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A Dynamic Model for Predicting Immune System Interactions with Infectious Diseases

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Abstract: In this paper we consider a model of interaction of the human immune system with infectious diseases with account changes in its conditions. We also consider an analytical approach for analyzing of the above interaction. It has been also considered possibility of acceleration and deceleration of the above interaction.

Keywords: interaction of the human immune system with infectious diseases; changing of conditions of interaction; prognosis of interaction; analytical approach for analysis.

1 Introduction

Currently, the development of immunology is proceeding so rapidly that its concepts are changing before our eyes, involving new facts and hypotheses in the arsenal of ideas about immune processes that correct various elements of the theory [1-5]. Updating information about immune processes leads to the need to correction of the considered treatment program. An actual issue in the correction of the treatment program is the prognosis of changes in the immune system during its control. In this paper we consider a model of the interaction of the human immune system with infectious diseases with account changes in its conditions. We also consider an analytical approach for analyzing of the above interaction. It has been also considered possibility of acceleration and deceleration of the above interaction.

2 Method of Solution

In this section we consider the following model of interaction of the human immune system with infectious diseases

$$\begin{cases} \dfrac{dV(t)}{dt} = \beta(t)V(t) - \gamma(t)F(t)V(t) \\ \dfrac{dF(t)}{dt} = \rho(t)C(t) - \eta(t)\gamma(t)F(t)V(t) - \mu_f(t)F(t) \\ \dfrac{dC(t)}{dt} = \xi(t)\alpha(t)F(t-\tau)V(t-\tau) - \mu_C(t)\left[C(t) - C^*\right] \\ \dfrac{dm(t)}{dt} = \sigma(t)V(t) - \mu_m(t)m(t) \end{cases} \tag{1}$$

where $V(t)$ is the concentration of proliferating antigens; $C(t)$ is the concentration of antigen-specific lymphocytes (carriers and producers of antibodies) in lymphoid tissue; $F(t)$ is the concentration of antibodies (molecules of an immune nature, - immunoglobulins, receptors of immunocompetent cells, etc. - neutralizing antigens) in the blood; $m(t)$ is the the proportion of cells destroyed by the antigen in the affected part of the target organ, affecting the weakening of the body's vital functions during the course of the disease, associated with a decrease in the activity of organs that provide the supply of immunological material: leukocytes, lymphocytes, antibodies, etc., necessary to combat multiplying antigens; $\beta(t)$ is the rate of reproduction of antigens; $\gamma(t)$ is the coefficient that takes into account the probability of encountering viruses with antibodies and the strength of their interaction; $\alpha(t)$ is the immune system stimulation factor; $\rho(t)$ is the rate of production of antibodies by a single plasma cell; $\mu_c(t)$ and $\mu_f(t)$ are the values inverse to the life span of plasma cells and antibodies, respectively; $\eta(t)$ is the amount of antibodies needed to neutralize a single virus; $\sigma(t)$ is the organ damage rate; $\mu_m(t)$ is the rate of recovery of the mass of the affected organ; $C(t)$ is the pre-existing level of immunocompetent cells (plasma cells); τ is the time required for the formation of a cascade of plasma cells; $\xi(t)$ is the a function that takes into account the disruption of the normal functioning of the immune system due to significant damage to the organ. The initial conditions of the desired functions described by the equations of system (1) can be represented in the following form

$$V(0)=V_0,\ F(0)=F_0,\ C(0)=C_0,\ m(0)=m_0. \tag{2}$$

Now we transform differential equations of the system (1) to the following integral form with account conditions (2)

