UDC 519.8.612.007 **https://doi.org/10.15407/biotech13.03.030**

INTEGRATED MATHEMATICAL MODEL FOR IMITATION OF THE COURSE OF VIRAL DISEASE AND CORRECTION OF THE INDUCED HYPOXIC STATE

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Received 21.03.2020
Revised 07.05.2020
Accepted 30.06.2020

The aim of the work was to create a complex mathematical model simulating the course of the disease caused by the SARS-CoV-2 virus on the level of interaction between functional systems of organism and pharmacological correction of organism hypoxic states arising in the complicated course of the disease. In the present work the methods of mathematical modeling and theory of optimal control of moving objects were used. The proposed integrated mathematical model consisted on the mathematical models of functional systems of respiration and blood circulation, thermoregulation, immune response, erythropoesis, and pharmacological correction. Individual patient data were taken for this model, and the disturbing effect in the form of viral disease was simulated. The reactions of functional respiratory and blood circulatory systems were predicted. Partial pressures of respiratory gases in alveolar spaces and their tensions in lung capillaries blood, arterial and mixed venous blood, and tissue fluid were calculated. Further the intravenous injection of antihypoxant was simulated and the values of the same parameters were calculated. In such a way it was possible to choose the most optimal way of hypoxic state correction for any individual. This model is theoretical only for today because the models of respiratory and blood circulation systems were designed for the average person and it does not suppose peculiarities of individual persons infected with SARS-CoV-2. In particular, this concerns the pequliarities of gas exchange in the alveolar space and characteristics of respiratory gases diffusion through the alveolar-capillary and capillary-tissue membranes. However, it is one of possible directions for solving the complex tasks related to treatment of the disease caused by SARS-CoV-2 virus. In the result of the work the complex of information support for the imitation of viral disease course was developed at the level of interaction of organism functional systems, as well as pharmacological correction of caused by it hypoxic states.

Key words: SARS-Cov-2 virus, immune response model, mathematical model of the respiratory system, hypoxic state, infection lesion

New coronavirus infection burst had happened in Republic of China with epicenter in Wuhan (Hubei Province) in late 2019. The World Health Organization officially named it COVID-19 (“Corona virus disease 2019”) on February 11, 2020. The International Committee on Viruses Taxonomy had assigned the official name to the agent of this infection — SARS-CoV-2 on February 11, 2020.

The information on epidemiology, clinical features, prevention, and treatment of this disease is limited until now. The most common clinical manifestation of the new variant of coronavirus strain infection was bilateral pneumonia: the development of acute respiratory distress syndrome was registered in 3–4% of patients [1]. This potentially severe acute respiratory infection causes dangerous disease [2]. It can occur both in the form of acute respiratory viral infection with mild course [3, 4] and in severe form with such specific complications as viral pneumonia caused acute respiratory distress syndrome or respiratory failure with a risk of the death [5]. However, full clinical picture is not yet clear [6]. There are no specific antiviral agents for the treatment or prophylaxis of this disease [7]. In most cases (approximately 80%) it turns out that no specific treatment is required, and recovery takes place on its own [2, 8]. In severe cases, specific means and methods are used to maintain functions of vital organs [9]. Respiratory insufficiency development is also possible against the background of this infection [3]. Less than a third of patients demonstrated the development of acute respiratory distress-syndrome [2]. In case of acute respiratory distress-syndrome, tachycardia, tachypnoea or cyanosis may also be appeared to accompany hypoxia [6].

Inflammatory processes can influence on cardiovascular system resulting in arrhythmias and myocarditis. Acute heart insufficiency is mostly found in severely or critically ill patients. Infection can occure long-term ~~influences~~ on the health of cardiovascular system. In case of patients with cardiovascular diseases in anamnesis, strict monitoring of their conditions may be required [2].

There is no specific antiviral therapy against SARS-CoV-2 virus [9] and there is no evidence of effective immunomodulating therapy [10]. Patients receive mainly symptomatic and supportive therapy. In severe cases, treatment aims to maintain vital functions of organs [9].

