Study of the human infectious safety model under the influence of SARS-CoV-2 on the example of the Perm Krai of the Russian Federation

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Abstract. In the new millennium, humanity is faced with infectious diseases that no one previously knew about. In the end of 2019, an outbreak of a new coronavirus infection occurred in the People's Republic of China (PRC) with an epicenter in the city of Wuhan (Hubei Province). On February 11, 2020, the International Committee on the Taxonomy of Viruses assigned an official name to the infectious agent - SARS-CoV-2. According to the results of serological and phylogenetic analysis, coronaviruses are divided into four genera: Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus. Currently, four seasonal coronaviruses (HCoV-229E, - OC43, -NL63 and -HKU1) are circulating among the world's population, which are present year-round in the structure of ARI, and, as a rule, cause damage to the upper respiratory tract of mild and moderate severity, as well as two highly pathogenic coronaviruses-Middle East respiratory syndrome virus (MERS) and new coronavirus infection COVID-19. To develop a model of human resistance to the disease caused by the coronavirus family, the elements, links and ways of protecting the Human-Virus-Environment system were identified. The destructive functions of sixteen proteins of the SARS-CoV-2 strain are considered. Deterministic and statistical models of cells infection risk development have been developed. A parameterized system of human protection against coronavirus infection is proposed.

1 Introduction

One of the most important problems of 2019-2021 is the search for optimal methods for creating human protective functions against coronavirus affect. The use of system analysis methods is one of the promising ways to consider and solve the problems of fighting viral

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infection in conditions of uncertainty. Currently, about 40 species of viruses are known, united in 4 subfamilies. They have this name because of the structure of their outer shell in the form of a crown. Coronaviruses – viruses with a positive RNA (+RNA) chain, compared to other RNA viruses, have an exceptionally big genome and have a unique replication mechanism. Viral particles of the SARS-CoV-2 strain have a spherical shape with a diameter of 60-120 nm. The height of the protrusions is 9-12 nm.

2 Development of the Human-Virus-Environment (HVE) system model)

Currently, coronaviruses of acute respiratory syndrome SARS, in particular SARS-CoV-2, are particularly dangerous among viruses. When developing a vaccine against the coronavirus family, it is necessary to have a methodology for studying the characteristics and assessing human life state. To formalize the elements of the HVE system, we introduce the following sets (Figure 1):

$H = \{h_1, h_2, ..., h_l\}$ – set of people types;

$V = \{v_1, v_2, ..., v_n\}$ – family of coronaviruses;

$E = \{e_1, e_2, ..., e_m\}$ – set of environment elements;

$U = \{u_1, u_2, ..., u_l\}$ – set of control elements.

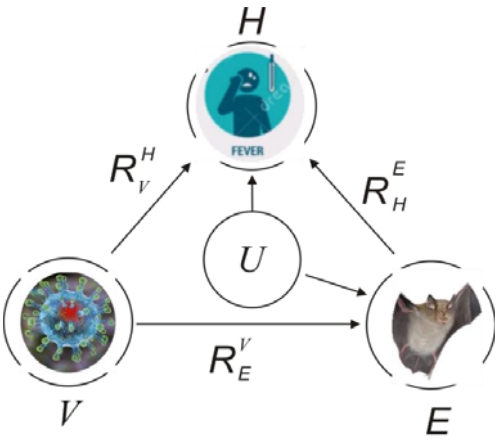


Fig. 1. Relationship of the HVE system elements under study.

The interrelations between system elements are defined by binary relations R (1), which can be understood as functional relations, preferences, sequences, and others that reflect the essence of the relationship of the HVE system elements:

$$\begin{matrix} VR_H{}^V H, & VR_E{}^V E, \\ URE, & URH, \\ ER_H{}^E H. \end{matrix} \quad (1)$$

Binary relations can be decomposed into more complex ones with the introduction of an additional variable C, called state. We decompose the binary relations R into two subsets: a healthy (1) and an infected (2) cell. The cell, like any real system, functions under certain physiological conditions determined by the environment. In this case, system (1) is transformed as follows:

$$VR_H^{V1}[C_H^V, H^1], C_H^V R_H^{V2} H^2,$$
$$VR_E^{V1}[C_E^V, E^1], C_E^V R_E^{V2} E^2, \quad (2)$$
$$ER_V^{E1}[C_V^E, H^1], C_V^E R_V^{E2} H^2.$$

