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Adaptation to Stresses Induced by the Effects of External Low Dose Ionizing Radiation

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Abstract

Objective

The cross adaptation of humans suffering the consequences of external low-dose ionising radiation impact (ELDIRI) was to be studied.

Methods

The observational investigation in a XXXXX secondary care centre included 507 non-smoking men (male, age 50.14 ± 10.39 years) and was approved by the commission on ethics.

Results

The radiation haematologic stress is not related to cytomegalovirus infection, unlike the haematologic stress. The latter is the response of the human body as an ecosystem, but it can be a synergist of cytomegalovirus, which is capable of inducing haematologic stress as well as systolic and isolated systolic hypertension.

Latent iron deficiency can cause hypertension, including diastolic hypertension, in humans, including those suffering from ELDIRI.

Conclusions

Many human biology features may be explained by the absence of inverse correlation between T3 and T4 (except in the case of patients with thyroid diseases). The health of Russian cosmonauts may be superior to that of US astronauts because of the use of reserpine for radioprotection in the USA. As long as biologic age is inversely correlated to the α_2-macroglobulin/α_1-protease inhibitor ratio, so it would be interesting to study the selection of humans with elevated α_2-macroglobulin contents for longitudinal interplanetary flights.

Advances in knowledge

The radiation haematologic stress has been described. It may be the more ancient stress in evolution than haematologic stress and Selye's general adaptation syndrome.

Keywords: Radiation haematologic stress; Coronary heart disease; Essential hypertension; Telehealth; Haematologic stress evolution; Trace elements

Introduction

Low-dose radiation research is vitally important for occupational, environmental and clinical medicine [1]. Ataxia telangiectasia-mutated (ATM), extracellular signal-related kinase (ERK), mitogen-activated protein kinase (MAPK), P53, ROS, tumor necrosis factor (TNF)- α-related signal transduction pathways are involved in low-dose ionizing radiation-induced genomic instability. ATM, ERK, phospho-c-Jun NH2-terminal kinase (JNK) and protein 53 (p53)-related signal transduction pathways may be involved in LDIR-induced hormesis. MAPK, p53 may be important for adaptive response. ATM, cyclooxygenase-2(COX-2), ERK, JNK, reactive oxygen species (ROS), p53 may be important in radioresistance. COX-2, ERK, MAPK, ROS, tumor necrosis factor receptor alpha may be relevant to LDIR-induced bystander effect [2]. A new approach is needed for further studies. Such an approach allowed us to investigate radiation haematologic stress as one of the mechanisms underlying induced radio resistance effects, adaptive responses and bystander effects. We consider the trace element estimation approach as the form of a new approach. We felt it was important for the concept of radiation haematologic stress to be distinguished from that of haematologic stress and of Selye's general adaption syndrome, as indicated by our studies. In particular, it was necessary to explain such an important form of cross adaptation, which has not been simulated in animals, as an opportunity to minimise other harmful effects in humans suffering the consequences of external low-dose ionising radiation impact (ELDIRI) [3-5]. Theoretically, radiation haematologic stress can be experienced by pilots, cosmonauts (astronauts travelling on Soviet/Russian spaceships) and astronauts. It may be possible during an exit from the limits of circumtellurian space in future piloted interplanetary expeditions [6]. Human evolution can be observed in the evolution of radiation haematologic stress in humans. The features of this evolution are relevant to the absence of an inverse correlation between T3 and thyroxin, which can be also observed as helpful in higher order primate diving as well [7,8].

Materials and Methods

With the approval of the commission on ethics, this study summarises the results of an investigation of 507 non-smoking men (to exclude the haematologic stress effects caused by smoking) aged 50.14 ± 10.39 years [9]. The investigation included healthy individuals with a low risk of atherosclerosis according to the Systemic Coronary Risk Evaluation (SCORE,) scale (50 persons) and coronary heart disease (CHD) patients with confirmation of professional harm due to a one-time exposure to an external technology-related source of ionising radiation at a dose less than 1 Gray not less than 25 years before the investigation (141 persons) [10,11].

In the latter group, cardiovascular diseases had been absent before the impact of ionising radiation. A system of reconstruction of doses to estimate a dose of external impact for each irradiated person based on place and the term of stay was used [12].