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$$\begin{cases} V(t)=\int\limits_0^t \beta(\chi)V(\chi)d\chi-\int\limits_0^t \gamma(\chi)F(\chi)V(\chi)d\chi+V_0 \\ F(t)=\int\limits_0^t \rho(\chi)C(\chi)d\chi-\int\limits_0^t \eta(\chi)\gamma(\chi)F(\chi)V(\chi)d\chi-\int\limits_0^t \mu_f(\chi)F(\chi)d\chi+F_0 \\ C(t)=\int\limits_0^t \xi(\chi)\alpha(\chi)F(\chi-\tau)V(\chi-\tau)d\chi-\int\limits_0^t \mu_C(\chi)\left[C(\chi)-C^*\right]d\chi+C_0 \\ m(t)=\int\limits_0^t \sigma(\chi)V(\chi)d\chi-\int\limits_0^t \mu_m(\chi)m(\chi)d\chi+m_0 \end{cases} \quad (3)$$

Next, we calculate solutions of equations of the system (3) by the method of averaging of function corrections [6-8]. In the framework of the approach, we replace the required functions in the right sides of equations (3) on their not yet known average values α_1. The substitution gives a possibility to obtain equations to determine the first-order approximations of the required functions in the following form

$$\begin{cases} V_1(t)=\alpha_{1V}\int\limits_0^t \beta(\chi)d\chi-\alpha_{1V}\alpha_{1F}\int\limits_0^t \gamma(\chi)d\chi+V_0 \\ F_1(t)=\alpha_{1C}\int\limits_0^t \rho(\chi)\,d\chi-\alpha_{1F}\alpha_{1V}\int\limits_0^t \eta(\chi)\gamma(\chi)d\chi-\alpha_{1F}\int\limits_0^t \mu_f(\chi)d\chi+F_0 \\ C_1(t)=\alpha_{1V}\alpha_{1F}\int\limits_0^t \xi(\chi)\alpha(\chi)F(\chi-\tau)V(\chi-\tau)d\chi-\left(\alpha_{1C}-C^*\right)\int\limits_0^t \mu_C(\chi)d\chi+C_0 \\ m_1(t)=\alpha_{1V}\int\limits_0^t \sigma(\chi)d\chi-\alpha_{1m}\int\limits_0^t \mu_m(\chi)d\chi+m_0 \end{cases} \quad (4)$$

Average values α_1 was determined by the following standard relation [6-8]

$$\alpha_1=\frac{1}{\Theta}\int\limits_0^\Theta G_1(t)dt, \quad (5)$$

where Θ is the continuance of observation on the considered process. Substitution of relations (4) into relation (5) gives a possibility to obtain relations to calculate the required average values α_1 in the following final form

$$\begin{cases} \Theta\alpha_{1V}=\alpha_{1V}\int\limits_0^\Theta (\Theta-t)\beta(t)dt-\alpha_{1V}\alpha_{1F}\int\limits_0^\Theta (\Theta-t)\gamma(t)\,dt+V_0\Theta \\ \Theta\alpha_{1F}=\alpha_{1C}\int\limits_0^\Theta (\Theta-t)\rho(t)dt-\alpha_{1F}\alpha_{1V}\Theta\int\limits_0^\Theta (\Theta-t)\,\eta(t)\,\gamma(t)\,dt-\alpha_{1F}\int\limits_0^\Theta (\Theta-t)\mu_f(t)dt+\Theta F_0 \\ \Theta\alpha_{1C}=\alpha_{1V}\alpha_{1F}\int\limits_0^\Theta (\Theta-t)\xi(t)\alpha(t)dt-\left(\alpha_{1C}-C^*\right)\int\limits_0^\Theta (\Theta-t)\mu_C(t)dt+\Theta C_0 \\ \Theta\alpha_{1m}=\alpha_{1V}\int\limits_0^\Theta (\Theta-t)\sigma(t)dt-\alpha_{1m}\int\limits_0^\Theta (\Theta-t)\mu_m(t)dt+\Theta m_0 \end{cases} \quad (6)$$

