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ELEMENTAL STATE OF THE ORGANISM OF WORKERS AND POPULATION AS MANIFESTATION OF ADAPTATION TO THE TECHNOGENIC EFFECT OF METALS: NEW METHODOLOGICAL APPROACHES

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Abstract. Elemental state of the organism of workers and population as manifestation of adaptation to the technogenic effect of metals: new methodological approaches. Andrusyshyna I.M. *The problem of adaptive, prepathological and pathological reactions of the body to the action of exogenous chemicals is closely intersected with the assessment of the norm and its fluctuations. The imbalance of chemical elements in the human body directly affects the functioning of almost all organs and systems, causing significant stress of adaptation mechanisms. In this article we study the elemental state of the human body depending on the physiological state (endocrine pathology and professional contact with heavy metals), analyze the correlation between macro- and microelements and assess the degree of adaptability of the body. In the work the elemental state of the human body, taking into account not only the absolute values of the concentrations of elements in the hair and whole blood was studied, the adaptability of the body according to the indicators of elemental imbalance in the blood and hair of volunteers, individuals with endocrine pathology (autoimmune thyroiditis and type II diabetes mellitus) and those working in conditions of contact with heavy metals (for jewelers, welders and battery technicians) is analyzed. The results of the study indicate that various non-specific adaptation reactions are accompanied by changes in the elemental state of a person. Under the prevailing pathology of the endocrine system (diabetes mellitus or autoimmune thyroiditis), the adaptation of the body was determined as a stage of tension and is associated with the duration of the disease. In persons exposed to professional contact with heavy metals (Mn, Cr, Pb, Ag), adaptation depended on the nature and duration of professional contact with them: the highest tension of adaptation processes was found in jewelers, and the least in welders and battery technicians, which is associated with the duration of professional contact with these metals. The high number of connections between the elements indicates the tension of adaptive reactions in people with endocrine pathology and especially in jewelry workers. Adaptation of welders and battery technicians to the high content of metals in the air is due to the longer experience of these workers and adaptation to production conditions with a decrease in the number of correlations between the elements, as a means of reliable operation.*

Реферат. Элементный статус организма работающих и населения как проявление адаптации к техногенному влиянию металлов: новые методические подходы. Андрусишина И.Н. *Проблема адаптационных, предпатологических и патологических реакций организма на действие экзогенных химических веществ тесно переплетается с вопросами оценки нормы и ее колебаний. Дисбаланс химических элементов в организме человека непосредственно влияет на функционирование практически всех органов и систем, вызывая значительное напряжение адаптационных механизмов организма. В работе изучен элементный статус организма человека в зависимости от физиологического состояния (эндокринная патология и профессиональный контакт с тяжелыми металлами), проведены анализ корреляционных связей между макро- и микроэлементами и оценка степени адаптированности организма. Дана оценка элементного статуса организма человека с учетом не только абсолютных значений концентраций элементов в волосах и цельной крови, выполнен анализ адаптированости организма по показателям элементного дисбаланса в крови и волосах волонтеров, лиц с эндокринной патологией и у работающих в условиях контакта с тяжелыми металлами (ювелиров, сварщиков и аккумуляторщиков) Резуль-*

таты проведенного исследования свидетельствуют о том, что различные неспецифические реакции адаптации сопровождаются изменениями элементного статуса человека. Содержание в цельной крови в группах работающих и лиц с эндокринной патологией по уровням нагрузки, как допустимом и критическом уровне, были подобны – Cr, Cd, Mn, Pb. У лиц с эндокринной патологией и, особенно, у работающих в ювелирном деле высокое количество связей между элементами свидетельствует о напряжении приспособительных реакций. Компенсация у сварщиков и аккумуляторщиков, то есть приспособление к высокому содержанию токсичных металлов в атмосферном воздухе, связана с большим стажем работы этих лиц и адаптацией к производственным условиям, о чем свидетельствует уменьшение количества корреляционных связей между элементами как средство надежного функционирования.

