheep erythrocytes. The contents of toxic and essential metals (Cd, Co, Cu, Fe, Hg, Mn, Ni, Pb, Sb, Sn, Zn) was defined by methods of atomic emission, atomic absorptive and cold vapour analysis on EMAS-200, AAS-3, «Saturn-3M», «Julia-2M» devices. Membrane bound, mitochondrial, lysosomal and cytoplasm marker enzymes activity, oxidative stress and apoptosis system components were measured by means of biochemical sets with spectrophotometers (SF-46), gas-chromatograph («Christall-lux-4000»), immunoenzyme (RT-2100C «Raito» and «Aution mini AM-4290») and luminescent (CM2203 «Solar») analysis. Morphological researches included light, faze-contrast and electronic microscopy. The carried out researches have shown, that time factor plays defining role in processes of binding, transport, accumulation, biotransformation and elimination of trace elements. There were allocated the limiting on time practically in all 5 of metals transport stages and their secondary mobilization. Quantitative toxicokinetic parameters of these processes which take an essential role in «omic» characteristics of toxicogenesis mechanisms are received and can be used as the basis for diagnostics, treatment and prognosis of metalopathies outcomes and consequences.

INFLUENCE OF EXOGENEOUS NUTRITIONAL SUPPLEMENTATION ON ACUTE LEAD POISIONING IN RATS

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The objective of this study was to evaluate the role of nutritional supplementation on lead-induced toxicity. Differentiation of micronutrients and heavy metals pose an inherent problem due to certain common properties shared by them. With this approach to the problem of heavy metal toxicity, in the present study two groups of male albino rats, one group supplemented exogenously with trace elements and micronutrients and other group (undernourished) without mineral supplements were used. Group I was subjected to acute lead exposure at the dose of 50 mg/kg *i.p.* for three days while second group received lead along with concurrent nutritional supplementation i.e. zinc, selenium, iron and calcium orally at the dose of 10, 0.5, 20 and 50 mg/kg *b.w.* respectively. After exposure blood and tissue lead were determined by atomic absorption spectroscopy, markers of oxidative stress and other biochemical variables were monitored. Exposure to lead produced a significant inhibition of δ-aminolevulinic acid dehydratase (ALAD) activity and reduced haemoglobin and haematocrit in lead control suggesting altered haem synthesis pathway. A marked reduction in GSH content and AChE activity while significant elevation in AST, ALT, ALAS, urea, uric acid, triglycerides and cholesterol was observed in undernourished rats. Results of the study showed a very high statistically significant increase in the lead levels in the undernourished subjects compared to the well-nourished subjects. Nutritional management of lead poisoning is of importance since essential elements and toxic heavy metals may interact to minimize the absorption of lead.

AMELIORATION OF ALUMINIUM INDUCED TOXICITY BY S-ALLYL-CYSTEINES

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S-allyl-cysteines (SAC) are a bioactive and bioavailable component of garlic. It is an organosulphur compound which regulates the thiol status of the cell and scavenges free radicals and work as an antioxidant. Aluminium is a trivalent cation found in its ionic form in most kinds of animal tissues and in natural waters everywhere. It is a potent neurotoxin and has been associated with Alzheimer's disease causality for decades. The aim of the study was to demonstrate the protective effect of SAC against aluminium-induced toxicity in rat model. Animals received aluminium nitrate 32.5 mg (1/2 LD50 of $Al(NO_3)_3$ i.p.) for the induction of toxicity. Different doses of SAC (25, 50 and 100 mg/kg) were given for 3 days after 24 h of Al toxicity. The activity of AChE was inhibited in all the parts of brain after Al intoxication. Significant rise were observed in the activities of serum LDH, AST and ALT whereas serum protein was found to be declined after toxicant exposure. The activity of δ-aminolevulinic acid dehydratase in blood and δ-aminolevulinic acid synthetase (ALAS) in brain was decreased after Al exposure. Al induced significant increase in the values of cholesterol, triglyceride, creatinine and urea level in serum. TBARS level was significantly higher and total glutathione content were significantly lower during toxicity. Total cholesterol and esterified cholesterol in liver, kidney and brain were increased after Al exposure. The protection afforded by SAC may be due to scavenging of free radicals produced by Al. Histopathological changes in liver, kidney and brain were also recouped with the therapy. In conclusion, SAC demonstrated amelioration against aluminium-induced cognitive dysfunction and oxidative damage.