Additional 316 men with CHD not influenced by technology-generated ionising radiation and working as machine operators were studied. Measurements of arterial pressure were conducted according to the recommendations of JNC experts (1999) [13]. All individuals surveyed, except for those who had been irradiated, worked in favourable sanitary and hygienic conditions. Stenocardia was assessed using Canadian classification.

The blood samples obtained for biochemical studies were collected between 9:00 and 10:00 in the morning. Blood samples for the estimation of lipids and lipoproteins were obtained 12 hours after food intake. Serum cholesterol and triglycerides were estimated using a Boehringer Mannheim (now Hoffmann–La Roche Diagnostic group) System 4030.4 analyser from Mannheim, Germany. Chylomicrons, β, pre-β and α-lipoprotein fractions were estimated by electrophoretic lipoprotein separation on acetate cellulose membranes from Sartorus (Germany) with the use of medinal-veronal buffers and film scanning on a densitometer in throughput mode at a wavelength of 570 nm. Values are expressed as percentages.

Recalcification time, activated recalcification time, and activated (partial) thromboplastin time (APTPT) were measured. The tolerance of plasma to heparin was defined using the techniques described by Poller.

Euglobulin clot lysis time, natural blood lysis in vitro, and fibrinogen were measured.

The quantity of uniform elements of blood was estimated using a SysmexF-820 analyser (Kyoto, Japan). Leukocytes were counted on stained blood smears. A unified method was used to calculate the number of red blood cells under a microscope in a count chamber.

Cu, Fe, and Zn were estimated by atomic-absorption analysis of blood serum samples on an AAS3 spectrometer.

Ca in blood serum was estimated by the unified techniques of colour reaction with cresolphtaleincomplexon.

K and Na in blood were estimated by the unified technique of flame photometry.

Inorganic phosphorus was estimated by the unified technique of phosphorus molybdenum heteropolyacid restoration.

The index of red blood cell deformability in standard units was measured [14,15]. The relative viscosity coefficient was estimated in standard units [15]. Indirect immunoenzymometric techniques with an Anti-CMV IgG EIA (DIAplus) (Roche-Moscow) set were used for the quantitative estimation of IgG antibodies against cytomegalovirus in blood serum.

The measurement of sulfhydryl and disulphide group (SH and SS) content in red blood cells was conducted by amperometric titrations with silver nitrate [16].

The total protein in blood serum was estimated by the unified techniques of the biuret reaction.

IDP CEBAK sets for the quantitative estimation of plasmatic proteins by the techniques of simple radial diffusion were used. IDP (IgG), IDP (IgA), and IDP (IgM) sets were used to measure G, A, and M antibodies, respectively. IDP (Trf), IDP (Cpl), IDP (A2M), and IDP (A1AT) sets for were used for the estimation of transferrin, ceruloplasmin, α_2-macroglobulin (A2M), α_1-antitrypsin (A1T), respectively.

Hormones were estimated from blood serum samples taken from an elbow vein between 9 and 11 o'clock. The steroid IFA-cortisol (Alkor-BIO, Russia) set of reactants was used for the quantitative estimation of cortisol in blood serum. The thyroid IFA-triiodothyronine (Alkor-BIO, Russia) set of reactants was used for quantitative estimation of triiodothyronine (T3). The thyroid IFA-thyroxin set of reactants was used for the quantitative estimation of thyroxin (T4). The steroid-IFA-testosterone (Alkor BIO, Russia) set of reactants was used for the quantitative estimation of testosterone.

An echocardiography examination of the patients was conducted.

An analysis of the responses of patient organisms to a test with psychological loading (PL) was conducted for 10-14 hours over the two days after the patient arrived at the clinic. A load simulating the work of an operator was used [17,18].

Arterial pressure was measured in patients performing this test. At data processing, the heart index (HI), specific peripheral vascular resistance (SPVR), stroke volume (SV) according to the Kubicheck formula, and minute volume (heart output) (MV) were calculated. The multiplication of a double product by ejection time produced the triple product (Tp). For each patient, the body weight index was calculated.