One of the priorities of modern hygiene and preventive medicine is to find objective methods and methodological approaches to assess the health of the population and workers, to prevent diruptions of the processes of adaptation and transition of prenosological conditions to the disease stage. One of the important factors that determine human health and its functional reserves is microelement homeostasis of organs and tissues. The level of accumulation of heavy metals and essential elements in various diagnostic biological environments can be judged by the state of health and adaptation of the organism to environmental conditions [5, 8].

From the standpoint of the theory of adaptation, the relationship of human microelement homeostasis with objects of the external environment is genetically determined. The full content of essential elements and the minimal presence of toxic and opportunistic elements does not threaten to disruption of the body's adaptation mechanisms and is one of the most important components of normal body function [4, 7].

To qualitatively assess the degree of resistance of the organism to man-made chemical environmental factors in modern medical elementology, various methodological approaches are used with the introduction of integrated assessments – an integrated indicator of elemental imbalance and other approaches to assessing elemental imbalances. The structure of elemental deviations is estimated in the form of normograms and diagrams. Thus, one of the known mechanisms that provides adequate responses of adaptation and resistance of the organism to the action of dangerous environmental factors is to increase the number of intra- and intersystem connections between macro- (MAE) and microelements (ME) as a means of reliable functioning. A number of studies [1-6] have shown that the redistribution of functional loads on different body systems compensates for the disorders caused and does not lead to disruption of adaptation, obvious dysregulatory disorders or the development of pathology. In this regard, the growth of correlations between the elements indicates the adaptive stress, and in the case of successful adaptation there is a decrease in the correlations between them.

The aim of the work was to study the elemental status of the human body depending on the physiological state (endocrine pathology and occupational exposure to metals), taking into account not only the absolute values of elements in the hair and whole blood, but also the results of analysis of their synergistic and antagonistic relationships.

MATERIALS AND METHODS OF RESEARCH

For this purpose, 3 groups of subjects were formed. Among them is the first group – volunteers (control), who had no signs of health disorders (58 people aged 25-45 years). The second group (aged 30-35 years) consisted of persons with a clinically established diagnosis – pathology of the thyroid gland (autoimmune thyroiditis – 14 people) or pathology of the pancreas (type II diabetes – 17 people). The third group consisted of people who had a history of professional contact with metals (welders – 23 people, jewelers – 12 people, battery technicians – 22 people).

The study was conducted in accordance with the principles of bioethics set out in the Declaration of Helsinki on Ethical Principles for Human Health Research and the Universal Declaration on Bioethics and Human Rights (UNESCO).

Biological media (whole blood, blood serum, hair) were taken according to generally accepted sampling methods [1, 8, 9, 10]. The content of 14 chemical elements (Ca, Mg, Al, Ag, As, Fe, Mn, Cu, Cd, Cr, Se, Pb, P, Zn) in the samples was determined using the method of multi-element analysis – optical emission spectrometry with inductive coupled plasma (OES-ICP) on the device "Ortima 2100 DV" from Perkin-Elmer (USA) [9].

Since chemical elements have a wide range of synergistic and antagonistic relationships, both the assessment of their relationships and the analysis of correlations between the elements and the assessment of the degree of resistance of the organism by calculating the index – the degree of adaptability of the elemental system (A) was performed by the following formula:

$$A=n\Sigma Kk/N,$$

where A is the degree of adaptability, in conventional units,
n is the number of correlations with a correlation coefficient of 0.5 or more,
ΣKk – the sum of correlation coefficients without sign,
N is the number of MaE and ME combined into a pleiad.

Calculated according to the proposed formula, the changes in correlations indicate the adaptive stress between physiological parameters (stress stage) and in the case of successful adaptation they decrease [4].

Statistical processing of the survey results was performed using statistical analysis software packages Statistica v.6.1., Microsoft Excel and Libre Office Calc based on the Linux operating system and software package R 3.2.5 [3].

RESULTS AND DISCUSSION

The results of the study indicate that various non-specific reactions of adaptation are accompanied by changes in the elemental status of man.