The security of the HVE system and the state (C) of each element as a whole depend on their properties, changing during the life cycle of the HVE system

$$C_H = F_1[\{S_H\}, C_H^V, C_H^E],$$
$$C_E = F_2[\{S_E\}, C_E^V], \quad (3)$$
$$C_V = F_3\{S_V\}.$$

The state of the HVE system is determined by the properties of the system elements (C_V, C_E, C_H). The nature of changes in these properties during the life cycle of the HVE system, as a rule, worsens due to the aging of the cell and a decrease in protective abilities. Therefore, to build dependencies of real state changes in the HVE system, it is necessary to know some functionality $\Im$ that would determine the safe state of the HVE system and its properties:

$$C_{HVE} = \Im (C_V, C_E, C_H). \quad (4)$$

The state C_V of destructive elements of coronaviruses affect the state of the C_{HVE} system: α-, β-, γ-, δ-CoVs, that have specific chemical and biological properties; on the own state of the C_H cell, which depends on the protective functions of the cell, climatogeographic features of human habitation and relations with animals - C_E.

3 Study of the HVE system state assessment model

The state of the HVE system is described by a functionality that characterizes the state of elements arrays (4). Let's examine human safety in more detail. The state of human safety (C_H) depends on the safety indicator of its own properties (Θ_H); change in the safety indicator from the influence of coronaviruses ($\Delta\Theta_H$(V)); on change in the safety indicator depending on change in environmental parameters ($\Delta\Theta_H(E)$) and is determined by the formula

$$C_H = \Theta_H + \Delta\Theta_H(V) + \Delta\Theta_H(E). \quad (5)$$

Let's describe in more detail the elements of equation (5).

The intrinsic properties of the cell (Θ_H) are determined by the susceptibility to destruction (modification) of nucleic acid elements that provide storage and transmission of genetic information (DNA and RNA) from the effects of coronavirus.

The change in the safety indicator $\Delta\Theta_H$(V) depends on the group and strain of coronaviruses and is described by the equation

$$\Delta\Theta_H(V) = \frac{\partial\Theta_H}{\partial\nu_\alpha}\Delta\nu_\alpha + \frac{\partial\Theta_H}{\partial\nu_\beta}\Delta\nu_\beta + \frac{\partial\Theta_H}{\partial\nu_\gamma}\Delta\nu_\gamma + \frac{\partial\Theta_H}{\partial\nu_\delta}\Delta\nu_\delta, \quad (6)$$

$\nu_\alpha = \{\text{HCoV - 229E, HCoV - NL63, TGEV}\}$ - α-type coronaviruses set;

$$v_\beta = \left\{ \begin{matrix} \text{Bat - SL ZXC21, 2019} - n\text{CoV}, \\ \text{SARS - CoV, MERS - CoV} \end{matrix} \right\}$$ - β-type coronaviruses set;

$$v_\gamma = \{\text{IBV, SW1}\}$$ - γ-type coronaviruses set;

$$v_\delta = \{\text{HKU11, HKU17}\}$$ - δ-type coronaviruses set.

The SARS-CoV-2 strain, which has a high destructive feature of modification of nucleic acid elements, cellular degradation, cleavage of polypeptides and other functions, is particularly dangerous [1]. Let's consider the destructive functions of sixteen non-structural and structural proteins (nsp) of the SARS-CoV-2 coronavirus strain:

$$\begin{aligned} \Delta V_{2019\text{-nCoV}}(\text{nsp}) = & \frac{\partial v_\beta}{\partial(\text{nsp}_1)}\Delta\text{nsp}_1 + \frac{\partial v_\beta}{\partial(\text{nsp}_2)}\Delta\text{nsp}_2 + \frac{\partial v_\beta}{\partial(\text{nsp}_3)}\Delta\text{nsp}_3 + \frac{\partial v_\beta}{\partial(\text{nsp}_4)}\Delta\text{nsp}_4 + \\ & + \frac{\partial v_\beta}{\partial(\text{nsp}_5)}\Delta\text{nsp}_5 + \frac{\partial v_\beta}{\partial(\text{nsp}_6)}\Delta\text{nsp}_6 + \frac{\partial v_\beta}{\partial(\text{nsp}_7)}\Delta\text{nsp}_7 + \frac{\partial v_\beta}{\partial(\text{nsp}_8)}\Delta\text{nsp}_8 + \frac{\partial v_\beta}{\partial(\text{nsp}_9)}\Delta\text{nsp}_9 + \\ & + \frac{\partial v_\beta}{\partial(\text{nsp}_{10})}\Delta\text{nsp}_{10} + \frac{\partial v_\beta}{\partial(\text{nsp}_{11})}\Delta\text{nsp}_{11} + \frac{\partial v_\beta}{\partial(\text{nsp}_{12})}\Delta\text{nsp}_{12} + \frac{\partial v_\beta}{\partial(\text{nsp}_{13})}\Delta\text{nsp}_{13} + \\ & + \frac{\partial v_\beta}{\partial(\text{nsp}_{14})}\Delta\text{nsp}_{14} + \frac{\partial v_\beta}{\partial(\text{nsp}_{15})}\Delta\text{nsp}_{15} + \frac{\partial v_\beta}{\partial(\text{nsp}_{16})}\Delta\text{nsp}_{16}, \end{aligned} \quad (7)$$