Solution of equations of the system (6) by standard approaches [9] could be presented in the following form

$$\alpha_{1C}=\frac{ch-cf^2-2dg-2eg}{3cg}+\frac{3c^2g\left(2cdf^2-2cef+d^2g+2\deg+e^2g-2cdh-2ceh\right)-c^2\left(ch-cf^2-2dg-2eg\right)^2}{4c^2g\left(c^6f^6+9bc^5ef^3g-3c^5df^4g\right)},$$

$$\alpha_{1V}=\frac{V_0\Theta}{\Theta-\int\limits_0^\Theta (\Theta-t)\beta(t)dt+\alpha_{1F}\int\limits_0^\Theta (\Theta-t)\gamma(t)dt},$$

$$\alpha_{1F}=\frac{\sqrt{b^2+4\alpha_{1C}\int\limits_0^\Theta (\Theta-t)\rho(t)dt-4\Theta F_0}-b}{2a}, \quad (7)$$

$$\alpha_{1m}=\frac{V_0\Theta\int\limits_0^\Theta (\Theta-t)\sigma(t)dt+\Theta m_0\left[\Theta-\int\limits_0^\Theta (\Theta-t)\beta(t)dt+\alpha_{1F}\int\limits_0^\Theta (\Theta-t)\gamma(t)dt\right]}{\left[\Theta-\int\limits_0^\Theta (\Theta-t)\beta(t)dt+\alpha_{1F}\int\limits_0^\Theta (\Theta-t)\gamma(t)dt\right]\left[\Theta+\int\limits_0^\Theta (\Theta-t)\mu_m(t)dt\right]},$$

where $a=\int\limits_0^\Theta (\Theta-t)\gamma(t)dt\left[\Theta+\int\limits_0^\Theta (\Theta-t)\mu_f(t)dt\right]$,

$$b=\left[\Theta-\int\limits_0^\Theta (\Theta-t)\beta(t)dt\right]\left[\int\limits_0^\Theta (\Theta-t)\mu_f(t)dt+\Theta\right],$$

$$f=2a\Theta-$$

$$-2a\int\limits_0^\Theta (\Theta-t)\beta(t)dt-2ab\int\limits_0^\Theta (\Theta-t)\gamma(t)dt,$$

$$c=\Theta+\int\limits_0^\Theta \mu_C(t)\,(\Theta-t)\,dt, \qquad e=V_0\Theta\int\limits_0^\Theta (\Theta-t)\xi(t)\alpha(t)dt,$$

$$h=b^2-4\Theta F_0,$$

$$g=4\int\limits_0^\Theta (\Theta-t)\rho(t)dt, \quad d=C^*\int\limits_0^\Theta (\Theta-t)\mu_C(t)dt+\Theta C_0.$$

The second-order approximations of the required functions in the framework of the method of averaging of function corrections could be calculated by replacement of the above functions on the following sums: $G(t)\to\alpha_2+G_1(t)$ [6-8]. The replacement gives a possibility to obtain the following equations to calculate the considered functions

$$\begin{cases} V_2(t)=\int\limits_0^t \beta(\chi)\left[\alpha_{2V}+V_1(\chi)\right]d\chi-\int\limits_0^t \gamma(\chi)\left[\alpha_{2F}+F_1(\chi)\right]\left[\alpha_{2V}+V_1(\chi)\right]d\chi+V_0 \\ F_2(t)=\int\limits_0^t \rho(\chi)\left[\alpha_{2C}+C_1(\chi)\right]d\chi-\int\limits_0^t \eta(\chi)\gamma(\chi)\left[\alpha_{2F}+F_1(\chi)\right]\left[\alpha_{2V}+V_1(\chi)\right]d\chi-\int\limits_0^t \mu_f(\chi)\left[\alpha_{2V}+V_1(\chi)\right]d\chi+F_0 \\ C_2(t)=\int\limits_0^t \xi(\chi)\alpha(\chi)\left[\alpha_{2F}+F_1(\chi-\tau)\right]\left[\alpha_{2V}+V_1(\chi-\tau)\right]d\chi+C_0-\int\limits_0^t \mu_C(\chi)\left[\alpha_{2C}+C_1(\chi)-C^*\right]d\chi \\ m_2(t)=\int\limits_0^t \sigma(\chi)\left[\alpha_{2V}+V_1(\chi)\right]d\chi-\int\limits_0^t \mu_m(\chi)\left[\alpha_{2m}+m_1(\chi)\right]d\chi+m_0 \end{cases} \quad (8)$$