Estimation of the degree of loading of the organism with toxic microelements of different groups of subjects is given in Tables 1 and 2. Professional contact led to an increase in the absolute number of cases of permissible and critical levels of metals in hair (Table 1), especially Al, Cr, Mn and Pb. The absolute number of cases of permissible levels of metals in the hair in people with endocrine pathology was found for Ag, Cd, Mn and the critical level – for Al, Cr. At the same time, similar levels of lead were observed in workers and persons with endocrine pathology.

Table 1

Content of chemical elements in hair of volontiers, workers and patients with endocrine pathology

Chemical element	Level of load with metal	Range of variations of metal in hair, mcg/g	Absolute number, %		
			control	workers*	endocrine pahtology
Al	Optimal content (physiological norm)	0.4-10.00	48.39	27.50	28.20
	Permissible level (metal carrier)	11-20	16.13	42.0	40.25
	Critical level (health hazard)	21-80	25.81	30.50	31.55
Ag	Optimal content (physiological norm)	0.004-0.05	56.52	54.60	55.75
	Permissible level (metal carrier)	0.06-0.10	30.43	26.95	34.25
	Critical level (health hazard)	0.11-0.20	13.04	18.45	10.0
Cd	Optimal content (physiological norm)	0.05-0.10	64.25	40.30	32.20
	Permissible level (metal carrier)	0.11-0.20	25.50	34.10	50.0
	Critical level (health hazard)	0.21-0.40	10.15	25.60	17.80
Cr	Optimal content (physiological norm)	0.002-0.5	53.33	39.80	40.50
	Permissible level (metal carrier)	0.6-1.99	33.33	45.0	39.50
	Critical level (health hazard)	2.0-6.0	13.33	15.20	20.0
Mn	Optimal content (physiological norm)	0.06-0.55	46.15	37.40	22.33
	Permissible level (metal carrier)	0.60-1.55	38.46	46.20	40.65
	Critical level (health hazard)	1.60-9.64	15.38	16.40	37.02
Pb	Optimal content (physiological norm)	0.50-2.40	52.46	23.70	26.66
	Permissible level (metal carrier)	2.5-4.9	37.14	50.02	50.04
	Critical level (health hazard)	>5.0	10.40	26.28	23.30

Note. In this and in the following table * – electric welders, battery technicians, jewelers together.

In whole blood, the distribution in the groups by levels of metal concentrations was as follows: the absolute number of cases of permissible and critical levels for Al in workers and people with endocrine pathology is the same, almost unchanged number of cases of permissible and critical levels for Ag in these groups. The content of Cr, Cd, Mn, Pb in whole blood in the groups of workers and persons with endocrine pathology by load levels as permissible and critical were similar. It should be noted that the share of level deviations, which characterizes the optimal content of metals Cr, Mn, is indicative of endocrine pathology and testifies to a deficiency of these metals.

For a more detailed assessment of elemental imbalances in the body, the change of the ratio of individual chemical elements as an important factor in changing metabolic processes is also of interest. The most significant ratios are Na/K, Ca/P, Ca/Mg, Cu/Zn, Cu/Fe, Ca/Pb, Fe/Pb.

Table 2

Content of chemical elements in whole blood of volontiers, workers and patients with endocrine pathology