where:
nsp_1 – degradation cellular mRNA [2];
nsp_2 – currently insufficiently studied [3];
nsp_3, nsp_5– cleaving polypeptides [4];
nsp_4, nsp_6– formation DMV [5];
nsp_7, nsp_8, nsp_{12} – DNA modification [6];
nsp_9 – dimerization RNA [7];
nsp_{10}, nsp_{14} and nsp_{16} – dsRNA sensors evasion [8];
nsp_{11} – currently insufficiently studied [3];
nsp_{13} - RNA destruction [8];
nsp_{15} – endoribonuclease [9].

The general destructive functions of the SARS-CoV-2 coronavirus can be described by the function (7). Human safety against the effects of coronaviruses can be estimated by the formula (6).

4 Necessary and sufficient conditions for human infection with coronavirus

A necessary condition of transition from one state of HVE system to another is the presence of the coronavirus (CoV), and sufficient – given distance (x) to the hazard (coronavirus), the speed of epidemic spread (w) and time effects (τ) (table 1).

Table 1. Necessary and sufficient conditions for the occurrence and the course of the infectious process in the body

Probability of state	Type of state	Parameters of viral activity
p_1	Safe state (lack of necessary and sufficient conditions)	$C^1 = \begin{pmatrix} c < c^d \\ x > x^d \\ \tau < \tau^d \\ w < w^d \end{pmatrix}$
p_2	Dangerous state of effect on the human immune system (the necessary is present (c), but there are no sufficient conditions)	$C^2 = \begin{pmatrix} c \geq c^d \\ x > x^d \\ \tau < \tau^d \\ w < w^d \end{pmatrix}$
p_3	State of infectious process in the body (presence of the necessary (c) and sufficient conditions (x, w)	$C^3 = \begin{pmatrix} c > c^d \\ x < x^d \\ \tau < \tau^d \\ w > w^d \end{pmatrix}$
p_4	State of cell death (destruction of the nucleus, cell organelles and cell membrane) (presence of the necessary (c) and sufficient conditions (x, τ, w)	$C^4 = \begin{pmatrix} c > c^d \\ x < x^d \\ \tau > \tau^d \\ w > w^d \end{pmatrix}$

Note – c^d, x^d, τ^d, w^d are the maximum allowed parameters for the spread of infection.

As a model of transition states of the HVE system, it is advisable to use semi-Markovian processes characterized by arbitrary probability distribution functions p_i. The transition of the system from the state C_i to the state C_j is carried out under the influence of viral activity with transition coefficients λ_{ij}. Determination of the probability $p_i(t)$ of the system state is determined by the solution of the Kolmogorov system of equations

$$\frac{\mathrm{d}p_i(t)}{\mathrm{d}t} = \sum_{j=1}^{n} \lambda_{ij}\, p_j(t) - p_i(t) \sum_{j=1}^{n} \lambda_{ij}, \ (i = 1,2,3,\ldots,n)$$

with initial conditions $p_1(0), p_2(0), \ldots, p_n(0); p_i(0) \geq 0, \ \sum_{i=1}^{n} p_i(0) = 1.$

Based on this, the HVE system from the point of view of a human safety to disease can be in one of four states:

C^1_{HVE} – safe state when the HVE system does not have the necessary conditions for the occurrence of a viral infection;

C^2_{HVE} – state of a dangerous situation when there is a viral infection in the HVE system, but there are no sufficient conditions for human coronavirus damage (the cell resists penetration into its virus, weak virulence of the coronavirus);

C^3_{HVE} – state of the infectious process in the body when the coronavirus entered the cell and the reproduction of the coronavirus began;

C^4_{HVE} – state of cell death, characterized by the destruction of the cell membrane and the cell nucleus.

