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Clinical and laboratory aspects of vibroacoustic therapy in the complicated course of acute exogenous poisoning in the rehabilitation period

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Abstract

Background*. An abrupt increase in the length of the rehabilitation period for acute poisoning (AP) is usually associated with concurrent pneumonia. In AP with psychopharmacological agents (pPPAs) we found a decreased tendency of platelets to spontaneous activation and hyperactivation, the pathology course being more favorable course*

against the background of vibroacoustic therapy (VAT). However, there are no detailed clinical and laboratory studies of VAT in various APs.

The objective *was to improve the efficacy of patient treatment for acute respiratory viral infection in a toxicological hospital by including VAT in the complex of therapeutic measures.*

Material and methods. *Thirty two patients with pPPAs, with neurotoxicants (pNTs) and corrosive substances (pCSs) complicated by pneumonia were studied. The main group consisted of 19 patients in whom VAT was used (2–9 daily sessions of 5 minutes each); and 13 who received only the basic therapy made the comparison group. Hemorheology parameters, morphofunctional status of erythrocytes and platelets, as well as endotoxicosis were assessed in the blood of all patients before VAT initiation and 1–2 days after VAT completion.*

Results*. In the main group, VAT made a moderate positive effect on hemorheology: a decrease in the initially increased (relative to normal) aggregation of red blood cells in motion (by 1.2 times) and an increase in the initially reduced (relative to normal) blood viscosity at shear rates of 2.5 s^{-1} and 62.8 s^{-1} (by 1.15 and 1.1 times, respectively); the impedance aggregometry revealed a statistically significant ($p<0.05$) 1.5-fold increase in platelet aggregation; their count increased (1.1-fold). At the same time, a statistically significant decrease (by 1.3 times) in the count of platelets with damaged membranes ($p=0.03$) and the elimination of the platelet tendency to spontaneous activation ($p=0.04$) were revealed. Among the standard indicators of endotoxicosis, there was a decrease in the leukocyte intoxication index (1.3 times) and blood leukocyte count (1.2 times). The VAT effect on the endotoxicosis severity was the greatest when assessed in terms of toxemia cellular component parameters: a statistically significant ($p<0.05$) decrease in the relative number of dead leukocytes (1.4 times) with the stabilization of their absolute count and an*

increase in the blood content of CD14+HLA-Dr+-monocytes (1.3 times). The VAT use significantly improved the AP course: in general, the length of pneumonia period decreased statistically significantly ($p<0.05$) (by 1.7 times) and the treatment duration was shortened (by 1.6 times); the length pneumonia period also decreased for $_{P}$PPAs (by 1.2 times), and statistically significantly ($p<0.05$) decreased for $_{P}$NTs (by 1.9 times); the treatment duration was reduced by 1.3 and 1.4 times, respectively.

***Conclusion**. An evidently increased efficacy of rehabilitation treatment with VAT has been demonstrated. Further enhancement of VAT capabilities is expected through optimizing the VAT regimen and combining it with other treatment methods. It is important to study the morphofunctional properties of platelets along with the determination of their aggregation activity.*

Keywords: acute poisoning, rehabilitation, vibroacoustic therapy, hemorheology, erythrocytes, platelets, morphofunctional status, endotoxicosis, toxemia cellular component

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AP, acute poisoning
BV, blood viscosity
$BV_{12.6}$, blood viscosity at a shear rate of 12.6 s^{-1}
$BV_{2.5}$, blood viscosity at a shear rate of 2.5 s^{-1}
BVE, blood viscoelasticity
$BVE_{62.8}$, blood viscoelasticity at a shear rate of 62.8 s^{-1}
CD14+ HLA-DR+ monocytes
CD95+ lymphocytes, lymphocytes that express the CD95+ receptor (apoptosis receptor) on their surface

EMs, monocytes expressing human leukocyte antigen D (HLA-DR+) on their surface
GCPs, granule-containing platelets
LII, leukocyte intoxication index
MDA, malonic dialdehyde
MFSP, morphofunctional status of platelets
MMWP, medium molecular weight peptide
$MMWPs_{280}$, medium molecular weight peptides identified at a wavelength of ultraviolet radiation equal to 280 nm
$MMWPs_{254}$, medium molecular weight peptides identified at a wavelength of ultraviolet radiation equal to 254 nm
NSI, Neutrophil Shift Index
pCSs, poisoning with corrosive substances
PMD, platelets with membrane damage
pNTs, poisoning with neurotoxicants
pPPAs, poisoning with psychopharmacological agents
RBC AI_M, red blood cell aggregation index at rest
RBC AI_M, red blood cell aggregation index in motion
RP, rehabilitation period
SSP, spindle-shaped platelet
TAS, total antioxidant status, blood serum total antioxidant activity
VAT, vibroacoustic therapy

Introduction

The rehabilitation period, the final phase of acute poisoning (AP), begins after completing the general resuscitation measures and related detoxification measures aimed at removing exogenous toxicants of a chemical nature from the body. It is an important stage in the AP course, where persistent changes in homeostasis parameters, although not life-threatening for patients, require their targeted correction for effective results of the treatment process.

According to our observations [1], an abruptly increased course of patient treatment in the rehabilitation period (from 2.5–11 to 13.5–24 days) usually depends on the complications of acute respiratory infections present at this stage, primarily pneumonia. The incidence of its development in various acute respiratory infections can range from 17 to 60% or more, and mortality can exceed 40–60% [2–6]. At the same time, literary data indicate a significantly lower incidence of pneumonia in cases of poisoning with corrosive substances (pCSs) [5].

The development, improvement, and implementation of rehabilitation therapy methods are largely aimed at preventing and treating such complications. In these cases, in addition to pharmacotherapy, non-drug treatment methods are successfully used, including vibroacoustic therapy (VAT), or vibration massage. VAT is currently used as a non-drug method for correcting respiratory disorders in various diseases. The therapeutic effect of this method is associated with improved bronchial drainage and ventilation-perfusion ratio in the lungs [7, 8].

In acute poisoning with psychopharmacological agents (pPPAs), we have found a decrease in the tendency of platelets to spontaneous activation and hyperactivation in response to the VAT effect, which was accompanied by a more favorable course of this pathology [9]. At the same time, extensive clinical and laboratory studies of the VAT efficacy in a wider range of AP have not yet been conducted. Meanwhile, our experience indicates the obvious benefit of such studies, since this allows us to better understand both the pathogenesis of AP complications and the sanogenetic mechanisms of the treatment methods used [1, 10].

Objective. To improve the efficacy of AP treatment by including the VAT technique in the treatment complex.

Material and methods

The studies were conducted in the rehabilitation period in 30 patients aged 18 to 80 years old (15 men, 15 women) transferred from the Intensive Care Unit to the Toxicology Department of the N.V. Sklifosovsky Research Institute for Emergency Medicine in 2022–2024. Eighteen patients had acute myocardial infarction, 10 more had poisoning with neurotoxicants (pNTs) (opioid drugs (methadone), psychodysleptics, ethanol, which impact caused the development of toxic-hypoxic encephalopathy), and 2 others had acute viral respiratory

infection. In all cases, the course of the disease was complicated by the development of unilateral or bilateral pneumonia. All patients underwent conservative standard treatment: enhanced natural detoxification (gastric lavage, bowel cleansing, forced diuresis), antibacterial therapy, vitamin, nootropic and symptomatic therapy; if necessary, sedatives were used. Besides, in pCSs, H2-histamine receptor blockers, antispasmodics, hormones and antacids were administered. Alongside with drug therapy for the treatment of pneumonia, we also used VAT. The patients were allocated into two groups: the main group (the VAT group) that included 17 subjects (9 with pPPAs, 7 with pNTs and 1 with pCSs) who in addition to the basic therapy received VAT, and the comparison group that 13 subjects (9 with pPPAs, 3 with pNTs and 1 with pCSs) who received only standard therapy.