Although unlicensed drugs and experimental therapies are used today in practice of coronaviral disease treatment, for example, with the use of antiviral agents, such treatment should be carried out within the framework of ethically based clinical trials [2]. Critically important is the use of tools that are justified both ethically and scientific researches [11, 12].

Bases for used methodology. Therapy prescriptions should not be based on hypotheses, but on clinical studies that confirm the effectiveness of such therapy. Hypotheses, however, may be the basis for a planned clinical trial [13]. Therefore, it seems reasonable to apply simulation modeling of coronaviral disease course and exposure to pharmacological drugs.

The methods of information technologies and mathematical modeling complement those of experimental biology and medicine. Modern diagnostic methods, whatever perfect they may be, give only a “slice” of current organism state. Therefore, the mathematical modeling of organism functional systems and an organism as a whole became widespread in the last third of the last century, allowing to simulate various processes taking place in the organism and to study these processes at the level inaccessible to the modern methodical diagnosis level, for example, to simulate extreme organism disturbances and forecast the functional state of organs and systems with this disturbance.

Mathematic model of functional respiratory system, developed by the united efforts of the scientists from Glushkov Institute of Cybernetics and Bogomoletz Institute of Physiology both of the National Academy of Sciences of Ukraine was based exactly on these principles.

The purpose of the work was to create integrated mathematical model to simulate the course of the disease caused by SARS-CoV-2 virus and pharmacological correction of complications — organism hypoxic states.

Mathematical models of respiration and blood circulation systems

Many mathematical models of various functional systems and organism as a whole exist nowadays. Let’s observe the models related to the respiratory and blood circulatory systems because of several reasons. First, according to the current information, exactly these systems are the most affected by the SARS-CoV-2 virus [14–27]. Secondly, in the theory of adaptation developed by Meyerson, exactly these systems responded most noticeably to changes of living conditions [28, 29]. Thirdly, in a number of publications there were shown that if we consider the human organism from the point of view of reliability theory, and assume it as a “chain with a weak link”, then such “weak links” are exactly the respiratory and blood circulatory systems [30–37].

First of all, Gray model should be highlighted, in which the respiratory system was presented as a feedback system and thus the background for studying the relationships between alveolar ventilation V and oxygen pressures pO_2, carbon dioxide pCO_2 and the arterial blood acidity pH was laid [38].

The next qualitatively important step was the model of Grodins, who suggested that the respiratory system should be considered as a dynamic system, which made it possible to use the appropriate mathematical apparatus [39, 40]. The ventilation dynamics was studied when the concentration of carbon dioxide in respiratory system changed. Therewith elements of system analysis were used. The control and controlled systems responsible for process of gas exchange were given up, tissue reservoirs of an organism in which oxygen was consumed and carbon dioxide was released were subdivided. Two reservoirs were identified as “brain” and “non-brain”. The first reservoir included vitally important organs, the second one — peripheral organs and tissues. Grodins derived the differential equations describing the dynamics of partial pressures and tensions of respiratory gases in the lungs, blood and tissues, basing on the principles of material balance and continuity of the flow [39, 40]. A significant disadvantage of the model was the assumption that during inspiration, a constant pCO_2 was maintained in the respiratory mixture, alveoli and blood.

Mathematical models of respiratory and blood circulatory systems: their use for the solution of practical and theoretical problems in medicine and physiology

Further development of Grodins model was a model of mass transfer and mass exchange of respiratory gases in human body and dolphin, proposed by Kolchinskaya and Misyura [41]. The model considers the process of mass transfer and mass exchange of respiratory gases through the alveolar-capillary and capillar-tissue membranes, taking into account their structural and functional pequliarities. This approach enabled to study gases transportation in human body during respiratory cycle: inspiration, expiration and pause, taking into account the biophysical and biochemical characteristics of the processes. Besides, tissue reservoirs were differentiated in the model, tissues of brain, heart, liver, kidneys, skeletal muscles, and etc. were defined. This made it possible to elaborate the models of gases saturation and to study the process of hypoxia development in them [41]. The proposed model contained equations for determining of alveolar ventilation and systemic blood flow obtained on the basis of experimental data. However in order to calculate oxygen and carbon dioxide regimes of human organism under changes in living conditions, it was required the data that were impossible to obtain at the current methodological level of bioexperiment. Therefore, it is quite problematic to use such type of models for the cases upon changing the levels of energy consumption, environmental conditions without solving the problem concerning control of respiratory system function.

