

## Case Report

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## Aseptic Necrosis of the Joints, As A Complication of Post-COVID Syndrome (Clinical Case)

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### SUMMARY

The COVID-19 coronavirus pandemic, declared by the World Health Organization (WHO) on 11.03.2020, has stimulated the search for treatment and prevention of this disease in many countries around the world. The rapid phase of the development of the disease is the viral phase, when it is still possible to use antiviral drugs, for example, ivermectin or hydroxychloroquine, and the inflammatory phase, when the virus penetrates into the lower parts of the lungs and enters the circulatory system. This phase of the disease is fraught with complications, sometimes requiring the use of ventilation, and with an unfavorable combination of risk factors - and to death. In the literature devoted to the topic of COVID-19, the term "Post-COVID syndrome" appeared, which describes the defeat of the central and peripheral nervous system, thrombosis of the vessels of various organs, damage to the gastrointestinal tract and skin. We present a rarer complication, however, characteristic of the Republic of Uzbekistan. We will talk about aseptic necrosis of the joints and tubular bones (bone infarction).

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bone marrow infarction of distal metadiaphysis of the femur, and proximal metadiaphysis of the tibia bones; degeneration of the medial meniscus on the right."

The clinic "Branch of the Academy of Hirudotherapy of Academician Krashenyuk A.I." in Tashkent was addressed by a man, 33 years old (Yu.S.S.) with complaints of pain in both hip joints, especially pronounced when walking and climbing stairs. In July (July 17, 2020), the patient was diagnosed with COVID-19 based on a PCR- test. The attending physician prescribed therapy at home: anticoagulant, antiplatelet, antibiotic therapy, antiviral, vitamin therapy, oxygen therapy, hormone therapy (dexamethasone in high doses). The patient received standard therapy: clopidogrel, sulbactam, remdesivir, favipiravir, dexamethasone, vobenzym, veroshpiron, ACC, slederone, tivortin, omega 3, magnesium B 6.

This therapy was carried out for 20 days. With an initial saturation of 70%, a saturation of 90% was achieved. During the treatment period, the patient could not move due to severe shortness of breath, which did not even allow to speak for more than 30 seconds. In January 2021, there were dull periodic pains in the hip and knee joints, more on the right side. The patient decided that nothing serious was happening to his health: the pain was not permanent; it arose periodically and he continued to work. At the end of April (April 22, 2021), pain in the hip and knee joints increased significantly, the patient could not walk, stand, drive a car. He could only move with a cane. He went to the doctor- the traumatologist who ordered the MRI.

According to the results of the MRI study, the diagnosis was made: "Aseptic bilateral necrosis of the femoral head of the 1st stage;

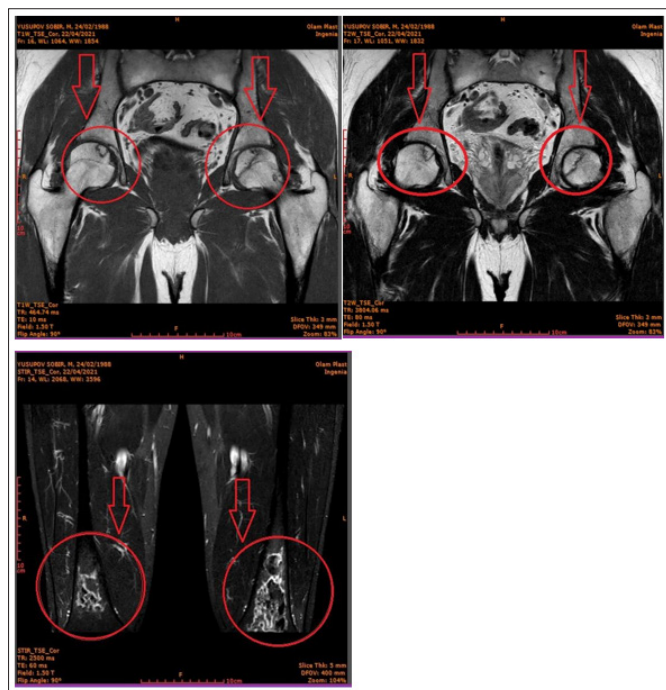
The patient was provided with surgical treatment to replace the hip and knee joints, which the patient refused. Appeal to other doctors, from other clinics, including foreign ones (Turkey, Germany, Tibet) was confirmed without alternative surgical treatment. As a result, the patient decided to be treated in the "Branch of the Academy of Hirudotherapy of Academician Krashenyuk A.I." in Tashkent. The attending physician Burkhonov A.B. prescribed to the patient the System Method of Leech treatment of Academician Krashenyuk A.I.

