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NEW APPROACHES TO HYGIENIC REGULATION OF OPTIMAL CONCENTRATIONS OF TOXIC METALS AND ESSENTIAL TRACE ELEMENTS IN HUMAN BIOLOGICAL MEDIA

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Introduction. The article presents approaches to the methodology of normalization of optimal levels of toxic metals and essential trace elements in human biological environments. Currently, the concept of norm is not a constant value due to the heterogeneity of geochemical living conditions, bad habits, diet, age and differences. The application of various analytical methods for the determination of chemical elements has led to significant disagreements in determining the boundaries of their physiological norm in human biological environments.

The aim of the study – to give an ecological and hygienic assessment of the influence of toxic metals and essential microelements (ME) on the formation of optimal levels of their content in biological environments.

Materials and methods of research. The content of toxic metals and essential trace elements was determined in the environment (atmospheric air, drinking water, food) and biological environments of healthy volunteers (hair, whole blood, serum). An optical emission spectrometry with inductively coupled plasma (OES-ICP), questionnaire methods, and mathematical statistics were used to determine the content of toxic metals.

Conclusions. The results of research have shown a close relationship between the chemical composition of air, drinking water, food in the formation of optimal levels of macroelements (MaE) and ME in human biological environments. The content of MaE and ME in the biological media studied in some cases corresponded to the minimum physiological levels (for Pb, Zn, Cd, Mg, Cr, Se), for Mn, Fe, Cu, Ni, Ca the optimal value was found, but for Al, As the content corresponded to the maximum physiological levels. Chemical elements, the concentration of which in biological media was in the range of «g – mg» (for Ca, Mg, K, Na, Fe, Cu, Zn in serum), were within the «conditional norm» when determined by the ECO-ISP method. To identify the risk of imbalance of MaE and ME in the human body, it is necessary to use an integrated approach (simultaneous determination of metal content in several biological media) and apply multi-element analysis methods at both individual and population levels.

Key words: toxic metals, trace elements, optimal levels of metal content, reference values, macro- and microelements, biological media

Introduction

It is known that microelement homeostasis of organs and tissues is an important factor determining human health and its functional reserves. The level of accumulation of toxic metals and essential elements in different diagnostic biological media may indicate the health status and adaptation of the body to the environment [1–3].

One of the factors of mass screening and control over the impact of the environment on human and animal organism is the lithium element analysis in biologic media, e.g. hair, whole blood and others [1–6].

In the last decade there have been attempts to establish normal physiological levels of the chemical elements [1, 11–13, 15, 19]. Thus, the term

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biologically permissible level was suggested for forming risk groups under conditions of metal intoxication, the notion of conditionally biologically acceptable level was introduced and the issue of «regional regulations» for certain toxic metals and essential trace elements (TE) was discussed [1, 5, 15]. Traditionally, clinical laboratory diagnostics use a term «reference values» when determining the amount of macronutrients (MN) and TE (this classification includes toxic metals and essential TE). This term also describes the limits. For most parameters each laboratory sets its own reference ranges due to the use of different equipment, examination methods, test systems and measuring units.

For optimal solution of this most important issue it is necessary to develop and further improve the methodological basis for studying the health indicators of certain population groups, including the identification of real exposure of the organism to toxic metals and other chemical components of the environment [5, 7]. Therefore the development of methodology of optimal (background) levels of metals content in biological media can be the basis of the system of diagnostics of pre-pathological (premalignant) conditions of human organism, including those working under hazardous conditions of chemical factors and implementation of new approaches to the establishment of background levels of chemical reagents in the biological environment for certain risk groups – people of different ages and status.

It should be noted that the diagnosis of early and preclinical stages of occupational diseases is the key to immediate treatment and their prevention. That is why the important point of this research was the analysis of the current state of normative-methodological basis for biomonitoring people, studying approaches to the procedures of evaluation of toxic metal and particulate matter content in the biological media of people of different functional status (age, health and professional groups).

Aim of research is to give ecological and hygienic assessment of exposure to toxic metals and environmental agents on optimal level of their content in biological environments, taking into account importance of environmental and geochemical conditions of living and nutrition, habits, gender peculiarities of people.

