ISSN: 2755-0125

Journal of Virology Research & Reports

SCIENTIFIC Research and Community

Research Article

Open Access

Pandemic "COVID-19 – POSTCOVID SYNDROME": A System Method of Leeching is a New and Effective Treatment

Krashenyuk AI

Academy of Hirudotherapy, St.-Petersburg, Russia

ABSTRACT

In March 2023 (March 11, 2023), it is 3 years since the **World Health Organization (WHO)** declared a pandemic of a new virus called "**COVID-19**". As of March 21, 2023, the WHO website has reported 761,071,826 confirmed cases of "**COVID-19**", including 6,879,677 deaths (0.9%). A total of 13,260,401,200 doses of various vaccines have been administered. **WHO** continues to collect statistics on the incidence of the disease in the world until the pandemic is stopped, despite the vaccination measures taken. What are the lessons of the pandemic that health authorities around the world have learned in three years? The mechanism of the "**COVID-19**" disease has become clearer. The concept of "**POSTCOVID SYNDROME**" or "**LONG COVID**" is developing. Work continues to improve vaccines, the use of which has revealed the negative aspects of vaccination.

The "**COVID-19**" pandemic that has swept the planet has caused a serious problem for survivors of this disease called "**POSTCOVID SYNDROME**". The article discusses the topic that the author designated as the pandemic "**COVID - 19**" - "**POSTCOVID SYNDROME**". The mechanisms of pathogenesis of this disease are affected. The most proven mechanisms of the pathogenesis of the disease and the most effective methods of treatment according to the literature are considered. In comparative terms, the advantage of the "**System Method of Leeching**" in comparison with the proposed methods of treatment is shown. The possibility of monotherapy with medical leeches **(Hirudotherapy)** of this disease is shown.

***Corresponding author**

Krashenyuk AI, Academy of Hirudotherapy, St.-Petersburg, Russia. Tel: 8 (931) -002-75-02.

Received: March 30, 2023; **Accepted:** April 10, 2023; **Published:** April 15, 2023

Keywords: Disease "**COVID-19**"-"**POSTCOVID SYNDROME**", damage to the nervous system (central and peripheral), antiviral effect of leech, DIC syndrome Thrombolytic and antithrombic effects of leech accumulation. Neurotrophic effect and neurotrophins. "**System method of leeching**" (**SML**)-hirudotherapy, new effects of hirudotherapy.

The author of the article belongs to a series of publications highlighting the new, recently discovered properties of medical leeches *Hirudo medicinalis*. As well as the features of the pathogenesis of the new disease: "**COVID-19**"- "**POSTCOVID SYNDROME**", a method of treating and preventing this disease based on the scientifically proven healing properties of hirudo medicinalis medical leeches [1-15]. At the same time, the editors of five scientific medical journals have already adopted the author's concept of the name of the disease- "**COVID - 19**" - "**POST-COVID SYNDROME**" [11-15]. This reflects the author's point of view that this is a single disease that has two phases: the first phase, this is an acute process, which usually lasts 2-3 weeks - ("**COVID - 19**") and the next phase is the development of a chronic process- ("**POSTCOVID SYNDROME**"), which can last for 18-24 months. Such a definition of the new pandemic is important not only from a taxonomic point of view, but, above all, from a mental point of view, so it gives the doctor an understanding of the complexity of the course of the disease and requires monitoring patients throughout the specified period, for example, monitoring the dynamics of: D-dimers, prothrombin time, platelet count and the level of fibrinogen in the blood of convalescents. This is reflected in the recommendations of the International Society on Thrombosis and Hemostasis (ISTH) [16-40]. Now these are the most informative markers of the danger of thrombosis. The term "**LONG COVID**" does not reflect the substance of the disease process [14]. It should be clearly distinguished that the cause of the disease is the virus "**COVID-19**" (**Beta coronavirus SARS-CoV-2**), and the disease itself, for these reasons, should be called "**COVID-19-POSTCOVID SYNDROME**".

The acute, viral phase of the disease undoubtedly requires the use of antiviral drugs. The pandemic took the pharmaceutical industry by surprise, so doctors used drugs with known antiviral properties in the pandemic in the treatment of influenza, Ebola, herpes and even fever. The liver of antiviral drugs on the pharmaceutical market is large, however, none of them, as practice has shown, could not stop the transition of the acute phase of the disease to the chronic, i.e. the transition of "**COVID-19**" to "**POSTCOVID SYNDROME**". A common drawback for all antiviral drugs is that they do not have time to work in preventing the development of a viral infection and "**The train has time to leave**." In this regard, the appointment of leeches from the first symptoms of the disease is also associated with the antiviral properties of this type of treatment. In this article, we present new arguments in favor of the use of the "**System Method of Leeching**" in the treatment

of the disease "**COVID -19**" - "**POST-COVID SYNDROME**". And, first of all, we draw the attention of readers to the cycle of works performed in Russia, when using the drug "**Piyavit**". This drug, "**Piavit**", was specially developed as a substance containing the entire secretion of salivary cells (SSC) of a medical leech, in which it fully retains its activity during long-term storage.

Approved for clinical use since 1994, this drug is described in detail in the monograph Baskova I.P. and Isakhanyan G.S [16]. The composition of "**Piyavit**" includes: hirudin, hyaluronidase, eglins and bdellins, prostacyclins, destabilase enzyme. It was experimentally confirmed that "**Piyavit**" does not have a teratogenic and embryotoxic effect and does not have a negative effect during the gestational period [17]. The healing properties of "Piyavit" have been proven in such a pathology as "**Delayed Fetal Development" (DFD)** [17]. With this disease, the most promising is the study of the indicators of the hemostasis system, the level of the endothelial dysfunction marker - fibronectin, as well as the concentration of placental proteins during pregnancy, complicated by DFD. It is proved that against the background of treatment with "**Piyavit**" there is a faster and more persistent positive dynamics in relation to the general symptoms of the disease. It is proved that the use of this drug can reduce reproductive losses, increase the number of pregnancies with a successful outcome, and also reduce the frequency of pregnancy complications by 25%! [17]. In pregnant women with DFD in 100% of cases, pathological changes in the indicators of the hemostasis system, hypercoagulation, activation of DIC syndrome with increased platelet aggregation are noted. In the blood of pregnant women, DFD, an increase in fibronectin was noted, as well as a decrease in the concentrations of specific proteins of the fetoplacental complex, which is an objective criterion for assessing the condition of the fetus during pregnancy, complicated by a delay in its development. The use of "**Piyavit**" in the complex treatment of DFD improves and normalizes the state of the blood coagulation system, improves the protein-synthesizing function of the placenta, increases the duration of the effect of therapy, which can significantly reduce the frequency of perinatal complications, premature birth, surgical interventions, than with traditional therapy aimed at improving the "**Uterine-placental - fetal blood flow**" [18]. Everything mentioned above about the properties of "**Piyavit**" is even more realized when using the "**System Method of Leeching**", i.e. when using treatment sessions with a live leech in the treatment of patients with the disease

"**COVID - 19 - POSTCOVID SYNDROME"**, including pregnant women [15].This topic turned out to be extremely relevant, due to its social significance. A significant role in substantiating the application of the "**System Method of Leeching**" in "**COVID-19-POSTCOVID SYNDROME**" was played by the work of professor I.P. Baskova of Lomonosov Moscow State University on the study of the role of the **secretion of salivary cells (SSC)** in the generation of the vascular endothelium of nitric oxide -NO [19]. In our publications, the topic of treatment of "**COVID-19-POSTCOVID SYNDROME**" [3, 4, 6-15] using the "**System Method of Leeching**" was repeatedly touched upon. In the article offered to readers, in addition to the well-known and published effects of leeching [1-15], attention should be paid to the previously unearthed in the literature effect, discovered by professor Baskova I.P. is the phenomenon of stimulation of the production of nitrous oxide by the vascular endothelium - NO, which has a pronounced antiviral effect [20,21]. of course, the topic of the functioning of the endothelium in the conditions of coronavirus damage is extremely interesting, not sufficiently covered in the literature, has prospects for further study. And it becomes extremely important, in relation to the discussed topic of treatment of the disease **"COVID-19 - POSTCOVID SYNDROME".**

Antiviral and Bactericidal functions of leech

The antiviral role of nitric oxide-NO has so far been proven by many works [20-23]. For the first time, the independent role of the endothelium in the regulation of vascular tone is stated in an article published in Nature by the authors Furchgott and Zawadzki [24].The authors first described the endothelium-dependent relaxation factor (NO) and discovered a new, NO-dependent way of regulating physiological processes. A review by S. Moncada discusses the role of NO in the cardiovascular system: in addition to maintaining vasodilation, NO inhibits platelet aggregation and modulates smooth muscle proliferation [25]. It affects many cardiovascular diseases, with each risk factor associated with a reduced ability of the endothelium to generate NO. Reduced basal synthesis of NO leads to vasoconstriction, increased blood pressure and thrombosis. In the proposed article, we are primarily interested in the problem of generating NO from the standpoint of antibacterial and antiviral action. Nitric monoxide (NO) is produced in the respiratory tract by nitrooxide synthases (NOS) of epitheliocytes, endotheliocytes, pro-inflammatory cells of the immune system and is involved in the regulation of many processes that are important in the development of lung pathology. NO has bactericidal and antiviral properties, regulates the tone of the bronchial tree, blood vessels, mobility of the cilia of the ciliated epithelium of the bronchi [21, 26], which is extremely important in pulmonary pathology caused by coronavirus.