VAT using the VibroLUNG device began on the 2nd day after the patients had been admitted to the Toxicology Department. For this, 2 acoustic radiators were used. They were tightly applied to the surface of the chest so that the sound waves would spread into the lungs, causing vibrations in the structures of the lung parenchyma, focusing on the projection zone of the inflammatory infiltrate (infiltrates) in lungs. The frequency of the acting signal was constantly changing, causing various effects, including the resonance one [7, 8]**.** One VAT session was performed daily. The session duration was 5 minutes, and the course included 2-9 sessions. VAT was performed until the resolution of the inflammatory process in the lungs, the appearance of positive dynamics in laboratory parameters and an improvement in the general condition of a patient. The duration of pneumonia course was determined by the series X-ray data indicating the resolution of the inflammatory process in the lungs.

All patients underwent complete blood count blood, urinalysis, and conventional biochemistry studies; and to assess the homeostasis in

venous blood, the parameters of hemorheology, the morphofunctional status of blood cells – erythrocytes and platelets were studied as well as the endotoxicosis characteristics according to its standard parameters and the toxemia cellular component indicators. The studies were performed before the start of VAT and before the discharge from the hospital (1–2 days after VAT completion).

During the hemorheology study, blood viscosity and viscoelasticity, erythrocyte aggregation and hematocrit were assessed. Blood viscosity and viscoelasticity were determined in the mode of decreasing shear rate from 62.8 to 2.5 s^{-1} on a capillary viscometer (BioProfiler, USA). The indices of erythrocyte aggregation at rest (RBC IA_M) and in motion (RBC IAm_1) were studied on MA-1 aggregometer (Myrenne GmbH, Germany). Among the hemostasis parameters, the collagen-induced platelet aggregation was assessed using Chronolog 590 aggregometer (Chrono-Log, USA). Hematocrit and platelet count were measured using an Act diff 2 hematology analyzer (Beckman Coulter, USA).

The rheology and hemostasis parameters of 45 blood donors (30 men and 15 women) aged 20–40 years were taken as reference values.

During the morphofunctional analysis of blood cells, the relative content of the main morphological types of erythrocytes was assessed: discoid erythrocytes (the norm being 85–92%), erythrocytes with jagged edges (normal 4–6%), echinocytes (normal 4–6%), and deformed erythrocytes (the norm 0–3%). Erythrocyte “shadows” (erythrocytes with very low hemoglobin content and marked damage to the plasma membrane) were also measured [11]. During the platelet analysis the following parameters were determined: the proportion of granule-containing platelets (GCPs) (normal 35–75%), morphofunctional status of platelets (MFSP) (normal 75–130 points); the content of platelets with pronounced membrane damage (PMD) (normal 1–3%); the intensity of

platelet adhesion to glass. In addition, the content of spindle-shaped platelets (SSPs) (%), which are absent in the blood of healthy individuals and appear in various diseases, was determined [12, 13]. Normally, the duration of adhesion of one platelet is 10–30 min from the moment of introducing their suspension onto the glass. During this period, the shape of the cell changes, and degranulation occurs with the release of platelet granules from it.

Endogenous intoxication was assessed by the level of fractions of medium molecular weight peptides (MMWPs), determined at a wavelength of ultraviolet radiation of 254 and 280 nm ($MMWP_{254}$ and $MMWP_{280}$) in the blood serum using the method by N.I. Gabrielyan [14]. The following hematological intoxication indices were assessed: the leukocyte intoxication index (LII) and the neutrophil shift index (NSI) [15, 16], as well as the leukocyte and lymphocyte counts in the complete blood count. In addition, the blood pro- and antioxidant activity was studied based on the content of malonic acid dialdehyde (MDA) in it [17] and the level of blood serum total antioxidant activity (total antioxidant status or TAS) studied by means of photometric method on the OLYMPUS AU 2700 biochemical analyzer (Olympus, China). The obtained data were compared with the normal values.

The study of the cellular component of toxemia parameters, lymphocyte apoptosis, and the counting of dead leukocytes were performed using flow cytometry. The count of lymphocytes ready to undergo apoptosis was determined by the expression of the Fas receptor using monoclonal antibodies CD95 and expressed as a percentage of the total lymphocyte count. The relative number of lymphocytes in the process of apoptosis was studied using the Annexin V-FITC/7AAD Kit (Beckman Coulter, USA).

Simultaneous staining of cells with the vital DNA-specific dye 7 amino-actinomycin D (7AAD) made it possible to differentiate cells at the early stages of apoptosis (Annexin V+/ 7AAD–, early apoptosis) from cells that had already died as a result of apoptosis (Annexin V+/7AAD+, late apoptosis). The number of dead leukocytes was determined using the vital dye 7AAD and monoclonal antibodies CD45 (pan-leukocyte marker) labeled with FITC [18–20]. The reference group consisted of 40 blood donors aged from 20 to 45 years.

In recent years, a more accurate assessment of the endogenous intoxication severity, has used the determination of antigen-presenting CD14+ monocytes in blood expressing the human leukocyte antigen D R (HLA-DR+) (CD14+HLA-DR+-monocytes, EM) on their surface, which decreased content in blood, especially below 55%, in combination with changes in other biochemical parameters may indicate the development of a severe infectious process, up to sepsis [21–23]. We also used this parameter in the presented study.

Statistical methods. To identify statistically significant differences between independent samples for parameters measured on quantitative and ordinal scales, the nonparametric Mann–Whitney U test (U-test) was used. For qualitative variables, 2x2 contingency tables, the χ^2 test, and Fisher's exact test were used [24]. When comparing dependent samples to assess the dominant trends, the nonparametric Wilcoxon tests were used for quantitative variables and the sign test for qualitative variables [25]. The results were expressed using the median and the 1st and 3rd quartiles: Me (Q_1;Q_3). Differences were considered statistically significant at a significance level of more than 95% ($p<0.05$) [26, 27].

Results

Hemorheological changes occurred in VAT-included treatment are presented in Table 1.

Table 1 shows that before treatment, among the parameters of blood viscosity and viscoelasticity (BV, BVE), there was a slight initial increase in BV at shear rates of 12.6 and 2.5 s^{-1} ($BV_{12.6}$, $BV_{2.5}$) in the comparison group (by 11.6% and 6.2%, respectively) and $BV_{12.6}$ in the main group (by 6.5%). At the same time, $BV_{62.8}$ was slightly lower than the reference value in both groups (by 3.8% and 4.1%, respectively). With regard to BVE values in the comparison and main groups, only a moderate increase was observed at a shear rate ėqual to 12.6 s^{-1} ($BVE_{12.6}$) (by 15.8% and 21.6%, respectively), whereas the values at $BVE_{62.8}$ in the comparison and main groups and $BVE_{2.5}$ in the main group was even moderately reduced (by 26.4%, 20.1%, and 13.65 %, respectively); and for a $BVE_{2.5}$ in the comparison group it remained virtually unchanged. Plasma viscosity and hematocrit were also slightly reduced. Erythrocyte aggregation at rest approached the reference value in the comparison group and was moderately reduced in the main group (by 21%), but in motion it was significantly increased (by 51.3% and 45.5%, respectively), being a statistically significant change ($p<0.05$). Platelet aggregation also significantly exceeded reference values (by 50% and 33.3%, respectively); the platelet content in blood was also moderately increased (by 30.2% and 19.8% above reference values, respectively).