In addition, blood circulatory system, contrary to respiratory one, is multifunctional, and this causes certain difficulties linked with determination of optimality criterion. Consequently, the concept of organism’s oxygen regimes regulation formulated by Kolchinskaya and Lauer was an actual one [42]. According to this concept, the regulation in organism is carried out by one complex system that coordinates joint functioning of various mechanisms and subordinates this system to its main task — to maintain optimal oxygen parameters along the oxygen pathes in organism. Herewith, the delivery speed should match the oxygen demand in tissues. In accordance with this concept, mathematical models should consider the united action of the systems of external respiration, blood circulation, and tissue respiration, aimed on the providing of tissues demand in oxygen.

There are numerous other mathematical models [43–52]. Let’s observe exactly the models developed by Onopchuk and representatives of his scientific school [37, 53–59]. Basing on above-described approach, few mathematical models of heat transfer and heat exchange [60–62], immune system [63–65], system of energy supply [66] and erythropoesis [67, 68] were developed.

These models were used to solve a number of practical and theoretical problems in medicine and physiology. Namely, the theoretical problems linked with investigations of cerebral blood circulatory tensions in operators of continuous interaction system were solved [69–74], compromise resolution of conflict situations in the problem of optimal control in decisions making in difficult situations was studied [37, 75–77], the role of hypoxia, hypercapnia and hypometabolism during adaptation of the respiratory system to intensive muscular activity and stay in conditions of hypoxic hypoxia were investigated [78–82], mathematical models of short-term, medium-term and long-term adaptation of the respiratory system to extreme environmental influences were developed [35, 37, 83, 84], parameters of self-organization of the rescue command members breathing system during short-term and medium-term adaptation to hypoxic hypoxia were studied [35, 82], the tasks of modeling of the hypoxic and hypercapnic stages of training athletes were considered [85, 86], dependence of parameters of functional self-organization for high qualification women-athletes on the hormonal status of their organisms were studied [87–89], algorithm for predicting of fatigue development in highly skilled athletes with refined muscular activity was constructed [90, 91], mathematic models for the development of hypoxia at coronary heart disease were developed [92–97], algorithm for the selection of data models and algorithms for their processing to build an integrated estimation of the reliability and performance of athletes was proposed [98–101]. Separately, it is necessary to highlight the use of these models in sports of the highest achievements, for the sportsmen specializing in cyclic sports [102], martial arts [103–107], alpinism [108], their practical application in research at the Elbrus Medical and Biological Station of Bogomoletz Institute of Physiology of the National Academy of Sciences of Ukraine [109–121], for solution of a broad range of problems connected with the examination of operators of continuously interacting systems and flying personnel.

Separately, it is necessary to write about the works [122–124] associated with the development of software for the improving of the tools and methods for operational data mining, processing and analysis of functional diagnostic data, and the person's stay in hyperbaric environment [125, 126].

There is also a number of works devoted to the research and identification of organism reserves under the extreme disturbances [127–132] and optimization of the recovery and rehabilitation processes after the extreme loads on an organism [133,134], thermoregulation processes under the extreme influences [116].

Therefore, the idea to apply such models for new class of problems related to studying and treatment of infectious organism lesions infected with SARS-CoV-2 seems quite reasonable and appropriate.

Integrated model of the functional system of respiration, blood circulation, heat transfer, and immune response

To simulate the hypoxic state caused by SARS-CoV-2 virus we proposed to use integrated mathematical model of the functional respiratory and blood circulatory system, thermoregulation, and immune response to predict the course of viral disease [37, 54, 55, 57, 60–65].

When studying the organism adaptation to one or another disturbances, including infectious disease, it is advisable to take into consideration the possibility of participation of intersystem mechanisms in process of organism state stabilizing, taking into account both intra-systemic and intersystemic conflict situations. In response to the environment disturbing influence (external or internal), all organism functional systems react against it to some extent, trying to stabilize the organism state, despite the contradictions between goals and interests. The structural scheme of complex mathematical model for investigation of the main functional systems (respiration, blood circulation, heat transfer, immune), their pharmacological correction as well as mechanisms of their interaction and interconnection during the life activities in extreme conditions of the external and internal environment was shown on Fig. 1.