The image obtained with an electron microscope, (https://echo.msk.ru/blog/nplus1/2576219-echo) shows the penetration of the coronavirus into the susceptible cell (Figure 2).

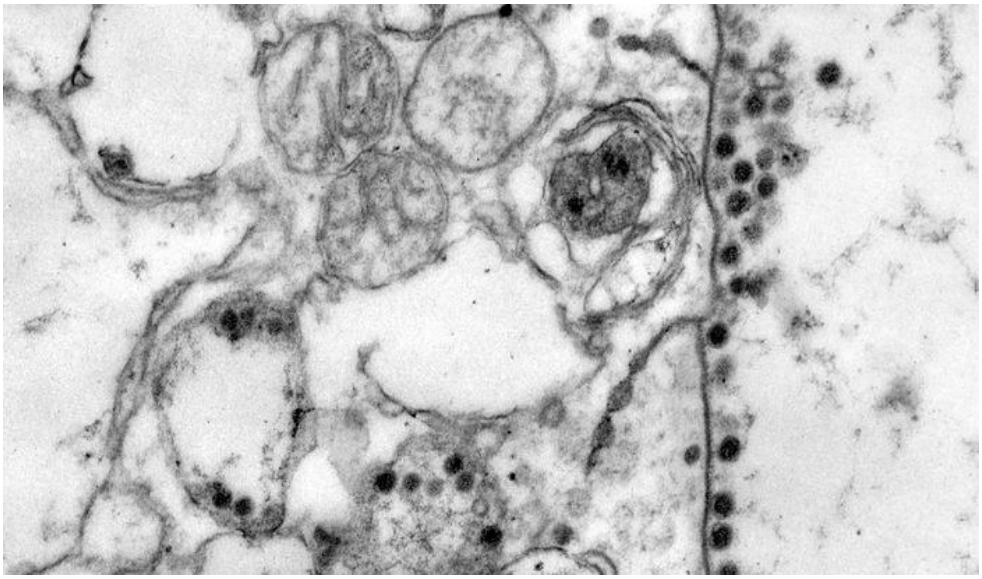


Fig. 2. Penetration of the coronavirus into susceptible cell (https://echo.msk.ru/blog/nplus1/2576219-echo/)

The article [10] also used approaches of applying the Kolmogorov system of equations to the development of a network model of human infection on the example of Wuhan City, Hubei Province of China.

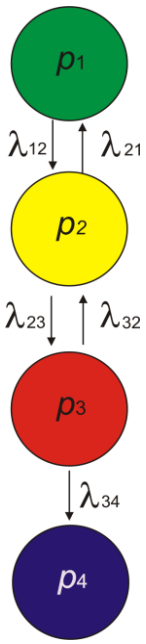
The interrelations between probabilistic states of the HVE system are presented in figure 3, which shows that the HVE system can go from a safe state (1) to dangerous state (2), infection state (3) and vice versa, while increasing the body's immune system, the cell prevents the penetration and reproduction of coronavirus. The transition from the infectious state to the state of cell death (4) is final, since the cell is destroyed and dies at this moment. The system of differential equations for the probability graph of states p_i and transition coefficients λ_{ij} of the HVE system is shown in Figure 3.

The system of coefficients λ_{ij} describing the dynamics of SARS-CoV-2 influence in accordance with the Kolmogorov system of equations (Figure 3) can be described by the transition matrix:

$$\Lambda = \begin{bmatrix} 0 & \lambda_{12} & 0 & 0 \\ \lambda_{21} & 0 & \lambda_{23} & 0 \\ 0 & \lambda_{32} & 0 & \lambda_{34} \end{bmatrix} \quad (8)$$

The probability matrix of the human condition P is described by an array:

$$P = [p_1, p_2, p_3, p_4]. \quad (9)$$



$$\frac{dp_1(t)}{dt} = \lambda_{21} p_2(t) - \lambda_{12} p_1(t)$$

$$\frac{dp_2(t)}{dt} = \lambda_{12} p_1(t) + \lambda_{32} p_3(t) - \lambda_{21} p_2(t) - \lambda_{23} p_2(t)$$

$$\frac{dp_3(t)}{dt} = \lambda_{23} p_2(t) - \lambda_{32} p_3(t) - \lambda_{34} p_3(t)$$

$$\frac{dp_4(t)}{dt} = \lambda_{34} p_3(t)$$

Fig. 3. Graph of the probability of states p_i and transition coefficients λ_{ij} of the HVE system: safe (1), dangerous (2), infectious (3) and cell death (destruction) (4).

