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Review Article

"Covid-19 - Post-Covid Syndrome" Pandemic: High Risks for Pregnant Women

Krashenyuk AI*

Academy of Hirudotherapy, St.- Petersburg, Russia

***Corresponding Author:** Krashenyuk AI, Academy of Hirudotherapy, St.- Petersburg, Russia.

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Abstract

The article discusses the mechanism of the disease "Covid-19 - Postcovid Syndrome". The mechanisms of pathogenesis of this disease in pregnant women are affected. The most proven mechanisms of the pathogenesis of the disease and the most correct methods of treatment according to the literature data are investigated. 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 and recommendations for pregnant women at risk of the disease are shown.

Keywords: Disease "COVID-19 - Postcovid Syndrome"; Damage to the Nervous System (Central and Peripheral); Endothelial Damage; Microthrombosis; Depression; "System Method of Leeching" (SML); Hirudotherapy; Neurotrophic Effect; Thrombolysis; Immunomodulatory Effect; Detoxification Effect; the Wave Effect; The Effect of Nitric Oxide Production - NO

Introduction

The new viral pandemic has created many challenges for all health services in the 205 countries affected by the pandemic. This is the high mortality of patients, especially in the group of elderly people, this is rehabilitation and attempts to prevent a high probability of thrombosis in convalescents, this is the problem of rehabilitation in brain damage, these are attempts to create vaccine preparations of various architectures, and other problems.

But the most dramatic was the problem of the most vulnerable contingent - pregnant women, both sick with coronavirus and vaccinated with various types of vaccines.

The author of the article owns a series of publications highlighting the features of the pathogenesis of a new disease: "COVID-19 - POSTCOVID SYNDROME", as well as a method of treatment and prevention of this disease based on the scientifically proven healing properties of *Hirudo medicinalis* medical leeches [1-14]. At the same time, the editors of four scientific medical journals have already adopted the author's concept of the name of the disease - "COVID-19 - POSTCOVID SYNDROME" [11-14], which reflects the understanding that this is a single disease that has two phases: the first phase 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.

The work [14] draws the attention of readers to the fact that such a definition of a 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 disease and requires monitoring of patients during the entire specified period, for example, monitoring the dynamics of D-dimers, prothrombin time, platelet count and fibrinogen levels in the blood convalescents. Now these are the most informative markers the danger of thrombosis. The term "Long COVID" does not reflect the essence of the disease process [13].

In addition, in this series of publications, we analyzed the most reasoned and proven various aspects of the pathogenesis of "COVID-19 - POSTCOVID SYNDROME" [3-14]. In this paper, we propose to consider the problem of this disease from the point of view of risk for pregnant women, taking into account the available publications [15-17]. If we consider the problem of the disease of pregnant women, then, first of all, it should be said that this group of women is at increased risk of the disease. This is due to the following reasons, firstly, pregnancy is a state of physiological hypercoagulation, in which these patients are prescribed anticoagulants during pregnancy. Most pregnancy complications are either caused by or combined with high thrombogenic potential. Genetic factors of blood clotting, especially antiphospholipid syndrome are risk factors for a large number of pregnancy complications - this is intrauterine fetal death, IVF failures, and delayed intrauterine development of the fetus, and premature abruption of the placenta, which leads to severe thrombohemorrhagic complications, these are thrombosis and embolism.

It can be expected that in the context of the disease "COVID-19 - POST-COVID SYNDROME", these complications may pose an even greater danger. After all, the «COVID-19» virus can be a factor that activates blood clotting factors. Some publications confirm the concerns expressed [18].

In recent years, the doctrine of genetic thrombophilia has become widespread.

Worldwide, this is up to about 20% of people who carry some form of genetic thrombophilia. You can live with this for a long time, but if there is an infection, trauma, an operation is performed - the patient can die from thromboembolism, even if the operation is performed at a high technical level. The reason for this is latent genetic thrombophilia - a mutation that makes its carrier susceptible to a high risk of thrombosis.