Average values of the second-order approximations α_2 was determined by the following standard relation [6-8]

$$\alpha_2 = \frac{1}{\Theta}\int_0^\Theta \left[G_2(t) - G_1(t)\right] d\,t \,. \tag{9}$$

Substitution of relations (8) into relations (9) gives a possibility to obtain the following relations to determine the required average values α_2

$$\begin{cases} \Theta\alpha_{2V} = \int_0^\Theta (\Theta - t)\beta(t)\left[\alpha_{2V} + V_1(t)\right]d\,t + \Theta V_0 - \int_0^\Theta (\Theta - t)\gamma(t)\left[\alpha_{2F} + F_1(t)\right]\left[\alpha_{2V} + V_1(t)\right]d\,t \\ \Theta\alpha_{2F} = \int_0^\Theta (\Theta - t)\rho(t)\left[\alpha_{2C} + C_1(t)\right]d\,t - \int_0^\Theta (\Theta - t)\eta(t)\gamma(t)\left[\alpha_{2F} + F_1(t)\right]\left[\alpha_{2V} + V_1(t)\right]d\,t + \Theta F_0 - \\ - \int_0^\Theta (\Theta - t)\mu_f(\chi)\left[\alpha_{2V} + V_1(t)\right]d\,t \\ \Theta\alpha_{2C} = \int_0^\Theta (\Theta - t)\xi(t)\alpha(t)\left[\alpha_{2F} + F_1(t-\tau)\right]\left[\alpha_{2V} + V_1(t-\tau)\right]d\,t - \int_0^\Theta (\Theta - t)\mu_C(t)\left[\alpha_{2C} + C_1(t) - C^*\right]d\,t + \Theta C_0 \\ \Theta\alpha_{2m} = \int_0^\Theta (\Theta - t)\sigma(t)\left[\alpha_{2V} + V_1(t)\right]d\,t - \int_0^\Theta (\Theta - t)\mu_m(t)\left[\alpha_{2m} + m_1(t)\right]d\,t + \Theta m_0 \end{cases} \tag{10}$$

Solution of equations of the system (10) by standard approaches [9] could be presented in the following form

$$\alpha_{2m} = \frac{\int_0^\Theta (\Theta - t)\sigma(t)\left[\alpha_{2V} + V_1(t)\right]d\,t - \int_0^\Theta (\Theta - t)\mu_m(t) m_1(t)\,d\,t + \Theta\, m_0}{\Theta + \int_0^\Theta (\Theta - t)\mu_m(t)\,d\,t}$$

$$\alpha_{2V} = \frac{p - \alpha_{2F}\int_0^\Theta (\Theta - t)\gamma(t)V_1(t)\,d\,t}{\left[q + \alpha_{2F}\int_0^\Theta (\Theta - t)\gamma(t)\,d\,t\right]},$$

$$\alpha_{2F} = \frac{\alpha_{2C} - A}{3x} - \frac{\sqrt[3]{2}\left(D - E\alpha_{2C}\right)}{2A^2\left(A + 2\alpha_{2C}\right)},$$

$$\alpha_{2C} = \frac{1}{2E\,p}\left[A^2\left\{\int_0^\Theta (\Theta - t)\mu_C(t)\left[C_1(t) - C^*\right]d\,t - \Theta C_0\right\} + \right.$$

$$\left. 2q\,x\int_0^\Theta (\Theta - t)\xi(t)\alpha(t)\,d\,t\int_0^\Theta \mu_f(\chi)(\Theta - t)\,d\,t\right]$$

$$\times\left[\int_0^\Theta (\Theta - t)\xi(t)\alpha(t)F_1(t-\tau)\,d\,t + \int_0^\Theta (\Theta - t)\xi(t)\alpha(t)V_1(t-\tau)\,d\,t\right]^{-1}\left[\Theta + \int_0^\Theta (\Theta - t)\mu_C(t)\,d\,t\right]^{-1}, \tag{11}$$