Chemical element	Level of load with metal	Range of variations of metal in whole blood, mg/l	Absolute number, %		
			control	workers*	endocrine pahtology
Al	Optimal content (physiological norm)	0.1-0.20	71.42	41.59	20.09
	Permissible level (metal carrier)	0.21-0.49	19.04	38.08	56.51
	Critical level (health hazard)	0.50-0.90	9.54	20.33	23.40
Ag	Optimal content (physiological norm)	0.0001-0.02	43.48	46.75	43.50
	Permissible level (metal carrier)	0.02-0.03	52.17	48.20	50.2
	Critical level (health hazard)	0.03-0.11	4.35	5.05	6.30
Cd	Optimal content (physiological norm)	0.001-0.005	66.90	28.72	32.10
	Permissible level (metal carrier)	0.006-0.01	36.90	42.55	55.78
	Critical level (health hazard)	>0.01	6.20	28.73	12.12
Cr	Optimal content (physiological norm)	0.001-0.02	45.45	40.50	34.20
	Permissible level (metal carrier)	0.028-0.04	40.91	50.42	45.60
	Critical level (health hazard)	0.05-0.20	4.54	9.08	20.20
Mn	Optimal content (physiological norm)	0.0002-0.075	84.0	53.83	38.90
	Permissible level (metal carrier)	0.076-0.08	12.0	41.67	55.50
	Critical level (health hazard)	0.08-0.10	4.0	4.50	5.60
Pb	Optimal content (physiological norm)	0.05-0.10	48.20	25.70	37.10
	Permissible level (metal carrier)	0.11-0.20	28.40	19.50	41.50
	Critical level (health hazard)	>0.21	23.40	54.80	21.40

Because chemical elements have a wide range of synergistic and antagonistic relationships in the body, an analysis of the correlations between them was performed. Characteristically, in the structure of correlation pleiads in the blood of volunteers (healthy individuals) there were found 4 positive strong correlations (r> | 0.6 |, p<0.05): Ca/Mg (r=0.77), Mn/Zn (r=0.99), Cr/Ni (r=0.86), Al/Ca (r=0.86), while in hair the following 3 relationships were recorded: Ca/Mg (r=0.71), Mn/Zn (r=0.60), Pb/Zn (r=0.81). The most significant correlations between the elements were in electric welders – Ca/Mg (r=0.70), Cr/Zn (r=0.60), Fe/Cu (r=0.60), battery technicians – Mn/Cu r=0.99), Mn/Mg (r=0.85), Se/Cr (r=0.90), Zn/Mg (r=0.60), Pb/Zn (r=0.60) and jewelers – Cr/Zn (r=0.80), Fe/Cu (r=0.65), Cu/Zn (r=0.90), Cu/Al (r=0.80), Al/Ca (r=0.99) (Fig. 1).

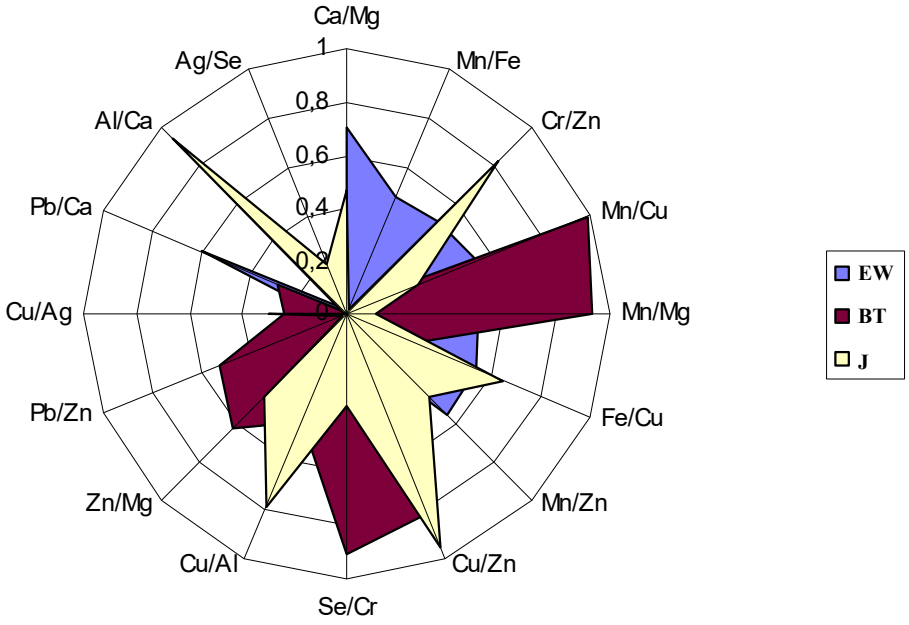

Fig. 1. The most significant correlations between the elements in the hair of various professional contingents (EW – electric welders, BT – battery technicians, J - jewelers). Significant correlation difference, p<0.05

