English version: VASCULAR PATHOLOGY IN LIQUIDATORS OF THE ACCIDENT AT CHERNOBYL NUCLEAR POWER PLANT: FORMATION, MANIFESTATION, AND PROGRESSING. LITERATURE REVIEW AND OWN INVESTIGATION*

Zhdan V.M., Shtompel V.Yu.

Higher State Educational Establishment of Ukraine "Ukrainian Medical Stomatological Academy", Poltava.

Vascular pathology keeps fundamental place in the morbidity structure among liquidators of the accident at Chernobyl Nuclear Power Plant in spite of the remote period after the catastrophe. This determines the significance for studying basic pathogenetic mechanisms of the diseases occurring due to the influence of complex disturbing factors. This research paper shows that the liquidators of the accident at Chernobyl Nuclear Power Plant demonstrate the changes in the indices of pituitary-thyroidal-adrenal hormones, shifts in the system of lipoperoxidation and antioxidant protection as well as in the system of vegetative and immune regulation. These factors determine the activity of compensatory and adaptive processes in the human body. The authors have found out that the adaptive functions of pituitary-thyroidaladrenal system fade inversely proportional to the growth of pathologies ranging from the functional (the first stage of discirculatory encephalopathy (DE)) to organic (ischemic heart disorder of the second stage of disculatory encephalopathy (IHD)), and these functions become weaker in combinations of IHD and DE in the liquidators of the Chernobyl accident. In the system of the free-radical lipid oxidation for theses patients the processes of lipoperoxidation are noticed to become more intensive, and the compensatory tension of antioxidant protective system shows the decrease in its activity in cases of comorbidities. There is a dependence of clinical manifestations of the diseases, hormonal and metabolic changes, state of central and peripheral hemodynamics on the direction of vegetative regulation and pathogenetic mechanisms of its disturbances. In proportion to the aggravation of vascular and concomitant segmental and suprasegmental vegetative pathologies in the liquidators of Chernobyl accident the capacity of vegetative regulation of circulatory system fails to function normally shifting towards the parasympathetic section and unbalancing of vegetative supply. Thus, the formation, manifestation, and progressing of cardio-vascular disorders under the influence of complex disturbing factors are mainly caused by the pathological changes determined by the decrease in activity of compensatory and adaptive processes of the organism and, therefore the proper correction is necessary.

Key words: hormones, lipid peroxidation, antioxidant system, vegetative nervous system, liquidators of Chernobyl accident.

The dynamics of morbidity among the liquidators of the Chornobyl accident which is known as the planetary technogeneous world catastrophe was characterized by gradual growth starting in 1989-1990-s. The functional syndromes as vascular dystonia, asthenic syndrome, astheno-neurotic syndrome developed at the first stage. Then this pathology turned into the organic one including hypertension (H), dyscirculatory encephalopathy (DE), ischemic heart disease (IHD). Most authors connect this process with an action of complex damaged factors that affected on the human organism in the conditions of liquidation consequences of Chernobyl disaster. It is important to mention diseases of circulatory system are widespread in the structure of liquidator's morbidity and in the further period from the beginning stage of catastrophe [4,7,10,12]. Undoubtedly, certain commonly known factors also contribute to the occurrence of thology in this population. [10,16,19]. However it is impossible to exclude an impact produced by the limited adaptive resources, unbalance of many mechanisms that may result not only in rapid development of the diseases but in its progression as well.

We examined the liquidators of Chernobyl accident who worked at the Chernobyl Nuclear Power Plant for 1986 –1987, when except the radial factor (a dosage of exterior homogeneous gamma-irradiation for patients ranged from 5 to 50 rem (roentgen equivalent man). The mean value for 85% of the liquidators made up18.5 rem

according to the information reported by the regional military registration and enlistment offices. These persons were also severely exposed to the influence of chemically aggressive substances, which were used for dust reduction and deactivation of surfaces, they also experienced long-time chronic stress (especially in the conditions of objective situation, which was often changing due to many factors) which disturbed the motivational personality sphere [6]. The impact produced by the complex of above-mentioned disturbing factors resulted in the following consequences which included the disturbance of general adaptative reactions, which failed to adapt to unwanted influences, and in some cases could lead to the development of pathologies [2]. The failure in functioning of compensatory and adapted process compensatory and adapted processes mainly consists in some changes that occur in the pituitary-thyroidal-adrenal system, in the system of lipid peroxidation and antioxidant protection, in immune status and hemostasis [11,15,18].