The resulting authentic functional connections and interrelations were confirmed by their presence in the dynamic measurements during the performance of a test with neuropsychological load, the logic analysis of causality, and statistical significance. The critical significance value to test hypotheses was set at 0.05. Statistica 6 of Statsoft was used to determine the allocation of independent factors by multiple linear regression, dispersion analysis ANOVA, MANOVA, Tukey's fair distribution according to the method described by Spietoli-Stolin accounting for the different number of investigations in each group, and logistical regression with calculation of the odds ratio. To reveal the force and direction of the linear connection between attributes, we used a correlation analysis with a calculation of Pearson's correlation coefficient (r) and its importance. Spearman's rank-order correlation coefficient was calculated at detection by means of Kolmogorov's criterion of essential difference from normal (Gaussian) distributions of attributes.

Results

The circulation systems is the core actuator of radiation haematologic stress similar to the general adaptation syndrome [14]. However, red blood cell relative viscosity has significant positive correlations with levels of cortisol ($r=0.26$, $p<0.05$) and testosterone ($r=0.28$, $p<0.05$). These hormonal levels are affected by the general adaptation syndrome but not by radiation haematologic stress. Red blood cell deformability had significant inverse correlations with SPVR ($r=-0.28$, $p<0.05$) and with body weight index ($r=-0.24$, $p<0.05$).

The observed increase in the level of SH-groups in red blood cells with the increase of the Cu/Zn ratio in blood serum ($r=0.44$, $p<0.05$ in people suffering from ELDIRI consequences, $r=0.4$, $p<0.05$ in others), the reduced SPVR in conjunction with an increased blood plasma Cu/Zn ratio and the decreased level of zinc in hypotension demonstrate the importance of the Cu/Zn ratio.

APTT has a direct correlation with the Cu/Zn ratio ($r=0.61$, $p<0.05$ in patients with ELDIRI, $r=0.57$, $p<0.05$ in others), copper has an inverse correlation with the level of phosphorus ($r=-0.4$, $p<0.05$), and phosphorus has a significant inverse correlation with the level of calcium in blood serum ($r=-0.4$, $p<0.05$).

According to our data, systolic blood pressure at rest has a significant direct correlation with the fibrinogen level in blood plasma ($r=0.24$, $p<0.05$), and diastolic blood pressure at rest has a significant negative correlation with the level of IgG antibodies to cytomegalovirus ($r=-0.38$, $p<0.05$), which explains the pathogenesis of isolated systolic hypertension.

The level of IgG antibodies to cytomegalovirus was reduced in high-normal blood pressure patients in comparison with the first ($p<0.05$), second ($p<0.05$), and third ($p<0.05$) hypertension stage patients according to JNC-VI.

Essential hypertension of the second and third stages according to JNC-VI (hypertension of the second stage according to JNC-VII) can be the result of sanogenesis, in contrast to the CHD pathological process developing in response to the effects of various manufacturing and environmental factors. This sanogenesis is marked by an increase in blood plasma fibrinolytic activity, which is amplified with an aging-related decrease in the α_2-macroglobulin/ α_1-antitrypsin ratio [22]. Euglobulin clot lysis time, reflecting the reduction of blood plasma fibrinolytic activity, has a significant negative correlation with age. Euglobulin clot lysis time significantly increases in angina pectoris (OR=5.3) and after myocardial infarction (OR=11.4) but decreases in the 2nd and 3rd stages of hypertension (OR=0.03). The increase in SPVR and arterial pressure can be the result of the enhanced lysis of angiotensinogen, ceruloplasmin and other substances with increases in the blood plasma fibrinolytic activity. Simultaneously, as a result of the change in the structure of blood plasma regulating the suppression, the effect on the central regulation of arterial pressure is realised [18].

Systolic blood pressure has a significant inverse correlation with the level of zinc-protein α_2-macroglobulin ($r=-0.2$, $p<0.05$) in patients with essential stage II-III hypertension, unlike those with stage I hypertension. The increase of blood plasma fibrinolytic activity can promote the development of hypertension while exerting a sanogenesis response on CHD development. One of the reasons for the increase in blood plasma fibrinolytic activity with aging can be demonstrated by a statistically significant inverse correlation between age and the α_2-macroglobulin/α_1-antitrypsin ratio, which can be used as markers of increases in biological age [22]. This ratio has a significant direct correlation with the T3/T4 ratio, which is lowered in patients suffering from distant exposure to ionising radiation effects. Therefore, radiation haematologic stress promotes accelerated aging.

Stenocardia 1	Stenocardia 2	Stenocardia 3	Stenocardia 4
2.8	4.4	4.84	5.12

Table 1: Odds relation of logistics regression of stenocardia class depending on Zn and IgG.