Let's give a description of the models of individual functional systems. Briefly,

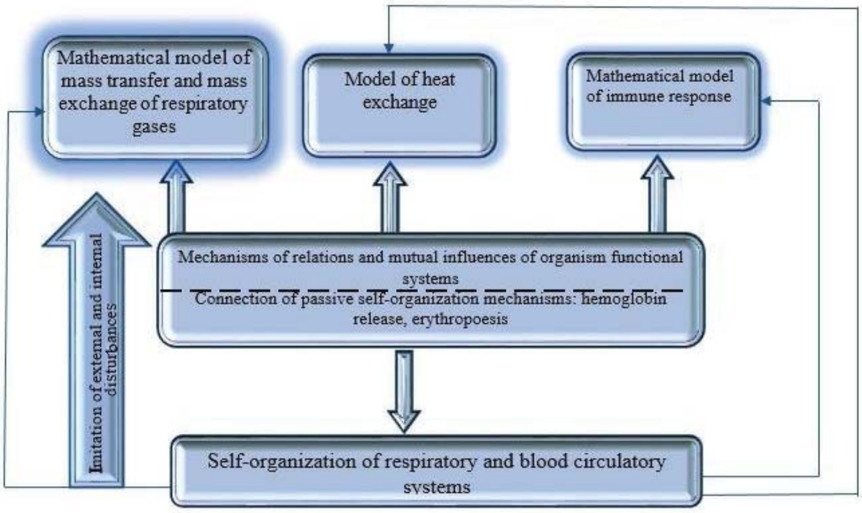

Fig. 1. **Integrated model of the functional system of respiration, blood circulation, heat transfer, and immune response**

the mathematical model of the functional respiratory system could be represented as follows. Mathematical model of respiratory and blood circulatory system is a controlled dynamic system, the phase state of which is characterized by partial pressures and tensions of respiratory gases in each element of the system.

The controlled part of the model is based on differential equations describing changes in average partial pressures of respiratory gases in each part of respiratory cycle — during inspiration, expiration and pause. Briefly, the model can be submitted as follows:

$$\frac{dp_iO_2}{d\tau} = \varphi(p_iO_2, p_iCO_2, \eta_i, \dot{V}, Q, Q_{t_i}, G_{t_i}O_2, q_{t_i}O_2) \quad , (1)$$

$$\frac{dp_iCO_2}{d\tau} = \psi(p_iO_2, p_iCO_2, \eta_i, \dot{V}, Q, Q_{t_i}, G_{t_i}CO_2, q_{t_i}CO_2) \quad , (2)$$

where the functions φ and ψ are described in detail in [54, 55], V is ventilation, η is a degree of hemoglobin saturation with oxygen, Q is volumetric velocity of systemic and Q_{t_i} — local blood flows, $q_{t_i}O_2$ is oxygen consumption rate by i-th tissue reservoir, $q_{t_i}O_2$ is the rate of carbon dioxide release in i-th tissue reservoir. The velocities $G_{t_i}O_2$ of oxygen flows from the blood into the tissue and $G_{t_i}O_2$ of carbon dioxide from the tissue into the blood are determined by the ratio:

$$G_{t_i} = D_{t_i} S_{t_i} (p_{ct_i} - p_{t_i}), \quad (3)$$

where D_{t_i} are gas permeability coefficients through the airhematic barrier, S_{t_i} is gas exchange surface area.