According to the authors [2, 4, 6, 9], one of the mechanisms that provide adequate responses of adaptation and resistance of the organism to the action of dangerous environmental factors is an increase in the number of intra- and intersystem connections as a means of reliable functioning. A number of physiological studies [5-11] have shown that the redistribution of functional loads to other systems compensates for the disorders and does not lead to disruption of adaptation, obvious dysregulatory disorders or the development of pathology. Changes in the adaptation of the organism by determining the correlations between the elements in biological media depending on the physiological state of the subjects are shown in Figure 2.

Under conditions of pathology of the endocrine system – diabetes mellitus (DM) or autoimmune thyroiditis (AIT), the degree of adaptability (indicator A) differed depending on the diagnosis. The exception was the degree of adaptability for whole blood, which was lower than its value in the control, indicating compensation for metabolic disorders associated with AIT (A=17.01). In persons diagnosed with type II diabetes, the stress of adaptive processes was more characteristic regarding whole blood, but indicator A was higher than the control (A=21.22).

In persons who underwent occupational contact with heavy metals (Mn, Cr, Pb, Ag), the degree of adaptability depended on both the nature of occupational contact with metals and its duration. The highest stress of adaptation processes was found in the group of jewelers (A=19.74, 5 years of experience) compared with the control (A=14.4), and the lowest A indicator was observed in the group of welders (A=7.50, 24 years of experience), in battery techniciancs – a slight deviation of the A indicator (A=12.61, 8 years of experience).