One of the forms of thrombophilia is the so-called hyperhomocysteinemia, which can be both acquired and genetically determined, can also be an important factor in thrombosis, heart attacks, and strokes. And now there is evidence that hyperhomocysteinemia is aggravated by "COVID-19" infection. Accordingly, the risk group includes all those who have elevated homocysteine levels in the blood, but a person may not be aware of this. The high contagiousness of the virus affects people with an overt or covert predisposition to thrombosis. These are patients not only with genetic thrombophilia or antiphospholipid syndrome, but also with diabetes mellitus, obesity, rheumatic diseases and other pathological conditions associated with increased blood clotting and/or inflammation.

Today, it can be unequivocally stated that with this viral pathology, from the very beginning there is activation of hemostasis, intravascular coagulation of blood and thrombosis in the vessels of small caliber of vital organs. At the same time, not only the lungs are damaged, but the blockade of microcirculation and its irreversible nature determine the outcome of the disease [19].

Late initiation of anticoagulant therapy is an unfavorable factor. Moreover, this process of intravascular coagulation in the capillaries of the lung plays an important role in the development of acute respiratory distress syndrome (ARDS). But it was not immediately possible to catch the connection between intravascular blood clotting and ARDS.

The term "Pulmonary intravascular coagulation" even appeared in Western literature. In almost all cases, there is an activation of the systemic inflammatory response. This is a general biological reaction, which is especially manifested in response to an infection of a viral nature. International organizations have recognized that coronavirus infection is sepsis.

On the other hand, the international organization for thrombosis and hemostasis in the absolute number of cases recognized the presence of DIC- syndrome in severe patients with "COVID-19". The combination of sepsis and coagulopathy is septic shock. Even Chinese colleagues pointed out that in 92% of cases, patients die from septic shock.

Of course, there is no denying that along with the virus, the cause of septic shock may be the addition of a secondary bacterial infection. Patients with "COVID-19" and disorders in the hemostasis system, as a rule, have hyperferritinemia, which occurs in critical conditions as a reactant of the acute phase of inflammation and is characterized by a cytokine storm due to hyperactivation of macrophages and monocytes. As a result, a large amount of ferritin

is produced - a complex protein complex that acts as the main intracellular depot of iron in humans and animals. In this case, it is always an acute phase protein, a marker of severe inflammation, and not an indicator of excess Fe^{+2}.

Thus, the cytokine and thrombotic storm aggravate the patient's condition and determine the severity. But there are some peculiarities. Perhaps "COVID-19" primarily damages fibrinolysis, a part of the hemostasis system that ensures the process of destroying already formed blood clots, thereby performing the protective function of preventing blockage of blood vessels by fibrin clots. Hence the fibrination syndrome with a lower frequency of hemorrhagic complications. And from here the prospect of using thrombolytics opens up, about which so much is written now.

Population analysis suggests that there are people not only with obvious, but also with latent hemostasis disorders predisposing to thrombosis - genetic thrombophilia, antiphospholipid syndrome and a number of other diseases accompanied by excessive activation of the hemostasis system; as well as people with a high readiness for a superinflammatory response (congenital factors and a number of rheumatological and immune diseases). And finally, "COVID-19" is blood clot inflammation.

Neutrophils and the extracellular neutrophil traps (NET) they secrete play a huge role in the development of so-called immunothrombosis. This is one of the priority scientific areas today.

When assessing ventilation-perfusion disorders in "COVID-19", perfusion disorders, microcirculation disorders prevail, which means that the main therapeutic target is the restoration of normal tissue perfusion, that is, antithrombotic therapy, and possibly even fibrinolytic. Mechanical ventilation cannot solve the issue of perfusion disorders.

Physiological changes associated with pregnancy increase the mother's susceptibility to infections in general.

Pregnancy is a state of relative immunosuppression caused by a change in the state of the body's immune system in order to prevent fetal rejection [20]. Increasing estriol levels also reduces CD4+ and CD8+ T cell levels, suppresses the production of inflammatory cytokines, and promotes the release of anti-inflammatory cytokines [20]. These immunological shifts and physiological changes predispose pregnant women to a more severe course of the disease and to diseases associated with respiratory infections, including coronavirus infections [20,21].

Features of the course of the disease «COVID-19» during pregnancy.