After 3 sessions of leeching (hirudotherapy), the patient felt significant relief, and, relief came after each session. The patient began to walk independently, without using a cane, to independently drive a car. The course of treatment with leeches was 23 days, daily productions, 1 leech.

After 23 sessions, the patient visited Turkey, the clinic "Acibadem", which has considerable experience in the surgical treatment of aseptic necrosis of the joints. The data of leech treatment in the clinic of Tashkent allowed the leading surgeon of the clinic "Acibadem", orthopedist-traumatologist professor Ibrahim Kaia to exclude surgical treatment of our patient. Since the control MRI data performed at the "Acibadem" clinic of May 25, 2021 showed that the degeneration of the patient's bone tissue was stopped by conservative treatment - medical leeches, moreover, even a slight regeneration of bone tissue is indicated. Until now (until the publication of this article), treatment with medical leeches

continues (1 session per week). The result of treatment: the patient walks, runs, and climbs the stairs without experiencing pain. Considers himself healthy.

We present the results of treatment in the dynamics of MRI. Fig. 1-4 shows the dynamics of bone tissue recovery in the process of leech treatment. Especially noticeable is the process of regeneration of the head of the right hip joint, Fig. 4 - 4A. The results of conservative treatment of aseptic necrosis of joints and bones, as a complication of Post-COVID syndrome, give hope that the surgical method of treating this disease has an alternative.



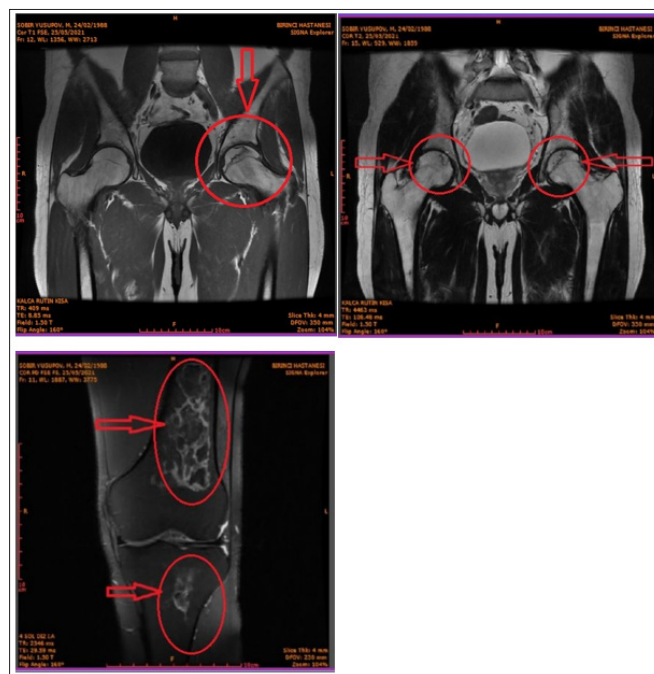
**Figure 1:** MRI from 22.04.2021, Tashkent

Indeed, the replacement of 4 joints at the same time with prostheses, even in the absence of complications, is a guarantee for 25 years. The increase in the number of endoprosthesis of large joints, and primarily the hip, is noted in most countries of the world and including Russia [1].