Materials and methods of research

The research involved hygienic, analytical and statistical analysis methods. Determinations of heavy metals were made in the environmental media (25 samples of atmospheric air, 728 samples of drinking water, 71 samples of food) and in 280 biological media of healthy volunteers (hair, whole blood and serum samples). All treated persons (persons aged 25–40 years) stayed in Kyiv and had no signs of metal intoxication.

The patients were also given a voluntary questionnaire to assess abnormal habits, health, occupational exposure to toxic metals and the nature of their dietary needs. To determine the content of 12 chemical elements in the samples the micro-wave method of mineralization of samples and spectral trace element analysis method (ICP-OES using OPTIMA 2100 DV) were used [5–8]. The obtained results were statistically evaluated using Microsoft Excel, correlation analysis was performed by the Verimax raw method [9].

Results of the research and their discussion

The research findings and available literature data [1, 10–13, 16, 17, 21] leave no doubt of the existence of a close connection between the chemical

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composition of the air, drinking water, foodstuffs and the formation of optimum physiological levels of metal content in biological environments. The contribution of food in the formation of optimal physiological levels takes the first place (from 59 to 98 % by day), drinking water – the second (from 1 to 35 % of the total consumption of mineral resources), and air – the third (from 0.1 to 2.0 % of total consumption). However, considering high adsorption capacity of respiratory organs and possibility of inhalation of low-dispersed metal particles and high sorption capacity of lung alveoli, aerogenic way is the main way of metal supply in some cases [1, 10–12, 18–20]. The obtained results are given in Table 1. The analysis of metal content in atmospheric air showed that zinc (Zn), cadmium (Cd), lead (Pb), manganese (Mn) and nickel (Ni) are the primary pollutants. A small number of drinking water samples exceeding the MACs for Mn, iron (Fe), Pb and chromium (Cr) were registered during the analysis of drinking water. MN and TE content in foodstuffs was mostly characterized by deficiencies in the elements.

The logical step of further research was the calculation of total dose of metals, taking into account inhalation and alimentary pathways of chemical reactions (Table 2) to the human body. The difference of this calculation in this research was that during the calculation of the supplied demand in one or another MN or TE the coefficient of ingestion for a skin element in the gastrointestinal tract was taken into account. The data obtained demonstrate that the total daily metal exposure of the inhabitants who live in the environmental and geochemical optimum zone does not exceed their daily exposure as compared with the recommended data from various literature sources [2, 12–15, 18–21]. The data obtained (Table 2) demonstrate that the total additional dose in the inhabitants who live in the environmental and geochemical optimum zone does not exceed the total dose with heavy metals and TE in comparison with the data recommended in the literature [12, 13, 19]. It should be noted that the main way of forming the physiological norm of metals is the intake of magnesium (Mg), Cd, Cr, Fe, Ni and Zn (over 50 %) with the intake of calcium (Ca), Cr, selenium (Se), Pb (fluctuations within 30–70 %) through water, but for Ni, Se through air (close to 20 %). Collective intake of all elements was lower for their permissible values given in various literature sources [1, 12–15].

It is well known that the amount of metals in the hair and blood of the population characterizes the processes of their translocation from environment into the human body. From the standpoint of current physiological concepts, unfavorable conditions of the environment and nutritional conditions can be a consequence of specific adaptation changes in the metabolism of reagents. Therefore, in order to determine these changes we carried out a correlation analysis (Table 3).

It was found that in the structure of factors of chemical nature according to correlation analysis, the highest relationship between the content in atmospheric air and content in biological media was found for copper (Cu) ($R = 0.37$), Fe ($R = 0.20$), arsenic (As) ($R = 0.29$) and Cd ($R = 0.24$). Correlation analysis showed an association between Ni ($R = 0.2$), Pb ($R = 0.52$), aluminium (Al) ($R = 0.24$) and Mn ($R = 0.2$) content in water and in hair of the surveyed.