In this model, respiratory, cardiac and vascular smooth muscles are the active mechanisms of self-regulation. Accordinly V, Q, Q_{t_i}, $i = 1,m$ are the control parameters in the dynamic system, which are determined as a result of solving the task of optimal output of the disturbed dynamic system into a stable equilibrium state characterized by the following retios:

$$G_{t_i}O_2 - q_{t_i}O_2 = 0, \quad i = \overline{1,m} \quad , \quad (4)$$

$$G_{t_i}CO_2 + q_{t_i}CO_2 = 0, \quad i = \overline{1,m} \quad . \quad (5)$$

The optimal values are those that provide a minimum of the functional:

$$I = \int_{t_0}^{T} \left(\rho_1 \sum_{t_i} \lambda_{t_i} \left(G_{t_i}O_2 - q_{t_i}O_2 \right)^2 + \rho_2 \sum_{t_i} \lambda_{t_i} \left(G_{t_i}CO_2 + q_{t_i}CO_2 \right)^2 \right) dt, \quad (6)$$

under the restrictions:

$$\dot{V}^{\min} \le \dot{V} \le \dot{V}^{\max}, \quad Q^{\min} \le Q \le Q^{\max}, \quad Q_{t_i}^{\min} \le Q_{t_i} \le Q_{t_i}^{\max}, \quad \sum_{t_i} Q_{t_i} = Q. \quad (7)$$

In (7) ρ_1, ρ_2 are organism sensitivity coefficients to the oxygen deficiency and carbon dioxide excess, λ_{t_i} characterize functionally the morphological features of tissue region.

The dynamics of infectious lesion of organism was given by Marchuk as a system of ordinary nonlinear differential equations with delay [135]. Let's consider one of the equations of this system:

$$\frac{dm}{d\tau} = \sigma\nu(1-m) - \mu_m, \quad (8)$$

where $m(\tau)$ is relative characteristics of an affected organ. If M is characteristics of healthy organ (mass or area), and M' is corresponding characteristic of the healthy part of affected organ, then

$$m = 1 - \frac{M'}{M}, \quad (9)$$

is a relative characteristic of lesion of an organ-target. The factor $(1 - m)$ in (8) determines the effect of antigens on unaffected part of an organ-target.

Decrease in this characteristic occur due to the regenerative activity of an organism with μ_m coefficient characterizing the rate of mass recovery of the affected organ.

The pathological state of an organism that developed due to the infectious lesion can be considered as disturbance during modeling of blood circulatory system. Then σ and μ_m in (8) are the functions depended on Q_{t_i}. When considering joint modeling of respiratory, circulatory and immune systems and their regulation, it is necessary to add the term

$$\rho_{\eta_i} f_i^2(m(\tau), V(\tau)), \quad (10)$$

to the quality criterion of regulation (6) into the integration element, where ρ_{η_i} is a coefficient characterizing the influence degree of the simulated disease type on the level of gas homeostasis. The function $f_i(m, V)$determines the damage degree of target-organ at current moment. At control points, this function was taken as:

$$f_i(m, V) = a_i m + b_i v \quad (11)$$

It could be assumed that the flow of energy processes in the tissues of an organ-target is supplied only due to its unaffected part. Then the mass of metabolizing part of the organ will be determined:

$$v_{t_i}(\tau) = v_{t_i}^0(1 - m(\tau)), \qquad (12)$$

where $v_{t_i}^0$ is a total mass (volume) of tissues of healthy organ.

In case of infectious disease, it is natural to assume a reaction of thermoregulatory system. Let's complete our model of the dynamics of the course of infectious disease by introducing the variable T (the temperature of internal sphere of organism [136, 137]) in the equation below:

$$\frac{dT_{t_k}}{d\tau} = K_T(Fv - (Fv)^*)\chi(Fv - (Fv)^*) - \mu_T(T_{t_k} - T_{t_k}^*), \qquad (13)$$

where K_T, μ_T are coefficients, $F\nu$ is concentration of $F\nu$ complexes, $(F\nu)^*$ is maximal permissible concentration of complexes, $T^*_{t_k}$ is normal temperature of core of organism, χ is Heaviside function. In this case, it was natural to put the coefficients in model (8)–(12) in the form of functions depending on T_{t_k}:

$$\overline{\beta}(T_{t_k}) = \frac{\overline{\beta}(T_{t_k}^*)}{1 + \alpha_{T_k}(T_{t_k} - T_{t_k}^*)}, \qquad (14)$$

$$\overline{\alpha}_{T_{t_k}} = \overline{\alpha}(T_{t_k}^*)[1 + b_{T_{t_k}}(T_{t_k} - T_{t_k}^*)], \qquad (15)$$

where $\overline{\beta}(T_{t_k}^*) = \overline{\beta}, \overline{\alpha}(T_{t_k}^*) = \overline{\alpha}, \quad \alpha_{T_{t_k}}, b_{T_{t_k}}$ are coefficients.