Despite the improvement in the quality of implants used, the improvement of endoprosthesis technologies, as well as the accumulation of practical experience among surgeons, the percentage of complications and unsatisfactory outcomes of arthroplasty remains quite high.

Thus, according to a number of authors, dislocations of the head of the endoprosthesis occur in 0.4 - 17.5% of cases, purulent - inflammatory complications in 1.5 - 6.0%, periprosthetic fractures in 0.9% - 2.8%, postoperative neuritis in 0.6 - 2.2%, thromboembolic complications in 9.3 - 20.7% [1].

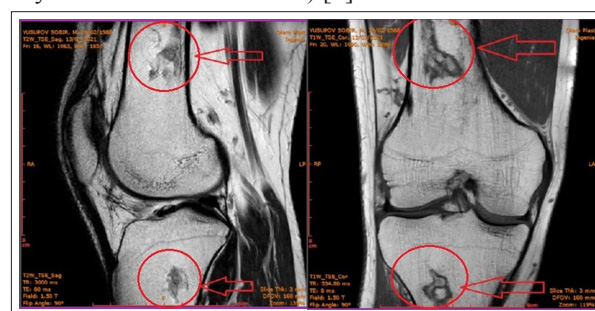
It is proved that these same complications after previous operations on the joint (osteotomy, osteosynthesis, etc.), as well as after revision endoprosthesis.



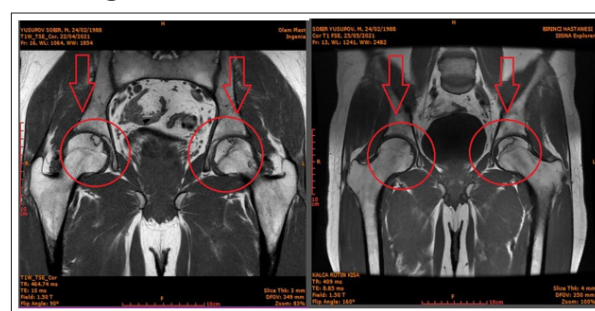
**Figure 2:** MRI from 25.05.2021, Turkey

Thus, the study of the causes and the development of ways to prevent the most frequent complications of hip arthroplasty have been and remain topical issues of traumatology and orthopedics. Obviously, conservative treatment with leeches of aseptic necrosis of bone tissue is not only the preservation of one's own joints, but also a unique opportunity to treat and prevent the entire range of complications of Post-COVID syndrome.

This thesis requires scientific substantiation, which allows us to remind the reader of some of the fundamental properties of leech. Professor Vorobyov A.P. expressed the hypothesis of Post-COVID syndrome (Chairman of the Moscow Scientific Therapeutic Society named after Botkin S.P.) [2].



**Figure 3:** MRI from 13.07.2021, Tashkent



**Figure 4:** MRI from 22.04.2021, Tashkent; Figure 4: A. MRI from 29.11.2021, Tashkent

**The main content of the diagnosis of Post-Covid syndrome: damage to the nervous system, as well as thrombosis of the capillary network of blood vessels. The remaining symptoms are a consequence of the above processes.**

Therefore, it was proposed pathogenetic technology for the treatment syndrome of complications from COVID-19: Direct anticoagulants and Plasmapheresis.

It is well known, that synthetic anticoagulants has a number of significant contraindications and complications in the defeat of the central nervous system and other organs.

As for plasmapheresis, the use of this technology requires special equipment and trained personnel, which does not allow the use of this technology outside of Moscow and large cities of regional significance.

We offer an alternative way to solve the problem of reducing mortality from pneumonia and other complications caused by COVID-19, without reducing the importance of the proposed therapy.