Table 1. Dynamics of hemorheology parameters in pneumonia during rehabilitation period with using vibroacoustic therapy

Parameter			Reference values (n=45)	Comparison Group (n=9)			Main Group (n=10)		
				Before treatment	After treatment	Δ%	Before treatment	After treatment	Δ %
Shear rate, s^{-1}	62.8	Blood viscosity, cPz	4.18 (3.79;4.29)	4.02 (3.39;4.78)	4.02 (3.68;4.56)	0,00	4.01 (3.58;4.78)	4.36 (3.56;4.59)	8.7
	12.6		4.89 (4.16;5.26)	5.46 (4.42;6.28)	5.40 (4.66;6.37)	-1,1	5.21 (4.08;6.25)	5.06 (3.86;6.12)	-2.9
	2.5		6.01 (4.96;6.51)	6.38 (5.13;6.93)	6.16 (5.45;7.25)	-3.4	5.92 (5.00;7.17)	6.98 (4.65;7.19)	17.9
Shear rate, s^{-1}	62.8	Blood viscoelasticity, cPz	0.53 (0.25;0.86)	0.39 (0.33;0.46)	0.40 (0.37;0.49)	2.6	0.42 (0.31;0.50)	0.45 (0.30;0.52)	7.1
	12.6		1.39 (1.04;2.07)	1.61 (1.05;1.96)	1.35 (1.20;1.68)	-16.1	1.69 (1.10;2.20)	1.97 (1.06;2.29)	16.6
	2.5		2.71 (2.39;4.04)	2.65 (1.70;2.99)	2.06* (1.96;2.28)	-22.3	2.34 (1.81;3.31)	2.91 (1.58;3.62)	24.4
Plasma viscosity, cPz			1.80 (1.70;1.80)	1.61 (1.42;1.72)	1.52 (1.43;1.65)	-5.6	1.75 (1.46;1.78)	1.61 (1.56;1.66)	-8.0
Hematocrit, vol.%			40.0 (40.0;43.0)	33.9 (33.0;40.9)	38.6 (33.7;42.0)	13.9	36.6 (30.8;37.6)	37.4 (27.4;42.8)	2,2
Erythrocyte aggregation, AI_M			15.2 (12.1;19.3)	14.9 (11.4;16.1)	9.70*,[1] (7.00;12.9)	-34.9	12.5 (11.0;20.7)	10.7↓ (8.80;13.6)	-14.4
Erythrocyte aggregation AI_{M1}			19.1 (14.4;23.6)	28.9* (26.7;30.9)	22.4[1] (20.2;26.5)	-22.5	27.8* (23.4;37.1)	23.5 (21.8;28.7)	-15.5
Platelet aggregation, O_M			12.0 (10.0;15.0)	18.0 (14.0;21.0)	18.0 (18.0;20.0)	0,00	16.0 (14.0;20.0)	17.5 (16.0;24.0)	9.4
Platelet count, 10^9 /L			199 (188;206)	259.0 (163.0;360.0)	301.0 (252.0;391.0)	16.2	238.5 (182.0;416.0)	373.0 (258.0;385.0)	56.4

Notes: * statistically significant ($p<0.05$) difference from reference values (Mann–Whitney test); [1] statistically significant ($p<0.05$) difference from standard (Mann–Whitney test); ↓ statistically significant ($p<0.05$) change in the parameter in relation to the standard (Wilcoxon test); Δ%, in relation to the standard parameter. AI_M, red blood cell aggregation index at rest; $AI_{M\,1}$, red blood cell aggregation index in motion

After treatment (see Table 1), some initially elevated parameters in the comparison group significantly decreased, such as $BVE_{12.6}$ by 16.1% (by 1.2 times) and the erythrocyte aggregation in motion by 22.5% (by 1.3 times) (statistically significant, $p<0.05$); the initially reduced hematocrit values slightly increased. Other shifts were associated with an undesirable increased deviation from the reference values, namely the decrease in $BVE_{2.5}$ by 22.3% (by 1.3 times) and erythrocyte aggregation at rest by 34.9% (by 1.5 times), as well as some further increase in the blood platelet count.

In the main group, positive changes included the increase in the initially reduced values of $BV_{62.8}$ and $BV_{2.5}$ (by 1.1 and 1.2 times) approaching the reference values, and a 1.2-fold decrease in the initially elevated erythrocyte aggregation in motion. Among the undesirable changes in the main group, a slight increase in the initially elevated $BVE_{12.6}$ (by 16.6%) should be noted; in addition, the initially elevated platelet aggregation increased slightly (by 9.4%) and their blood platelet count increased 1.5-fold; plasma viscosity and erythrocyte aggregation at rest, which were initially below the reference values, on the contrary, decreased slightly (by 8% and 15.5%, respectively).

Along with hemorheological tests, we studied the morphofunctional properties of blood cells (erythrocytes and platelets). All examined patients were found to have normal quality of erythrocytes with the proper ratio of their main morphological types before the treatment and before discharge, and no erythrocyte “shadows” were found in their blood. In most patients of both groups, columns of cells containing 4–7 erythrocytes (small erythrocyte sludges) were found in blood before treatment.), which they retained even after treatment.

Before treatment, the morphofunctional parameters of platelets in both groups did not differ statistically significantly. In both groups,

normal values of GCPs and MFSP were noted, and the level of PMD was only slightly higher than normal (Table 2), the level of SSPs was also low, their content in most patients was within 1-2%. The number of microscopically distinguishable granules in all SSPs was noticeably lower than that in normal discoid platelets; most of the granules in SSPs were bound to the cell membrane, thereby revealing their readiness for exocytosis (release). In both groups, contacts of SSPs with other platelets were absent, they did not affect the activity of individual platelets to glass during adhesion. In 9 of 16 patients in the main group and 6 patients of the comparison group (n=11), platelets with granules were characterized by marked readiness for spontaneous activation and hyperactivation, since upon contact with glass they began to adhere within 1–2 minutes, often forming flattened platelet aggregates up to 20 μm in diameter; the granule release rate was also increased, amounting to 3 to 10 minutes from the onset of adhesion. SSPs could be detected along the periphery of such aggregates. In 3 patients of the main group and in 3 of the comparison group, the platelet hyperactivation was accompanied by the appearance of platelet conglomerates up to 10 μm in diameter in the peripheral blood. In patients without hyperactivation before the treatment no platelet conglomerates were noted in blood in both groups. In the group where VAT was used, the statistically significant differences were found only in the SSP content in patients with and without platelet hyperactivation, amounting to 2 (1;4)% and 1 (0;1)%, respectively ($p<0.05$). There was no such difference in patients in the comparison group. There were no statistically significant differences between the groups in other platelets morphofunctional parameters.

Table 2. Morphofunctional parameters of platelets in donors and when using vibroacoustic therapy for the treatment of acute exogenous poisoning

Main group (n=16)				
The study stage	GCPs, %	MFSP, score	PMD, %	SSPs, %
Before treatment	50(45;57)	95 (81;108)	4 (3;6)	1 (0;2)
Before discharge	51 (45;60)	94 (82;111)	3 (2;5)*	1 (0;1)
Comparison group (n=11)				
The study stage	GCPs, %	MFSP, score	PMD, %	SSPs, %
Before treatment	52 (48;60)	97 (91;113)	5 (4;8)	1 (1;2)
Before discharge	53 (38;60)	96 (81;109)	4 (4;9)	1 (0;2)

Notes: * statistically significant ($p<0.05$) relative to similar parameters in the comparison group (Mann–Whitney test). GCPs, granule-containing platelets; MFSP, morphofunctional status of platelets; PMD, platelets with membrane damage; SSPs, spindle-shaped platelets.