Testing in non-pregnant women most often occurs when they show symptoms or have been in contact with infected people, while pregnant women are often tested for «COVID-19» when seeking medical care for pregnancy or causes unrelated to the «COVID-19» outbreak [16,22]. A systematic review of 28 studies involving 11,432 patients found that one in 10 pregnant or postpartum women admitted to the hospital tested positive for «COVID-19» [17]. Of these, 75% were asymptomatic carriers, and one in 20 asymptomatic pregnant women tested positive for «COVID-19» [17]. As in the general population, the predominant symptoms of "COVID-19" in pregnant women were hyperthermia, cough, shortness of breath, and lymphopenia [17].

Compared with non-pregnant women of reproductive age, pregnant or recently pregnant women with «COVID-19» were less likely to report myalgia [17]. A French cohort study found that the presence of gastrointestinal symptoms was associated with a more severe course of the disease [25]. The clinical symptoms of infection generally did not differ depending on the gestational age [26].

Data on the course of "COVID-19" in pregnant women is mixed.

International data indicate a similar course of the disease in pregnant and non-pregnant women. Most studies show that the critical course of the disease is rarely observed in pregnant patients, but slightly increases compared to the age population [27-31]. One study reported that approximately 90% of pregnant women diagnosed with «COVID-19» recovered without the need for early delivery [17].

A recent study found an increased risk of severe illness and mechanical ventilation (ventilator) in pregnant women compared to non-pregnant women adjusted for age, race, and comorbidities [32]. In addition, "COVID-19" is associated with the development of cardiomyopathy in 7-33% of the general population [33,34].

Data on «COVID-19» cardiomyopathy during pregnancy are limited, as this complication manifested itself in only two pregnant patients [35]. Due to the lack of data, it is unclear whether the risk of developing «COVID-19» -related cardiomyopathy in pregnant women is increased compared to the general population.

The differential diagnosis of «COVID-19» symptoms in pregnancy is complex and includes preeclampsia, cardiomyopathy, pleural or pericardial effusion, gestational rhinitis, physiological shortness of breath, and manifestations of other viral-bacterial pneumonias. Many conditions associated with fever, coughing, or shortness of breath can trigger early termination of pregnancy, including preeclampsia and pulmonary embolism [17]. The frequency of admission to intensive care increases with increasing gestational age, with one study reporting that more than 90% of pregnant patients require intensive care in the third trimester [28]. Evidence suggests that 40% of pregnant women who died from «COVID-19» were obese, had diabetes, or the mother was 40 years of age or older [17,28,36,37]. Complications of severe disease include the need for invasive ventilation or extracorporeal membrane oxygenation, preterm birth, and «COVID-19»-related cardiomyopathy [37].

Late maternal age, high body mass index, pre-existing hypertension and diabetes mellitus (DM) were associated with severe «COVID-19», and the presence of extragenital diseases was an unfavorable prognostic marker for ventilators [17,24-26].

These indicators were closely related to the risk of neonatal death [28]. Other studies also demonstrate severe outcomes in pregnant women with "COVID-19" While the estimated mortality rates of pregnant women with "COVID-19" are 0.6-2%, which is comparable to the general population, critically ill patients account for the vast majority of deaths secondary to «COVID-19» [17,28].

Features of the results of laboratory and functional methods of examination in pregnant women with "COVID-19".

In pregnant women with «COVID-19», both leukocytosis and leukopenia can be detected. In a small clinical study, it was noted that leukocytosis, lymphopenia, a shift in the leukocyte formula to the right and normal body temperature are more common in pregnant women compared to non-pregnant women with "COVID-19" [24]. In contrast to previous data, more recent studies have found that leukopenia is the most common laboratory abnormality in these patients (66.1%) [22].

Other general laboratory norms described in the literature include elevated levels of C-reactive protein, D-dimer, and lactate dehydrogenase [24,28].

The combination of elevated levels of D-dimer and interleukin-6 was also associated with a more severe course of the disease and was found in 60% of severe and 80% of critically severe pregnant women with "COVID-19", respectively [28]. Unfortunately, data on baseline levels of these laboratory parameters during pregnancy are limited, making comparisons difficult.