NO inhibits many viral proteinases and transcription factors necessary for viral replication and also enhances the antiviral effect of **IFN-γ** [21, 22]. The effect of **activated oxygen-containing metabolites (AOM)** on infectious agents is also associated with the rate of their interaction with **activated nitrogen-containing metabolites (ANM)**, which leads to the formation of ONOO- [27-29]. Currently, a new understanding of the synergy of the action of reactive oxygen and nitrogen radicals in the nonspecific protection of the body is presented [27]. According to modern research, the production of **AOM** and **ANM** is the most important sign of activation of phagocytic cells - macrophages, neutrophils and monocytes. The generation of NO and O2-• occurs almost in an equimolar amount. The balance in the level and rate of generation of NO and O2–• in the development of the ocisisative explosion is crucial in the formation of the additive result of their joint influence. Simultaneous production by macrophages and epitheliocytes in an almost equimolar ratio of the superoxide anion of the radical and NO leads to the formation of peroxynitrite **$ONOO^-$**, which is more toxic than NO for most bacterial, viral and fungal infectious agents[28-30]. Peroxynitrite interacts with virus capsule proteins, inhibiting the penetration of viruses into the cell [22, 23].

The bronchodilating effect of NO leads to moderate relaxation of the smooth muscles of the predominantly large bronchi. Nitrosothiols formed during nitrosylation have a powerful bronchodilating effect [21].

Bronchoprotective effect of NO and effect on the Drainage function of the Respiratory Tract

cNOS deficiency has been shown to be associated with the development of bronchial tree hypersensitivity [21-31]. With a low level of NO, it promotes the restoration of the extracellular matrix, inducing prostaglandin E2-dependent collagen synthesis, and actively participates in the processes of repair of the mucous membrane of the respiratory tract [32, 33]. Active nitrogen radicals increase the production of mucin and epithelial mucus, enhancing

the activity of the submucosal glands, accelerate the movement of the cilia of the ciliated epithelium. NO induces the activity of apical anionic and basolateral potassium channels of epitheliocytes, contributing to the mechanical elimination of infectious agents [21-31]. The work cited leads us to an understanding of the role of the medical leech's CSCs in influencing the synthesis of NO in **human vascular endothelial cell culture (HUVEC)**. A series of works carried out at Lomonosov Moscow State University under the guidance of **Professor** I.P. Baskova using three methods: fluorescence microscopy, flow cytometry and the method of measuring the fluorescence of solutions proved the following. The use for the determination of NO in living cells of the fluorescent dye Cu-Fl, which is a complex of ferrous copper with a derivative of fluorescein [34,35], can be successfully applied to analyze the synthesis of NO in living endothelial cells using microscopy and flow cytometry. The researchers' next step was to prove that different concentrations of SSC affect the synthesis of

NO in Human Vascular Endothelial Cell Culture (HUVEC)
Analysis of cells under microscopy showed that in **HUVEC** culture the intensity of NO synthesis increases in the centers located near the cytoplasmic membrane, while NO molecules have time to diffuse into the intercellular medium for a sufficiently long distance. The data obtained on the models on the effect of the drug "**Piyavit**" and SSC suggest that the live leech ***Hirudo medicinalis*** will have a similar effect of stimulating the production of nitric oxide - NO in the endothelium of blood vessels and human tissues, but this also requires direct experimental evidence, although empirically in the treatment of patients we observe a powerful therapeutic effect of the broncho-pulmonary complex.

The immunomodulatory effects of medical leeches have not been studied enough. Analysis of the literature shows that this is a multifactorial process, while discussing the activation of the macrophage link of immunity, the complement system and other levels of immune system response when using leeches. For the first time, we drew attention to the currently unexplored property of leeching – **autohemohirudotherapy**, and proposed this term to refer to a new therapeutic factor of leech accumulation. We are talking about subcutaneous microhemorrhages resulting from the process of bloodsucking, Fig. 1. As for the topic of autohemotherapy, many publications talk about its benefits. Detailed reviews on this topic are of interest [36, 37]. With regard to the topic under discussion "**COVID-19**", attention should be paid to the work [38]. Immunomodulatory effect of hirudotherapy aimed at a specific restructuring of regulatory subpopulations of lymphocytes was discovered.

Figure 1: Subcutaneous hemorrhages are visible at leech bite points. This is an illustration of autoimmune hydrotherapy, a phenomenon that was not given importance in the evaluation of immunomodulatory effect of leeching before our research
Thus, in some patients whose blood had an increased initial amount of CD4 (helper T-helpers) and CD25 (T-regulators) of subpopulations of lymphocytes, these indicators decreased to physiological values. Simultaneously with the inhibition of CD4 and CD25 subpopulations, there was an increase in the number and functional indicators among CD8 (T-killers / suppressors) and CD16 (natural killers). To objectify the assessment of helper-suppressor relationships of subpopulations in immunogenesis, the authors proposed a CD2 regulatory index (CD2 RI) in relation to the amount of CD4 to the sum of CD8 and CD16, on the grounds that the latter subpopulations have common molecular cellular mechanisms of inhibition of immunogenesis. Before hirudotherapy, CD2 RI was 1.24 ±0.07, which indicates a strain on the immune system and an increase in the activity of CD4 (helper activation of immunogenesis). After hirudotherapy, this indicator changed to 0.86±0.07 due to the suppression of excessive activation of immunogenesis.

These data allow us to expect that the "**Cytokine Storm" [73],** which many publications talk about when analyzing the pathogenesis of "**COVID-19**", will not arise, but will go into the "**Cytokine Calm**"[39-73]. And we see this in practice. Applying the "System Method of Leeching" on a large group of patients (more than 500 people), we did not observe a single case of "**Cytokine Storm**". A very important aspect of the problem under discussion is the fate of those who have recovered from" **COVID-19**". Leech treatment can prevent and treat the development of pulmonary fibrosis. The instrument of treatment is the presence in the leech secretion of enzymes collagenase and elastase which affect connective tissue scars, causing their resorption [16]. The transition from the acute stage of "**COVID-19**" to its transition to the chronic phase of "**POST-COVID SYNDROME**" requires a completely different tactic in treatment. Consider the analysis of the pathogenesis and treatment offered by two authoritative scientific schools in Russia. One of them is the analysis and opinion of doctors united in the **Moscow City Scientific Society of Therapists (MCSST)** named after Professor S.P. Botkin. After examination and treatment of a significant number of patients (more than 2,000 people), with a confirmed diagnosis of "**COVID-19**", during 2020-2021, the diagnosis of "**POSTCOVID SYNDROME**" was formulated. According to **MCSST**, "**POSTKOVID SYNDROME**" is: **Chronically occurring thrombovasculitis with a predominant lesion of the nervous system (Central, autonomous and peripheral) and skin [39]**. The team of **MCSST** doctors, represented by its Chairman - professor A.P. Vorobyov, offers the following treatment for "**POSTCOVID SYNDROME**":
1. Apply direct oral anticoagulants, twice a day;
2. Plasmapheresis - at least 900 ml, for 1 procedure, at least 5 procedures, daily, with plasma replacement with saline to reduce intoxication [39]. It should be noted that the use of direct anticoagulants has a number of limitations and significant complications with damage to the central nervous system, they can cause nasal, throat and renal bleeding. Plasmapheresis is applicable only if there is special equipment and trained personnel in the clinics. Given the huge masses of the population affected by the pandemic, the proposed treatment technology has no chance of large-scale application.

Another clinical school, headed by academician Makatsaria A.D., believes that the leading pathological sign of this disease is the "**Syndrome of disseminated intravascular coagulation**" **- (DIC) syndrome** [40]. The most unfavorable prognostic sign, according to the authors of this school, is coagulopathy. If the parameters of the main markers of coagulopathy (D-dimers, prothrombin time, platelet count and fibrinogen levels) worsen, more "aggressive" resuscitation care should be carried out: Low molecular weight

heparin (**LMWH**) should be prescribed to all patients with diagnosed "**COVID-19**" infection (including non-critical patients) who require hospitalization, in the absence of contraindications to **LMWH** in these patients. The use of **LMWH** drugs by this school (Enaxiparin, Nadroparin, Dalteparin) in a prophylactic dose is also justified, which does not require special control. It is recommended to take these drugs to all patients, even with a mild course of the disease, excluding active bleeding, platelet count < $25x10^9$ / l, intolerance to **LMWH**, severe renal failure. At the same time, it is not known how these drugs will behave with prolonged use, except for the above limitations for them. Both schools recognize the pathogenesis of the "**POSTCOVID SYNDROME**" of DIC syndrome, although the school of academician A.D. Makatsaria considers coagulopathy, i.e. DIC -syndrome, to be the leading one. In this regard, the international experience in the treatment of DIC- syndrome in the treatment of "**COVID-19**", especially of Chinese colleagues, is also very important. Chinese scientists from the Institute of Biotechnology of Beijing found that the anticoagulant heparin, which is used in the treatment of a new coronavirus infection, causes deadly complications in patients with "**COVID-19**". The research materials are published on the preprint portal medRxiv. BEIJING, May 1, 2020, 8:25 PM — **REGNUM** . It is noted that doctors in the treatment of patients with a new coronavirus infection use an anticoagulant - heparin. Observations showed that this improved lung function by dissolving blood clots and reducing inflammation.