The formalization of the space of hazard parameters i of the CoV virus allows to assess the degree of safety of human infection:

$$\theta_i = \begin{cases} \frac{1}{4}\left(\frac{c_i^d - c_i}{c_i^d} + \frac{x_i - x_i^d}{x_i^d} + \frac{w_i^d - w_i}{w_i^d} + \frac{\tau_i^d - \tau_i}{t_i^d} \right), \text{ at } \left(c_i < c_i^d\right) \wedge \left(x_i > x_i^d\right) \wedge \left(w_i < w_i^d\right) \wedge \left(\tau_i < \tau_i^d\right); \\ 0, \text{ at } \left(c_i \geq c_i^d\right) \vee \left(x_i < x_i^d\right) \vee \left(\tau_i > \tau_i^d\right) \vee \left(w_i > w_i^d\right). \end{cases} \quad (10)$$

Thus, the total indicator for multiple virus sources is calculated as an arithmetic mean or equal to zero if at least one of the virus sources is dangerous:

$$\Theta = \begin{cases} \frac{1}{N} \sum_{i=1}^{N} \theta_i, \forall\, i = \overline{1,N} : \theta_i > 0; \\ 0 \qquad\quad , \exists\, i = \overline{1,N} : \theta_i = 0. \end{cases} \quad (11)$$

Based on the sanitary and epidemiological norms in force on the territory of the Russian Federation, the minimum permissible distance between people x^d =1.5 m is determined, the permissible exposure time τ^d is set by the employer based on the epidemiological situation in the region.

Using equations (10) and (11),it is possible to calculate the epidemiological level of safety in the studied region (province).

5 Statistical model of cell infection

Coronaviruses have some unique features in RNA transcription, protein composition, and assembly mechanisms. They penetrate into the cell by adsorptive endocytosis. After that, genomic RNA is attached to ribosomes, which leads to the synthesis of viral RNA-

dependent RNA-polymerase. During transcription of genomic RNA, a complementary minus-chain of full-length RNA is formed. Its synthesis is completed in 5–6 hours after infection. Let's make a statistical model of cell infection with respect to the probability function $\vartheta(t)$.

In the course of human life, the parameters of infections sources (c, x, w and τ) of the HVE system can change both deterministically (for example, natural cell aging) and stochastically (under the influence of external influences, for example, viruses):

$$c = c(\vartheta_c(t), t),\ x = x(\vartheta_x(t), t),\ \ w = w(\vartheta_v(t), t),\ \tau = (\vartheta_\tau(t), t), \tag{12}$$

where $\vartheta(t)$ is a random event.

Differentiating complex functions (10), we obtain

$$\frac{\mathrm{d}c(\vartheta_c(t), t)}{\mathrm{d}t} = \frac{\partial c(\vartheta_c(t))}{\partial \vartheta_c(t)} \cdot \frac{\mathrm{d}\vartheta_c(t)}{\mathrm{d}t} + \frac{\partial c(t)}{\partial t}, \qquad \frac{\mathrm{d}x(\vartheta_x(t), t)}{\mathrm{d}t} = \frac{\partial x(\vartheta_x(t))}{\partial \vartheta_x(t)} \cdot \frac{\mathrm{d}\vartheta_x(t)}{\mathrm{d}t} + \frac{\partial x(t)}{\partial t}, \tag{13}$$

$$\frac{\mathrm{d}w(\vartheta_v(t), t)}{\mathrm{d}t} = \frac{\partial w(\vartheta_v(t))}{\partial \vartheta_v(t)} \cdot \frac{\mathrm{d}\vartheta_v(t)}{\mathrm{d}t} + \frac{\partial w(t)}{\partial t}, \qquad \frac{\mathrm{d}\tau(\vartheta_\tau(t), t)}{\mathrm{d}t} = \frac{\partial \tau(\vartheta_\tau(t))}{\partial \vartheta_\tau(t)} \cdot \frac{\mathrm{d}\vartheta_\tau(t)}{\mathrm{d}t} + \frac{\partial \tau(t)}{\partial t},$$

where $\frac{\partial c(\vartheta_c(t))}{\partial \vartheta_c(t)}, \frac{\partial x(\vartheta_x(t))}{\partial \vartheta_x(t)}, \frac{\partial w(\vartheta_v(t))}{\partial \vartheta_v(t)}, \frac{\partial \tau(\vartheta_\tau(t))}{\partial \vartheta_\tau(t)}$ is the density of the probability distribution of a random variable of cell infection;