The priority metals responsible for the body's load from food intake are Cd ($R = 0.28$), Se ($R = 0.35$), silver (Ag) ($R = 0.37$), Zn ($R = 0.44$), Cu ($R = 0.23$), Ni ($R = 0.20$). A positive correlation between the content of metals in environmental objects and whole blood was found for Ca ($R = 0.49$), Mn ($R = 0,25$), Ni ($R = 0,35$) and Zn ($R = 0,26$)

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Table 1

Amount of chemical elements in the environment

Chemical element	Statistical indicator	Atmospheric air, mg/m^3	Water, mg/l	Food products, mg/kg
Aluminium	M Min/max TLV	0.097 0.083–0.11 0.01	0.031 0.01–0.054 0.1	10.40 0.35–20.44 1.0–30.0
Silver	M Min/max TLV	– – 0.20	0.017 0.015–0.018 0.050	0.19 0.025–0.36 0.1–0.65
Arsenic	M Min/max TLV	0.005 0.005–0.007 0.003	0.023 0–0.045 0.05	0.03 0.01–0.05 0.05–1.0
Calcium	M Min/max TLV	0.027 0.0001–0.054 0.3	33.97 1.75–72 100	875.0 800–950 800
Cadmium	M Min/max TLV	0.0001 0.00007–0.0001 0.0003	0.005 0–0.017 0.001	0.034 0.002–0.004 0.01–0.1
Chromium	M Min/max TLV	0.001 0.0001–0.0016 0.0015	0.13 0.0003–0.053 0.05	0.001 0.0002–0.003 0.1–0.3
Copper	M Min/max TLV	0.002 0.00007–0.0038 1.0	0.05 0.021–0.15 1.0	0.27 0.029–0.50 0.5–10.0
Iron	M Min/max TLV	0.03 0.0001–0.006	0.13 0.002–0.71 0.3	3.30 0.6–6.0 3–50.0
Magnesium	M Min/max TLV	0.014 0.0002–0.028 0.05	4.57 0.23–7.03 50	11.27 3–19.03 280
Manganese	M Min/max TLV	0.005 0.0001–0.01 0.01	0.008 0.002–0.025 0.1	0.18 0.001–0.35 0.4–10
Nickel	M Min/max TLV	0.006 0.0004–0.012	0.006 0.002–0.017 0.1	0.085 0.02–0.15 0.1–0.5
Selenium	M Min/max TLV	0.001 0–0.002 0.05	0.12 0–0.33 0.01	0.016 0.002–0.03 0.5–1.0
Lead	M Min/max TLV	0.014 0.0001–0.028 0.01	0.05 0.004–0.17 0.01	0.11 0.1–0.12 0.05–1.0
Zinc	M Min/max TLV	0.018 0.0002–0.036 0.05	0.015 0.009–0.28 5.0	4.60 2.2–7.0 5–40

Note. MPCs are indicated for cadmium, lead, arsenic, copper, zinc, iron, and background levels for other elements.