However, heparin can spontaneously cause acute platelet insufficiency, which leads to the formation of new blood clots and often leads to the death of patients

The researchers said that "**COVID-19**" patients develop antibodies that combine with heparin molecules. The resulting complex damages platelet cells with which heparin interact. This leads to the mass death of platelets. Such complications occurred in 40% of patients with "**COVID-19**", in whom the disease proceeded in a complex form. At the same time, usually such complications occur in 1% of patients. If patients were connected to the apparatus "artificial kidney" to purify the blood of toxins, then patients were guaranteed to die from the resulting platelet insufficiency.

Thus, the scientists conclude, other anticoagulants should be used to thin the blood in COVID-19 patients, but not heparin

The author of this article spoke at the 11th European Congress for Integrative Medicine in 2018 in Ljubljana (Slovenia) and at the 5th International Meeting on Traditional and Alternative Medicine in Rome (Italy) April 2019 with a report: "The Renaissance of hirudotherapy in Russia: The end of XX and the beginning XXI century" [2]. These speeches and publications were positively received by the medical community, which served as an incentive for a more complete coverage of the topic of the current state of hirudotherapy in Russia [3-15, 41]. Without reducing the importance of the recommendations of the two mentioned scientific schools of Russia and the Chinese experience in the treatment of "**POSTCOVID SYNDROME**", we offer an alternative way to solve the problem of reducing mortality from pneumonia and other complications caused by **COVID-19**.This is the application of the "**System Method of Leeching**" **(SML)** - (hirudotherapy). The method is based on a combination of the principles of homeopathy and hirudopuncture ("Hirudopuncture", the author's definition). The proposed solution is based on almost 30 years of use of SMP in elderly people with multi-organ pathology and children treated at the Academy of Hirudotherapy of **St. Petersburg** [42]. The preventive and therapeutic plan for anticoagulant and antiplatelet therapy for the prevention of DIC -syndrome, distress syndrome is considered step by step from the standpoint of the SML in recent publications [4-12]. We remind readers about the advantage of early anticoagulant therapy in the form of SML. Early anticoagulant therapy is certainly the right tactic. We offer this therapy in the form of the appointment of a medical leech (ML) ***Hirudo medicinalis***.

Thrombolytic and antithrombotic activity of Hirudo medicinalis.

1. On the role of hirudin

Professor of King's College Birmingham (England) John Highcraft (J.B. Haycraft ,1884) was the first who managed to obtain from ML an extract that has an anticoagulant effect in vivo and in vitro. Although J.B. Haycraft did not find glands that produce an anticoagulant, he showed that they should be sought in the front of the body of the ML. And this is his great merit and priority. It received the name "Hirudin" in 1904 as a result of the work of F. Franz, performed in 1903. in the laboratory of Y. Jacoby (quoted in [43]. The complete primary structure of hirudin was established in 1976 [44]. It was later confirmed and in 1985 the location of disulfide bonds in the hirudin molecule was established [45, 46]. In 1986, the first publications on the production of recombinant desulfated hirudin appeared [47]. Thus, it is obvious that **hirudin is a unique thrombin inhibitor**. It is the only inhibitor capable of blocking the activity of a proteolytic enzyme in picomolar concentration. The unique specificity of the medical leech hirudin is explained by a previously unknown mechanism of multiple interactions between the enzyme and the inhibitor. Hirudin forms an exceptionally strong complex with thrombin, and the molecular basis of such strength is a large number of contacts between thrombin and hirudin, which are detected by X-ray diffraction analysis of the corresponding hirudin crystals with an inhibitor. The format of this article allows us to make only the most general overview of the properties of hirudin. But even these properties allow us to judge its unique anticoagulant potential. Research in the field of obtaining recombinant hirudin has led to the emergence of various structural variants of the natural inhibitor, common to which is the presence in the molecules of the residue of unsulfated Tyr-63.Which determined their common name **"desulfogyrudines" or "desirudins"** [48]. Unlike natural recombinant hirudins, they have less affinity for thrombin, although their anticoagulant properties are the same as those of a natural inhibitor.

Hirudin inhibits not only free thrombin in solution, but also an enzyme bound to the fibrin clot [49]. Aspects of the clinical use of hirudin are diverse, the limitation is only the use of high doses of hirudin, in which increased bleeding in patients is possible. Inhibiting thrombin activity is not the only function of hirudin. In its presence, the reaction of thrombin activation of coagulation factors V, VIII, XIII slows down. Hirudin prevents the reaction of release and aggregation of platelets, inhibiting the binding of thrombin by blood platelets. Hirudin causes dissociation of the thrombin complex with specific proteins - receptors on platelets, since thrombin has a higher affinity for hirudin than for high-affinity receptors on platelets.

2. On the role of the Destabilizing Complex secret of ML. Destabilase, endo- and exo- ε - (γ -Glu) - Lys isopeptidase was first discovered in the secretion of the salivary glands in 1986. The enzyme carries out its fibrinolytic (thrombolytic) activity through the hydrolysis of isopeptide bonds formed during the stabilization of fibrin in the presence of blood coagulation factor XIII, complementing new ideas about the mechanism of fibrinolysis.

Taking into account the behavior of destabilase in aqueous and organic solvents, it has been suggested that the micellar nature of this compound, i.e. the ability to aggregate destabilase into larger complexes is realized in the layout of the micelle, which changes its spatial orientation depending on the polarity of the solvent.

Experiments have shown that destabilase has a powerful prophylactic antithrombotic effect, due primarily to blocking platelet aggregation (platelet-vascular link of hemostasis) by the lipid component of destabilase. Attention is drawn to the fact that destabilase also manifests its effect when administered orally to animals. Obviously, destabilase has such a spatial structure that provides it with protection from proteolytic hydrolysis in the digestive tract. That is, destabilization is able to form aggregates that, thanks to the lipid component, can change their spatial configuration, i.e. has a certain "fluidity". This assumption is supported by the fact that destabilase exhibits its properties (hydrolysis of isopeptide bonds) both in an aqueous medium and in organic solvents.

When analyzing the effect of destabilase on the parameters of blood coagulation, it is shown that in its presence the thrombin time and the time of recalcification of blood plasma are significantly lengthened. It is natural to assume that such an effect is provided by hirudin and a blood plasma kallikrein inhibitor, which were found in destabilase preparations. These facts suggest that the destabilizing complex is a natural liposome [50].The composition of the "**Destabilizing Complex**" (DC) includes: destabilizing and prostaglandin components, hirudin and an inhibitor of blood plasma kallikrein (IR). The strength of this complex is evidenced by the fact that the known methods of biochemistry, suitable for the destruction of liposomes, it is not possible to destroy it. This is possible only as a result of the destruction of the polypeptide chain of destabilization. In this case, the prostaglandin component of destabilase, hirudin and a kallikrein inhibitor are released. The prophylactic antithrombotic effect of destabilase is due to both the blockade of the internal mechanism of blood coagulation (inhibition of platelet adhesion and aggregation and the activity of blood plasma kallikrein) and the antithrombin activity of hirudin. DC also shows its activity when administered orally at a protein concentration of 2 mg / ml [50].The liposomal nature of DC also provides an important physiological role of this complex as a universal thrombolytic agent: fast and deep (due to the wave-ultrasonic effect penetration of DC through the cell membrane, attachment due to the lipid component of destabilase to the damaged part of the vascular wall and parietal thrombus, slow lysis of the fibrin clot due to the isopeptide activity of destabilase and obstacles to further thrombosis due to blockade of thrombin, blood plasma kallikrein, platelet aggregation and adhesion [51]. Thus, the natural liposome - DC is an agent that provides both prophylactic and thrombolytic (therapeutic) action, which is an extremely important point in the treatment of thrombosis.

3. On the role of ML proteinase inhibitors

Another powerful argument for the use of SMP in the treatment of **COVID-19** is the publication of scientists from the United States and Germany on the suppression of the reproduction of coronavirus by inhibitors of cellular proteases. For **SARS-CoV-2** to penetrate into cells, it is necessary that its surface glycoprotein S be cut by cellular proteases. One such protease is the transmembrane enzyme TMPRSS2. However, as shown by studies of German scientists conducted on the culture of cells of the human epithelium of the airways, in addition to TMPRSS2, the virus needs another cellular protease - furin. Furin and TMPRSS2 introduce breaks in different regions of the S protein, and both breaks are critical to the virus's ability to enter the cell. The TMPRSS2 knockdown with antisense RNA prevented the proliferation of SARS-CoV-2 in cell culture. In addition, the reproduction of the virus was suppressed under the action of two inhibitors of TMPRSS2 (MI-432 and MI-1900) and aprotinin, an inhibitor of serine proteases of a wide spectrum. Viral replication was also suppressed by a furin inhibitor known as MI-1851. Moreover, the simultaneous action of TMPRSS2 inhibitors together with MI-1851 gave a more pronounced antiviral effect than the action of the equimolar amount of each of the studied TMPRSS2 inhibitors without MI-1851.