The most common manifestations of pneumonia in pregnant women were changes according to multispiral computed tomography (MSCT) of the lungs by the type of "frosted glass" and bilateral infiltrates [17,22,24,28]. A meta-analysis of 42 studies involving 247 pregnant patients with «COVID-19» found that focal-beam or asymptomatic glossal opacities are the most common, while all patients with severe disease had diffuse bilateral glossal opacities with subpleural involvement and pleural effusion on imaging [16,22]. This study revealed abnormal imaging in 89% of patients, 8.7% of whom showed signs of disease during MSCT [28]. These similar studies showed that abnormal imaging results were common in asymptomatic pregnant patients [16,22]. Given the high rate of positive testing, it is important to prevent premature delivery in women who test positive for «COVID-19» but without clinical symptoms [19]. Pregnant women should be diagnosed on the basis of anamnesis, clinical picture, results of laboratory and instrumental methods of examination, including MSCT.

Complications and outcomes of pregnancy against the background of "COVID-19".

One large cohort study included 242 «COVID-19"-positive pregnant women and 248 newborns from these mothers observed during the third trimester of pregnancy and one month after childbirth [28]. The results of this study showed a higher incidence of cesarean section and preterm birth in hospitalized patients with symptoms of "COVID-19" [28]. It was noted that preterm birth occurred in about a third of pregnant women with "COVID-19", of which 40.0% were ultra-early and early (from 24.0 to 33.6 weeks of pregnancy) and 60.0% were late preterm births (from 34.0 to 36.6 weeks of pregnancy) [28].

Similar results were obtained in another study, which included 179 children born to Covid-positive mothers and 84 children born to «Covid -19»-negative mothers, confirmed an increased risk of preterm birth, the need for intensive care for newborns [23-28,31,35,39-44].

It is not yet clear whether the higher rate of prematurity is a consequence of the need for delivery secondary due to complications associated with "COVID-19" in the mother, or a consequence of the impact of the disease on pregnancy. The caesarean section rate is extremely high in patients with "COVID-19" in the U.S. - a meta-analysis showed a frequency of almost 85% [43,44].

Notably, the only documented indication for a C-section, in about half of these cases, was the mere presence of "COVID-19" in the mother. The frequency of preterm birth and caesarean sections increase in patients with «COVID-19» regardless of the severity of the disease [29], which may suggest that early delivery, and even by operative means, may be iatrogenic in nature.

Spontaneous miscarriage is more common in patients who become ill in the first trimester, compared with the second trimester, with a frequency of 16.1% and more than 3.5%, respectively [45-48].

Somewhat more often during pregnancy, patients with a new coronavirus infection show fetal growth retardation, placental insufficiency with morphologically confirmed changes in the placenta in the form of uterine-placental vascular malperfusion, interventricular inflammation and thrombosis of the interventricular vessels of the fetus [26].

The findings confirm the results of the following studies reporting histopathological studies of 14 placentas of patients with a clinically mild form of "COVID-19", which found occlusive fibrin deposition and non-occlusive blood clots with placental hypoperfusion in all samples [27,29]. Half of these cases ended in premature birth. Placental abruption, miscarriage in the second trimester of pregnancy and the birth of a low-weight child for gestational age (one case each) has also been reported [42-44,49].

The frequency of spontaneous preterm birth does not increase compared to the general population, and cesarean section was the main mode of delivery in all cases of preterm birth [17].

Accordingly, most complications in newborns born to mothers diagnosed with «COVID-19» are the result of prematurity, not «COVID-19» infection.

Infants with mothers who were diagnosed with the disease closer to childbirth were more likely to have a severe course than those whose mothers tested positive two or more weeks before delivery [26]. In a recent cohort study, nearly a tenth of newborns from COVID-19-positive mothers were tested for antibodies in the first month of life [42].

Stillbirths and neonatal mortality do not increase compared to the general population [26]. None of them tested positive for «COVID-19» [50-53]. The findings are consistent with the findings of another study that reported no cases of pneumonia or lower respiratory tract disease in newborns less than 6-8 weeks of age born to "COVID-19" positive mothers [51,53]. Several cases of mild symptoms have been reported in newborns diagnosed with «COVID-19» at birth or shortly thereafter [50-53].

The most common manifestations of "COVID-19" in newborns are fever, pneumonia, cyanosis, respiratory distress [26]. Most of these children showed moderate symptoms and the outcome was favorable. It was found that most of the complications were related to prematurity and sepsis, and not to «COVID-19» [27,42].

Complications and outcomes of pregnancy due to vaccination against "COVID-19".