Before discharge from hospital (after VAT), the GCP, MFSP and SSP parameters in both groups did not change statistically significantly (see Table 2), but the PMD content in the main group was 1.3 times lower than in the comparison group, being statistically significant ($p=0.03$). Also, in the comparison group, the spontaneous activation and hyperactivation of platelets persisted in 5 of 6 patients, who initially had platelets prone to spontaneous activation. At the same time, in the group where VAT was performed, the spontaneous activation and hyperactivation of platelets were observed only in 2 patients, statistically significantly differing from the data obtained in the comparison group ($p=0.04$); platelet conglomerates were absent in blood of such patients. As can be seen, the treatment with VAT made it possible to eliminate the tendency of platelets to spontaneous activation in 77.8% of patients in the main group, while only in 16.7% of cases in the comparison group. The above presented data on the study of the morphofunctional properties of blood cells confirm the results we had obtained earlier [9].

We also assessed the changes in the most frequently used endogenous intoxication parameters in practical work that occurred as a result of VAT (Table 3).

Table 3. Dynamics of endotoxicosis parameters in the presence of pneumonia in the rehabilitation period with using vibroacoustic therapy for acute poisoning

Parameter	Normal	Comparison group (n=10)			Main group (n=12)		
		Before treatment	After treatment	Δ %	Before treatment	After treatment	Δ %
LII, units	1.0 (0.03;1.7)	1.98 (0.57;2.76)	1.51 (1.11;3.43)	-23.7	1.71 (0.48;2.17)	1.35 (0.88;2.19)	-21.0
NSI, units	0.06 (0.03;0.09)	0.05 (0.02;0.09)	0.03 (0.02;0.05)	-40.1	0.03 (0.03;0.04)	0.04 (0.03;0.06)	33.3
Leukocyte count, 10^9/L	6.81 (5.89;7.57)	9.75 (8.60;16.3)	8.98 (7.90;11.8)	-7.9	9.26 (7.23;10.8)	7.78 (6.69;10.8)	-16.0
Lymphocyte content, %	29.7 (21.6;36.4)	17.5 * (9.50;21.0)	18.0* (18.0;21.0)	2.9	17.0* (12.0;22.5)	15.0* (15.0;27.0)	-11.8
MDA	2.27 (2.11; 2.47)	4.59* (3.82;5.75)	4.48* (3.86;5.05)	-2.4	4.60* (3.98;5.07)	4.85* (4.65;5.27)	5.4
TAS	1, 61 (1.56;1.68)	1.37 (1.25;1.43)	1.35 (1.18;1.63)	-1.5	1.21 (1.15;1.30)	1.20 (1.17;1.28)	-0.83

Notes: * statistically significant ($p<0.05$) difference from the normal (Mann –Whitney test); Δ%, in relation to the standard. NSI, neutrophil shift index; LII, leukocyte intoxication index; MDA, malonic dialdehyde; TAS, total antioxidant activity of blood serum

As can be seen from Table 3, there were no serious shifts in the values of the studied endogenous intoxication parameters in either group. Initially, the comparison group and the main group showed an increase in the LII values (2-fold and 1.7-fold, respectively) and the leukocyte count (1.4-fold in both cases); the lymphocyte count decreased noticeably and statistically significantly ($p<0.05$) (1.7-fold in both groups). In both groups, the blood prooxidant activity increased 2-fold, which was reflected by a statistically significant increase in the MDA content in it compared to the norm, and which was compensated by the maintenance of TAS values close to the norm.

After the treatment, some positive changes were noted in both groups: a decrease in the LII values (by 1.3 times in both groups), while

the NSI values did not statistically significantly differ from the norm, being below it. After the treatment, a slight increase in NSI (by 33.3%) was noted in the main group, while in the comparison group it was significantly reduced (by 40%) compared to the level before treatment. In both groups, the concentration of leukocytes in blood decreased slightly after treatment, but these changes were statistically insignificant.

The changes in MDA and TAS values after treatment were not statistically significant. As can be seen, under the VAT impact, no significant shifts occurred in the anti- and prooxidant factors of blood.

The most noticeable effect of the treatment was in relation to apoptosis parameters (Table 4).

Table 4. Dynamics of the toxemia cellular component in patients with pneumonia in the rehabilitation period using vibroacoustic therapy

Parameter	Reference values (n=40)	Comparison Group (n=8)			Main group (n=8)		
		Before treatment	After Treatment	Δ %	Before treatment	After treatments	Δ %
Venous blood leukocyte count, ×109/L	6.3 (5.5;7.3)	9.90 * (7.90;11.3)	7.65 (5.90;8.45)	-22.7	8.10 (7.70;12.4)	8.15 (7.40;10.1)	0.62
CD95+ lymphocytes, % (Fas receptor)	44.8 (41.5;47.5)	33.2 (18.5;53.1)	42.5 (35.1;49.0)	28.0	46.5 (36.8;54.6)	46.8 (42.3;67.3)	0.65
Number of lymphocytes in early apoptosis, %	2.82 (2.05;3.43)	4.30 (2.87;5.73)	5.28* (3.24;7.45)	22.8	3.79 (2.52;8.40)	3.56 (2.41;6.35)	-6.1
Number of lymphocytes in later apoptosis, %	0.11 (0.04;0.16)	0.03 * (0.02;0.10)	0.06 (0.02;0.09)	100	0.05 (0.03;0.08)	0.07 (0.04;0.12)	40.0
Relative number of dead leukocytes (%)	0.62 (0.38;0.92)	1.40 (0.95;1.95)	1.80*,[1] (1.64;2.94)	28.6	0.77 (0.60;0.91)	0.80 (0.54;1.55)	3.9
Absolute count of dead leukocytes, cells/μL	44,0 (23.0;59.0)	114.8 * (96.7;195.8)	160.6* (100;211.5)	39.9	71.0 (59.4;77.8)	73.7 (49.5;123.8)	3.8
CD14+HLA-Dr+-monocytes	80–100%	53.2 (43.0;66.3)	90.5 [1] (71.3;91.8)	70.1	60.2 (51.7;84.7)	85.3 (66.5;95.6)	41.7

Notes: * statistically significant ($p<0.05$) difference from the reference data (Mann –Whitney test), [1] statistically significant ($p<0.05$) difference from the standard (Mann –Whitney test); Δ%, in relation to the standard. CD14+ HLA-DR+ monocytes mean the monocytes that express human leukocyte antigen D (HLA-DR+) on their surface; CD95+ lymphocytes are the lymphocytes that express the CD95+ receptor (apoptosis receptor) on their surface

As can be seen from Table 4, before treatment, the parameter values in both (comparison and main) groups indicated the activation of apoptosis: the number of lymphocytes in early apoptosis was significantly higher than the reference values, by 1.5 and 1.3 times, respectively. Meanwhile, the number of lymphocytes in late apoptosis (dead cells) before treatment in the same groups was significantly lower than the reference values, 3.7 times (statistically significant, $p<0.05$) and 2.2 times, respectively.

The content of dead leukocytes before treatment in the above-mentioned groups was markedly higher than the reference values: the relative one by 2.25 times and 1.2 times, and the absolute one by 2.6 times (statistically significant, $p<0.05$) and 1.6 times, respectively.

Before the treatment, a noticeable decrease in the EM content was also observed in both groups: by 1.5 times in the comparison group and 1.3 times in the main group.

After the treatment (see Table 4), the number of lymphocytes in late apoptosis in the comparison group increased by 2 times, while in the main group it increased only by 1.4 times, that is, they died 2.5 times less often than in the comparison group.

After the treatment, the relative number of dead leukocytes in the comparison group had unfavorable dynamics, statistically significantly ($p<0.05$) increasing by 1.3 times and being statistically significantly higher ($p<0.05$) than that of donors, while in the patients of the main group it remained virtually unchanged. The absolute content of dead leukocytes after the treatment in the comparison group increased by 1.4 times, while the statistically significant ($p<0.05$) initial excess of their content over that of donors increased even more; meanwhile, in the main group their level also remained virtually unchanged.