INTERVENTION OF TRACE ELEMENTS AND CHELATORS AGAINST METAL TOXICITY

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There is growing evidence that micronutrient and trace element intake has a significant effect on the toxicity caused by various heavy metals. This paper examines the effect of micronutrient and trace elements: zinc, selenium, iron, magnesium and calcium on the toxicity of few nonessential metals: beryllium and aluminium. Micronutrients can affect toxicity of metals by interacting with the metal at its primary site of action. Trace metal administration together with chelating agents decreased the uptake of these toxic metals in soft tissues and reduced metal induced biochemical, histological and ultra structural alterations. Micronutrients interact with toxic metals at several points in the body: absorption and excretion of toxic metals; transport of metals in the body; binding to target proteins; metabolism and sequestration of toxic metals and finally, in secondary mechanisms of toxicity such as oxidative stress. Therefore, intervention of trace elements with chelators should be preferred to provide the best defence against metal intoxications.

THE INFLUENCE OF INTRAMUSCULAR INJECTIONS OF COPPER NANOPARTICLES TYPE CU10X ON THE RATS' LIVER AND SPLEEN ELEMENTAL CONTENT

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INTRODUCTION. Beneficial and toxic effects of metal nanoparticles are one, of interesting problems of modern biology. Nanoparticles of essential metals can influence on different important function of living organism through its synergistic, antagonistic or other effects on macro - and TE metabolism. AIM: To investigate the influence of i.m. administration of copper nanoparticles type Cu10x (CuNP) on the liver and spleen elemental content. METHODS: 60 Wistar male rats (150—180 g) were treated by CuNP suspension i.m. (2.0 mg/kg body weight) once a week during 12 weeks of experiment. The rats were decapitated in day after 1st injection (Gr 1), (Gr 2), 7 days after 2nd (Gr 3), 7 days after 3rd (Gr 4) and 7 days after 12th injection (Gr 5). In control group the distilled water in the same days was im injected. Immunogystochmical investigations were provided of monoclonal antibodies (Ki-67, Caspase-3, Bcl-2) and Bio Genex Super Sensitive Detection System, USA, and macro and trace elements were determined by ICP-MS (ELAN 9000, Perkin-Elmer, USA). RESULTS: In rat spleen the gradually increasing of Cu Content since Gr 1 till Gr 3 was observed. The Fe, Zn, Se, I, Mn content was very sensitive to CuNP i.m administration. The controversial changes in elemental content were obtained. In Gr 2 I, Se, Ni, Mn, Fe, As, Cr, Cu content was elevated, for Gr 3, Gr 4, the accumulation of essential of elements was typical. But after long term i.m. injections of CuNP (Gr 5) there was the significant decreasing of majority of elements (excluding B, Ni, V, K, Al) content in the spleen samples. Immunohistochemical tests the modulating influence of CuNp on apoptosis recalled. CONCLUSION: I.m. administration of CuNP significantly deranges the macro- and TE content of the liver and spleen. Long-term (N 12) ingestions of CuNP can produce the secondary deficiencies of majority of essential macro- and trace elements and related pathological processes. ACKNOWLEDGEMENT: Work is supported by grant of the Russian Fund of Fundamental Research № 08-04-13544-ofi_c.