Analysis of published materials on the relationship of vaccination against "COVID-19" and complications of pregnancy is contradictory. Nevertheless, some preliminary conclusions can be drawn: Studies that talk about the safety of vaccination of pregnant women do not inspire confidence in the population, since these publications show the interest of companies that produce vaccines and order such publications, despite the large statistics of observations.

Oddly enough, but the most trust is caused by the speech of politicians who reflect the information and interests of their voters. As an example, we can cite the speech of the member of the Canadian Parliament from Ontario Rick Nicholls on December 10, 2021 (His speech is cited by many publications on the Internet).

Addressing Canada's Minister of Health, Christine Elliot R. Nicholls said: "There were 86 stillbirths in the Waterloo area from January to July (2021), and this usually occurs with a frequency of approximately 1 stillbirth every two months. But here's the most important thing. Mothers of stillborn babies were fully vaccinated. And you've made it clear many times that vaccines are safe".

Minister Christine Elliott did not respond to a member of parliament's question regarding the facts of a large number of stillbirths, but instead gave a standard religious response to the cult of the vaccine.

"It's safe. This has been verified. We recommend that pregnant women receive the vaccine to protect themselves as well as protect the baby. And it's been proven, it's been approved by Health Canada. The World Health Organization, the Food and Drug Administration".

Let's supplement this information with the materials of the United States. The latest update to the U.S. government's National Vaccine Side Effects Reporting System (VAERS). VAERS now has recorded 2,893 cases of intrauterine fetal death after COVID-19 vaccinations over the past year, which means more fetal deaths after all vaccines in the last 31 years. (Materials from the Internet).

The capabilities of the "System Method of Leeching" in preventing the development of complications in pregnant women infected with «COVID-19».

In our previous publications, we have dwelt in detail on the use of hirudotherapy as a pathogenetic method of treating the disease "COVID-19 - POSTCOVID SYNDROME". However, to an even greater extent, these grounds for reducing the severity of the disease and mortality apply to pregnant women [3-14]. We analyzed in our previous publications the main pathogenetic mechanisms implemented in the "System Method of Leeching".

Let's remind readers about them:

- Discovery of the energy effect (information-entropic);
- Discovery of the neurostimulating effect of the medical leech;
- Discovery of the acoustic effect of leech burning (hirudotherapy);
- Discovery of the detoxification effect of leech accumulation (hirudotherapy);
- Discovery of the negentropic effect of leech accumulation (hirudotherapy);
- The role of autohemogyrudotherapy in the formation of the immunomodulatory effect of leech accumulation (hirudotherapy) is shown;
- Discovery of the aquastructuring effect of leech burning (hirudotherapy);
- Discovery of the "Resonance-wave effect" of leech on the state of the human aquasystem.

In addition to these mechanisms, in this article we give new arguments in favor of the use of the "System Method of Leeching" in the treatment of pregnant women from the disease "COVID-19 - POSTCOVID 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 of Baskova I.P. and Isakhanyan G.S. [54].

The composition of "Piyavit" includes: hirudin, hyaluronidase, eglins and bdellins, prostacyclins, destabilase enzyme. It was experimentally confirmed that "Piavit" does not have a teratogenic and embryotoxic effect and does not have a negative effect during the gestational period [55].

The healing properties of "Piyavit" have been proven in such pathology as "Delayed Fetal Development" (DFD) [56]. 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%! [55].

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 [57], aimed at improving the "Uterine-placental - fetal blood flow".

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 pregnant women with the disease "COVID-19 - POSTCOVID SYNDROME".

A significant role in substantiating the application of the "System Method of Leeching" in "COVID-19 - POSTCOVID SYNDROME" was played by the work of Lomonosov M.V Moscow State University professor Baskova I.P. on the study of the role of salivary cell secretion (SCS) in the generation of the vascular endothelium of nitric oxide -NO [58].

In our publications, the topic of treatment "COVID-19 - POSTCOVID SYNDROME" [3,4,6-14] was repeatedly touched upon, but in relation to the topic of treatment of pregnant women, a specially responsible attitude is required, since we are talking about the health of a pregnant woman and her unborn child.

In favor of the "Systemic method of Leeching" of pregnant women says, in addition to the known and published effects of leeching [1-14], discovered by professor Baskova I.P. M.V. the phenomenon of stimulation of the production of nitrous oxide by the vascular endothelium - NO, which has a pronounced antiviral effect [59,60]. Of course, this topic is interesting, not sufficiently covered in the literature, has prospects for further study. The antiviral role of nitric oxide-NO has so far been proven by many works [59-62].