The EM content after the treatment increased in both groups: by 1.7 times in the comparison group (statistically significantly, $p<0.05$), and by 1.4 times in the main group.

The clinical results of VAT are shown in Table 5. As can be seen from Table 5, in general, VAT during the RP allows a 1.5 time reduction in pneumonia course duration versus the results in the comparison group, the difference being statistically significant ($p<0.05$). In the main group, there was a clear tendency towards a noticeable reduction in the inpatient treatment duration (the mean, by 1.3 times). At the same time, the greatest reduction, by 2 times in the pneumonia duration occurs in pNTs (statistically significant, $p<0.05$), and by 1.2 times 1.2 times in pPPAs; the treatment periods were also reduced by 1.1 times. We could also see that the use of VAT has a positive effect on pCSs as well.

Table 5. Clinical efficacy of complex treatment for acute exogenous poisoning, using vibroacoustic therapy

Parameter (days)	Total number of patients with poisoning and pneumonia in the study (pPPAs+pNTs+pCSs)			pPPAs			pNTs			pCSs		
	Without VAT treatment (n=13)	VAT treatment (n=17)	Δ%	Without VAT treatment (n=9)	VAT treatment (n=9)	Δ%	Without VAT treatment (n=3)	VAT treatment (n=7)	Δ%	Without VAT treatment (n=1)	VAT treatment (n=1)	Δ%
Length of pneumonia period (according to X-ray data), days	6.0 (4.9;6.75)	4.0 [1] (3.0;6.0)	-33.3	6.00 (4.9;6.6)	5.1 (4.0;6.25)	-15.0	6.0 (4.0;9.0)	3.0^ (3.0;4.0)	-50.0	24	4	-83.3
Treatment duration, days	13.0 (10.0;17.0)	10.0 (6.0;15.0)	-23.1	12.8 (9.9;14.3)	11.8 (10,5;16.0)	-7.8	9.0 (8.0;17.0)	8.0 (6.0;10.0)	-11.1	52	15	-71.2

Notes: [1] $p<0.05$ relative to the group without VAT treatment according to the Mann–Whitney test; ^ $p<0.05$ relative to the group without VAT treatment according to the median criterion

Discussion

The clinical results we have obtained indicate the obvious efficacy of VAT, which implementation during RP contributes to a statistically significant, 1.5-fold reduction in the duration of pneumonia in the entire cohort of examined patients. Including the greatest reduction in the pneumonia duration occurring in pNTs (by 2 times, statistically significantly), and by 1.2 times in pPPAs; this has also brought about a 1.1-fold reduction in the total treatment time in both groups. Taking into account a complete period of pneumonia resolution, the following data were obtained: for pNTs, it made 6.0 (5.14;7.4) days in the main group and 6.9 (5.9;7.4) days in the comparison group (a reduction of 13%); and for pPPAs it was 7.6 (6.0;10.0) days and 9.1 (6.8;11.4) days, respectively (a reduction of 16.5%). Apparently, the observed difference, in addition to the therapeutic effect, was also due to the pneumonia genesis: the predominant dependence on somatic disorders in pPPAs (long comatose state with impaired evacuation of bronchial tree secretions and with the aspiration of gastric contents), and the prevalence of the impact of psychopathological disorders in pNTs, at which result at the intensive care stage associated mainly with the use of antibiotic therapy, the treatment turned out to be more effective for pPPAs, and in the rehabilitation period with the use of VAT a more effective treatment was for pNTs. Apparently, the observed difference, in addition to the therapeutic effect, was also due to the pneumonia genesis: the predominant dependence on somatic disorders in pPPAs (long comatose state with impaired evacuation of bronchial tree secretions and with the aspiration of gastric contents), and the prevalence of the impact of psychopathological disorders in pNTs, at which result at the intensive care stage associated mainly with the use of antibiotic therapy, the treatment turned out to be more effective for pPPAs, and in the

rehabilitation period with the use of VAT a more effective treatment was for pNTs.

We should note less frequent cases of pneumonia development in pCSs despite the accompanying severe inflammatory changes associated with a chemical burn of the gastrointestinal tract, which the possible causes will be discussed below, using laboratory data. The lower frequency of pneumonia development in this pathology is also evidenced by the above-mentioned literature data [5].

Comparison with our earlier obtained results [1, 28] shows that the VAT results are similar to those obtained using mesodiencephalic modulation, hyperbaric oxygenation, and intravenous laser hemotherapy for the treatment of pPPAs. A significant advantage of VAT is its non-invasive nature and short duration of the procedure. In connection with the above, a more detailed study of the therapeutic effect of this method using a set of laboratory parameters was of interest.

The study of changes in hemorheological parameters showed the absence of serious impairments at this treatment stage without signs of hyperviscosity syndrome in a significant number of cases. We should note that these changes are noticeably less pronounced than those we noted in previous years [1, 29]. In our opinion, this can be associated with the regular use of the enteral homeostasis correction program at the previous stage of detoxification, resuscitation and intensive therapy [30], as a result of which disturbances of its parameters in the rehabilitation period become less significant. Meanwhile, it was in one of the patients of those with pCSs who underwent VAT and who had had pronounced signs of high viscosity syndrome before its start with an excess in $BV_{2.5}$ and $BVE_{2.5}$ from reference values by more than 1.5 times (with their normalization after VAT). From this we can conclude that, as we have already noted earlier and taking into account the results of multifactorial

statistical analysis [1], in the development of pneumonia in a toxicology clinic, the disruption of the central nervous system is of priority importance, which is just typical of the other two types of poisoning we have considered: pPPAs and pNTs.

In general, we should note that the above-mentioned shifts, both before and after treatment, which are mainly within 20%, can, in our opinion, have a certain effect on the results of the treatment process, and therefore the VAT-involving program correction of the detected impairments, in homeostasis parameters, including hemorheological ones, should be recognized as an appropriate one in this case as well. Among the most useful and fundamentally important hemorheological effects of VAT in the main group, it is necessary to highlight the changes in $BV_{2.5}$ and $BVE_{62.8}$ values as a result of treatment, which reflect the blood flow in capillaries and large vessels, respectively, towards their reference values with their initial decrease, as well as the observed trends towards normalization of hematocrit and erythrocyte aggregation in motion. In the comparison group, on the contrary, it is necessary to note such statistically significant undesirable effects as a further decrease in the values of $BVE_{2.5}$ and the aggregation activity of erythrocytes at rest, which were initially below the reference values.

The moment that was clearly revealed in the course of this study, and which, in our opinion, deserves special attention, is a further, although moderate, increase in the initially increased platelet aggregation in the main group while maintaining its increased value in the comparison group, as well as an increase in their number in blood, more noticeable in the main group. The increase in the content of platelets in blood could be explained taking into account the available literature data indicating such possibilities when the iron level in blood decreases and, accordingly, does hemoglobin. For example, thrombocytosis is noted in many cases of iron

deficiency anemia, whereas iron deficiency is an important pathogenetic mechanism of secondary thrombocytosis for example, in inflammatory bowel disease. Iron intake led to decreased platelet count, even at absence of pre- existing thrombocytosis [31–33]. In our study, before and especially after VAT, no significant changes were observed in either group in such parameters as total hemoglobin content, the erythrocyte count, and the hemoglobin content in them, both the mean and its mean concentration, which values were either extremely close to the norm, being below it by only 1.2–5% (total hemoglobin content), or were within its reference range. This, by the way, characterizes the safety of the treatment measures taken.