The problem of vegetative dysfunctions as one of the leading mechanisms of dysadaptation takes on special significance for the liquidators of Chernobyl accident (LCA) [3,13,17]. Segmentary and suprasegmentary vegetative centers affect on the functional condition of human systems and organs as well as they are responsible for regulating blood circulation. Clinical researches convincingly demonstrate the close interdependence between the nervous system, non-specific resistance and immu-

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nogenesis. There has also been shown the development of immune suppression in humans under stress [9,18]. The investigations on immunosympathetic animals have demonstrated the sympathetic section of vegetative nervous system (VNS) is an efferent section in the regulation of immune response. Depression of adrenergic mechanisms is accompanied with the suppression of specific reaction on antigen. Sympathetic nervous system stimulates functions of lymphoid tissue, and catecholamines serve as mediators activating leukocytes and phagocytes. Control influence of catecholamines on immune reactions is performed by means of adrenoreceptors [9, 29].

Clinical studies confirm the interrelation between the VNS dysfunction and hormonal homeostasis [23, 24]. It has been shown the progress of vascular pathology in LCA which ranges from functional DE of the 1st stage to organic condition (coronary heart disease (CHD) - stable exertional angina of II-III FC, DE of the 2nd stage) is accompanied by the changes in the pituitary-thyroidaladrenal system, and its adaptative functions steadily fade, and in cases of comorbidities, for instance, in a case of CHD and DE of the 2nd stage they become considerably exhausted [22]. So, the highest level of cortisol was observed in DE of the 1st stage (943,56±34,48 nmol/l), while in the patients with CHD, DE of the 2nd stage it was likely < lowered (548,37±27,61 and $461,47\pm21,34$ nmol/l accordingly, $p_1 < 02,01$, $p_2 < 0,01$). Thus, the prolonged tension of compensatory adaptative processes can lead to exhaustion of the main adaptative mechanisms.

The patients with the comorbidities of CHD and DE of the 2nd stage manifested the course which was marked by more expressed clinical, biochemical and functional severity, and the level of cortisol was likely lowered (287,38±16,56 nmol/l) in comparison not only with the indices of the patients with DE of the 1st stage ($p_1 < 0.01$), but also with the indices of the patients who had CHD (p_2 < 0.01) and DE of the 2^{nd} stage (p₃ < 0.01). At the same time the patients were observed to show the changes in the vegetative reaction. The analysis of neurohumoral regulation of the heart rhythm spectrum power [5] in LCA under the observation found out its decrease simultaneously with the growth of pathology severity (in DE of the 1^{st} stage - 2367±1706 mc^2 , in CHD - 1737±1241 mc^2 , in DE of the 2nd stage - 1737±1241 Mc², CHD in combination with DE of the 2nd stage - 531±314 mc²) with the shift of regulation balance towards the parasympathetic sec-

The dynamics of triiodthyronin (T_3 hormone) in the patients was identical to the dynamics of cortisol indices (in DE of the 1st stage - 2,4± 0,16 nmol/l, in CHD-2,13±0,07 nmol/l, in DE of the 2nd stage - 1,69±0,17 nmol/l, in CHD combined with DE of the 2nd stage - 1,41 nmol/l, p_1 <0,01, p_2 <0,01, p_3 <0,05). The level of thyroid-stimulating hormone was changing statistically uncertainly.

The increase in activity of pituitary-thyroidal-adrenal system and sympathico-adrenal system which are the most important components of human adaptative system performs a major protective function. But prolonged tension of these mechanisms may turn into a damaging factor with time, which can interfere the blood supply of systems and organs, lower the immunity and promote transformations of functional vascular disorders into severe forms of vascular pathology as CHD, DE, essential hypertension. It is possible to assume that these dis-

eases which have developed against the background of prolonged stress produce an influence upon the depression of compensatory – accommodative processes. In our study this is pointed out by the indices of cortisol, triiodthyronin in the patients with CHD, DE of the 2nd stage and with their combination.