$\frac{\partial c(t)}{\partial t}, \frac{\partial x(t)}{\partial t}, \frac{\partial w(t)}{\partial t}, \frac{\partial \tau(t)}{\partial t}$ – functions of deterministic changes in the coronaviruses parameters;

$\frac{\mathrm{d}\vartheta_c(t)}{\mathrm{d}t}, \frac{\mathrm{d}\vartheta_x(t)}{\mathrm{d}t}, \frac{\mathrm{d}\vartheta_w(t)}{\mathrm{d}t}, \frac{\mathrm{d}\vartheta_\tau(t)}{\mathrm{d}t}$ – density of distribution of the time of infection.

In the case of a normal distribution law of a random variable of human infection with an exponential law of time for cell destruction, we obtain the following expressions:

$$c(t) = \int_0^t \frac{\mathrm{d}c(\vartheta_c(t), t)}{\mathrm{d}t}\mathrm{d}t = \int_0^t \left(\frac{1}{\sigma_c\sqrt{2\pi}} \exp\left(-\left[\frac{\vartheta_c - \mathrm{M}(\vartheta_c)}{2\sigma_c} \right]^2 \right) \exp(-\lambda_c t) \right) \mathrm{d}t +$$

$$+ \int_0^t \frac{\mathrm{d}c(t)}{\mathrm{d}t}\mathrm{d}t = c(t) + \frac{1}{\sigma_c\sqrt{2\pi}} \exp\left(-\left[\frac{\vartheta_c - \mathrm{M}(\vartheta_c)}{2\sigma_c} \right]^2 \right) \exp(-\lambda_c t), \tag{14}$$

$$x(t) = x(t) + \frac{1}{\sigma_x\sqrt{2\pi}} \exp\left(-\left[\frac{\vartheta_x - \mathrm{M}(\vartheta_x)}{2\sigma_x} \right]^2 \right) \exp(-\lambda_x t),$$

$$w(t) = w(t) + \frac{1}{\sigma_v \sqrt{2\pi}} \exp\left(-\left[\frac{\vartheta_v - \mathrm{M}(\vartheta_w)}{2\sigma_w} \right]^2 \right) \exp(-\lambda_w t),$$

$$\tau(t) = \tau(t) + \frac{1}{\sigma_\tau \sqrt{2\pi}} \exp\left(-\left[\frac{\vartheta_\tau - \mathrm{M}(\vartheta_\tau)}{2\sigma_\tau} \right]^2 \right) \exp(-\lambda_\tau t).$$

With the known laws of a random variable distribution, using the system of equations (14), it is possible to determine the probability of cell infection in order to take timely measures to prevent the protection of the population. To further simplify the calculations, we take as the defining equation the function of coronavirus presence $c(t)$ and the argument of the equation λc, which we take as the corresponding coefficients λ_{ij} of the transition matrix (8).

6 Influence of SARS-CoV-2 viral infection on the development of human disease

SARS-CoV-2 refers to the viruses of pulmonary pneumonia. Figure 4 shows reticular (fibrous) changes in the human lungs. Indirectly, SARS-CoV-2 affects other vital organs, cardiovascular pathology, myocardial infarction, renal failure can develop.

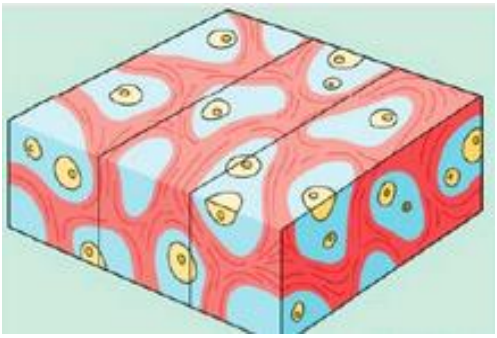


Fig. 4. Reticular changes in the lungs.

At the next stage of research, we will select the coefficients of the matrix (8) taking into account the full-scale data on pandemic development on the example of the Perm Krai of the Russian Federation**.** Let's consider the dynamics of the pandemic development in the period from November 15 to December 15, 2020 on the example of the Perm Krai of the Russian Federation (Figure 5). The number of deaths (state p_4) is marked with a red line, the number of tests with a positive reaction (state p_3) is marked with a blue line, the number of people cured (state p_1) is marked with a green line. The article [11] shows approaches to the development of an express analyzer for the presence of SARS-CoV-2 antibodies using a solid-phase immunochromatographic method, which can also increase the detection of infected people in the Russian Federation.