It is natural to assume that at the initial stage of disease, the passive mechanisms of self-regulation such as erythropoesis, release of hemoglobin and mioglobin into blood were involved. An increase of the content of red blood cells and the content of hemoglobin in them is powerful regulatory mechanism for maintaining of organism stable state in conditions that lead to oxygen deficiency under the various disturbances. In [67] the linear dependences of erytropoetin (EPO), *Ht* and *Hb* were obtained and than they were introduced into the mathematical model of functional respiratory and blood circulatory system to enhance the regulation of respiratory system main function in hypoxia.

Further, due to the fact that severe hypoxia develops in organism as a result of lung damage, the injection of antihypoxants into the organism is advisable in order to study the possible ways of organism state relief in case of hypoxia. The integrated model described above for this case has to be supplemented by the equations of transport of pharmacological preparations in organism in forms, suggested previously [107, 118, 138]. The algorithm for the application of this approach is given in Fig. 2.

Our developed mathematical model of pharmacological correction of hypoxic states clarifies the role of pharmacological preparation use for prevention of hypoxic states development in organism (for organism state perfection). It was assumed that the withdrawal of antihypoxant *f* from the organism is carried out through the kidneys. It was assumed as well that we use pharmacological preparations that improve oxygen permeability through the capillary tissue membranes of blood vessels. According to this scheme it was assumed that the most effective was intravenous administration of antihypoxant, although the model enabled to simulate as well as respiratory, oral and intramuscular way of antihypoxants administration.

Procedure for the work with the model

1. Patient examination is carried out.
2. The data obtained from the survey are the source for calculation of organism oxygen regimes [121, 122].
3. The data obtained during patient examination and some data obtained as a result of calculation of organism oxygen regimes were taken as input source data in the models of functional respiratory system, blood circulatory system and thermoregulation. In such a way the models individualization was fulfilled.
4. Further, using the model of immune response, the effect of virus is simulated; with the interaction and interinfluence of the models, the partial pressures and tensions of respiratory gases in all parts of respiratory system, alveolar ventilation and systemic blood flows are calculated.
5. The next step is to simulate the effects of pharmacological preparations and, consequently, the values of the same indicators have to be calculated again.
6. The obtained data are analyzed and further, in case of unsatisfactory result, another effect of antihypoxant is simulated, or if the obtained indicators are acceptable, then this scheme of pharmacological preparation use is chosen.

Thus in this publication, the results of development of comprehensive integrated mathematical model for simulation of the course of disease caused by SARS-CoV-2 were suggested. It could be used