**This pathway is also the prevention of the development of aseptic bone necrosis**

Previously, we have published our position in the treatment of elderly people with multi-organ pathology, namely, they become primarily victims of Post-COVID syndrome, in particular, pneumonia [3]. We suggested using the systemic method of leech treatment (SML). This one is based on a combination of the principles of acupuncture (hirudopuncture) and homeopathy.

Our experience and offer is based on almost 30 years of use of SML at the Academy of Hirudotherapy of St. - Petersburg [4]. The detailed therapeutic mechanism of action of SML, offered by us in recent publications [3, 5]. The thrombolytic function of leech treatment well known.

Russian scientists Baskova I.P. and Nikonov G.I. made a significant contribution to the understanding of the thrombolytic effect of the medical leech – they discovered the enzyme destabilase.

Due to the limited size of this publication, we will refer to our publications on the mechanism of thrombolysis using medical leeches [3, 4, and 20]. We remind readers about some unknown properties of leech. The Academy of Hirudotherapy in St. - Petersburg has received a number of new fundamental facts over the past 30 years of research.

On the analysis of the main mechanisms of the pathogenesis of the COVID-19 virus, and details of the therapeutic effects of medical leeches in relation to the treatment of Post-COVID syndrome, our work was published (priority of April 21, 2021) [6]. Perhaps in this regard, our readers will be interested and our other article: "COVID-19 - Theoretical and practical justifications for reducing mortality and complications" [3]. This work is devoted to the treatment of Post-COVID syndrome and the treatment of complications from vaccinations against coronavirus.

The International Conference, dedicated to the 25<sup>th</sup> anniversary of the first in Russia and the world Department of Hirudotherapy was held in September 2021 in Russia. The conference discussed the fundamental discoveries of the department in the field of hirudology and hirudotherapy [5].

These achievements are based on the application of the systemic method of leech treatment (SML).

1992 - discovery of the phenomenon of "Girudobiopsia"

(A.I. Krashenyuk, S.V. Krashenyuk);

1993 – discovery of the energy effect (information-entropic) (A.I.Krashenyuk, S.V.Krashenyuk) [7,8].

1996 – discovery of the neuritstimulating effect of the medical leech

(A.I. Krashenyuk, S.V. Krashenyuk, N.I. Chalisova) [9,10,11].

2001 – discovery of the acoustic effect of leech treatment (hirudotherapy). (A.I.Krashenyuk, D.I.Frolov) [12].

2003 – discovery of the detoxification effect of leech treatment (A.I.Krashenyuk) [13].

2004 - discovery of the phenomenon of local hyperthermia in the body brain tumor - neurinoma (Kamynin Yu.F., Krashenyuk A.I.) [14,15].

2005 – discovery of the negentropic effect of leech treatment (hirudotherapy). (A.I.Krashenyuk, G.N.Dulnev) [14].

2007 – the role of autohemogyrudotherapy in the formation of the immunomodulatory effect of leech treatment (hirudotherapy) is shown. (A.I.Krashenyuk, S.V.Krashenyuk, Krylov A.A.) [4].

2010 – discovery of the aquastructuring effect of leech treatment (hirudotherapy). (Semikhina L.P., Krashenyuk A.I.) [16].

2016 – discovery of the "Resonance-wave effect" of leech treatment on the state of the human aquasystem (Vlaskin S.V., Dubovitsky S.A., Krashenyuk A.I., Petrosyan V.I.) [17].

The above-mentioned new fundamental knowledge has allowed us to offer pathogenetic treatment of Post-COVID syndrome, as well as the prevention of aseptic bone necrosis and bone infarction.

**1.Thrombolytic strategy:** The use of antiplatelet therapy (dipyridamole, aspirin) to prevent disturbances in microvascular blood flow in all patients is not required when using the systemic method of leech treatment.

The use of thrombolytic drugs of recombinant tissue plasminogen activators in patients with multiple organ failure when using the SML, is not required.

A marker of a high risk of an unfavorable outcome should be considered a D-dimer level of more than 1000 ng / ml.