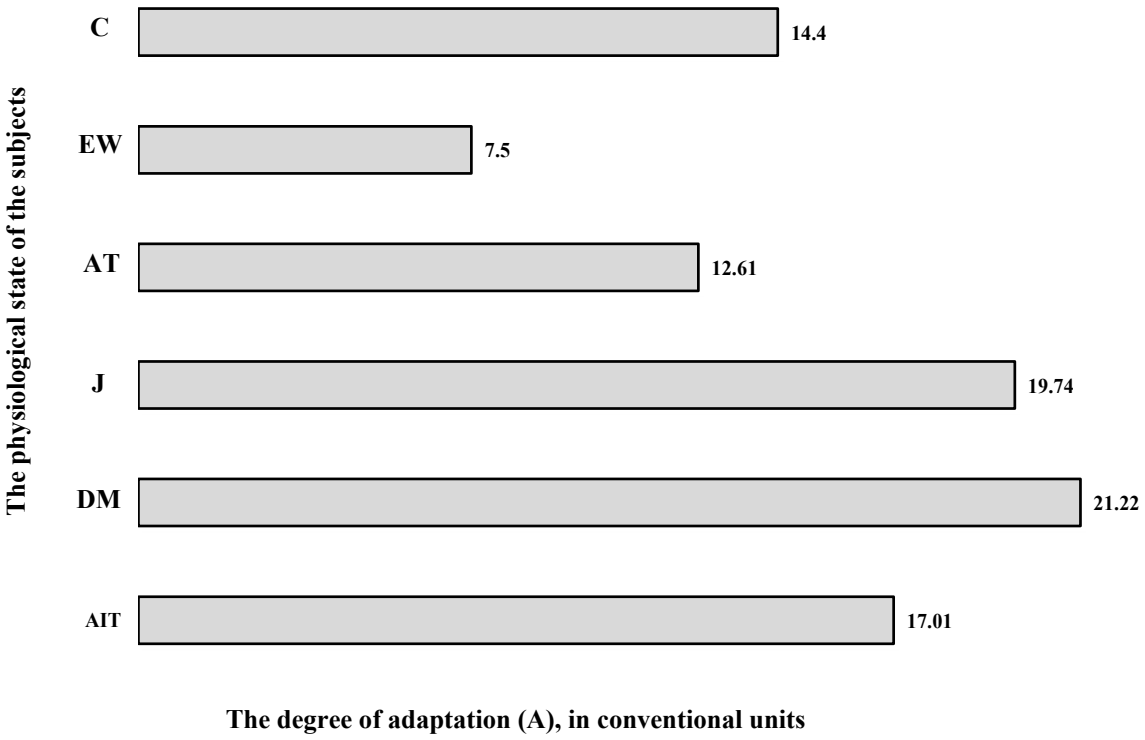

Fig. 2. The degree of human adaptation depending on the physiological state: disease (AIT - autoimmune thyroiditis, DM –diabetes mellitus), professions (EW - electric welders, AT – battery technicians, J - jewelers) and control (C)

Thus, it should be noted that the negative impact of heavy metals on the body is due to the combined action of the components of the environment and has a multidirectional nature. The latter can be manifested both through the stress of regulatory and adaptive systems, and through the clinical manifestations of pathological changes in individual organs and systems.

CONCLUSIONS

1. The results of research indicate that professional contact has led to an increase in the absolute number of cases of permissible and critical levels of Al, Cr, Mn and Pb in the hair. The content in whole blood in groups of workers and persons with endocrine pathology by load levels is characterized as an permissible level and critical one for Cr, Cd, Mn, Pb. It should be noted that the number of deviations in the content of Cr, Mn in the hair in endocrine pathology characterizes them as a deficiency that has important diagnostic value.

2. In the conditions of the formed pathology of the endocrine system (diabetes mellitus or autoimmune thyroiditis) the adaptation of the organism was defined as a stage of stress, and was associated with the duration of the disease. The greatest stress of adaptation processes was found in jewelers, and the least - in welders and battery technicians, which is due to the duration of professional contact with these metals.

3. Predicting the severity of the pathological process (endocrine pathology or occupational contact) is possible by establishing dynamic quantitative parameters of the ratio of elements in invasive and non-invasive diagnostic biosubstrates, which will expand the criteria for early clinical diagnosis of those working in hazardous conditions.

Conflict of interest. The author states that there is no conflict of interest.

In further research it is planned to conduct biochemical analysis of metalloenzymes and forms of metals to find markers of adaptation to man-made effects of priority pollutants among metals.

REFERENCES

1. Andrusyshyna IM, Golub IO, Lampeka OG. [Prior to the problem of better understanding of the optimal rationalization of important metals in the biological treasures of people]. Ukrainian Journal of Occupational Health. 2015;44(3):48-56. Ukrainian.
doi: https://doi.org/10.33573/ujoh2015.03.048

2. Andrusyshyna IN, Golub IA, Lampeka EG. [Elemental homeostasis – a strategy of a person's activity under conditions of anthropogenic loading with metals]. The survival strategy in terms of bioethics, anthropology, philosophy and medicine. Kishenev. 2018;24:161-3. Ukrainian.

3. Antomonov MYu. [Mathematical processing and analysis of biomedical data 2nd ed.]. Kyiv; 2017. p. 576.

4. Baevsky RM, Maximov AL, Bersenev AP. [Fundamentals of ecological human valeology]. Magadan: SECC FEB RAS; 2001. p. 267. Russian.

5. Kashapova RA. [Adaptation of an organism in conditions of low-intensity chemical pollution]. Modern problems of science and education. 2015;3. Russian. Available from: http://www.science-education.ru/ru/-article/view?id=19710

6. Lugovaya EA, Stepanova EM, Gorbachev AL. [Approaches to the body element status assessment]. Microelements in medicine. 2015;16(2):10-17. Russian. doi: https://doi.org/10.19112/2413-6174-2015-16-2-10-17

7. Miroshnikov SV, Notova SV, Kvan OV. [Elemental status features during some unspecific adaptation reactions (abnormally high activation and reactivation)]. Vestinik OSU. 2011;15(134):88-90. Russian. doi: https://doi.org/10.25198/1814-6457

8. Oberlis D, Harland B, Skalny A. The biological role of macro- and micronutrients in humans and animals. Sankt-Peterburg: Nauka; 2008. p. 544. Russian.