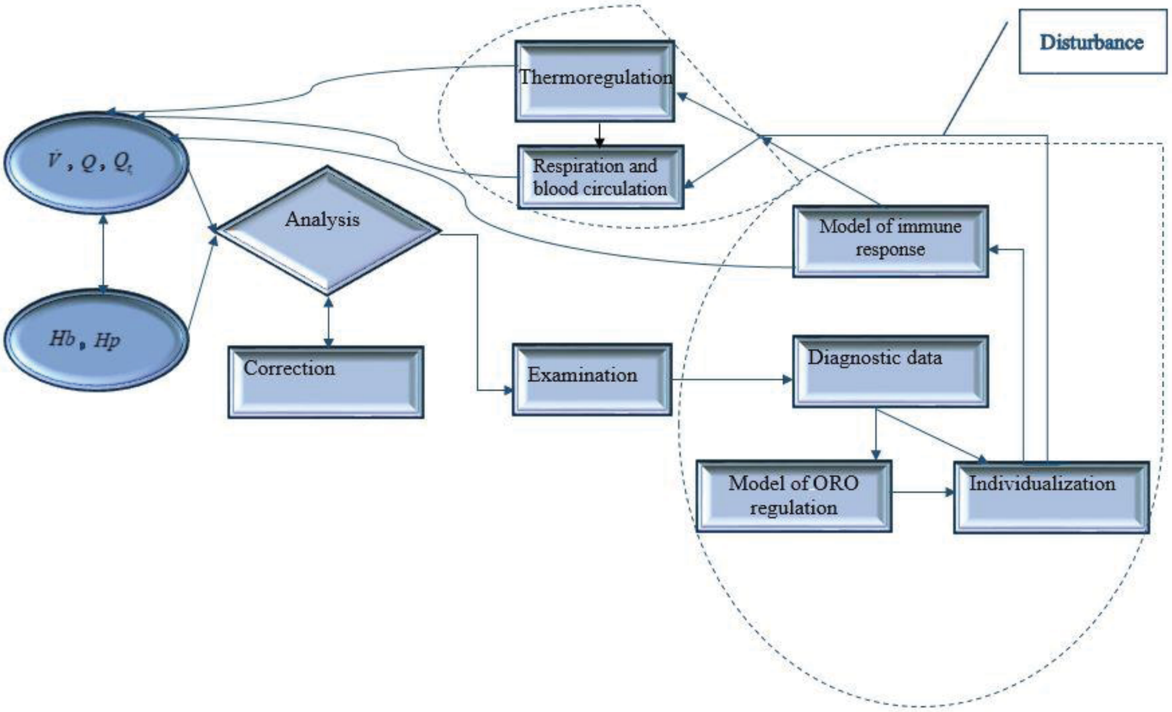

Fig. 2. **Scheme of mathematical model for simulating the course of viral disease and its pharmacological correction:** *Hb*, *BH* — concentrations of hemoglobin and buffer bases in blood; ***Q*** — volurimetric velocity of systemic blood flow; Q_{t_i} — volurimetric velocity of local blood flows; *ORO* — oxygen regimes of organism; ν — alveolar ventilation (air volume that pass through alveolar space during 1 min)

for pharmacological correction of hypoxic states that occur with the complication of disease course as well. The bases for the used methodology were observed as well as mathematical models of respiration and blood circulation systems. The information about the developed models of respiratory and blood circulatory systems and their use for the solution of practical and theoretical problems in medicine and physiology were suggested. For simulation of hypoxic state caused by SARS-CoV-2, we proposed to use the integrated mathematical model of functional respiratory and blood circulatory systems, thermoregulation, and immune response one to forecast the course of viral disease. The structural scheme of complex mathematical model for the investigations of main functional systems (respiration, blood circulation, heat transfer, and immune response), their pharmacological correction as well as mechanisms of their interaction and interconnection during the life activities in extreme conditions of the external and internal environment was demonstrated. In the result, the complex of information support for imitation of viral disease course as well as for it pharmacological correction caused by the organism hypoxic states were developed.

For today, this mathematical integrated model has theoretical significance only. It is based on the information about the clinically registered manifestations of coronaviral (SARS-CoV-2) disease available in the public domain. Therefore, this model requires further perfection. In particular, it seems necessary to clarify some characteristics of respiratory gases transport through the alveolar-capillary membrane, peculiarities of gas exchange in the alveolar space, which cause the decrease of blood oxygenation. These are the problems that need to be solved in close collaboration with the professionals in medicine. At the same time, the imitation on this model the development of infectious disease and associated hypoxic state is one of the possible and quite effective tool for solving the tasks associated with the support of patients in acute hypoxic respiratory and heart failure caused by the complications of viral (SARS-CoV-2) disease.

“To develop mathematical models of the integration organisms of functional systems for a body and methods of integration of their mathematical models to maintain the reliability and safety of human life in extreme conditions” (State registration number 0114U001052). 2014–2018 Research work B.F.170.09.