It is necessary to emphasize that the patients with CHD and DE who did not take part in the elimination of the Chernobyl Nuclear Power Station accident show the reverse dynamics of cortisol and triiodthyronin levels which increases in accordance with the aggravation of the pathology. The highest cortisol level was observed in the patients with CHD (it exceeded in 1,4 times), in the patiens with DE of the 2nd stage (it exceeded in 1,5 times), and in the patients with both CHD and DE of the 2nd stage this level was doubled in comparison with the patients who had DE of the 1st stage. The changes in triiodthyronin level were characterized by the identical directedness.

The prolonged stress and the presence of vascular pathology in LCA lead to the activation of lipid peroxidation processes and to the tension of SAOP which gradually runs out as the vascular disorders progress [22, 24]. It results in the cellular membranes damage, the disturbances in microcirculation, rheological blood properties, immunity, and complicates the course of the disease. The patients with CHD and DE who did not take part in the elimination of consequences of the Chornobyl accident demonstrate the increase in the activity of prooxidant system but against the background of SAOP tension according to the severity of the pathology.

We investigated the characteristics of the course of CHS in LCA against the background of thyroid-vegetative dysfunctions [23]. It is known that CHD is complicated with disturbances of vegetative nervous system (VNS) [3, 20, 21, 28, 30]. These disturbances rank the leading position in the development of lethal arrhythmias [8], latent myocardial ischemia [14], sudden cardiac death [27].

When comparing the parameters of the functional state of the VNS and the thyroid gland (TG) it is possible to observe an interdependence between the character of autonomic reactions and the concentrations of thyroidal hormones: thus, sympathicotony is characterized by their elevation, while parasympathicotony is characterized by their lowering. Some attention should also be pain to the absence of appropriate response of central regulatory mechanisms to the dynamics of thyroidal hormones (comparing the indices of thyroid-stimulating hormone in the patients with both their elevated and lowered level, p> 0.5), that may contribute to the aggravation of thyroid dysfunction.

The patients with elevated indices of thyroidal hormones mainly demonstrate the increase in autonomic reactivity (AR), vegetative supply of body vitality (VSV) that determines the disturbances in regulatory mechanisms, in the adaptive responses of the cardiovascular system and affects the clinical manifestations of CHD. The patients were observed to have not only anginal pain, but long-lasting diffuse cardiac pain, palpitation, vegetative crises of sympatho-adrenal character, tachycardia, cardiac fibrillation, extrasystole, the growth of arterial pressure. According to the data obtained by rheoencephalography (REG) and rheovasography (RVG) the patients predominantly had increased vascular tone. Such conditions as the thyroid hyperplasia (TH), essential hypertension (EH) of the I stage, EH of the II stage, and DE of the I stage were registered to be the concomi-

tant pathologies for CHD. The patients with lowered indices of thyroidal hormones mainly manifested the reduction of vegetative reactions and VSV. This might be considered as a sign of profound disturbances in adaptive functions of VNS and was accompanied with the absence or even paradoxical vascular response under exertion that was shown with the REG functional tests. This may lead to the failure of compensatory reserves as well as to the inadequacy of myocardial blood supply and in this way to the aggravation of coronary pathology. The patients of this group were observed to have the respiratory disorders, vegetative-vascular paroxysms of vago-insular nature, signs of heart failure, bradycardia, extrasystole. TH and the DE of the II stage were registered as the commonest concomitants diseases. REG findings found out the weakening of vascular tone and difficulties in venous outflow.