In this case, there is reason to assume that the increase in platelet aggregation activity is associated with an increase in their total concentration in blood after VAT. According to some researchers, aggregometry parameters depend on the platelet count in the sample [34–37]. In addition, an increase in platelet aggregation activity may also be associated with an increase in the absolute content of platelets with granules (thousands/μL) in blood after VAT. We have previously shown that there is a correlation between some parameters of the impedance aggregometry and the absolute content of biologically complete platelets in blood [12]. Considering that the relative level of platelets with granules in blood of patients after VAT did not change, the increase in the total concentration of platelets should have been accompanied by an increase in the absolute concentration of platelets with granules, which in turn could stimulate higher values of platelet aggregation activity. However, this does not reflect their more subtle morphofunctional characteristics.

It is also worth noting that there is no statistically significant difference in platelet aggregation activity before and after treatment between the main group and the comparison group, despite the fact that

VAT causes a decrease in the tendency of circulating platelets to spontaneous activation and hyperactivation upon contact with the adhesive surface (glass). This indicates that the selected impedance aggregometry parameter (amplitude of the platelet aggregation curve**)** does not allow predicting the morphofunctional properties of platelets associated with their spontaneous activation.

The limited capabilities of aggregometry in the area of detecting increased platelet activity have been repeatedly pointed out [38–40]. In addition, the spontaneous activation and hyperactivation of platelets can be seen against the background of low values of the total platelet concentration or a decrease in the total coagulation activity of blood [12, 41]. In this regard, the assessment of the morphofunctional characteristics of platelets seems particularly relevant.

Patients with AP have an increased risk of damage to blood cells, primarily platelets and erythrocytes [8, 42–44]. At the same time, exposure to various physical factors can cause changes in the structural and functional organization of platelets and erythrocytes. Determination of the morphofunctional status of blood cells from this point of view is an important addition to the generally accepted methods of studying hemorheology [11–13]. According to our data, despite the absence of morphofunctional disorders in platelets for most of the parameters used, in many cases, platelets, as it turned out, before the treatment had a tendency to increase the spontaneous activation and hyperactivation. This, in our opinion, may be associated with the known high sensitivity of platelets to various effects, including a possible long-term increase in their reactivity under the impact of potentially toxic substances [11, 41–43]. The use of VAT, as can be seen, makes it possible to reduce this undesirable tendency, which was observed when studying the blood of such patients in vitro. It can also be noted that the observed initial

hyperactivation of platelets is less dangerous for the development of rheological disorders, where a more important role is played by the aggregation of erythrocytes, which number in blood by more than an order exceeds the number of platelets, and which condition improves under the VAT impact. However, the correction of functional disorders in the platelet link of hemostasis is also necessary.

As can be seen, the precision semiautomated microscopic determination of the morphofunctional properties of platelets used in this study is a valuable alternative, allowing us to identify the direct positive effect of the applied treatments on patients' blood cells, which otherwise may have been unattainable using standard instrumental methods. In our opinion, these results go beyond the scope of solely toxicological studies. This is also evidenced by a recent publication on the verification of the platelet aggregometry results [39]. It is also noted that a method free from the "platelet number-aggregation" relationship is a light transmission aggregometry [37]. However, it is less available method due to its greater labor intensity, and, in addition, it is associated with difficulties in interpreting the results.

We have managed to establish that VAT contributes to a more intensive elimination of platelets with marked membrane damage from the bloodstream. Despite the fact that in both groups after the treatment their content in the blood only slightly exceeded the norm, i.e. platelets with pronounced membrane damage did not have a serious pathophysiological impact that could have been imposed only under conditions of their high content (more than 10%), nevertheless, a more intensive removal of damaged platelets from the bloodstream during VAT was a favourable effect, allowing us to expect an improvement in the circulating platelet population. It also produces an effect on the platelet link of hemostasis, contributing to a significant decrease in the

tendency of the platelet population to spontaneous activation. The above changes occurring with VAT, may have a sanogenetic effect in the AP rehabilitation period.

The initial changes in the generally accepted endogenous intoxication indices in clinical studies in the examined patients were mainly characterized by an initially slight leukocytosis and a moderate increase in the LII values in combination with a short decrease in the relative lymphocyte count and a significant increase in the prooxidant activity of blood. As can be seen, we are talking about moderate manifestations of endotoxicosis, which, judging by the nature of the changes in the studied parameters, are more related to immune system status [1, 15]. The conducted treatment demonstrated a positive effect on the parameters under study manifested as tendency towards the LII normalization and the leukocytosis reduction; in addition, the changes in the NSI values towards normal in the main group should be recognized as more physiological ones than in the comparison group. As can be seen, as in relation to hemorheological parameters, the assessment of the positive effect of correction of homeostasis parameter disorders in the absence of critical situations should often take into account not only their quantitative changes, but also their vector, which in certain cases, in the presence of a modulating effect, can be of fundamental importance.

The positive effect of the VAT-included treatment on the endotoxicosis severity was most evident in the immune system shifts in late apoptosis [20], associated with its severity reduction that we had previously observed during the rehabilitation period [1] and that confirmed our assumption about the predominantly immune nature of endotoxicosis at this stage of treatment. When assessing the dynamics of the cellular component of toxemia in the present study, we found that initial cell state corresponded to the pattern of apoptosis activation with

an increase in the lymphocyte count in early apoptosis above the reference values in both groups in response, apparently, to the presence of an infectious process reflected by a significant decrease in the content of CD14+HLA-DR+ monocytes in both groups [23].

The effect of VAT was manifested as a less prominent increase in the lymphocyte count in late apoptosis compared to that in the comparison group, as well as in the stabilization of relative and absolute numbers of dead leukocytes in blood, which content increased significantly in the comparison group. Both groups are characterized by changes in the number of CD14+HLA-DR+ monocytes towards their reference values, which, in our opinion, indicates positive dynamics in the course of inflammatory changes in the lungs.

As can be seen, the shifts in the values of endogenous intoxication parameters, both commonly used and, especially, the cellular component of toxemia, clearly indicate a significant predominance in this segment of the treatment results obtained by using VAT.

Conclusion

Rehabilitation therapy, although is not a direct life-saving modality, nevertheless, requires careful multifaceted monitoring of the homeostasis state, since the full restoration of patient health depends on targeted interventions in this direction, allowing the patients to overcome the asthenia phenomena, return to active work and other aspects of full life activities. Judging by the data presented, the above presented also applies to the outpatient management of toxicological patients, since upon their discharge from the hospital, some impairments in homeostasis parameters still persist.

In this regard, the efficacy of rehabilitation treatment is clearly increased by using vibroacoustic therapy. The results obtained aim to

further enhance the capabilities of vibroacoustic therapy in terms of optimizing its regimen and its complex use with other pharmacological and non-pharmacological methods; the prospects of such an approach in acute poisoning management, taking into account the existing experience [1, 45–47], are beyond doubt.

Based on the study results we have made the following summarizing conclusions:

1. The use of vibroacoustic therapy in the rehabilitation period of acute poisoning with psychopharmacological agents, neurotoxicants and corrosive substances is associated with its moderate positive effect on hemorheological parameters: a tendency to decrease the initially increased parameters of erythrocyte aggregation in motion from the reference values (by 1.2 times), an increase in the initially decreased blood viscosity at shear rates equal to 2.5 s^{-1} and 62.8 s^{-1} from the reference values (by 1.2 times and 1.1 times, respectively); when measured by the impedance aggregometry method a pronounced tendency ($p=0.07$) towards an increase in the platelet content in blood is seen with its 1.5-fold increase. Meanwhile, undesirable effects of both quantitative and qualitative (vector) nature in the comparison group have been observed, such as a further decrease in blood viscosity at a shear rate of 2.5 s^{-1} and the aggregation activity of erythrocytes at rest (by 1.3 times and more than 1.5 times, respectively), initially being below the reference values.