Patients	Average mg/l	Std
Without angina pectoris	0.73+ -	0.28
Stenocardia 1	0.91+ -	0.21
Stenocardia 2	0.83+ -	0.33
Stenocardia 3	0.93+ -	0.49
Stenocardia 4	1.05+ -	0.2
Healthy control group	0.7+ -	0.24

Table 2: Zn in serum.

Discussion

The lower prevalence of angina pectoris among people suffering from the consequences of ELDIRI may be the result of the lower values of Zn and InG according to the Tables 1 and 2.

Other authors have reported no numerical connections between blood pressure and trace elements in blood [19]. This we can explain by the following: 1)blood pressure is the product of specific peripheral vascular resistance, the squire of body surface area, heart index, the latter being the product of stroke volume and heart rate divided by body surface area; 2) at all measurements and at all loads, specific peripheral vascular resistance (SPVR) has a significant inverse correlation with the Cu/Zn ratio; 3) stroke volume demonstrates a significant inverse correlation with Zn content; 4) the heart index shows a significant positive correlation with Cu content. Demonstrating the myocardium requirement for oxygen, the triple product at and after psychological load (but not at other types of loads) shows a significant positive correlation with Zn content.

The observed interrelations among values, parameters of homeostasis, trace element contents in blood serum, including those at normal levels that were much reduced in comparison with maximum permissible exposure limits, can be used to study the influence of various harmful factors that have a rather small influence on an organism. The present research demonstrates that the effects of harmful factors connected to trace element deficiency, surplus or imbalance can be exhibited at trace element concentrations much below their maximum permissible exposure concentration, which often occurs under the influence of harmful factors of small intensity, including ELDIRI. This finding is especially important for additional research on copper and zinc because it was impossible to distinguish between their toxic actions and physiological activities [20]. Although much previous research on copper and zinc (mainly on their toxic actions) exists, no fruitful physiological research into the numerical connections among copper and zinc contents in blood plasma and haemodynamic parameters has been conducted prior to the present study. The effects of harmful factors can be predicted based on physiological research on work processes, both in industrial environments and in the laboratory. In the latter case, research is conducted without the influence of harmful environmental factors. The absence of this influence avoids the possibility of combined effects on workers and may therefore produce confounding results due to cross adaptation because of immunity, general adaption syndrome, haematologic stress and radiation haematologic stress [3,9,21]. Radiation haematologic stress may be a more evolutionarily ancient response than haematologic stress and general adaptation syndrome. Therefore, the harmful effects of non-ionising high-frequency radiation and of ELDIRI can be diminished simultaneously due to radiation haematologic stress induced by ELDIRI [4]. Similar features of the combined influence of these factors do not allow us to determine the harmful effects of each environmental factor and of the work environment process separately based on research only at a workplace. The basic paradigm of occupational medicine is the concept of non-threshold actions of harmful factors and the summation of effects of different harmful factors, particularly their combined influence. Therefore, professional suitability, as well as professional selection, to avoid the phenomenon of cross adaptation effect, should be examined in laboratories using tests simulating the essential characteristics of work environment (work, labour) processes [3].

Because copper and zinc blood levels differ in inhabitants at different geographical latitudes and depend on the industrial microclimate, the observed correlations between HI and Cu and between SPVR and the Cu/Zn ratio explain distinctions in the pathogenesis of diseases associated with a change in myocardium afterload under various climate and occupational microclimate conditions [20]. As long as zinc plays a key role in the function of the sensory systems of an organism and its exchange in an organism is interconnected with an exchange of copper and iron, changes in the levels of zinc, copper and iron in blood plasma can be associated with the various parameters describing workplace conditions under the influence of various harmful occupational factors of small intensity [20]. Levels of the trace elements copper, zinc, and iron in blood plasma were associated with disease pathogenesis due to either trace element deficiency or surplus because of the intake of these heavy metals from a polluted environment or previous exposure [20]. We demonstrated the mechanisms of Cu, Fe, and Zn homeostasis in blood plasma within their normal physiological levels, which is important for the progress of preventive medicine and for stress biology and human biology as a whole. According to Bergomi et al., it was not possible to reveal numerical interrelations between blood serum levels of copper and zinc and blood pressure [19]. Our research solved this important theoretical problem by applying the scientific principles we developed to calculate SV, SPVR, heart index, body surface area, and Cu/Zn and Fe/Cu ratios and by finding interrelations among them.