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Table 2

Total daily intake of heavy metals in human body

Way of intake	Statistical data	Metal, mg/day													
		Magnesium	**Calcium**	**Silver**	**Aluminium**	**Arsenic**	**Cadmium**	**Copper**	**Chromium**	**Iron**	**Nickel**	**Manganese**	**Selenium**	**Lead**	**Zinc**
Food products	M	144.7	131.5	0.215	14.41	0.50	0.06	0.60	0.04	4.73	0.13	0.3	0.04	0.09	6.90
	Min	4.5	120	0.18	12.19	0.15	0.03	0.45	0.03	0.45	0.03	0.015	0.03	0.02	3.3
	max	285	143	0.25	16.62	0.75	0.09	0.75	0.05	9.0	0.23	0.53	0.05	0.16	10.5
	%	63.86	20.01	95.45	32.02	9.26	81.08	8.70	55.56	92.56	72.22	8.82	14.81	50.0	98.29
Drinking water	M	6.86	50.96	0.0098	0.050	0.039	0.008	0.075	0.025	0.20	0.009	0.012	0.18	0.08	0.023
	Min	0.35	2.63	0.0045	0.012	0.005	0.002	0.032	0.005	0.003	0.003	0.003	0.005	0.006	0.014
	max	10.5	108.0	0.015	0.087	0.07	0.026	0.22	0.05	1.07	0.026	0.038	0.20	0.26	0.42
	%	**30.27**	77.54	4.45	0.11	7.22	**10.81**	**10.87**	**34.72**	3.91	5.0	3.53	**66.67**	**44.44**	0.33
Air	M	1.33	1.61	0.0056	0.26	0.0036	0.006	0.012	0.007	0.18	0.036	0.03	0.05	0.009	0.10
	Min	0.37	0.59	0.0026	0.23	0.0029	0.0042	0.0042	0.0059	0.059	0.024	0.01	0.018	0.006	0.012
	max	1.70	2.21	0.0086	0.28	0.0042	0.01	0.016	0.0095	0.24	0.06	0.05	0.034	0.012	0.056
	%	5.87	2.45	2.55	0.58	0.67	8.11	0.17	9.72	3.52	20.0	8.82	18.52	5.0	1.42
In total per day	M	226.6	657.2	0.081	4.91	0.54	0.074	0.69	0.072	5.11	0.18	0.34	0.27	0.18	7.02
	Min	11.7	152.2	0.062	4.14	0.16	0.036	0.49	0.041	0.69	0.057	0.028	0.07	0.032	3.33
	max	407	1245.1	0.091	5.66	0.82	0.13	0.99	0.11	10.31	0.32	0.62	0.28	0.43	10.98
Daily need		280–350	800	0.22	45	0.001	0.04–0.9	1.0–1.5	0.03–0.15	10-15	0.4	2.0–5.0	0.03–0.07	0.43	7–10

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Table 3

Correlation dependence between metal content in environmental objects and biological media of adult humans

Element	Biological media	Environmental objects		
		Atmospheric air	Drinking water	Food products
Silver	Hair	0.052	0.01	**0.37****
	Whole blood	0.07	0.13	0.13
Aluminium	Hair	-0.05	**0.28***	0.16
	Whole blood	0.21	0.12	0.07
Calcium	Hair	0.12	0.11	0.10
	Blood serum	**0.49****	0.11	0.04
Cadmium	Hair	**0.48****	0.05	**0.28***
	Whole blood	**0.23**	0.20	**0.23**
Copper	Hair	**0.37****	-0.01	**0.23**
	Whole blood	0.19	0.11	0.14
Chromium	Hair	**-0.27***	-0.15	**0.28***
	Whole blood	0.13	0.03	**0.29***
Iron	Hair	0.20	0.03	0.03
	Blood serum	0.001	0.12	0.03
Magnesium	Hair	-0.10	0.21	**0.30***
	Blood serum	0.15	**0.37****	**0.35**
Manganese	Hair	0.07	**0.28***	-0.12
	Whole blood	**0.25***	**0.21***	0.03
Nickel	Hair	-0.14	0.20	0.20
	Whole blood	**0.35****	0.07	**0.49****
Selenium	Hair	-0.034	0.07	**0.35****
	Blood serum	0.038	0.08	**0.27**
Lead	Hair	**-0.29***	**0.52****	0.14
	Whole blood	0.02	0.12	0.18
Zinc	Hair	-0.05	-0.10	**0.44****
	Blood serum	**0.26***	0.06	**0.43****

*Note. Probability p < 0,001, **p < 0,05.*

in atmospheric air, for Mg (R = 0,37) and Mn (R = 0,27) in water and for Cd (R = 0,23), Cr (R = 0,29), Mg (R = 0,30), Ni (R = 0,49), Se (R = 0,27) and Zn (R = 0,43) in food.