2. The use of vibroacoustic therapy has a moderate positive effect on the dynamics of commonly used indicators of endotoxicosis: there is a noticeable tendency to a decrease in the value of the leukocyte intoxication index (by 1.3 times) and the same tendency in the leukocyte content in blood (by 1.2 times); an undesirable effect that occurs in the

comparison group is a significant (by 1.7 times) further decrease in the value of the neutrophil shift index, which was initially below the norm.

3. The greatest effect of vibroacoustic therapy on the endotoxicosis severity is reflected in the toxemia cellular component parameters in the form of stabilized relative and absolute number of dead leukocytes in the main group, while in the comparison group there is a noticeable increase in the values of these parameters: by 1.3 times (statistically significant, $p<0.05$) and 1.4 times, respectively, with a final excess of their content in the main group by 2.25 times and 2.2 times, respectively. In addition, the positive effect of vibroacoustic therapy in the main group is the complete restoration of the level of CD14+HLA-D R + monocytes in blood with an increase by 1.4 times compared to the initial values.

4. The use of vibroacoustic therapy in the above-mentioned kinds of poisoning is accompanied by a noticeable improvement in their clinical course: in the total number of patients, there is a significant statistically significant ($p<0.05$) reduction (by 1.5 times) in pneumonia duration; whereas, there is a tendency for its decreased incidence in poisoning with psychopharmacological agents (by 1.2 times) and a considerable, statistically significant ($p<0.05$) reduction in the duration of pneumonia in poisoning with neurotoxicants (by 2 times); the duration of treatment is also reduced by 1.1 times in both groups.

References

1. Goldfarb YuS, Badalyan AV, Gerasimenko MYu, Shchetkin VA, Potskhveriya MM, Elkov AN. *Reabilitatsionnye meropriyatiya pri ostrykh otravleniyakh khimicheskoy etiologii v toksikologicheskom statsionare.* Saratov: Nauka Publ.; 2023. (In Russ.).

2. Goldfarb YuS, Glukhovskaya NYa, Shirinova MN, Burykina IA, Potskhveriya MM. Ultrafioletovoe obluchenie krovi pri ostrykh

ekzogennykh otravleniyakh v profilaktike i lechenii pnevmoniy. *Klinicheskaya meditsina.* 1987;(3):49–52. (In Russ.).

3. Gembitskiy EV, Gayduk VA. Ostraya dykhatel'naya nedostatochnost' pri otravlenii fosfororganicheskimi insektitsidami (klinika, patogenez, differentsirovannaya terapiya). *Terapevticheskiy arkhiv.* 1977;(1):75–80. (In Russ.).

4. Ilyashenko KK, Luzhnikov EA. *Toksicheskoe porazhenie dykhatel'noy sistemy pri ostrykh otravleniyakh.* Moscow: ID Medpraktika-M Publ.; 2004. (In Russ.).

5. Gorbakov VV. *Kliniko-immunologicheskaya kharakteristika tyazhelykh otravleniy uksusnoy kislotoy i immunokorrektsiya lizotsimom:* Cand. med. sci. diss. Synopsis. Moscow; 1991. Available at: http://www.dslib.net/anestezia/kliniko-immunologicheskaja-harakteristika-tjazhelyh-otravlenij-uksusnoj-kislotoj-i.html [Accessed April 7, 2025]. (In Russ.).

6. Luzhnikov EA, Goldfarb YuS. *Fiziogemoterapiya ostrykh otravleniy.* Moscow: Medpraktika-M Publ.; 2002. (In Russ.).

7. Eremenko AA, Zyulyaeva TP, Kalinina AA, Rozina NA. Evaluation of effectiveness of vibroacoustic lung massage in self-breathing patients after cardiosurgical operations. *Clinical and Experimental Surgery. Petrovsky Journal.* 2020;8(4):126–134. (In Russ.). https://doi.org/10.33029/2308-1198-2020-8-4-126-134

8. Garus YN, Antoshkieva RM. The effectiveness of treatment of chronic generalized catarrhal gingivitis with mild antiseptic octenisept, vibroacoustic and antioxidant therapy. *Astrakhan medical journal.* 2011;6(4):119–121. (In Russ.).

9. Makarov MS, Goldfarb YuS, Badalyan AV, Simonova AYu, Potskhveriya MM. The effect of vibroacoustic therapy on the structural integrity of erythrocytes and platelets in patients with acute exogenous

poisoning. *Transplantologiya. The Russian Journal of Transplantation.* 2024;16(3):303–312. (In Russ.). https://doi.org/10.23873/2074-0506-2024-16-3-303-312

10. Goldfarb YS, Badalyan AV Marina M.Y, Shchetkin VA, Potskhveriya MM. Rehabilitation program for acute poisoning in a toxicological hospital. *Russian Journal of Physiotherapy, Balneology and Rehabilitation.* 2021;20(2):99–117. (In Russ.). https://doi.org/10.17816/1681-3456-2021-20-2-2

11. Alentiev AYu, Belov NA, Nikiforov RYu, Polunin EV, Borovkova NV, Evseev AK, et al. Gas permeation and hemocompa-tibility of novel perfluorinated polymers for oxygenation of blood. *Membranes and Membrane Technologies.* 2018;8(4):217–223. (In Russ.). https://doi.org/10.1134/S2218117218040028

12. Khvatov VB, Makarov MS, Borovkova NV. The morphologic evaluation of adhesive activity of human thrombocytes using vital dye. *Klinicheskaya Laboratornaya Diagnostika (Russian Clinical Laboratory Diagnostics).* 2013;(7):58–61. (In Russ.).

13. Makarov MS. Morphofunctional properties of spindle-shaped platelets. *Bulletin of Experimental Biology and Medicine.* 2022;174(11):646–649. (In Russ.). https://doi.org/10.47056/0365-9615-2022-174-11-646-649

14. Gabrielyan NI, Dmitriyev AA, Kulakov GP, Melikyan AM, Shcherbaneva OI. Diagnosticheskaya tsennost opredeleniya srednikh molekul v plazme krovi pri nefrologicheskikh zabolevaniyakh. *Klinicheskaya meditsina.* 1981;59(10):38–42. (In Russ.).

15. Kalf-Kalif YaYa. O leykotsitarnom indekse intoksikatsii i yego prakticheskom znachenii. *Vrachebnoye delo.* 1941;(1):31–36. (In Russ.).

16. Kapitanenko A.M., Dochkin I.M. *Klinicheskiy analiz laboratornykh issledovaniy v praktike voyennogo vracha*. Moscow: Voyenizdat Publ.; 1985. (In Russ.).

17. Gavrilov VB, Gavrilova AR, Mazhul LM. Methods of determining lipid peroxidation products in the serum using a thiobarbituric acid test. *Voprosy Meditsinskoi Khimii*. 1987;33(1):118–122. (In Russ.).

18. Zelenin AV, Poletaev AI, Stepanova NG, Barsky VE, Kolesnikov VA, Nikitin SM, et al. 7-Amino-actinomycin D as a specific fluorophore for DNA content analysis by laser flow cytometry. *Cyto-metry*. 1984;5(4):348–354. PMID: 6468175 https://doi.org/10.1002/cyto.990050410

19. Morse EE, Yamase HT, Greenberg BR, Sporn J, Harshaw SA, Kiraly TR, et al. The role of cytometry in the diagnosis of lymphoma: a critical analysis. *Ann Clin Lab Sci*. 1994;24(1):6–11. PMID: 8147568

20. Borovkova NV, Aleksandrova IV, Valetova VV, Kobzeva EN. Blood lymphocyte apoptosis in norm and pathology. *Molecular medicine (Molekulyarnaya Meditsina)*. 2013;(4):41–45. (In Russ.).