where

$$q = \Theta - \int_0^\Theta (\Theta - t)\beta(t)\,d\,t + \int_0^\Theta (\Theta - t)\gamma(t)F_1(t)\,d\,t,$$

$$p = \int_0^\Theta (\Theta - t)\beta(t)V_1(t)\,d\,t + \Theta V_0 - \int_0^\Theta (\Theta - t)\gamma(t)F_1(t)V_1(t)\,d\,t,$$

$$r = \int_0^\Theta (\Theta - t)\rho(t)C_1(t)\,d\,t - \int_0^\Theta (\Theta - t)\mu_f(\chi)V_1(t)\,d\,t + \Theta F_0 - \int_0^\Theta (\Theta - t)\eta(t)\gamma(t)F_1(t)V_1(t)\,d\,t,$$

$$u = \int_0^\Theta (\Theta - t)V_1(t)\times$$

$$\times\beta(t)\,d\,t - \int_0^\Theta (\Theta - t)\gamma(t)F_1(t)V_1(t)\,d\,t + \Theta V_0,$$

$$s = \Theta + \int_0^\Theta (\Theta - t)\eta(t)\gamma(t)V_1(t)\,d\,t,$$

$$v = \Theta - \int_0^\Theta (\Theta - t)\beta(t)\,d\,t + \int_0^\Theta (\Theta - t)F_1(t)\times$$

$$\times\gamma(t)\,d\,t,$$

$$x = \int_0^\Theta (\Theta - t)\gamma(t)\,d\,t\left[\int_0^\Theta (\Theta - t)\gamma(t)\,d\,t - \int_0^\Theta (\Theta - t)\gamma(t)V_1(t)\,d\,t\int_0^\Theta (\Theta - t)\eta(t)\gamma(t)\,d\,t\right],$$

$$y = v\int_0^\Theta (\Theta - t)\gamma(t)\,d\,t -$$

$$- v\int_0^\Theta (\Theta - t)\gamma(t)V_1(t)\,d\,t\int_0^\Theta (\Theta - t)\eta(t)\gamma(t)\,d\,t + \left[q + p\int_0^\Theta (\Theta - t)\eta(t)\gamma(t)\,d\,t\right]\int_0^\Theta (\Theta - t)\gamma(t)\,d\,t,$$

$$w = \left[\int_0^\Theta (\Theta - t)\mu_f(\chi)\,d\,t + \right.$$

$$\left. + \int_0^\Theta (\Theta - t)\eta(t)\gamma(t)F_1(t)\,d\,t\right],$$

$$A = y - r\int_0^\Theta (\Theta - t)\gamma(t)\,d\,t\int_0^\Theta (\Theta - t)\gamma(t)\,d\,t + w\int_0^\Theta (\Theta - t)\gamma(t)V_1(t)\,d\,t\int_0^\Theta (\Theta - t)\gamma(t)\,d\,t,$$

$$B = \int_0^\Theta (\Theta - t)\rho(t)\,d\,t\int_0^\Theta (\Theta - t)\gamma(t)\,d\,t,$$

$$D = v\left[q + p\int_0^\Theta (\Theta - t)\eta(t)\gamma(t)\,d\,t\right] + qw\int_0^\Theta (\Theta - t)\gamma(t)V_1(t)\,d\,t - rq\int_0^\Theta (\Theta - t)\times$$

$$\times\gamma(t)\,d\,t + wu\int_0^\Theta (\Theta - t)\gamma(t)\,d\,t + r\,v\int_0^\Theta (\Theta - t)\gamma(t)\,d\,t,$$

$$E = q\int_0^\Theta (\Theta - t)\rho(t)\,d\,t\int_0^\Theta (\Theta - t)\gamma(t)\,d\,t + v\int_0^\Theta (\Theta - t)\rho(t)\,d\,t\times$$

$$\times\int_0^\Theta (\Theta - t)\gamma(t)\,d\,t \,.$$

Analysis of the considered function has been done analytically by using the second-order approximation in the framework of method of averaging of function corrections. The approximation is usually enough good approximation for to make qualitative analysis and to obtain some quantitative results. All obtained results have been checked by comparison with results of numerical simulations.