Numerous observations show, the use of SML can reduce the level of D-dimer to the clinical norm.

**2.Effect on the pathogenesis of the central and peripheral nervous system:**

As stated above, in 1996, for the first time in the world, we discovered and patented the neurotrophic and neurostimulations effect of the medical leech [11].

We have installed 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) [19-22].

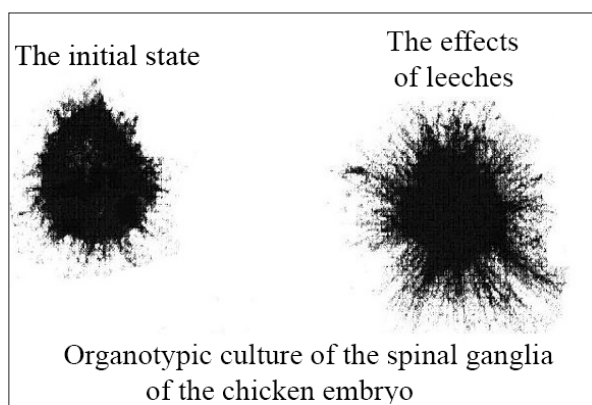
A long-term analysis of scientific publications to date has shown, no clinic in the world for the treatment of cerebral palsy and muscle spasticity has reached this level of treatment. The video-film is proof of our priority in this area "Cerebral palsy is treated only in Russia" can be viewed on our website: [academia-hirudo.ru](http://academia-hirudo.ru) For the first time this problem was raised by our research, thanks to the results of treatment of children diagnosed with Cerebral Palsy (Cerebral Palsy), patients with myopathy and children suffering from alali and autism [19-22].



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, Fig. 1.

The discovery of the neurotrophic (neuritstimulating) effect of medical leeches was confirmed in the laboratory of Moscow State University (MSU). The group of professor Baskova I.P. showed that the neurotrophic (neuritstimulating effect) is associated with the presence of destabilase-M, bdelastazine and bdelin-B in the secretion of the salivary glands of the leech [34].

The phenomenon of removal (reduction) of spasticity in the treatment of leeches is associated with the effect of the secretion of the salivary glands of the leech on the nerve endings and neurons, which is very important in the treatment of Cerebral Palsy, Post-COVID syndrome, Post-stroke syndrome.



**Figure 1:** (Photo). 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 interneuron bridges [9].

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 (MBD), 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 much more active than that of drugs known from scientific publications. For example, this activity 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. They can be used during pregnancy and in breastfeeding women.

Due to intravascular thrombosis, it cannot cope with the elimination of toxins that occur during tissue damage.

## Comparative evaluation of the neuritstimulating effect of some biologically active compounds [34]. Table 1

Biologically active compounds	Effective concentration, ng / ml	Literary source
Proteincinase 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	Goncharova V.P. et al., 1985
Fibroblast growth factor	100,0	Gospodarowicz D. et al.,1989
Cortexin	100,0	Havinson V.Kh. et al., 1997
Epithalamine	200,0	Havinson V.Kh. et al., 1997
Destabilase-M	0,01 и 0,05	Chalisova N.I. et al., 1999

Professor Vorobyev P.A., analyzing brain damage in COVID-19, notes that with the standard picture of hemorrhagic stroke with anatomic analysis of dead people observe, an unusual mechanism of brain tissue damage - diapedesis (penetration) of erythrocytes through the wall of cerebral capillaries [2]. This fact indicates a pronounced effect of the virus on the connective tissue of the vascular endothelium. Even so, leech therapy has been shown as a method of regenerating vascular connective tissue [23, 24].

**3.Treatment of depression.** 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. An essential 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 play not only the role of a neurotransmitter, but also a neuromodulator (neurohormon) [25].

As follows from the description of the symptoms of Post-COVID syndrome, we observe a pronounced lesion of the serotonin system of the brain, which, in our opinion, leads to the development of depression [2].