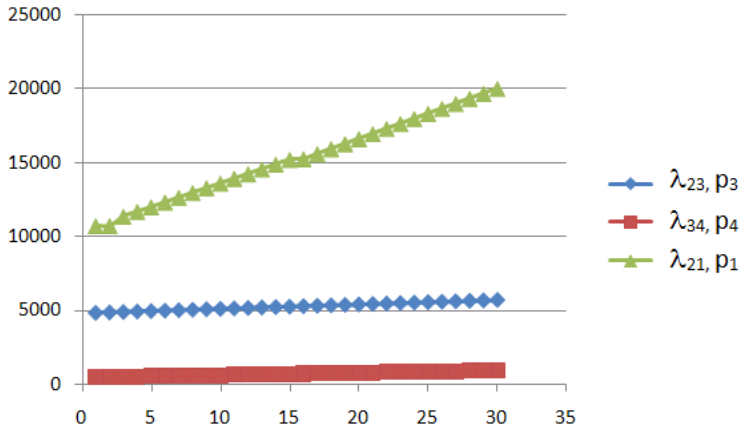


Fig. 5. Dynamics of the pandemic development in the period from November 15 to December 15, 2020 on the example of the Perm Krai of the Russian Federation, transition to a safe state - p_1, λ_{21}; infectious state - p_3, λ_{23}; death - state p_4, λ_{34}

7 Simulation modeling

In the article [12], a logistic model of SARS-CoV-2 population development based on the solution of the Reimersequation was studied. Consider the dynamics of cell damage caused by pulmonary pneumonia using formula (14). Results of simulation modeling of the severity of human disease with coefficients $\lambda = -0.05, -0.01, 0.1, 0.2, 0.3$ within 30 days of the disease development are shown in Figure 6.

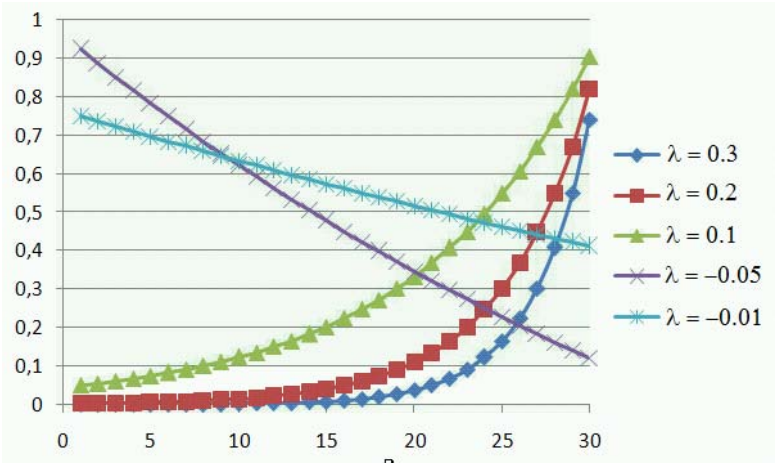


Fig. 6. Results of simulation modeling of human disease with the coefficient $\lambda = -0.05, -0.01, 0.1, 0.2, 0.3$ within 30 days of the disease development

With 90% of lung damage, pulmonary insufficiency occurs, gas exchange processes in the body are disrupted, so it is very difficult to save a person, 50-60 % of lung damage refers to a severe form of the disease.

When comparing the results of a full-scale experiment (Figure 5) and the results of simulation modeling (Figure 6), based on the severity of the disease, it is possible to form the coefficients of the matrix (8) in the following form:

$$\Lambda = \begin{bmatrix} 0 & 0.1 & 0 & 0 \\ -0.01 & 0 & 0.2 & 0 \\ 0 & -0.05 & 0 & 0.3 \end{bmatrix} \quad (15)$$

The matrix of probabilities of outcomes of residents P, given the data of field researches on the example of Perm Krai of the Russian Federation, given the population of the Perm Krai according to the latest All-Russian population census in the amount of 2 635 276 people can be described by the array, in accordance with (9):

$$P = [0.008, -, 0.01, 0.0004]. \quad (16)$$

8 Development of a human protection system against coronavirus infection

Currently, active methods are underway to develop a vaccine against the SARS-CoV-2 virus strain. By the end of 2020, in the Russian Federation, the "Sputnik V" vaccine from the National Research Center for Epidemiology and Microbiology n.a. N.F. Gamalei (Moscow) and "EpiVacCorona" developed by the State Scientific Center for Virology and Biotechnology "Vector" (Koltsovo) have passed clinical trials and are widely used for vaccination of the population.