SUBACUTE LEAD POISONING BY USE OF EARTHENWARE JARS

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OBJECTIVE: Blood lead concentrations among the general population have fallen mainly due to the elimination of lead in gasoline. Nevertheless, other sources of exposure still exist. We describe two cases of subacute lead poisoning caused by use of earthenware jars. MATERIAL AND METHODS: CASE 1 — a 60 year old patient. He complains of 4 months of asthenia, lumbar and abdominal pain, constipation, decreased libido and personality changes. After discarding neoplasia, a blood lead test was requested as he had occupational exposure. CASE 2 — a 59 year old hospital employee visiting the laboratory for a hypertension test. The patient presents bradypsychia and complains of personality changes with clear irritability. It is decided to add a blood lead test to the requested analyses. Blood lead was measured by electrothermal atomic absorption spectrometry with Zeeman background correction using a PerkinElmer AAnalyst 800 spectrometer. We administered the PESA® questionnaire to identify the source of exposure. RESULTS: Patient n°1 presented a blood lead concentration of 110 µg/dL. Multiple sources of exposure were identified: occupational, hunter, consumption of homemade wine ([Pb] = 27 µg/dL) and consumption of tomatoes marinated in vinegar and stored in old earthenware casseroles for the last six months. The liquid of the tomatoes was analyzed and a concentration of 550 000 µg/L was obtained, showing that this was the main cause of the lead poisoning. Patient n°2 presented a blood lead concentration of 38.2 µg/dL. The employee habitually consumed olives prepared with vinegar in an old earthenware jar. The liquid of the olives was analyzed and a lead concentration of 4700 µg/L was obtained. CONCLUSIONS: The consumption of pickles and olives in vinegar prepared in old earthenware jars is still an important source of exposure to lead in Spain. It is essential to research sources of exposure to lead in a systematic manner, as evidence of one source does not exclude the existence of others.

STUDY OF BIOLOGICAL ACTIVITY AND D/H RATIO OF WATER WITH THE AID OF CELLULAR BIOSENSOR *SPIROSTOMUM AMBIGUUM*

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Deuterium depleted water — is thoroughly purified water, whose molecules contain the heavy hydrogen isotopes and oxygen in minimum quantities. In literature it has been shown that such water received from snow and relic ice, has favourable influence on plants, animals and the man. OBJECTIVES of the given work are the following: (1) determination of biological activity of samples of deuterium depleted water; (2) determination of optimum D/H ratio; (3) determination of activation energy (E_a) of destruction of cell of S. ambiguum in samples of deuterium depleted water. MATERIALS AND METHODS: for the analysis 8 samples of water with D/H ratio 4, 20, 61, 90, 117, 137 ppm have been used. In each well 100—150 μl of water different D/H ratio were introduced. Furthermore three infusorians *S. ambiguum* were sat out in one well with pipette (diameter of the bill more than 1 mm). The duration of life of cell was calculated as range from the moment of landing to the loss of cell. The loss of cell was established by the immobilization with the absence of contracting reaction to the mechanical irritation. CONCLUSIONS: (1) Biomonitoring of a light water with various D/H ratios has revealed three samples which decreased cell's lifetime in 5 times without changes in Ea. They are samples of water with D/H ratio 4, 20 and 32 ppm. Other samples of water did not show activity concerning test object; (2) proceeding from diagrams dose-response there was optimum correlation D/H — 75—125 ppm; (3) true values of energy of activation of process of ligand-induced destruction of *S. ambiguum* in water with various D/H ratio were defined.

HAIR DISTRIBUTION OF TOXIC METALS IN NOVOSIBIRSK RESIDENTS

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At present, latent health disorders in humans became widespread due to high level of environmental pollution with toxic chemical elements. In this connection, multielement analysis of hair samples from 3602 residents of Novosibirsk city, Russia, was made. Content of 25 biologically important chemical elements was determined by ICP-AES/ICP-MS method in the laboratory of ANO Centre for Biotic Medicine, Moscow, Russia. Excess level of conditionally toxic chemical elements, including heavy metals, was detected: for Pb — in 11.9% of cases, for Cd — in 11.3%, for Al — in 9.6%, for Sn — in 4.5%, for Ti — in 4.2%, for V — in 4.0%, for Ni — in 3.2%, for As — in 2.0%, for Hg — in 1.8% of cases. It is notable that Cd excess takes the 2nd place of prevalence among Novosibirsk residents, being one of the most dangerous environmental pollutants. The main sources of the pollution are industrial plants, thermal power plants, and motor transport.