Scientists believe that TMPRSS2 and furin are promising targets for the treatment of "**COVID-19**", and the use of their inhibitors, alone or in combination, should be considered as a way to treat the disease. Source: Dorothea Bestle, et al. // **TMPRSS2 and furin** are both essential for proteolytic activation and spread of **SARS-CoV-2** in human airway epithelial cells and provide promising drug targets. bioRxiv, April 15, 2020; DOI: 10.1101/2020.04.15.042085 In connection with the mentioned publication of the activation mechanism of the coronavirus "**COVID-19**", readers should be reminded of the inhibitors of the proteases of the medical leech.

Bdellins-are a group of polypeptides with a small molecular weight, among which bdellins A with a molecular weight of 7 kDa are distinguished (in this group, bdellastazine with a molecular weight of 6.3 kDa is most studied) and Bdellin B with a molecular weight of 5 kDa. By the method of equilibrium chromatography, numerous forms of bdellins A and B have been isolated; they are designated from A1 to A6 and from B1 to B6. Both are strong inhibitors of trypsin, plasmin and sperm acrosine. They do not block the activity of chymotrypsin, tissue and plasma kallikreins, subtilisin. They were first discovered by H. Fritz and co-authors in 1969. A recombinant form of bdellastazine was obtained.

Hirustazin-belongs to the same family of antistasine inhibitors of serine proteases. Isolated in 1994 from extracts of the medical leech. The molecular weight of hirustasin is 5.9 kDa. It inhibits tissue kallikrein (but not plasma), trypsin, chymotrypsin and G-cathepsin neutrophils. The ability of hirustasin to block tissue kallikrein is a very important property, since the latter catalyzes the release of highly active kinins. Kinins through specific receptors on target cells modulate a wide range of biological activities, including those involved in maintaining normal blood pressure. Hirustazin is also obtained in recombinant form.

LDTI (Leech Derived Tryptase Inhibitor) –tryptase inhibitor derived from an extract of medical leeches. Tryptase is the main component of secretory cytoplasmic granules of mast cells and leads to the destruction of extracellular matrix proteins. The important role of tryptase in allergic and inflammatory reactions is known. As for many of the compounds already described, a recombinant LDTI.

LCI (Leech Carboxypeptidase Inhibitor)-inhibitor of carboxypeptidase A. It was isolated in 1998 and has two isoforms with molecular weights of 7.3 and 7.2 kDa. Stable over a wide range of pH and temperatures. Since this inhibitor is found in the secretion of the salivary glands of the medical leech, it can be assumed that it can block the hydrolysis of kinins by metalloproteinases at the site of the leech bite of the skin, thereby enhancing the kinin-induced increase in blood flow. Created recombinant LCI.

Eglins-are low molecular weight proteins from medical leech extracts with molecular weights of 8.073 and 8.099 kDa ("b" and "c" forms, respectively). They were first described in 1977 by U. Seemuller and co-authors. Inhibit the activity of alpha-chymotrypsin, mast cell chymase, subtilisin and neutrophil proteinases, elastase and cathepsin G. They have a high resistance to denaturation and warming. The inhibitory spectrum of eglin "c" allows us to consider it one of the most important anti-inflammatory agents. However, there are very serious reasons to believe that the eglins that are isolated from the extracts of the medical leech are not present in the secretion of its salivary glands, but are secreted by the stomach gland [16].

On The Role of Neurotrophins ML

Effect on the pathogenesis of the central and peripheral nervous system. In 1996, for the first time in the world, we discovered and patented the neurotrophic and neuritstimulating effect of a medical leech (A.I. Krashenyuk, S.V. Krashenyuk, N.I. Chalisova) The scientific foundation of unique clinical results on the treatment of muscle spasticity and the restoration of motor activity in children diagnosed with **"Cerebral Palsy" (CP)** was established. Until now, no clinic in the world for the treatment of cerebral palsy and muscle spasticity has reached this level of treatment [52-54].Video-"Cerebral palsy is treated only in Russia" proof of our priority in this area, can be viewed on our website: academia-hirudo.ru This aspect is associated with the effect of the secretion of the salivary glands of the leech on the nerve endings and neurons.

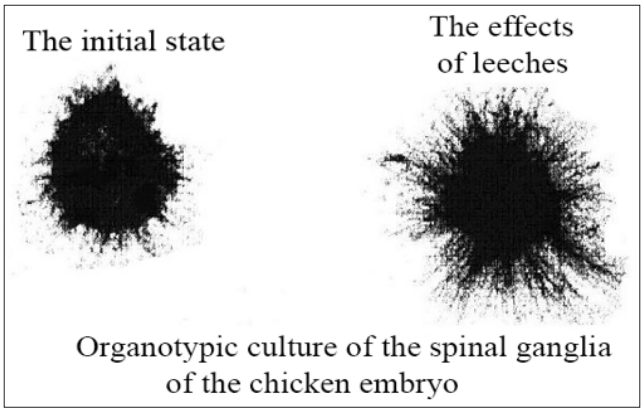

Figure 2: Stimulation of nerve cells (neurons) observed by phase-contrast microscopy in the culture of nerve ganglion cells of a 10-day-old chicken embryo. After exposure to an aqueous extract of the head of the leech, we observe a characteristic growth of neurites (processes) that act as interneuronal bridges [52].

For the first time, this problem was raised by our research, as a consequence of the results of treatment of children diagnosed with «**Cerebral Palsy**" (**CP**), patients with myopathy and children suffering from alalia and autism [53-55]. Neurotrophic factors are low-molecular proteins that are secreted by target tissues, are involved in the differentiation of nerve cells and are responsible for the growth of their processes. Neurotrophic factors play an important role not only in the processes of embryonic development of the nervous system, but also in the adult body. They are necessary to maintain the viability of neurons. The study of the processes that ensure the viability of the neuron is directly related to the study of the role of neurotrophic factors (NTP) in the functioning of the central and peripheral nervous system.

In 1986, **Rita Levy-Montalcini Stanley Cohen was awarded the Nobel Prize for the discovery of the "Nerve Growth Factor" (NGF)**, which led to the rapid development of this direction and the discovery of other neurotrophic factors. Our task is not to provide a broad overview of neurotrophins, so a detailed discussion of this topic can be found in the attached sources [56-58]. In the context of this article, the relationship of neurotrophins with heart and vascular disease is of great importance [58]. Over the past decades, neurotrophins have become the object of increased attention not only from neuroscientists, but also from cardiologists and angiologists. Neurotrophins have significant cardiac functions.

In the process of development of the "Cardiovascular System" (CVS), neurotrophins and their receptors are the most important factors in the formation of the heart and the regulation of vascular growth. In the postnatal period, they control the survival of endothelial and smooth muscle cells of blood vessels, cardiomyocytes, and also regulate angiogenesis and vasculogenesis using autocrine and paracrine mechanisms. The expression of neurotrophins continues throughout life and their activity changes in cardiovascular diseases. Neurotrophins have been shown to have a protective effect on CVS and can be used as biomarkers of coronary heart disease (CHD). Elevated blood levels of brain-derived neurotrophic factor (BDNF) are associated with a low risk of CHD and mortality. In "Acute myocardial infarction" (AIM), the neurotrophic factor of the brain and the nerve growth factor (Nerve Growth Factor, NGF) increase by 2-4 times their concentration is maintained during the first few days, triggering a signal transmission mechanism mediated by the central nervous system to protect the myocardium after damage. The high level of neurotrophins in the blood has a protective effect on cardiomyocytes and stimulates angiogenesis in the postinfarction period [58].In patients with stable angina pectoris and progressive atherosclerosis, a low level of BDNF is determined, which is associated with the development of adverse cardiovascular events over the next 4 years and increased mortality from all causes [58]. Understanding these mechanisms can be crucial for the long rehabilitation period of patients who have undergone "**COVID-19**"-"**POSTCOVID SYNDROME**" and the use of leeches during the rehabilitation period. The priority of the discovery of neurotrophic factors of the medical leech belongs to us [52]. Fig. 2. In the further development of this direction, the group of professor Baskova I.P. showed that the neurotrophic (neuritstimulating effect) is associated with the presence of destabilase-M, bdellastazine and bdellin-B in the secretion of the salivary glands of the leech [16]. It should be especially noted that the discovery of neurotrophic factors of the medical leech allows us to determine hirudotherapy as one of the leading technologies in the treatment of diseases of the nervous system: Parkinson's disease, multiple sclerosis, Alzheimer's disease, the consequences of traumatic brain injury, stroke, minimal brain dysfunctions (MMD), cerebral palsy, alalia, dysarthria, epilepsy, autism and other diseases of the nervous system.

From Table 1 it follows that the neuritstimulating activity of destabilase-M is 10,000 times more active than that of the drug Cortexin, which is popular in the treatment of neurological diseases. In addition, "Cortexin" has the ability to cause allergic reactions, it is not recommended for pregnant women and when breastfeeding a child. The use of medical leeches has no such limitations.

Comparative evaluation of the neuritstimulating effect of some biologically active compounds [16].