Taking into the consideration the important role of VNS in the regulation of the cardiovascular activity [26], we carried out the studied vegetative status conjunction with the parameters of central and regional hemodynamics in the patients who had underlaying CHD and such comorbidities as vegetative disorders in spinal osteochondrosis (SOCH), DE, TH [25]. The patients having CHD and no comorbidities demonstrated the prevalence of eutony, adequate VR and VSV, and in most patients (40%) the eukinetic type of hemodynamics was observed. In cases of CHD and concomitant SOCH the sympathicotony and hypokinetic type of hemodynamics dominated (cardiac index - CI - 1,76 ± 0,05 l/ min • m², total peripheral resistance - GPR - 2591,56 ± 65,71 dyn • cm • s⁻⁵) mainly in patients who had longer course of SOCH, pronounced pain syndrome, muscular tonic neurodystrophic changes, anxiety and hypochondriacal disorders. The LCA made up 59% of there patients. According to the RVG and REG findings there were registered differently directed vectors of vascular tone, but mostly it increased, that led to the lowering of CI and the formation of hypokinetic circulation type. The patients with CHD and increased indices of thyroidal homeostasis demonstrated the predominance of sympathopathy was dominated, increased VR and VSV. 69.8% patients (among whom LCA constituted 31%) were observed to have hyperkinetic type of hemodynamics. REG findings pointed to the signs of vascular dystony, neuropsychological status showed increased anxiety, neuromuscular excitability, irritability.

59.7% of the patients with CHD and DE (among whom LCA made up 42%) demonstrated hypokinetic type of hemodynamics (CI - 1,83 ± 0,04 l/min•m², General peripheral resistance (GPR) - 2001,4 ± 92, 8 prevalent dynes•cm•s⁻⁵), parasympathycotony, weakening of mechanisms responsible for autoregulation of VNS and especially its sympathetic division. In the patients with DE of $2^{\rm nd}$ and $3^{\rm rd}$ stages GPR was recorded to decrease in all the hemodynamic types that pointed out the decrease in sympathetic influences upon the vascular tone. According to REG findings most patients had venous outflow obstruction, decreased volume and rate of cerebral circulation. Thus, in cases of the combination of CHD and DE, especially in increasing severity of DE, sympathetic (hyperergic) regulatory influences become weaker while parasympathetic (trophotropic) ones become stronger, the hypokinetic type of hemodynamics develops as well as depressive disorders and passive attitude to the disease, which complicates the rehabilitation of the patients may occur.

The analysis of parameters of autonomic balance obtained by cardiointervalography has shown that the most appropriate reactivity is registered in hyperkinetic type of hemodynamics. Lowered and reversed reactivity points to the disturbances in interaction between ergotropic and trophotropic structures. The sufficient autonomic balance was combined hypokinetic type of hemodynamics and prevailed in patients with CHD and such comorbidities as SOCH and / or DE. There was a particular regularity in changes of vegetative supplying of vitality (VSV) in different variants of circulation. The hyperkinetic variant was marked by excessive VSV in heart rate and blood pressure, while hypokinetic variant was characterized by insufficient or uncoordinated with components (excessive in heart rate and insufficient in blood pressure), which might be regarded as the most inadaptative Decompensation of autonomic functions disturbs the adaptive responses of the heart and blood vessels, the adequacy of myocardial blood supply in a variety of conditions and certainly produces an impact on the development of CHD.

Thus, the formation, manifestation and progression of vascular disease in liquidators of the Chernobyl accident is based on the mechanisms of inadaptability, among which the leading role belongs to hormonal disorders, changes in lipid peroxidation and antioxidant protection system, immune homeostasis in close association with autonomic disorders of the central and peripheral genesis. This should be taken into account when developing patient-oriented therapeutic and preventive measures for the rehabilitation of each member of those tragic and at the same time heroic events.

A quarter of a century has passed since the Chernobyl accident happened, but it gave rise to grave medical and social consequences which are still urgent nowadays. This is evidenced by recent events in the nuclear power plant "Fukushima" in Japan. Unfortunately, the consequences of technogenous catastrophes are still threatening the mankind.

References

- Afanas'eva N.I. Osoblivosti tireoïdnogo gormonal'nogo gemostazu pri zachvoryuvannyach schitovidnoï zalozi u suchasnich radiaziyno-ekologichnich umovach Ukraïni URZh.–1998.–№3–s.354–357.
- Bazhan K.V.Prirodni fizichni chinniki v likuval'ni pazientiv , scho zaznali vplivu ekstremal'nich faktoriv.