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 и Zawadzki [63]. The authors were the first to describe endothelium-dependent relaxation factor (NO) and discovered a new, NO-dependent way of regulating physiological processes. A review by S. Moncada [64] discusses the role of NO in the cardiovascular system: in addition to maintaining vasodilation, NO inhibits platelet aggregation and modulates smooth muscle proliferation. It affects many cardiovascular diseases, each factor of rice is 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 [60,65]. NO inhibits many viral proteinases and transcription factors necessary for viral replication [61] and enhances the antiviral effect of IFN-γ [60].

The effect of activated oxygen-containing metabolites (AOCM) on infectious agents is also related to the rate of their interaction with activated nitrogen-containing metabolites (ANCM), which leads to the formation of $ONOO^-$ [66-68]. Currently, a new understanding of the synergy of the action of reactive oxygen and nitrogen radicals in the nonspecific defense of the body is presented [66]. According to modern research, the production of AOCM and ANCM is the most important sign of the activation of phagocytic cells - macrophages, neutrophils and monocytes. The generation of NO and O_2-• occurs almost in an equimolar amount.

The balance in the level and rate of generation of NO and O_2-• 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 $ONOO^-$, more toxic than NO for most bacterial, viral [61,62] and fungal infectious agents [69]. Peroxynitrite interacts with virus capsule proteins, inhibiting the penetration of viruses into the cell [62]. 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 [60].

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 [60,70]. At low levels, NO contributes to 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 [71,72].

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 [60,70].

The work cited prepares us to understand the role of the medical leech's SCS in influencing the synthesis of NO in human vascular endothelial cell culture (HUVEC). A series of works carried out at Lomonosov M.V. Moscow State University under the guidance of professor Baskova I.P. 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 divalent copper with a derivative of fluorescein [73,74], 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 the 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 in the models on the effect of the drug "Piyavit" and SCS allow us to hope 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.

Conclusion

«COVID-19» is a potentially fatal infection, but data on its course in pregnant women today is limited. The heterogeneity of the information obtained is most likely due to the diversity of the studied populations of people, survey methods and, as a result, the results obtained.

The existing different approaches to the treatment of pregnant women with «COVID-19» make it difficult to analyze the course of infection, the development of specific and non-specific complications during pregnancy, approaches to delivery.

Pregnant patients with a mild form of infection and the absence of concomitant diseases, obstetric complications should be delivered naturally in due time and can be safely discharged home. Women in the third trimester of pregnancy, especially with obesity, diabetes, chronic arterial hypertension, have the highest risk of a critical course of the disease, complicated by the course of pregnancy, in such conditions the tactics of early delivery are collegially discussed.

Of fundamental importance is the question of the use of hirudotherapy during pregnancy. The works presented in the review on the preservation of pregnancy and gestation of the fetus when using the drug "Piyavit" unequivocally proves its effectiveness. The literature indicates that the use of hirudotherapy in preparation for pregnancy has a pronounced positive effect even with such a serious pathology as chronic pyelonephritis. The authors of the work [75] found that in chronic pyelonephritis there are violations of the antioxidant system, which negatively affects the course of pregnancy. The use of pregravidal preparation with the inclusion of hirudotherapy helped to improve the indicators of

the antioxidant system during pregnancy, reducing the frequency of exacerbations of pyelonephritis and pregnancy complications to a greater extent than the standard course of treatment.

Observations in our clinic for infertile couples and materials published in 2012 for a period of 18 years of observations showed that children born to these couples using the "System Method of Leeching" were born with a high level of physical health (Apgar Scale 9/10 points), but they showed good dynamics of physical and mental development, better than their peers born with normal childbirth.

By 2012, more than 3,000 such children had been born using the "System Method" [76]. They had the highest score on the Apgar scale. By 2022, more than 5,000 such children were born in various regions of Russia, with the participation of students of our department: for 26 years, more than 2,000 doctors in Russia who own the "System Method of Leeching" have been trained. The use of the "System Method of Leeching" in pregravidal preparation and during pregnancy allows you to avoid complications and give birth to a healthy child on time against the background of the current pandemic.

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