The results of MN and TE content in biological media (Table 4) in persons of ecological and hygienic optimum (the examinees lived within Kyiv city without industrial load) were compared with the reference values [1, 5, 11, 15]. The content of MN and TE in whole blood and serum of the examined persons predominantly corresponded to the minimum physiological levels of elements in comparison with the «conditional norm» published in the literature. Identified values of elements content in whole blood taking into account their daily intake are within physiological minimum (or biologically

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Table 4

Content of macro- and microelements in whole blood, serum and hair of adult humans in the control

Chemical element	Statistical Indicator	Blood/serum, mg/l	Hair, mcg/g
Aluminium	M ± m Min/max Median	0.120 ± 0.005 0.010–0.13 0.12	10.81 ± 4.33 6.48–15.14 10.18
Silver	M ± m Min/max Median	0.08 ± 0.02 0.06–0.10 0.08	0.08 ± 0.03 0.05–0.11 0.10
Arsenic	M ± m Min/max Median	0.020 ± 0.005 0.010–0.033 0.02	0.30 ± 0.03 0.003–2.10 1.11
Magnesium	M ± m Min/max Median	17.43 ± 1.37 16.06–18.80 16.88	59.14 ± 13.39 17–655 177.98
Calcium	M ± m Min/max Median	86.44 ± 5.54 80.90–91.98 87.02	1157.23 ± 151.16 239–2241 1087
Cadmium	M ± m Min/max Median	0.005 ± 0.003 0.002–0.010 0.003	0.07 ± 0.02 0.01–1.27 0.083
Chromium	M ± m Min/max Median	0.023 ± 0.004 0.019–0.030 0.02	0.53 ± 0.07 0.002–5.970 5.28
Copper	M ± m Min/max Median	0.70 ± 0.07 0.63–0.80 0.71	10.79 ± 1.24 1.07–26.82 10.09
Iron	M ± m Min/max Median	1.07 ± 0.37 0.70–1.44 1.10	16.08 ± 6.38 1.32–44.44 24.53
Manganese	M ± m Min/max Median	0.035 ± 0.007 0.028–0.042 0.032	1.31 ± 0.16 0.06–0.35 1.22
Nickel	M ± m Min/max Median	0.002 ± 0.001 0.001–0.003 0.002	0.59 ± 0.03 0.02–2.72 0.72
Selenium	M ± m Min/max Median	0.07 ± 0.01 0.06–0.08 0.074	0.66 ± 0.11 0.003-0.80 0.06
Lead	M ± m Min/max Median	0.10 ± 0.012 0.08–0.12 0.088	0.66 ± 0.09 0.05–8.55 1.3
Zinc	M ± m Min/max Median	1.15 ± 0.08 1.07–1.23 1.10	100.56 ± 14.22 11.05–445.75 101.99

Note. For magnesium, calcium, copper, iron, zinc, selenium, chromium the data of content in blood serum are given.

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acceptable level) for Ni and Cr, within optimum – for Pb, Cd and As and only for Mn maximal value in whole surveyed blood was found. Reference values of TE in blood serum were found within the minimum for Mg, Ca, Cu, Se, for Fe the content was within the physiological optimum and only for Zn the maximum content was found.

The TE content in the hair of the examined persons in some cases corresponded to the minimum of physiological levels (for Pb, Zn, Cd, Mg, Se), for Mn, Fe, Cu, Ni, Ca the optimum value was detected, but for As the detected content corresponded to the maximum physiological level.

Obtained reference values of elements content in whole blood taking into account their daily intake are within physiological minimum (or biologically acceptable level) for Ni and Cr, within optimum – for Pb, Cd and As and only Mn maximal value in whole blood of examined people was revealed. Reference values of TE in blood serum were found within the minimum for Mg, Ca, Cu, Se, for Fe the content was within the physiological optimum and only for Zn the maximum level of this element was found. In the hair of the examined persons the DOE content in some cases corresponded to the minimum physiological levels (for Pb, Zn, Cd, Mg, Se), for Mn, Fe, Cu, Ni, Ca the optimum value was detected, but for As and Al the content detected corresponded to the maximum physiological levels.