Table 1: Resource requirements by component

Biologically active compounds	Effective concentration, ng/ml	Literary source
Proteincanase C	10,0	Edgar D.,1978
Brain-derived neurotrophic factor	0,04	Barde Y.et al.,1980
Nerve growth factor	20,0	Levi-Montalcini R.,1982
Ciliary neurotrophic factor	10,0	ManthorpheM., et al.,1982
Monosialgangliosides	200,0	Facci L.,et al.,1984
Brain Neuritstimulating Protein	4,0	Гончарова В.П. с соавт.,1985
Fibroblast growth factor	100,0	Gospodarowicz D. et al.,1989
Cortexin	**100,0**	**Khavinson V.Kh. et al., 1997**
Epithalamine	200,0	Khavinson V.Kh. et al., 1997
Destabilasese-M	**0,01 и 0,05**	**Chalisova N.I. et al., 1999**

Professor Vorobyov P.A., analyzing brain damage in "**COVID-19**", draws attention to the fact that in addition to classical hemorrhagic strokes during pathological autopsies of dead people, an unusual mechanism of brain tissue damage is observed - diapedesis (penetration) of erythrocytes through the wall of cerebral capillaries [39]. This fact indicates a pronounced effect of the virus on the vascular endothelium. In this case, the mechanism of development of fibrosis of the lung tissue is also clear. If the virus also affects the endothelium of the pulmonary capillaries, this leads to the development of pneumonosis - edema and inflammation of the lung tissue, followed by the development of its fibrosis - the replacement of alveolar tissue with connective tissue. But even in this case, leech therapy has been shown as a method of regenerating vascular connective tissue [59, 60].

Treatment of depression

The ability to show a neuroendocrine effect. The ability of medical leeches to affect the level of neurohumoral mediators (neurohormones) in the central nervous system, which underlies the numerous neuroendocrine effects of hirudotherapy, was also significant. A significant factor in reducing the level of depression is the ability to increase the level of serotonin in the leech session and after it. **Serotonin** (5-hydroxytryptamine, 5-HT) plays an important role in the regulation of emotional behavior, motor activity, eating behavior, sleep, thermoregulation, is involved in the control of neuroendocrine systems. Serotonin can perform not only the role of a neurotransmitter, but also a neuromodulator (neurohormone) [61]. As follows from the description of the symptoms of "**POSTCOVID SYNDROME**" [39], we observe a pronounced lesion of the serotonin system of the brain, which, in our opinion, leads to the development of depression in this syndrome. In our work we investigated in detail the effect of leeching on the secretion of various neurotransmitters, including serotonin in the human brain [3-62]. At the same time, a violation of sensory functions - smell, vision, hearing, indicate a deeper lesion of other sensory systems.We are talking about the dophamine system (damage to the olfactory bulb), histamine - a violation of the regulation of blood pressure, thermoregulation - a decrease in body temperature). Given that leech therapy affects the level of almost most neurotransmitters, it follows an unequivocal conclusion that this method is pathogenetic in terms of the mechanism of lesions of the "**COVID-19**" virus of the central regulatory systems of the human brain.

On The Role of The Detoxification Effect of ML

With the defeat of "COVID-19", the human body experiences a state of intoxication, since intravascular thrombosis affects the capillary network of many organs. As a consequence of this process, hypoxia occurs in various organs, which inevitably leads to the accumulation of toxins - products of toxic metabolism. Today, this has been proven in patho-anatomical autopsies of people who have died of "**COVID-19**" in many countries, not just China. That is why, leech therapy is indicated for a disease of moderate and high severity, especially since plasmapheresis is simply not available in many medical institutions. «For six months after suffering "**COVID-19**", there remains a high risk of death from complications caused by infection."

This was announced on the air of the TV channel "**Russia 24**" by the Minister of Health of Russia Mikhail Murashko on August 31, 2021.The Minister of Health noted the need to undergo an in-depth medical examination of those who have had coronavirus infection in recent months. According to Minister M. Murashko, at this time the appearance of various kinds of complications associated with the formation of blood clots, damage to the nervous and cardiovascular system is possible, i.e. confirmed the conclusions of MGNIT and the symptoms of the development of "**POSTCOVID SYNDROME**"[39].Extended medical examination in order to identify complications after coronavirus infection and further treatment began in the regions of Russia from July 1, 2021. The minister also warned of greater lethality of the "**Delta strain**" of the coronavirus. **"The mortality rate for the disease "COVID-19" caused by the Delta strain may be higher than in the previous period of the rise in the incidence,"** he admitted.

Hemorrhagic complications with prolonged use of SML have not been identified (the observation period in some patients was more than 23 years of continuous use [71]. The phenomenon of detoxification described by us in the process of hirudotherapy allows you to remove toxic products (endo - or exogenous origin) that have not undergone metabolic transformations that allow them to be removed from the body with the help of excretory organs [62,63].

They are capable of causing "**Attached Leeches**" (the definition of zemstvo doctors for leeches that have passed the stage of bloodsucking) to vomit or die. This property of attached leeches allows us to consider their behavior after bloodsucking as a "**Method for assessing the integral toxicity of the patient's blood**" (author's definition).The accumulation of clinical material on the topic of blood toxicity of patients made it possible to discover a number of unknown patterns and new facts.

For example, if the death of leeches after bloodsucking occurs in a patient only after 5 to 6 months of treatment, this leads to the conclusion that the patient's toxic substances are **in the matrix or intercellular space**. And the task of the doctor is to understand how toxins entered the human body and accumulated in the matrix and how to remove them. And they could get into the matrix as a result of illness or long-term treatment, or with chronic poisoning from the patient's environment: food, air, water, by contact during work. If leeches die from the very beginning of treatment, from the first month of treatment, this clearly indicates that toxins are in the circulating blood. For example, in the treatment of drugs containing $\mathbf{F}^{+3}$ or salts of heavy metals. Then we will observe in the attached leeches the regurgitation of blood and their death. It should be noted that we will be able to observe the mentioned changes in the behavior of attached leeches only if we do not kill them, but control their behavior by regularly changing their water. With this observation, leeches are collected monthly in a separate jar. As a result of this observation, we receive unique information and answers to the questions:

1. Is the patient's blood toxic?
2. And if it does, where are the toxins, are the blood currently circulating or are they in the matrix? To prove the above concept, here are a number of clinical cases demonstrating the **"Integral toxicity of patients' blood"**.

Clinical case No1. Patient. V.M.Z., 33 years old.

The main diagnosis: "Chronic fatigue syndrome"?

Concomitant diagnosis: "Depressive state". Anamnestic diagnosis: "Kozhevnikov form of epilepsy (small form) of epilepsy at the age of 7 years." The treatment period is 11 years From the anamnesis. At the age of 7 years, 2 months after starting school, the patient developed tics of the facial muscles. A council of doctors during the examination of the child established the presence of a focus of epileptic excitation in the left hemisphere of the brain. Diagnosed: Kozhevnikovskaya epilepsy, simple partial motor local seizures. Drugs of 4 groups are prescribed: anticonvulsants, nootropic, vasodilators, antihypertensives. During school life, the child took from 9 to 12 drugs of this specificity. By the third grade of school, parents began to notice a decrease in the child's memory and inhibition when performing parental assignments. Treatment of the disease continued throughout the school life of the child, for 11 years. In the "**Academy of Hirudotherapy**" treatment with medical leeches was started 16 years after the completion of treatment. Final diagnosis at discharge: chronic drug poisoning. Bad habits: does not suffer. The patient's height is 185 cm, weight is 80 kg. Observation period: 18 months, from June 1999 to November 2000. Complaints of the patient upon admission to the Academy of Hirudotherapy: Constant pronounced physical fatigue by 12-14 o'clock in the afternoon, sleep disturbance in the form of frequent awakenings, due to lack of physical strength does not maintain contact with fellow students, school friends. Frequent depressive thoughts and low mood. Heaviness in the lumbar spine and lower extremities.

When examining blood by PCR for a group of herpes viruses (8 serotypes) in May 1999, the herpes virus carrier was not detected, which allowed the diagnosis of "**Chronic Fatigue Syndrome**" to be questioned. In the "Dynamic Hirudotest of Krashenyuk-Akabane" at the beginning of treatment, disturbances were noted in the channels: the large intestine (GI), the pericardium (MC), the stomach (E), the small intestine (IG), the bladder (V), three heaters (TR), the gallbladder (VB) [5,64-66].

Dynamics of leech death in the treatment of a patient in 1999 - 2000

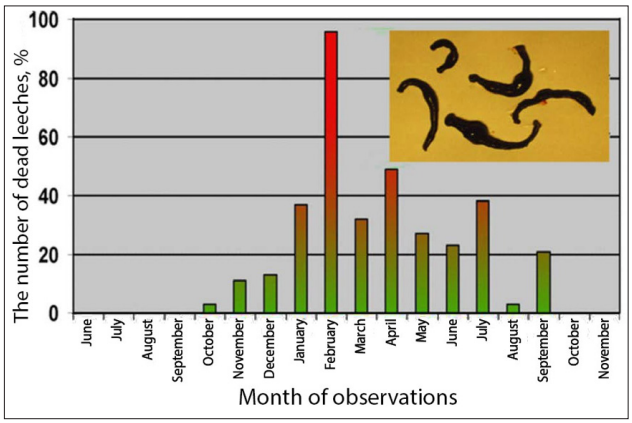

Figure 3: Dynamics of leech death in the treatment of a patient with chronic drug poisoning. Diagnosis: "A small form of epilepsy." The treatment period is 11 years. [13].