21. Mengos AE, Gastineau DA, Gustafson MP. The CD14+HLA-DR$^{lo/neg}$ monocyte: an immunosuppressive phenotype that restrains responses to cancer immunotherapy. *Front Immunol*. 2019;10:1147. PMID: 31191529 https://doi.org/10.3389/fimmu.2019.01147

22. Minkov G, Dimitrov E, Yovtchev Y, Enchev E, Lokova R, Halacheva K. Prognostic value of peripheral blood CD14+HLA-DR+ monocytes in patients with acute pancreatitis. *J Immunoassay Immunochem*. 2021;42(5):478–492. PMID: 33818295 https://doi.org/10.1080/15321819.2021.1903491

23. Kvasnikov AM, Borovkova NV, Petrikov SS, Godkov MA, Andreev YuV, Storozheva MV, et al. Regulation of lymphocyte apoptosis in intensive care patients with COVID-19. *Russian Journal of Anesthesiology and Reanimatology*. 2023;(1):49–55. (In Russ.). https://doi.org/10.17116/anaesthesiology202301149

24. Runion R. *Spravochnik po neparametricheskoy statistike: sovremennyy podkhod*. Moscow: Finansy i statistika Publ.; 1982. (In Russ.).

25. Smirnov NV, Dunin-Barkovskiy IV. *Kurs teorii veroyatnostey i matematicheskoy statistiki dlya tekhnicheskikh prilozheniy*. Moscow: Nauka Publ.; 1969. (In Russ.).

26. Kobzar AI. P*rikladnaya matematicheskaya statistika dlya inzhenerov i nauchnykh rabotnikov*. 2nd ed. Moscow: Fizmatlit Publ., 2012. (In Russ.).

27. Le˜meshko BYu. *Kriterii proverki otkloneniya raspredeleniya ot normalnogo zakona. Rukovodstvo k primeneniyu*. Moscow: Infra-M Publ.; 2023. (In Russ.).

28. Lapshin VP, Goldfarb YuS, Chzhao AV, Krasilnikov AM, Seraya EV, Shipilov IV, et al. Transcranial electric stimulation in therapy of critical states range of application and perspectives of development. *Russian Journal of Physiotherapy, Balneology and Rehabilitation.* 2007;(1):45–47. (In Russ.).

29. Badalyan AV, Bitkova EE, Goldfarb YuS, Khvatov VB, Elkov AN, Levina OA. Disturbances of rheological blood parameters and their correction in acute chemical poisonings at rehabilitation stage. *Tromboz, Gemostaz i Reologiya.* 2016;1(65):81–90. (In Russ.).

30. Potskhveriya MM, Matkevich VA, Goldfarb YuS, Simonova AYu, Stolbova NE, Tyurin IA, et al. The program of enteral correction of homeostasis disorders and its effect on intestinal permeability in acute

poisoning. *Transplantologiya. The Russian Journal of Transplantation.* 2022;14(1):45-57. (In Russ.). https://doi.org/10.23873/2074-0506-2022-14-1-45-57

31. Kadikoylu G, Yavasoglu I, Bolaman Z, Senturk T. Platelet parameters in women with iron deficiency anemia. *J Natl Med Assoc.* 2006;98(3):398–402. PMID: 16573304

32. Talamo G, Oyeleye O, Paudel A, Tayyab H, Khan M, Meseeha MG, et al. Platelet levels before and after iron replacement therapy in patients with iron deficiency anemia. *Hematology.* 2025;30(1):2458358. https://doi.org/10.1080/16078454.2025.2458358

33. Kulnigg-Dabsch S, Evstatiev R, Dejaco C, Gasche C. Effect of iron therapy on platelet counts in patients with inflammatory bowel disease-associated anemia. *PLoS One.* 2012;7(4):e34520. PMID: 22506024 https://doi.org/10.1371/journal.pone.0034520

34. Olivier CB, Meyer M, Bauer H, Schnabel K, Weik P, Zhou Q, et al. The ratio of ADP- to TRAP-induced platelet aggregation quantifies P2Y12-dependent platelet inhibition independently of the platelet count. *PLoS One.* 2016;11(2):e0149053. PMID: 26885820 https://doi.org/10.1371/journal.pone.0149053

35. Wustrow I, Ebner C, Langwie-ser N, Haller B, Luppa PB, Bradaric C, et al. Influence of diagnosis of venous thromboembolism on immature platelets, absolute platelet count and platelet aggregation over time. *Platelets.* 2021;32(3):398–403. PMID: 32316806 https://doi.org/10.1080/09537104.2020.1754380

36. Ma L, Wu Q, Ma Q, Liang S, Mo Q, Huang C. Platelet aggregation in apparently healthy elderly populations: reference ranges and influence of hematology parameters. *Clin Lab.* 2023;69(2). PMID: 36787562 https://doi.org/10.7754/Clin.Lab.2022.220438

37. Scavone M, Podda GM, Tripodi A, Cattaneo M. Whole blood platelet aggregation measurement by Multiplate™: potential diagnostic inaccuracy of correcting the results for the sample platelet count. *Platelets.* 2023;34(1):2156493. PMID: 36550076 https://doi.org/10.1080/09537104.2022.2156493

38. Stolyar MA, Olkhovsky IA. On issue of detection of limits of normal reaction of thrombocytes in testing of impedance aggregometry. *Russian Clinical Laboratory Diagnostics.* 2016;61(6):359–363. (In Russ.). https://doi.org/10.18821/0869-2084-2016-61-6-359-363

39. Markhulia DC, Popugaev KA, Sychev DA, Vatsik-Gorodetskaya MV, Gazaryan GA, Godkov MA, et al. Laboratory evaluation of the platelet component of hemostasis in acute coronary syndrome with ST segment elevation. *Russian Sklifosovsky Journal "Emergency Medical Care".* 2025;14(1):47-60. (In Russ.). https://doi.org/10.23934/2223-9022-2025-14-1-47-60

40. Giordano S, Franchi F, Rollini F, Al Saleh T, Uzunoglu E, Costa F, et al. Effect of lipid-lowering therapy on platelet reactivity in patients treated with and without antiplatelet therapy. *Minerva Cardiol Angiol.* 2024;72(5):489–505. PMID: 37870424 https://doi.org/10.23736/S2724-5683.23.06411-6

41. Makarov MS. Non-canonic ways to human platelet activation. *Medical alphabet.* 2015;3(11):30–35. (In Russ.).

42. Surovikina MS, Samoilenko VV, Vlasova EA, Vasilenko IA, Suslov VP. Changes in plasmic and platelet hemostasis in patients with chronic renal failure in hemodialysis. *Urologiia.* 2012;(1):25–29. (In Russ.).

43. Baaten CCFMJ, Nagy M, Bergmeier W, Spronk HMH, van der Meijden PEJ Platelet biology and function: plaque erosion vs. rupture.

Eur Heart J. 2024;45(1):18–31. PMID: 37940193 https://doi.org/10.1093/eurheartj/ehad720

44. Kikuchi Y, Koyama T. Red blood cell deformability and protein adsorption on red blood cell surface. *Am J Physiol.* 1984;247(5 Pt 2):H739–47. PMID: 6496755 https://doi.org/10.1152/ajpheart.1984.247.5.H739

45. Luzhnikov EA, Goldfarb YuS, Musselius SG. *Detoksikatsionnaya terapiya: rukovodstvo dlya vrachey.* Saint Petersburg: Lan Publ.; 2000. (In Russ.).

46. Goldfarb YuS. Kompleksnaya detoksikatsiya pri lechenii ostrykh otravleniy. In: *Meditsinskaya toksikologiya: natsionalnoye rukovodstvo.* Moscow: GEOTAR-Media Publ.; 2012. Sect. 4.5. 294–304. (In Russ.).

47. Luzhnikov EA, Goldfarb YuS, Badalyan AV. Present-day detoxification therapy for acute poisonings of chemical etiology. *Toxicological Review.* 2014;3(26):9–17. (In Russ.).

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