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ІНТЕГРОВАНА МАТЕМАТИЧНА МОДЕЛЬ ДЛЯ ІМІТАЦІЇ ПЕРЕБІГУ ВІРУСНОГО ЗАХВОРЮВАННЯ ТА КОРЕКЦІЇ СПРИЧИНЕНОГО НИМ ГІПОКСИЧНОГО СТАНУ

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Метою роботи було створення комплексної математичної моделі, що імітує перебіг захворювання, спричиненого вірусом SARS-CoV-2, та фармакологічної корекції гіпоксичних станів організму в разі ускладнення цього захворювання. В цій роботі було використано методи математичного моделювання та теорії оптимального керування рухомими об’єктами. Запропонована математична модель складалася з математичних моделей функціональних систем дихання та кровообігу, терморегуляції, імунної відповіді, еритропоезу та фармакологічної корекції. Для цієї моделі було взято індивідуальні дані пацієнта і здійснено імітацію вірусного захворювання. Прогнозували реакції органів дихання та кровообігу: розраховано парціальний тиск дихальних газів у альвеолярних просторах та їхню напругу в крові легеневих капілярів, артеріальної та змішаної венозної крові та тканинної рідини. Далі імітували ін’єкцію антигіпоксанту та розраховували значення тих самих параметрів. Таким чином можна було вибрати найбільш оптимальний спосіб корекції гіпоксичного стану для будь-якої людини. На сьогодні ця модель є суто теоретичною, оскільки моделі системи дихання та кровообігу було розроблено на усереднені дані, і вони не враховують особливостей окремих осіб, інфікованих SARS-CoV-2. Зокрема, це стосується газообміну в альвеолярному просторі можливих особливостей проникності дихальних газів через альвеолярно-капілярну мембрану. Однак це один із можливих напрямів вирішення складних завдань, пов’язаних з лікуванням захворювання, спричиненого вірусом SARS-CoV-2. У результаті було розроблено комплекс інформаційної підтримки для імітації перебігу вірусних захворювань, а також фармакологічної корекції спричинених ними гіпоксичних станів.

Ключові слова: вірус SARS-CoV-2, модель імунного відгуку, математична модель дихальної системи, гіпоксичний стан, інфекційне ураження.

ИНТЕГРИРОВАННАЯ МАТЕМАТИЧЕСКАЯ МОДЕЛЬ ДЛЯ МОДЕЛИРОВАНИЯ ТЕЧЕНИЯ ВИРУСНОГО ЗАБОЛЕВАНИЯ И КОРРЕКЦИИ ВЫЗВАННОГО ИМ ГИПОКСИЧЕСКОГО СОСТОЯНИЯ

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Целью работы было создание комплексной математической модели, имитирующей течение заболевания, вызванного вирусом SARS-CoV-2, и фармакологической коррекции гипоксических состояний организма, возникающих в случае осложнения этого заболевания. В этой работе использовались методы математического моделирования и теории оптимального управления движущимися объектами. Предлагаемая математическая модель состояла из математических моделей функциональных систем дыхания и кровообращения, терморегуляции, иммунного ответа, эритропоэза и фармакологической коррекции. Для этой модели были взяты индивидуальные данные пациента и смоделирован эффект в виде вирусного заболевания. Спрогнозированы реакции дыхательной и кровеносной систем: рассчитаны парциальное давление дыхательных газов в альвеолярных пространствах и их напряжение в крови капилляров легких, артериальной и смешанной венозной крови и тканевой жидкости. Далее имитировали инъекцию антигипоксанта и рассчитывали значения тех же параметров. Таким образом можно было выбрать наиболее оптимальный способ коррекции гипоксического состояния для среднестатистического человека. На сегодняшний день эта модель является чисто теоретической, поскольку модели системы дыхания и кровообращения были разработаны усредненные данные, и не учитывающие особенности отдельных лиц, инфицированных SARS-CoV-2. В частности, это касается газообмена в альвеолярном пространстве и возможных особенностей проницаемости дыхательных газов через альвеолярно-капиллярную мембрану. Однако это одно из возможных направлений решения сложных задач, связанных с лечением заболевания, вызванного вирусом SARS-CoV-2. В результате был разработан комплекс информационной поддержки для имитации течения вирусных заболеваний, а также фармакологической коррекции вызванных ими гипоксических состояний.

Ключевые слова: вирус SARS-CoV-2, модель иммунного отклика, математическая модель дыхательной системы, гипоксическое состояние, инфекционное поражение.