In our work we have studied in detail the effect of leech treatment on the secretion of various neurotransmitters, including serotonin in the human brain [14]. 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 dopamine system (damage to the olfactory bulb), histamine - a violation of the regulation of blood pressure, thermoregulation - a decrease in body temperature).

Given the mechanism of damage to the brain and peripheral nervous system by the COVID-19 virus, it should be recognized

that the mechanisms of action of medical leeches on the nervous system are pathogenetic (correct) for the treatment of Post-COVID syndrome.

**4. Detoxification effect of leech treatment:** For the first time described by us, the phenomenon of detoxification in the process of hirudotherapy, allows us 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 [13].

They are able to cause “Attached Leeches” (the definition of zemstvo doctors for leeches that have passed the stage of bloodsucking) vomiting or death. This property of attached leeches allows us to consider their behavior after bloodsucking as a way to assess the integral toxicity of the patient’s blood (author’s definition). The cause of intoxication with COVID-19 is the defeat of the capillary network of blood vessels, which, due to thrombosis, does not cope with the removal of toxins that occur when tissues are affected.

Today, this has been proven in patho-autopsies of people who have died of COVID-19 in many countries, not just China [26, 27]. 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 it is possible to have various kinds of complications associated with the formation of blood clots, damage to the nervous and cardiovascular system, i.e. confirmed the conclusions of professor A.P. Vorobyev and the hypothesis of the development of Post-COVID syndrome [2].

The minister also warned of greater lethality of the delta- strain of the coronavirus.

**“The mortality rate for COVID-19 disease caused by the delta-strain may be higher than in the previous period of rising incidence,”** he admitted.

Hemorrhagic complications with prolonged use of SML, were not detected (the observation period) in some patients was more than 2 years of continuous use.

**5. 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 leech treatment.

For the first time, we drew attention to the currently unexplored property of leech treatment - autohemogyrudotherapy, and proposed this term to refer to a new therapeutic factor of leech treatment. We are talking about subcutaneous microhemorrhages resulting from the process of bloodsucking.

As for the topic of autohemotherapy, many publications speak about its benefits. Extensive reviews on this topic are of interest

[28,29]. With regard to the topic of COVID-19 under discussion, attention should be paid to the work [30].

The immunomodulatory effect of leech treatment, aimed at a specific restructuring of regulatory subpopulations of lymphocytes, was discovered. 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. Prior to leeching, CD2 RI was  $1.24 \pm 0.07$ , which indicates a strain on the immune system and an increase in the activity of CD4 (helper activation of immunogenesis). After GT, this indicator changed to  $0.86 \pm 0.07$  due to the suppression of excessive activation of immunogenesis.

These data allow us to expect that the “Cytokine storm” [31], which many publications talk about when analyzing the pathogenesis of COVID-19, will not arise, but will go into the “Cytokine calm”.

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 [24].

**6. The discovery of the wave effects of leeches:** in the kilohertz range and the ability to change the radiation of the body’s aquasystem in the microwave/EHF range allows us to consider another possible aspect of the therapeutic and preventive effect of the SML [32,33].

In conclusion, in conclusion of the proposed publication, I would like to express the hope that the materials presented in the publication will effectively treat various complications of Post-COVID Syndrome, in particular, aseptic necrosis of bone tissue, without resorting to surgical treatment of this disease.

## Conclusions

Today in Russia and 30 countries of the world there are doctors who have received training and knowledge of the technology of the Systemic Method of Leeching (SML) at the Academy of Hirudotherapy, in St. - Petersburg. For the whole world, 1500 doctors familiar with the technology of the SMLt is clearly not enough.

But it is these specialists who today really save people with Post-COVID Syndrome of varying severity, as well as with complicated cases of vaccination. Extended training of doctors from different countries on the technology of the SML can be implemented with the support of International Health Organizations.

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