 – Poltava, 1998.–207s.
- Veyn A.M. (red.) Zabolevanie vegetativnoy nervnoy sistemi. Rukovodstvo dlya vrachey .M., Medizina,1991.– 622s.
- Diszirkulyatornaya enzefalopatiya i eye sochetanie s drugimi zabolevaniyami nervnoy sistemy u uchasnikov likvidazii posledstviy avarii na ChAES (diagnosticheskie i terapevticheskie podchody) / T.V.Mironenko, V.N.Penner, N.L.Pizul i dr. // Mezhdunarodnyy nevrologicheskiy zhurnal.–2010.–№4(34).–s.25–28.
- Doslidzhennya variabel'nosti serzevogo ritmu u kardiologichniy prakizi/ V.O.Bobrov, V.M.Chubuchniy, O.Y.Zharinov ta in../ Metodichni rekomendazii, K., 1999.– 24 s.
- Druzhinin A.M. Izmenenie motivazii povedeniya imeyuschich ofizial'nyy status postradavshich v rezul'tate avarii na ChAES // Materialy nauchnoy konferenzii «Aktual'nye problemy epidemiologii i pervichnoy profilaktiki medizinskich posledstviy avarii na ChAES (Kiev ,15–16 okt.1997).– K. : Chernobyl' –interform.1999.– S.269–273.
- Zhdan V.N. Poltavskiy bishofit v kompleksnoy reabilitazii likvidatorov posledstviy avarii na ChAES/ V.N.Zhdan, Yu.M.Kazakov, V.Yu.Shtompel'// Tezisy VIII Yubileynoy rossiyskoy nauch.konf. s medunar.uch. "Reabilitaziya i

- vtorichnaya profilaktika v kardiologii".-Moskva,2009.-S.63-64.
- Zheludochkovoe narushenie ritma u bol'nych ishemicheskoy bolezn'yu serza: Vozmozhnaya rol' avtonomnoy nervnoy sistemy/ V.A.Bobrov, V.N.Simorot, A.P Stepanenko. i dr. // Kardiologiya. – 1993.–T.33.–№1.– S.11–14.
- Ismagilov M.F. Rol' vegetativnoy nervnoy sistemy v regulyazii ne- spezificheskich immunnych reakziy organizma / M.F.Ismagilov, Yu.V Korshun.// Kazanskiy medizinskiy zhurnal–1991.– T.72, №1.– S.69–72.
- Karamova L.M. Medizinskie posledstviya Chernobyl'skoy katastrofy/ L.M.Karamova, G.R.Basharova, M.Ch.Gibidulina // Fundamental'nye issledovaniya.– 2009.–№7.–S.64–65.
- Meerson F.Z. Adaptaziya, stress i profilaktika. M.: Nauka.–1981. – 278s.
- Meshkov V.A. Effektivnost' lecheniya serdechnososudistoy patologii u likvidatorov posledstviy avarii na Chernobol'skoy atomnoy elektrostanzii/ N.A Meshkov., T.A.Kulikova, M.V.Fokeeva //Radiaziya i risk (Byulleten' nazional'nogo radiazionno-epidemiologicheskogo registra).-2011.- T20.- №3.- S.47-57.
- Nyagu A.Ch. Psichonevrologicheskie i psichologicheskie aspekty posledstviy avarii na Chernobyl'skoy AES//Vestn.AMN SSSR,1991.–11– S.31–32.
- Osoblivosti vegetativnogo statusu u chvorich z bezbol'ovoyu ishemicyu miokarda / O.S.Polyans'ka, V.K.Taschuk, N.V.Bagun ta in..// Bukovins'kiy medichniy zhurnal,1998.– №3.– S.47–50.
- Petrov R.V. Rol' gormonov i mediatorov v funkzionirovanii immunnoy sistemy // Vesti AMN SSSR.1980.–T.7.–S.11– 17.
- Serdechno-sosudistye zabolevanie i ich faktory riska u likvidatorov posledstviy avarii na chernobyl'skoy AES po itogam skriniruyuschego obsledovaniya/ V.I.Shamarin, S.A.Shal'nov, S.K.Kukushkin i dr. // Kardiologiya.–1996.– №3.–S.44–46.
- 17. Tayzlin V.Y. Vegetativnaya distoniya i zerebrovaskulyarnye narusheniya// Mezhdunarodnyy medizinskiy zhurnal, 1999. №3.–S. 31–34.
- Fomin V.V. Gipotalamo-gipofizarnaya sistema i immunnyy otvet pri infekzionnych zabolevaniyach/ V.V.Fomin, S.N.Kozlova, Yu.A.Knyazev - Sverdlovsk : Izd-vo Ural.unta,1991.–240s.
- Chomazyuk I.N. Psichoemozional'nye faktory i bolezni sistemy krovoobrascheniya u postradavshich pri Chernobyl'skoy katastrofi. // Materialy mezhdunar. konf. « Aktual'nye i prognoziruemye narusheniya psichicheskogo