The reduction of triiodothyronine without changes in thyroxin levels and cortisol arousal appears to occur because of radiation haematologic stress, unlike the general adaptation syndrome [23]. The increased glycosaminoglycan levels resulting from the aforementioned T3 reduction without thyroxin reduction explain the increased hypercalcaemia in the aging process with the decrease in general blood protein levels [24]. The cause of hypercalcaemia in aging after ELDIRI was unclear before this study [27].

The blood plasma level of endogenous radio-protectors such as glycosaminoglycans (including heparin) increases with an increase in SH-groups in red blood cells and with an increase in the Cu/Zn ratio in blood plasma. The increase in heparin level leads to an increase in APTT, the value of which changes within the normal values and is an indicator of bradykinin secretion. The reduction in SPVR and/or increase in APTT values (including, as the result of heparin infusion and of ethanol, ACE inhibitor intake) and the increase in the Cu/Zn ratio are interconnected with an increase in the level of SH-groups in red blood cells. This effect demonstrated in the present research allows us to explain the consistent action of known radio-protectors (including heparin, ethanol, aminothiols, indolealkylamine derivatives, and angiotensin-transforming enzyme inhibitors, even those not containing SH-groups) [18, 29]. In addition, the Cu/Zn ratio is directly connected to the interleukin-1 level because of its opposing influences on copper and zinc levels, and changes in the Cu/Zn ratio can thus explain the radio-protector action of interleukin-1 [20].

The longitudinal application of standard radio-protectors (aminothiols, indolealkylamine derivatives) causes either hypotension or hypertension accompanied by hypoxia, and the long-term use of ethanol and longitudinal heparin therapy can increase the risk of coronary heart disease [29]. Zinc ligands (ACE inhibitors) in low (non-hypotensive) doses do not have this drawback because APTT increases moderately with the insignificant decrease in the zinc level (excessively high values of APTT can be connected with thrombocytopenia, haemorragia, and a reduction of bradykinin secretion [18].

It is possible to conclude that the blood concentration of a substance or substances toxic to the nervous and cardiovascular systems under conditions of ionising radiation decreases simultaneously with the reduction in blood pressure. Such substances include zinc and plasmin. Nerve cells perish as the result of the combined cytotoxic actions of zinc and plasmin, and the plasmin level is increased in hypertension along with the decrease in euglobulin clot lysis time [18]. The content of zinc in blood plasma is reduced by radio-protectors such as heparin, which increases natriuresis [30]. SPVR decreases because of the decrease in both Zn and sodium content. The direct correlation between sodium level and SPVR both at rest and during loads shows that the increased consumption of sodium not only causes an increase in blood pressure but can also promote CHD development due to the afterload increase. Therefore, it is necessary to optimise the consumption of salt, rather than eliminating salt from a diet, because Na is a vital element. A deficiency of sodium consumption, in particular, causes aldosteronism and subsequent hypertension. Hyponatremia is especially undesirable in the elderly [31]. The level of sodium in blood plasma showed a significant direct correlation with the level of T3, the potassium in blood plasma showed a significant negative correlation with the level of T3, and the level of T3 in blood serum showed a significant positive correlation with the level of copper in blood serum among all subjects studied. Triiodothyronin showed no correlation with zinc in blood serum (zinc content had a significant direct correlation only with the level of thyroxin). Hence, hypocupraemia can be relevant to hyponatraemia and hyperkalaemia, which explains why CHD patients poorly tolerate even moderate salt restriction [31]. Therefore, it is possible to limit the consumption of table salt to a physiological optimum due to a diet rich in copper and the normalisation of the exchange of copper. All hypertensive patients have an increased level of sodium in their red blood cells which explains the need for a reduction in plasma blood sodium levels. Sodium level was correlated with SPVR in all study subjects.