3 Discussion

In this section we analyzed the considered concentrations and proportion of cells destroyed by antigen. Figs. 1, 2 and 3 show typical dependences of the considered concentrations on time for developing disease, fading disease and stabilizing disease at different values of the considered parameters. Changing the values of the model parameters with time gives a possibility to accelerate or slow down the development or stabilization of the disease, as well as the recovery of the body or change the mode of development of the situation.

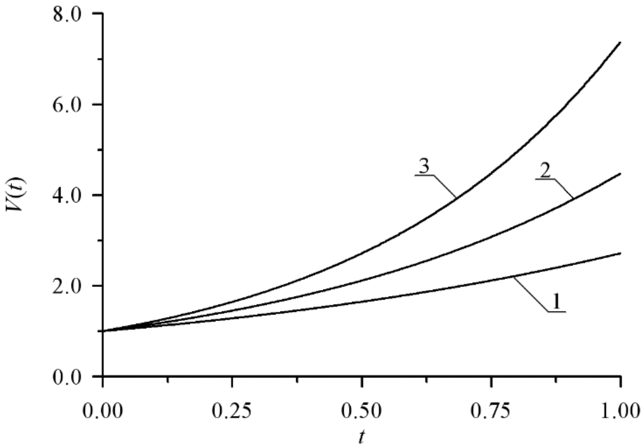

Fig. 1: Typical dependences of the concentration of proliferating antigens on time for developing disease

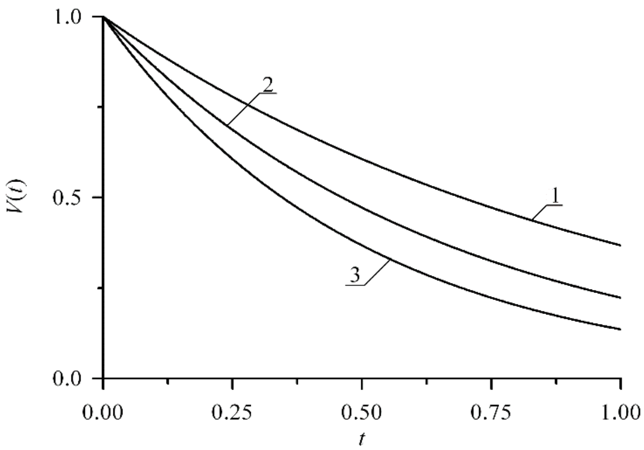

Fig. 2: Typical dependences of the concentration of proliferating antigens on time for fading disease

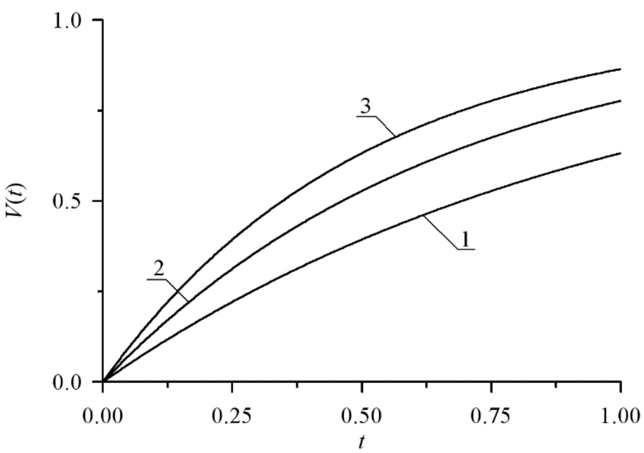

Fig. 3: Typical dependences of the concentration of proliferating antigens on time for stabilizing disease

5 Conclusions

We consider a model of interaction of the human immune system with infectious diseases with account changes in its conditions. Also, we consider an analytical approach for analyzing of the above interaction. It has been also considered possibility to change speed of the above interaction.

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