9. Andrusyshyna IM, Lampeka OG, Golub IO, Lubyanova IP, Kharchenko TD. [Methodical recommendations (111) 72.14/133.14 "Evaluation of the destruction of mineral exchange in profeccional contingents by the method of atomic emission spectrometry with inductively coupled plasma"]. Kyiv: Avicena; 2014. p. 60. Ukrainian.

10. Saravanabhavan G. et al. Human biomonitoring reference values for metals and trace elements in blood and urine derived from the Canadian Health Measures Survey. International Journal of Hygiene and Environmental Health. 2017;220(2 Pt A):189-200.
doi: https://doi.org/10.1016/j.ijheh.2016.10.006

11. Stojsavljević A, Jagodić J, Vujotić L. et al. Reference values for trace essential elements in the whole blood and serum samples of the adult Serbian population: significance of selenium deficiency. Environ Sci Pollut Res Int. doi: https://doi.org/10.1007/s11356-019-06936-8

СПИСОК ЛІТЕРАТУРИ

1. Андрусишина І. М., Голуб І. О., Лампека О. Г. До проблеми обгрунтування оптимальних рівнів умісту важких металів у біологічних середовищах людини. *Укр. журнал з проблем медицини праці*. 2015. Т. 44, № 3. С. 48-56.
DOI: https://doi.org/10.33573/ujoh2015.03.048

2. Андрусишина И. Н., Голуб И. А., Лампека Е. Г. Елементний гомеостаз – стратегия виживання человека в условиях антропогенной нагрузки металлами. *The survival strategy in terms of bioethics, anthropology, philosophy and medicine*. Kishinev. 2018. Vol. 24. P. 161-163.

3. Антомонов М. Ю. Математическая обработка и анализ медико-биологических данных 2-е изд. К., 2017. 576 с.

4. Баевский Р. М., Максимов А. Л., Берсенева А. П. Основы экологической валеологии человека. Магадан: СВНЦ ДВО РАН, 2001. 267 с.

5. Кашапова Р. А. Адаптация организма в условиях химического загрязнения малой интенсивности. *Современные проблемы науки и образования.* 2015. № 3. URL: http://www.science-education.ru/ru/article/-view?id=19710

6. Луговая Е. А., Степанова Е. М., Горбачев А. Л. Подходы к оценке элементного статуса организма человека. *Микроэлементы в медицине*. 2015. Т. 16, № 2. С. 10-17.
DOI: https://doi.org/10.19112/2413-6174-2015-16-2-10-17

7. Мирошников С. В., Нотова С. В., Кван О. В. Особенности элементного статуса при некоторых неспецифических реакциях адаптации (повышенной активации и переактивации). *Вестник ОГУ*. 2011. Т. 134. № 15. С. 88-90.
DOI: https://doi.org/10.25198/1814-6457

8. Оберлис Д., Харланд Б., Скальный А. Биологическая роль макро- и микроэлементов у человека и животных. Санкт-Петербург: Наука, 2008. 544 с.

9. Оцінка порушень мінерального обміну у професійних контингентів за допомогою методу атомно-емісійної спектрометрії з індуктивно зв'язаною плазмою: метод. рек. (111)72.14/133.14 / І. М. Андрусишина та ін. Київ: Авіцена, 2014. 60 с.

10. Human biomonitoring reference values for metals and trace elements in blood and urine derived from the Canadian Health Measures Survey / G.Saravanabhavan et al. *Inter. Journal of Hygiene and Environmental Health*. 2017. Vol. 220, No. 2 Pt A. P. 189-200.
DOI: https://doi.org/10.1016/j.ijheh.2016.10.006

11. Reference values for trace essential elements in the whole blood and serum samples of the adult Serbian population: significance of selenium deficiency / A. Stojsavljević et al. *Environ Sci Pollut Res Int.* 2020. Vol. 27, No. 2. P. 1397-1405.
DOI: https://doi.org/10.1007/s11356-019-06936-8

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