Insufficient in comparison with haematologic stress, radiation haematologic stress lowering of zinc and iron levels does not provide protection against the majority of microorganisms, whereas radiation haematologic stress, apparently, can protect against the influence of some microorganisms. For example, we found that systolic and systolic-diastolic hypertensions are not features of radiation haematologic stress. However, these forms of hypertension are connected to cytomegalovirus (human herpes virus 5) infection. In CHD patients suffering from the consequences of ELDIRI, blood pressure is significantly raised in comparison with other CHD patients, and the diastolic pressure is increased to a greater degree than the systolic pressure. CHD patients suffering from ELDIRI have significantly increased fibrinogen and low-density lipoprotein levels; reduced high-density lipoprotein, chylomicron, triiodothyronine, IgM, and IgG levels; and reduced euglobulin clot lysis times. These changes can promote the development of arterial hypertension and CHD. Despite the existence of several mechanisms of arterial pressure regulation, stage I and II essential hypertension is not present in the case of simultaneous decreases of triiodothyronine, zinc and iron. According to the literature, the same correlation has also been observed in people with haematologic stress without nephropathy [9]. However, the decrease in triiodothyronine level with the increase in zinc (usually in the second stage of hypertension) and/or iron (usually in the third stage) levels promotes a greater frequency of stage I and II hypertension among CHD patients with ELDIRI and causes diastolic hypertension in these patients.

The level of IgG antibodies to cytomegalovirus is reduced in comparison with high normal blood pressure patients in the first ($p<0.05$), second ($p<0.05$), and third ($p<0.05$) stages of hypertension. This finding may be evidence of reduced immunity to cytomegalovirus (CMV) in essential hypertension that promotes the development of atherosclerosis and arterial hypertension. Cytomegalovirus, as well as other latent herpes viruses, is a major problem of interplanetary space flights because it influences the response of an organism to other pathogens and is the marker of aging of the immune system [26]. Along with the ability of all herpes viruses to damage endothelium, CMV distinguishes itself by the damage it causes to cellular immunity by the compression of T-cellular compartments, its long persistence in leukocytes and hematopoietic cells, its ability to cause the origination of cold autoantibodies promoting RBC haemolysis, the extraction from the RBC surface and from the RBC of fibrinogen, RBC clotting factors and haeme iron [19,24].

The reduction of zinc in lymphocytes is associated with the suppression of cellular immunity [20,24]. The reduction of zinc and iron in blood plasma can be an adaptive reaction to the impact of infections [20,18]. Correspondingly, haematologic stress [9,25] can be a response to infections and the display of cross adaptation to infections during the impact of non-infectious factors increasing sensitivity to infections (for example, non-ionising radiation). Mechanisms of radiation haematologic stress links to CHD are most likely similar to those of haematologic stress. However, unlike radiation haematologic stress, haematologic stress, which can be a response to infectious diseases, has an impact on blood pressure similar to the impact of cytomegalovirus infections [9]. According to our data, the cytomegalovirus can promote only systolic and systolic-diastolic hypertension, and it is the cause of haematologic stress. Cytomegalovirus infection is the synergist of haematologic stress in the regulation of blood pressure, and haematologic stress concept may even lead to cytomegalovirus infection as a marker of immune system aging and of its failure to protect from other infections [28]. Therefore, haematologic stress and radiation haematologic stress essentially differ. Nevertheless, the accelerated aging in radiation haematologic stress can be the consequence of latent stem cell pool reduction and of the disorganisation of a stem cell niche of bone marrow similar to haematologic stress [25].

According to our data, radioprotection is often accompanied by an increase in APTT (for example, because of hypotension and the reduction of zinc content in hypotension); thus, myocardial calcification due to the longitudinal application of radioprotectors explains the increased CHD risk in patients treated with standard chemical radioprotectors and heparin, often exceeding CHD risk due to the impact of ionising radiation[28,29].In the USA, doses of standard chemical radioprotectors in astronauts are considerably decreased by addition of the biological radioprotector reserpine, reducing arterial pressure and, after onset of hypotension, zinc content[28,29]. Vasodilatation is the main effect of the reserpine doses [32]. However, intracranial pressure can be increased as the result of long-term reserpine intake. The intracranial pressure increases and often remains elevated even after discontinuation of reserpine intake [32]. Reserpine is also capable of causing depression [33]. This effect may have an impact on the health and longevity of astronauts after flights, unlike cosmonauts, who do not receive reserpine.