After 4 months of treatment, the patient felt the restoration of physical strength, and by the sixth month of treatment (December 1999), the patient notes a pronounced positive effect of treatment and begins training in the section of martial arts "Taykwan-do". In May 2000 he entered the amateur theater at the place of residence for residents of his municipal body. In a patient with a very severe history, effective treatment was carried out without the development of attachment reactions and with minimal blood loss resulting from post-ping bleeding. By the end of November 2000 the patient stated that he considered himself healthy.

Clinical case No2. Patient U.O.S., 33 years old. **The main diagnosis: "Ovarian cysts, a condition after two operations to remove ovarian cysts, cystic fibrous mastopathy of both mammary glands." Concomitant diagnosis: "Chronic tonsillitis, tonsillectomy surgery in 2013; spinal injury in an accident (2005); ulcer of the 12th duodenum (2007); stomach ulcer (2009)"**. Bad habits: smoking experience of 12 years. Height 165 cm, weight 95 kg (overweight). Observation period: 25 months. Complaints of the patient upon admission to the Academy of Hirudotherapy: menstrual irregularities in the form of irregular and painful periods. Pulling pain in the lower abdomen, does not feel the right leg, constant headaches, insomnia, itching of the whole body, pain in the liver, periodic twitching pain in the mammary glands, constant congestion in the nose. Intense hair loss, loose stools up to 5 times a day, lethargy, pain in the small and large joints of the lower extremities, severe sweating, shooting pain along the front wall of the abdomen in the vagina.

Dynamics of leech death in the treatment of patient in 2014-2016

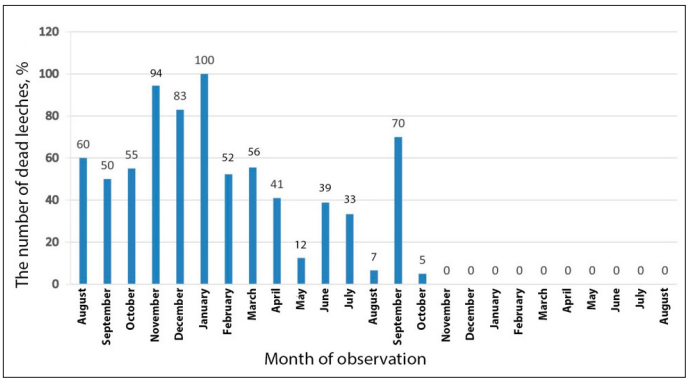

Figure 4: Patient U.O.S., 33 years old. Diagnosis: "Ovarian cysts, a condition after two operations to remove ovarian cysts." Bad habits: smoking experience of 12 years. The follow-up period is 25 months.

In the "**Dynamic Hirudotest of Krashenyuk-Akabane**" at the beginning of treatment, disturbances were noted in the channels: the large intestine (GI), the pericardium (MC), three heaters (TR), the spleen-pancreas (RP) [5, 64-66]. Six months after the start of treatment, a pronounced positive clinical effect has been achieved. By September 2015, the regularity of the menstrual cycle was restored. In a patient with a burdened history and manifestations of an allergic reaction in the anamnesis, effective treatment was carried out without the development of attached reactions and with minimal blood loss resulting from post leeching bleeding. A weight loss of 15 kg has been achieved. Edema of the lower extremities has gone, considers herself practically healthy after 25 months of treatment of the **SML**.To understand the mechanism of detoxification with medical leeches, it is necessary to recall the fundamental research of the German scientist H.-H. Reckeweg, which formed the basis of his theory of "**HOMOTOXICOLOGY**" [67, 68]. The author devoted an entire article to the discussion of the mechanism of detoxification with medical leeches [13]. In conclusion, it is necessary to dwell on the important observations of our students trained in the "**Academy of Hirudotherapy**". In patients who complained of a condition after an illness (in mild, moderate or severe form) vaccination against coronavirus infection (Increased blood pressure, lethargy, headaches), **then when setting leeches, their death was noted**. And there were several hundred such observations. These episodes clearly indicate the high toxicity of the drugs used for vaccination. Of course, this causes concern for both doctors and the population and cannot but cause concern among Russian developers and manufacturers of vaccines. And in this case, the study of the state of **integral blood toxicity** using medical leeches can be of significant help in testing vaccines of a new generation of vaccines. Especially dangerous in new coronavirus vaccines is the presence of highly toxic graphene oxide. This problem is thoroughly analyzed in the review [69-74].

On The Role of Wave Effects of ML

The discovery of the wave effects of leeches in the kilohertz range and the microwave SHF/EHF band allows us to consider another possible aspect of the therapeutic and preventive effect of the SML [62,69,72]. To date, it has been established that a significant part of medical personnel in different countries fall ill with the coronavirus "**COVID-19**". At the same time, the most likely version is that medical personnel violated the anti-epidemic regime. However, there is another reason - this is the remote (remote) interaction of the aquasystems of a sick and healthy person. Namely, we are talking about the discovery of academician V.P. Kaznacheev, L.P. Mikhailov, S.P. Shurin "The phenomenon of intercellular distant electromagnetic interactions in the system of two tissue cultures" (Number and priority date: No. 122, dated February 15, 1966).

The Authors Discovered a New Way of Transmitting Biological Information

The essence of the discovery: in two vessels, a culture of normal living cells was grown. One culture was infected with the influenza virus. Almost simultaneously, cells in another vessel, which are only in optical contact with infected cells (the vessels touched the bottoms of quartz glass), reproduced a similar pathological process. When quartz glass was replaced by ordinary glass, the situation changed: cells infected with the virus died, and their neighbors normally divided and developed perfectly.

The authors of the discovery believe that there are electromagnetic interactions between two tissue cultures in the optical range. They showed the conditions under which the mirror cytopathic effect develops, developed ways to increase the sensitivity of healthy cells to the perception of electromagnetic radiation of the affected cells. With the help of quantometric equipment, it was found that the process of cell damage, in particular, by viruses, is accompanied by the characteristic kinetics of its own electromagnetic radiation in the frequency range of the visible and ultraviolet regions of the spectrum.

The discovery discovered a new information channel in biological systems, helping to develop a new approach to assessing the role of quantum phenomena in the mechanisms of functioning of the genetic program of the cell and the processes of encoding information in specialized cellular systems, for example, neurons. The correctness of the authors' experiments has been confirmed by many laboratories, including abroad.

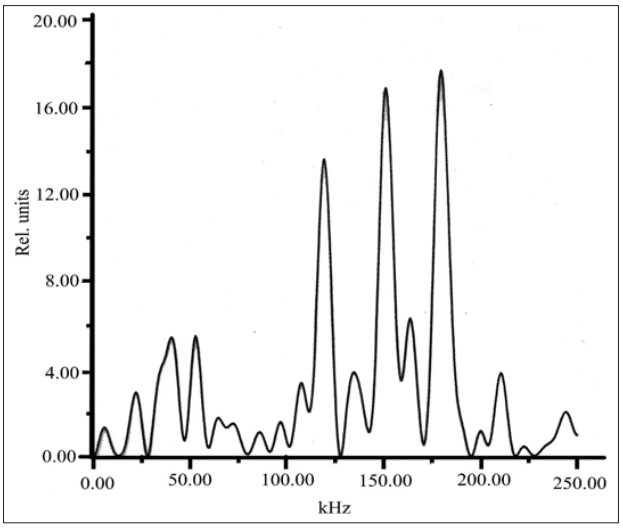

Figure 5: Recording of the acoustic signal of the leech in the process of bloodsucking after the Fourier transform. The details of the experiment are set out in the work [69].

Confirmation was also carried out at our department on the model of ultraviolet irradiation of people with the definition of the chaos criterion (**Kch**) and the order criterion (**Ko**) on the device of academician G.N. Dulnev "**Eniotron**" [62,70]. From this point of view, the protection of health workers requires a different design of protective clothing for doctors, i.e. protection from

electromagnetic radiation of the aquatic system of a person sick with the coronavirus "**COVID-19**". The wave emissions of leeches significantly exceed the radiation of influenza and herpes serotype 2 viruses (from the literature 800 and 440 Hz, respectively).

We do not yet know the frequency of radiation from the "**COVID-19**" coronavirus, but we assume that it is lower significantly than that of a medical leech. And this is the basis of our assumption about the preventive role of SML in health workers in contact with infected with the "**COVID-19**" virus. This conclusion is also based on practical material. Doctors who used ML in the "**Red Zone**" not only saved their patients, but also did not get sick themselves, using the SML as a preventive and therapeutic agent.

Conclusion

In conclusion of the proposed publication, I would like to express the hope that the materials presented in the publication will save many more human lives, since training in the **SML** methodology is now available in Russia. It is well known that the governments of **India, China** and other countries are actively promoting traditional methods of treatment and prevention against COVID-19.

The Government of India has issued a memorandum stating as potentially useful: yoga, Ayurveda, Unani, Siddha, homeopathy and and naturopathy. **Note that leech therapy is one of the branches of Ayurveda**. The Chinese government attributes the relatively rapid turnaround in this country to the integration of traditional Chinese medicine with traditional biomedicine in 90% of its patients. **We remind readers about some unknown properties of leech**. Over the past 30 years, the **Academy of Hirudotherapy in St. Petersburg** has obtained a number of new fundamental facts in the use of **SML**, which can significantly enhance the clinical effect of its use, and will reduce the mortality of patients with pneumonia caused by the "**COVID-19**" virus.