It should also be noted that preliminary studies have established that it is reasonable to assess risks of adverse effects of heavy metals on health of population and workers using developed criterion indicators (regional background levels, regional maximum permissible load levels). Migration peculiarities have been calculated for 4 chemical elements (Table 5). A high level of accumulation of Al and Cr by blood cells was revealed. The elimination index in hair is highest for Al, Ag and Cr, and with urine for Cr. Thus, the optimum levels of metals in blood are: Al – 0.2 mg/l, Ag – 0.02 mg/l, Cr – 0.02 mg/l,

Table 5

Migration features of metals in human body

Metals	Level of alimentary intake, mg/day (M ± m)		Content in biosubstrates, mg/l (M ± m)				Estimated indices, units			
							Penetration index		Index of retention of blood forming elements	Index of elimination (hair/urine)
	women	men	whole blood	serum	hair	urine	whole blood	blood serum		
Aluminium	1.640 ± 0.004	7.23 ± 0.70	0.120 ± 0.005	0.10 ± 0.03	10.81 ± 4.33	0.090 ± 0.002	0.013 / 0.06	0.073 / 0.02	0.83	6.59–1.49 / 0.06–0.012
Argentum	0.0220 ± 0.0005	0.110 ± 0.0007	0.08 ± 0.02	–	0.08 ± 0.03	–	–	3.63 / 0.73	–	3.64–0.73 / –
Chromium	0.030 ± 0.003	0.033 ± 0.003	0.023 ± 0.004	0.012 ± 0.002	0.53 ± 0.07	0.07 ± 0.01	0.36 / 0.40	0.77 / 0.70	0.52	17.67–16.06 / 2.33–2.12
Manganese	0.15 ± 0.06	0.16 ± 0.01	0.035 ± 0.007	0.006 ± 0.001	1.31 ± 0.16	0.020 ± 0.009	0.038 / 0.04	0.23 / 0.22	0.17	8.73–8.19 / 0.13–0.13

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Mn – 0.038 mg/l, and in hair – Al – 5.20 μg/g, Ag – 0.03 μg/g, Cr – 0.80 μg/g, Mn – 0.45 μg/g.

Data on the degree of the population's exposure to toxic TE are given in comparison with the available estimates of the content of these toxicants in the human body: «optimum level» (physiological norm), «acceptable level» and «critical level» (health-threatening level of content).

The obtained results allow to improve an estimation of trace element balance in biological environments of the workers at the enterprises, connected with heavy metals influence by application of multielement and highly sensitive method of spectral analysis (ICP-OES, ETAAS, MS-ISP), determination of reasons of mineral exchange disturbances, increase of information content of clinical diagnostics by application of complex approach in definition of MN and TE in several biological environments simultaneously.

Conclusions

1. The obtained results leave no doubt of a close connection between chemical composition of air, potable water, foodstuff in formation of concentrations representing risk for health. It has been calculated that the main way of formation of physiological norm of metals is the alimentary ingress of Mg, Cd, Cr, Fe, Ni, Mn and Zn (over 50 %) with food, for Al, Ca, Cr, Se, Pb (ranging from 30–70 %) the main way of ingress is aquatic, and for Ni , Se it is air (about 20 %).
2. The content of metals in one medium does not always adequately reflect the nature of their metabolism in the human body. Therefore, to increase reliability and efficiency of early clinical diagnostics of diseases it is necessary to use a complex approach (simultaneous determination of metal content in several biological media).
3. The content of MN and TE in the biological media of those examined in a number of cases corresponded to the minimum physiological levels (for Pb, Zn, Cd, Mg, Cr, Se), for Mn, Fe, Cu, Ni, Ca the optimum value was found, but for Al, As the content detected corresponded to the maximum physiological levels. Chemical elements whose concentration in biological media was within «g–mg» (for Ca, Mg, K, Na, Fe, Cu, Zn in blood serum) were within the «conditional norm» when determined by the ECO-ISP method. The optimum content of metals in blood was calculated, which is: Al – 0.2 mg/L, Ag – 0.02 mg/L, Cr – 0.02 mg/L, Mn – 0.038 mg/L, and in hair – Al – 5.20 μg/g, Ag – 0.03 μg/g, Cr – 0.80 μg/g, Mn – 0.45 μg/g.
4. Optimal levels of content of heavy metals in biological media are justified for Al, Ag, Cr, Mn, due to the combined effect of the environment. Cases of excess of content of these metals can manifest as a strain of regulatory-adaptation systems and clinical manifestations of pathological changes in individual organs and systems.

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