CHD was present in all studied patients after ELDIRI. Epidemiological techniques failed to demonstrate increased CHD morbidity and mortality after ELDIRI [27]. One of the reasons for this finding may be cross-adaptation in cases in which there had been a combined influence of ELDIRI and some other harmful factors, in which case even easing of symptoms can be observed [4]. It is possible to explain this effect by the concept advanced herein of novel radiation haematologic stress appearing after ELDIRI. Radiation haematologic stress is an organism-protective response promoting resistance in conditions of an extreme factor impact. Radiation haematologic stress features in humans can be explained by the absence of an inverse correlation between thyroxin and triiodothyronine content. This correlation is present in other ground mammals, including lower monkeys used for the simulation of radiation impact in long flights [18]. The human radiation haematologic stress phenomenon could be used to solve problems of long-duration space travel to other planets. Apart from strengthening the protection of spaceships, development of optimal radioprotection for astronauts and cosmonauts should be researched, and the study of selection of people with increased levels of α_2-macroglobulin in biological fluids for long interplanetary space flights will advance our understanding of the risk of radiation exposure. Occupational and environmental medicine applications of disease prevention, diagnostics, treatment, and rehabilitation should be designed with an understanding of human biology factors, including the availability of combination of general adaptation syndrome, haematologic stress and radiation haematologic stress effects in humans.

The reduction of myocardial oxygen requirements and of the triple product reflecting a higher pain threshold at the same type of load due to a lower zinc content, as, for example, results from the intake of angiotensin-converting enzyme inhibitors (zinc ligands) , results in an increased tolerance to loads and an improvement in work tolerance [18].

The transferrin level increases with latent iron deficiency [20]. Specific peripheral vascular resistance at rest has a significant inverse correlation with the ceruloplasmin/transferrin ratio. As a result, essential hypertension associated with latent iron deficiency, under the influence of the harmful factors of working conditions and environment, can precede the development of CHD. We have seen that factors interconnected with SPVR, both at rest and at loads, are directly correlated with the body weight index and the sodium content of blood plasma and are inversely correlated with the Cu/Zn ratio and the red blood cell deformability index, the latter having an inverse linear correlation with zinc content and a direct linear correlation with the zinc-protein α_2-macroglobulin level (most likely due to the direct correlation of α_2-macroglobulin and ceruloplasmin levels, whose receptors are on red blood cells) [20]. Therefore, the early influence of harmful factors of small intensity, diets, and medicines on peripheral vascular resistance-if they do not influence the plasma sodium level-is mediated by a change in either the Cu/Zn ratio or Zn content of blood plasma. More long-term effects, especially those of sedentary lifestyles, diets, longitudinal stresses and biological factors of the environment, can also be connected to changes in body weight index, body surface area and latent iron deficiency, which effect SPVR at rest.

Essential hypertension and myocardial hypertrophy can most likely be explained by endogenous diszincosis. The significant positive correlation between zinc content in blood serum and the triple product reflects the myocardial oxygen requirement only at psychological load and at rest after psychological load has been applied, but not at rest before applying the load. This phenomenon is connected to the psychological capabilities of Homo sapiens and can be explained by the neuro-cardiologic hypothesis of mammalian evolution, which is connected to the evolution of red blood cell properties [14].