In addition to the already known properties of hirudotherapy - antithrombotic and thrombolytic, anti-inflammatory, anti-edematous, new properties of medical leeches were discovered in the "Academy of Hirudotherapy":
-**Discovery** of the energy effect (information-entropic);
- **Discovery** of the neurostimulating effect of the medical leech;
-**Discovery** of the acoustic effect of leech accumulation;
- **Discovery** of the detoxification effect of leech accumulation;
-**Discovery** of the phenomenon of local hyperthermia in the body of a benign brain tumor -neuroma;
-**Discovery** of the negentropic effect of leech accumulation;
-the role of **autohemogyrudotherapy** in the formation of the immunomodulatory effect of leech is shown;
-**Discovery** of the aquastructuring effect of leeching;
- **Discovery** of the "Resonance-wave effect" of leech on the state of the human aquasystem.

All these discoveries are detailed in the author's publications [1-15]. Therefore, as soon as the pandemic caused by the "**COVID-19**" virus began in Russia, our doctors, trained in the SMLR technology, began to actively apply this method in the treatment of the disease "**COVID-19**" - "**POSTCOVID SYNDROME**".

At the same time, it was shown that **SML** is a pathogenetic method of treating this disease, including damage to the central and peripheral nervous system, (loss of smell, hearing and vision loss, depression, impaired cognitive function). The use of SMP restores all sensory functions, prevents the development of DIC - syndrome. Thanks to the use of the **SML**, hundreds of lives were saved and their working capacity and interest in life were fully restored. The use of SMP in some cases required from 18 to 24 months of treatment. And prolonged use of anticoagulants poses a serious risk of internal bleeding: spontaneous retroperitoneal hematoma, intra- or extraperitoneal bleeding, gastrointestinal or intracranial hemorrhage [74]. It should be noted that the use of SML has no restrictions on the timing of use, so a patient with a brain tumor - **the neurinoma** (**schwanoma**) received treatment for 23 years, demonstrating a positive result of treatment (Clinical case described [71].

Why do we consider hirudotherapy a method of information medicine? [14]. Not only because this method has about 20 types of therapeutic effect. But also because in the process of treatment with medical leeches, which is shown for the first time in our studies, there is an impact on the information-entropy processes in the aquasystem of patients, which leads to a process of harmonization between the indicators of the chaos criterion (**Kch**) and the order criterion (**Ko**), with access to the harmony parameters - "**Golden Proportion**" or "**Golden Section**", which is typical for a high level of health [62]. **"Health" in terms of thermodynamic characteristics**. Known for many centuries, the method of hirudotherapy, as part of "Ayurveda" or "Ayurvedic medicine", is still revered and used in India and the countries of Southeast Asia. At present, thanks to new knowledge in the field of hirudology and hirudotherapy, reflected in the **"System Method of Hirudotherapy"**, **the Ayurveda method has acquired a new image, content and capabilities**.

Inference

The SML method has a wide range of properties that are pathogenetic, for the treatment of the disease "**COVID - 19-POSTCOID SYNDROME**": **antiviral**, **immunomodulatory**,**an tithrombotic**, **thrombolytic**, **anti-inflammatory**, **neurotrophic**, **antidepressant regenerative**.

The SML method has no complications and can be used as monotherapy in the acute and chronic stages of the disease "COVID - 19 - POSTCOVID SYNDROME". [75].

References

1. Krashenyuk AI, Krashenyuk SV (2018) New understanding of Ancient Technology –Leech therapy. Abstracts for 11th European Congress for Integrative Medicine. Int.J.Integrated Medicine 43: 195.
2. Krashenyuk AI (2019) The Renaissance of hirudotherapy in Russia: The end of XX and the beginning XXI century. Journal of Regenerative Medicine 8: 42.
3. Krashenyuk AI (2020) Neurotrophic (Neural Stimulating) and Neuromediator Effects of Hirudo medicinalis. Pathogenetic Mechanism of Treatment of Diseases of the Nervous System of the Human. Acta Scientific Medical Sciences 4: 01-06.
4. Krashenyuk AI (2020) Coronavirus «COVID-19»-Theoretical and Practical Substantiations for Reducing Mortality from Complications. Acta Scientific Medical Sciences 6: 115-123.
5. Krashenyuk AI (2020) Aquapathogenesis is the Nature of Human Diseases. Dynamic Hirudotests: New Possibilities of Integral Diagnostics of the State of Human Bodies and his Systems-Study of the Dynamism of the Human Aquasystem. Acta Scientific Medical Sciences 4: 76-90.
6. Krashenyuk AI (2021) Covid-19: Prospects for the Treatment and Rehabilitation of «POST-COVID SYNDROME» by Ayurvedic Method-Hirudotherapy. Acta Scientific Medical Sciences 5: 133-144.

7. Krashenyuk AI (2021) «COVID-19»: The Importance of the Renaissance of Hirudotherapy to Overcome the Pandemic in Russia and in the World. Journal of Clinical Case Studies, Reviews & Reports 3: 1-8.
8. Krashenyuk AI, Burkhonov AB (2022) Aseptic Necrosis of the Joints, As A Complications of «POSTCOVID SYNDROME» (Clinical Case). Journal of Clinical Case Studies, Reviews & Reports 4: 1-6.
9. Krashenyuk AI (2022) Hirudotherapy and Scientific Arguments Substantiation of Pathogenic Treatment «POST-COVID SYNDROME». J. Inter. Medicine Research & Reports 1: 1-10.
10. Krashenyuk AI (2022) COVID-19: Is there any legitimate optimism in the treatment of «POSTCOVID SYNDROME» and complication from vaccination? 2nd Edition of International Conference on TRADITIONAL MEDICINE, ETNOMEDICINE AND NATURAL THERAPIES. VIRTUAL EVENT. 18-19. 22-23.
11. Krashenyuk AI (2022) "COVID-19»-«POSTCOVID SYNDROME" Pandemic: Solutions of the Problem are Visible in the Application of Modern Hirudotherapy and Integrative Medicine. Open Access Journal of Biomedical Science 4: 1907-1909.
12. Krashenyuk AI (2022) "COVID–19»-«POSTCOVID SYNDROME" Pandemic: How to Protect Doctors and Nurses in the "Red Zone" of Hospital?. J. of Medical & Clinical Nursing 3: 1-9.
13. Krashenyuk AI (2022) "COVID-19»-«POSTCOVID SYNDROME" Pandemic: Complex Treatment with Medical Leeches, Including Detoxification. Confirmation of the Validity of the "HOMOTOXICOLOGY" of H. - H. RECKEVEG. Journal of Clinical Epidemiology & Toxicology 3: 1-7.
14. Krashenyuk AI (2022) "COVID-19»-«POSTCOVID SYNDROME" Pandemic: The Problem is Solved by Information Medicine-Hirudotherapy. PriMera Scientific Medicine and Public Health 1: 05-09.
15. Krashenyuk AI (2023) "COVID-19"-"POSTCOVID SYNDROME" Pandemic: High Risks for Pregnant Women. Acta Scientific Medical Sciences 7: 71-82.
16. Baskova IP, Isakhanyan GS (2004) Hirudotherapy. Science and practice 507s.
17. Baskova IP (2015) scientific foundations of hirudotherapy. Humoral link M 189.
18. Kazennova YuS, Strizhova RI, Sheikhov MR, Ibragimov AA, Balabanova IB (2005) Conceptual scheme for the treatment of fetal development delay with the use of hirudopharmacotherapy//Theses of reports of the VII Russian Forum "Mother and Child". M 89-90.
19. Baskova IP, Alekseeva AYu, Kostyuk SV, Neverova ME, Smirnova TD, et al. (2012) The use of a new reagent Cu- Fl for analysis of stimulation of NO synthesis by the secret of salivary cells of medical leech in human endothelial culture (HUVEC) and cardiomycetes of rats // Biomed. Chemistry 58: 65-76.
20. Akaike T, Maeda H (2000) Nitric oxide and virus infection 101: 300-308.
21. Ricciardolo FLM (2003) Multiple roles of nitric oxide in airways 58: 175-182.
22. Cao W, Baniecki ML, McGrath WJ (2003) Nitric oxide inhibits the adenovirus proteinase in vitro and viral infectivity in vivo. FASEB J 17: 45-2346.
23. Padalko E, Ohnishi T, Matsushita K (2004) RNA Peroxynitrite inhibition of coxsackievirus infection by prevention of viral entry. Proc Natl Acad Sci USA v.101: 11731-11736.
24. Furchgott RF, Zawadzki JV (1980) the obligatory role of endothelial cells in relaxation of arterial smooth muscle by acetylcholine. Nature 288: 373-376.
25. Moncada S, EAHiggs (2006) the discovery of nitric oxide and its role in vascular biology // British Journal of Pharmacology 147: 193-201.
26. Allain A, Hoang VT, Lasker GF (2011) Role of nitric oxide in developmental biology in plants, bacteria, and man. Curr. Top. Pharmacol 15: 25-33.
27. Fang FC (2004) Antimicrobial reactive oxygen and nitrogen species: concepts and controversies. Nat Rev Microbiol 2: 820-832.
28. Li H, Wallerath T, Forstermann U (2002) Physiological mechanisms regulating the expression of endothelial-type NO synthase. Nitric Oxide 7: 132-147.
29. Lang JD, McArdle PJ, O Reilly PJ, Matalon S (2002) Oxidant-Antioxidant Balance in Acute Lung Injury. Chest 122: 314-320.
30. Stamler JS, Lamas S, Fang FC (2001) Nitrosylation the prototypic redox-based signaling mechanism. Cell 106: 675-683.
31. Ricciardolo FLM, Sterk PJ, Gaston B, Folkerts G (2004) Nitric Oxide in Health and Disease of the Respiratory System. Physiol. Rev 84: 731-765.
32. Shi HP, Most D, Efron DT (2001) the role of iNOS in wound healing // Surgery 130: 225-229.
33. Wong SH, Santambrogio L, Strominger JL (2004) Caspases and nitric oxide broadly regulate dendritic cell maturation and surface expression of class II MHC proteins. // Proc. Natl. Acad. Sci. USA 51: 17783-17788.
34. Lim MN, Xu D, Lippard SJ (2006) Visualization of nitric oxide in living cells by a copper-based fluorescent probe. Nat.Chem.Biol 2: 375-380.
35. Pluth MD, McQuade IE, Lippard SJ (2010) Cell-trappable fluorescent probes for nitric oxide visualization in living cells Org. Lett 12: 2318-2321.
36. S Hale Shakman (2010) Autohemotherapy.Reference Manuel. (Russian ed.). www.Institute of Science.com p 254.
37. Dagmar Lanninger Bolling (2001) the healing power of blood. Guidelines for autohemotherapy. Arnebia 158.
38. Frolov AK, Litvinenko RA, Fedotov ER (2013) Study of the immunotropic action of hirudotherapy. First World Hirudotherapy Congress Moscow Abstracts 119-120.
39. Lecture by professor PA Vorobyov "POSTCOVID SYNDROME" https://youtu.be/FB4EGWgb4VQ.
40. Makatsaria AD, Grigorieva KN, Mingalimov MA (2020)"Coronavirus infection (COVID-19) and disseminated intravascular coagulation syndrome. Obstetrics. Gynecology and Reproduction 14: 123-131.
41. AI Krashenyuk (2021) Renaissance of hirudotherapy in Russia. XX-XXI Century. Renaissance of hirudotherapy in Russia. XX-XXI Century. Ed. by Professor, Academician of the European Academy of Natural Sciences. Team of authors 8: 344.
42. Krashenyuk AI, Krashenyuk SV, Krylov AA (2007) the role of the "System method of hirudotherapy" in the treatment of the elderly. Non-drug medicine. Scientific and practical journal 59-73.
43. Baskova IP, Isakhanyan GS (2004) Hirudotherapy. Theory and Practice M 159.
44. Bagdy D Barabas E, Graf L (1976) Hirudin. Methods Enzymol 45: 669-678.
45. Dodt J, Mller HP, Seemüller U, Chang JY (1984) The complete amino acid sequence of hirudin, a thrombin specific inhibitor. FEBS Lett 165: 180-183.