- zdorov'ya posle yadernoy katastrofy v Chernobyle (Kiev, 24–28 maya 1995g.).– K.– 1995.– S.276.
- Shtompel V.Yu. Vetebrogennye bolevye sindromy: mechanizmy razvitiya, svyaz' s koronarnoy patalogiey // Mezhdunarodnyy medizinskiy zhurnal.–1999.– t.5,4.– S. 25–27
- Shtompel' V.Yu. Osobennosti diagnostiki i lecheniya IBS na fone vegetativnych disfunkziy u likvidatorov posledstviy avarii na ChAES // Mezhdunarodnyy medizinskiy zhurnal.– 1999.– t.5,4.–S.27–29.
- 22. Shtompel' V.Yu. Disadaptaziyni mechanizmi formuvannya sudinnoyi patologiyi u likvidatoriv avariyi na ChAES// Ukrayins'kiy radiologichniy zhurnal.-2000.-№4.-S.376-378
- Shtompel' V.Yu. Perebig ishemichnoyi chvorobi serzya pri tiroyidno-vegetativnich disfunkziyach// Ukrayins'kiy radiologichniy zhurnal.–2000.–№3.–S.328–330.
- 24. Shtompel' V.Yu. Vpliv vegetativnich disfunkziy zentral'nogo i periferichnogo r'enezu na kliniko-patogenetichni osoblivosti IChS u likvidatoriv avariyi na ChAES// Medizina segodnya i zavtra.–2000.–№3.–S.68–71.
- Shtompel' V.Yu. Osoblivosti funkzional'nogo stanu serzevo - sudinnoyi sistemi i varianti yogo regulyaziyi chvorich na IChS z vegetativnimi porushennyami // Aktual'ni problemi suchasnoyi medizini. Visnik UMSA.–2001.– T.1.vip.1–2.– S.53–55.
- 26. Shchvazabaya I.K. O Novom podchode k ponimaniyu gemodinamicheskoy normy./ I.K.Shchvazabaya, E.N.Konstaninov, I.A.Gundarov // Kardiologiya .–1981.– №3.–S.10–14.
- Yabluchanskiy N.I. Osnovy prakticheskogo primeneniya neinvazivnoy technologii isledovaniya reflektornych sistem cheloveka/ N.I.Yabluchanskiy, A.V.Martynenko, A.S.Isaeva – Char'kov, Osnova, –2000.–86s.
- De Ferrari G.M. Cardiac vagal activity, myocardial ischemia and sudden death/ G.M.De Ferrari, E.Vanoli, F.J.Schwartz // Cardiac Electrophysiology, From Sell to Badside.–1995–Vol.30.–№1– p.422–434.
- Modulation of the immune system by the autonomic nervous system and it's implication in immunological changes after training/ K.Nagatomi, T.Kaifu, M.Orutsu at al.// Exerc.Immunol.Rev.-2000.-vol.6.-p.54-74.
- Shtompel V. Iu. Rehabilitation of coronary patients with psychovegetativ disturbances // World congress on rehabilitation in psychiatry. Abstracts.-Belgrade. Yugoslavia. August 27–30, 1997.–p.78

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