References

1. Barcellos-Hoff MH, Brenner DJ, Brooks AL, Formenti S, Hlatky L, et al. (2011) Low-dose radiation knowledge worth the cost. Science 332: 305-306.
2. Loke WK, Tang FR (2015) Molecular mechanisms of low dose ionizing radiation induced hormesis, adaptive responses, radioresistance, bystander effects, and genomic instability. Int J Radiat Biol 91: 13-27.
3. Ushakov IB, Bogomolov AV, Kukushkin YA (2010) The patterns of functional states of a human machine operator. Moscow, Russia, Science.
4. Artamonova VG, Leckar PG, Samorodova LN (1978) To the problem of biologic effects of radio frequency electromagnetic waves. The Works of LSGMI 124:102-106.
5. Ivanova OM (2007) Radiation hematologic stress due to non-lethal doses of technogenic radiation. Thesis Sixth all-Russian symposium on battle stress. Battle stress: stress mechanisms in extreme conditions of activity. State research and testing institute of defense medicine Moscow, Russia 2007: 40-41.
6. Ivanova OM (1991) Some topics of human machine operator health research.The All-Union conference on flight safety and human factor in aviation– St-Petersburg, Russia, Civil aviation academy :81-82.
7. Ivanova MA (2012) The studies of human evolutionary physiology due to differential sphygmography systems. Journal of New Medical Technologies 1:9-11.
8. Bender R, Bender N (2013) Brief communication: Swimming and diving behavior in apes (Pan troglodytes and Pongo pygmaeus): first documented report. Am J Phys Anthropol 152: 156-162.
9. Reizenstein P (1979) The haematological stress syndrome. Br J Haematol 43: 329-334.
10. http://www.escardio.org/communities/EACPR/toolbox/health-professionals/Pages/SCORE-Risk-Charts.aspx
11. Belenkov YN, Oganov RG (2007) The guide to ambulance cardiology. Moscow, Russia, Geotar-Media, 2007 : 398 c.
12. Shubik VM (2003) Radiation accidents and health. St. Petersburg: 336p.
13. 1999 World Health Organization-International Society of Hypertension Guidelines for the Management of Hypertension. Guidelines Subcommittee. J Hypertens 17: 151-183.
14. Ivanova OM, Ivanova MA (2011) Research of red blood cell properties. Preventive and clinical medicine 4:75-82.
15. Fyodorova ZD, Bessmeltsev SS, Kotovschikov MA (1989) The techniques of red blood cell aggregation, viscosity and deformability. St-Petersburg, Russia, Fyodorova, 1989: 12p.
16. Sokolovsky VV (1996) Thiol-disuflide ratio of blood as the parameter of the inspecific resistance of an organism. Saint-Petersburg, Russia: 30c.
17. Ivanova O, Simon S (1997) New methods of telemedicine due to just-in-time education systems. J. Telemed Telecare 3: 106.
18. Ivanova OM (2002) Anatomy and molecular principles in the new technologies of the coronary heart disease (CHD) research and of CHD accompanying functional system disorder research. Journal of New Medical Technologies IX: 54–58.
19. Bergomi M, Rovesti S, Vinceti M, Vivoli R, Caselgrandi E, et al. (1997) Zinc and copper status and blood pressure. J Trace Elem Med Biol 11: 166-169.
20. Avtzyn AP, Zhavoronkov AA, Rish MA, Strochkova LS. (1991) Trace element diseases in humans. Moscow, Russia, Medicine: 495 p.
21. Cox T. Stress (2nd edition) 1985- New York, Macmillan.
22. Ivanova OM (2002) Relationship between blood pressure, blood cell counts, cardiovascular dynamics and serum copper, zinc and iron. Biogerontology 3: 68-69.
23. Ivanova OM (2000) The parameters of an endocrine system and the psychoemotional load. The proceedings of the 3rd All-Russian conference: 104-105.
24. Shanin VY (1998) Clinical pathophysiology. Saint-Petersburg, Special literature: 563p.
25. Tzeng YS, Li H, Kang YL, Chen WC, Cheng WC, et al. (2011) Loss of Cxcl12/Sdf-1 in adult mice decreases the quiescent state of hematopoietic stem/progenitor cells and alters the pattern of hematopoietic regeneration after myelosuppression. Blood 117: 429-439.
26. Shigematsu I, Kamaola N, Kyama A, Sasaki H (1995) Effects of A-bomb radiation on the human body. Harwood Academic Publishers-Tokyo: 200p.
27. Ripa S, Ripa R (1994) Zinc and blood pressure. Minerva M
28. Stowe RP, Peek MK, Cutchin MP, Goodwin JS (2012) Reactivation of herpes simplex virus type 1 is associated with cytomegalovirus and age. See comment in PubMed Commons below J Med Virol 84: 1797-1802.edica 85: 455-459.
29. Kuna P (1989) Chemical radioprotection. Moscow, Medicine: 190 p.
30. Kutzenko SA, Butomo NV, Grebenuk AN, Ivnitsky YT, Melnichuk VP, et al. (2004) Military toxicology, radiobiology and medical defense. St-Petersburg, Russia, Foliant: 528p.
31. Shustov SB, Yakovlev V, Baranov V, Karlov V (1997) Arterial hypertensions. St-Petersburg, Russia, Special literature.
32. Tzarenko SV, Kryshov VV, Tyurin DN, Lazarev VV, Tsymlyakov DL (1999)The correction of arterial hypertension in the intensive therapy of patients with a head and brain injury and vessel diseases of brain. Journal of intense therapy 2:60-64.
33. Gawade BV, Fegade SA Rauwolfia (2012) Reserpine as a potential antihypertensive agent. A review. Int J Pharm Phytopharmacol 2: 46-49.