46. Dodt J, Seemüller U, Maschler R, Fritz H (1985) The complete amino acid sequence of hirudin. Localization of disulfide bonds. Biol Chem Hoppe – Seyler 366: 379-385.
47. Harvey RP, Degryse E, Stefani L (1986) Cloning and expression of cDNA coding for the anticoagulant hirudin from the blood sucking leech, Hirudo medicinalis. Proc.Nat. Acad.Sci.USA 83: 1084-1088.
48. Matheson AJ, Goa KL (2000) "Desirudin: a review of its use in the management thrombotic disorders. Drugs 60: 679-700.
49. Markwardt F (2002) "Hirudin as alternative anticoagulant -a historical review". Seminar.Thromb. Haemost 5: 405-414.
50. Nikonov GI, Latrile Zh (2002) Scientific foundations of hirudotherapy. In kn. "Hirudotherapy and hirudopharmacotherapy". (Edited by G.I. Nikonov) 4: 28-38.
51. Krashenyuk AI, Frolov DI (2001) Interpretation of the nature of the energy-informational effect of hirudotherapy on the basis of acoustic phenomenon. V kn. Nauka.Informatsiya. Soznanie, SPb 89-90.
52. Krashenyuk AI, Krashenyuk SV, Chalisova NI (2000) Method of modeling the influence of a medical leech on stimulating the growth of nerve fibers in tissue culture. RF. Patent 2144698.
53. Krashenyuk AI, Krashenyuk SV (1997) Hirudotherapy as a method of rehabilitation of children suffering from cerebral palsy. International Journal of Immunoreabilitation 4: 118p.
54. Krashenyuk AI, Krashenyuk SV (1998) Cerebral palsy In Nikonov GI "Medical leech. Basics of hirudotherapy". "SDS", St.-Petersburg 154-155.
55. Krashenyuk AI, Kondratyeva S Yu, Krashenyuk SV, Legkova AV (2001) Application of hirudotherapy in defectology. Practical and experimental hirudology: results for the decade (1991-2001). Materials of the VII scientific and practical conference of the Association of Hirudologists of Russia and CIS countries Lyubertsy, Moscow region 27-28.
56. Gomazkov OA (2011) Aging of the brain and neurotrophins. M., Izd. "Icarus" 92 p.
57. Sokolova MG, Alekseeva TM, Lobzin SV (2014) Neurotrophic factors. Prospects of application in clinical neurology. Bulletin of the North-Western State Medical University named after I.I.Mechnikov 6: 75-81.
58. Atamas OV, Antonyuk MV, Kytikova OY (2022) Neurotrophins in coronary heart disease (Literature review). Bulletin of new medical technologies. Electronic Edition 1: 1-2.
59. Nikonov GI, Lebedeva AO, Titova EA, Romanenko EB, Klochkov OI, et al. (2014) Gel "GIRUDO" in the complex treatment of vascular pathologies. Asclepeion 29-34.
60. Efimova AO (2019) Pharmacological properties of Hirudo Medicinalis extract, ointment and gel based on it for skin application. (Experimental study) Dissertation Ph.D., Staraya Kupavna 123.
61. IP Ashmarin, PV Stukalov, ND Yeshchenko Ed (1999) Biochemistry of the brain: A textbook. Ed. by St. -Petersburg University 328.
62. Dulnev GN, Krashenyuk AI (2010) From synergetics to information medicine.St.- Petersburg, Institute of Biosensory Psychology 167.
63. Krashenyuk AI (2003) Medical leech as an indicator of integral blood toxicity (detoxification effect of hirudotherapy). "HIRUDO-2003". Materials of the Conference of the Association of Hirudologists of Russia and CIS countries. Edition 2nd, supplemented.M 69-71.
64. Krashenyuk AI, Kamynin Yu F (2006) Neuroendocrine nature of Krashenyuk's hirodotest. In: "Science. Information. Consciousness" 119-121.
65. Sokovikov VI, Seroshtanova EV (2006) Dynamic hirudotest Krashenyuk A.I. Experience of application in the territory of the Altai Territory. In: Second International Scientific Congress "NEUROBIOTELECOM-2006".Sbornik nauchnykh trudov, St.-Perersburg, Izd. "POLYTECHNICA" 116-117.
66. Krashenyuk AI (2021) Method of treatment with medical leeches. RUSSIA. Patent for invention No. 2787525.
67. Rückwege HH (1963) Von den Grundlagen den Homotoxinlehre. Biol.Med 1: 182-184.
68. Reckeweg HH (1963) Pathogenetisches, Homotoxicologisches und Pharmakologisches Prinzip. Biol.Med 1: 1-17.
69. Krashenyuk AI, Frolov DI (2001) Interpretation of the nature of the energy-informational effect of hirudotherapy on the basis of acoustic phenomenon. V kn.: Nauka.Informatsiya. Soznanie., St.-Petersburg 89-90.
70. Krashenyuk AI, Dulnev GN, Tonkov VV (2010) "Aquacommunication effect of ultraviolet irradiation and the phenomenon of remote transmission of this effect from person to person". In: "Science. Information. Consciousness." Abstracts of the XIV International Congress on Bioelectrography. St.-Petersburg 27.
71. Krashenyuk AI (2020) Clinical case of Conservative Leech Treatment of Neurinoma of the Brain. Acta Scientific Medical Sciences 1: 108-110.
72. Vlaskin SV, Dubovitsky SA, Krashenyuk AI, Petrosyan VI (2016) Resonance-wave therapy and diagnostics. The results of the study and prospects of application in leech treatment. Second World Hirudotherapy Congress. Abstracts. Moscow 8: 35-39.
73. Mehta P, Mc Auly DF, Brrown M (2020) COVID-19: consider cytokine storm syndromes and immunosuppression. 395: 1033-1034.
74. Redko AA, Ivanov DV (2023) On the mechanism of action of modern immunobiological drugs (Scientific review of the literature). Bulletin of New Medical Technologies Electronic http://www.medtsu.tula.ru/VNMT/Bulletin/E2023 - 1/3-8.pdf.
75. Evrev D, Sekulovsky M, Gulinac M (2023) Retroperitoneal and Abdominal bleeding in anticoagulated "COVID-19" hospitalized patients Case series and brief literature review. World Journal of Clinical Cases 11: 1528-1548.