Let's draw a schematic representation of the cell protection system shown in Figure 7.

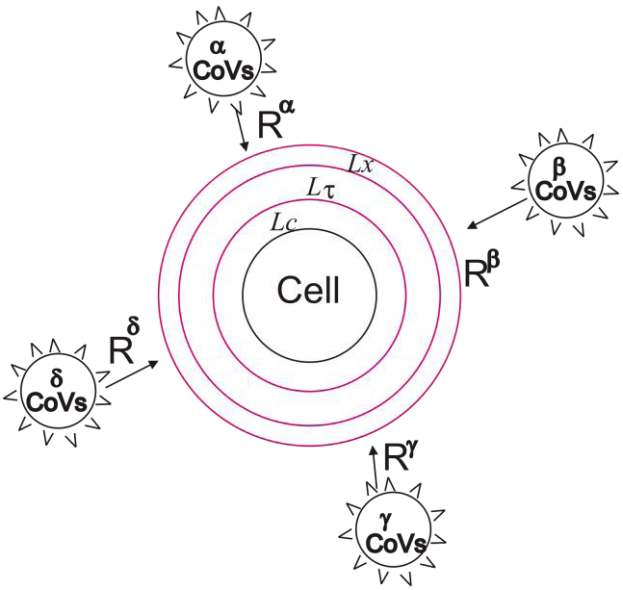


Fig. 7. Model of the cell protection system: L - protection system.

Protection L should ensure that exposure to coronavirus hazards does not exceed the permissible values (Figures 8a, 8b, 8c).

$$L_c \cdot c(t),\ L_x \cdot x(t), L_v \cdot v(t),\ L_\tau \cdot \tau(t). \quad (15)$$

Fig. 8a. Protection by virus intensity, L_c

Fig. 8b. Protection by distance, L_x

Fig. 8c. Protection by exposure time, L_t

The safety of the HVE system according to the parameters of the source of coronaviruses danger will be ensured if the inequalities are met:

$$c^d - L_c \cdot c(t) \geq 0,\ L_x \cdot x(t) - x^d \geq 0,\ v^d - L_v \cdot v(t) \geq 0,\ \tau^d - L_\tau \cdot \tau(t) \geq 0. \quad (16)$$

The safety assessment of the HVE system for the *i*-th source of coronavirus danger, taking into account the protection coefficients, will be determined by the expression (13), taking into account the fulfillment of inequalities (14)

$$\theta_i = \frac{1}{4}\left[\left(\frac{c_i^d - L_{ci} \cdot c_i(t)}{c_i^d}\right) + \left(\frac{L_{xi} x_i(t) - x_i^d}{x_i^d}\right) + \left(\frac{w_i^d - L_{vi} \cdot w(t)}{w_i^d}\right) + \left(\frac{\tau_i^d - L_{\tau i} \cdot \tau(t)}{\tau_i^d}\right)\right].$$

Protection L must ensure that the impact of coronavirus hazards is not higher than acceptable values, it can be defined as means and measures to combat coronavirus that reduce the parameter values to acceptable values.

$$L_x \geq \frac{\theta_i^d}{\theta_i},\ L_w \leq \frac{\theta_i^d}{\theta_i},\ L_c \leq \frac{\theta_i^d}{\theta_i},\ L_\tau \leq \frac{\theta_i^d}{\theta_i},$$

where θ_i^d is the permissible value of the viral danger source.

The development and implementation of this model will allow timely and reliable monitoring of the epidemiological state of the HVE system from the influence of coronaviruses.

9 Conclusion

A method of instrumental assessment of the state of the Human-Virus-Environment (HVE) system based on structural and functional analysis has been developed, which allows calculating models for the development of the SARS-CoV-2 epidemic, taking into account its destructive features. The scientific and practical value lies in the generalization of assessment criteria for monitoring of the safe state of the HVE system, based on the methods of general system theory and implementing instrumental approaches to identification and management of the protective properties of the HVE system. The conducted modelling showed the adequacy of the mathematical model. The probability of disease of residents of the Perm Krai of the Russian Federation in the autumn-winter period

of 2020 was calculated. A method for assessing the safety of the HVE system, taking into account the protection coefficients, has been developed. The use of the developed models in practice will reduce the risk of human disease, taking into account vaccination and other organizational and technical means of protection.

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