Mathematical Modelling of Immune Response to Infectious Diseases with Ecological Factor

Yaroslav Bihun, Oleh Ukrainets

Abstract

The abstract generalizes G.I. Marchuk's mathematical model of the human immune system's response to infectious disease. The negative impact of environmental pollution, described by the Hutchinson equation, on the course of the disease is considered. Stationary solutions are found, their stability is investigated, and a medical interpretation of the obtained results is provided.

Keywords: immune response, infectious disease, mathematical model, delay, stationary solution

The immune response involves the production of specific objects (antibodies, $F(t)$), which are generated by a cascade of plasma cells $C(t)$. Antibodies are capable of neutralizing or destroying foreign materials (antigens), the amount $V(t)$ of which changes over time $t \geq t_0 = 0$.

An effective mathematical model of the immune response to infectious diseases was developed by G.I. Marchuk, and other researchers elaborated it in numerous works [1], [2]. The course of infectious diseases, such as hepatitis and acute respiratory diseases, is influenced by factors such as chemical, radioactive, and other environmental pollutants [3]. The model takes into account an integral factor $E(t)$, which is the sum of m factors $E_i(t)$ and is represented as follows:

$$E(t) = a_1 E_1(t) + ... + a_m E_m(t),$$

where $a_i \geq 0$, $a_1 + ... + a_m = 1$.

Let's assume that the change of $E(t)$ occurs according to the generalized Hutchinson equation, which has the following form:

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$$\frac{dE(t)}{dt} = r\left(1 - \left(\frac{E(t-\Delta)}{E^*}\right)^n\right)E(t), t > 0, \tag{1}$$

where $r > 0$ – coefficient of linear growth, $0 < \Delta$ – average time for the restoration of ecological balance, amount of which $E^* > 0, n > 0$.

It has been shown that the equilibrium state $E = E^*$ is locally asymptotically stable if

$$0 < rn\Delta < \pi/2. \tag{2}$$

The change over time of the factors V, E, F, C and the magnitude m, where $o \leq m(t) \leq 1$ is the extent of organ damage against which the antigen V is directed, is proposed to be described by a system of equations:

$$\begin{aligned} \frac{dV}{dt} &= (\beta - \gamma F)V, \\ \frac{dC}{dt} &= \alpha\xi(m)V_\tau F_\tau - \mu_c(C - C^*) - \varepsilon_c E, \\ \frac{dF}{dt} &= \rho C - (\mu_f + \eta\gamma V)F, \\ \frac{dm}{dt} &= \sigma V - \mu_m m + \varepsilon_m E, \end{aligned} \tag{3}$$

where $\xi(m) = 1$ for $m \in [0, m^*]$ and $\xi(m) = (m-1)/(m^*-1)$ for $m^* < m \leq 1$, having $m^* \in (0,1)$ and considering for $m \in [0, m^*]$ the immune system functions normally; $V_\tau(t) = V(t-\tau), F_\tau(t) = F(t-\tau)$.

Theorem 1. *If the coefficients in equations (1), (3) are non-negative and the initial functions $V_0(t) \geq 0, F_0(t) \geq 0$ for $t \in [-\tau, 0]$ and $E_0(t) \geq 0$ for $t \in [-\Delta, 0]$, then there exists a unique non-negative solution to the initial value problem for the system of equations (1), (3).*

There always exists such a stationary solution

$$E_1 = E^*, V_1 = 0, C_1 = C^* - \frac{\varepsilon_c E^*}{\mu_c}, F_1 = \frac{\rho C_1}{\mu_f}, m_1 = \frac{\varepsilon_m E^*}{\mu_m} \tag{4}$$

that defines the state of a healthy organism under permissible environmental pollution levels. Let's perform a substitution in system (3): $E = \overline{E} + E^*, V = \overline{V}, C = \overline{C} + C_1, F = \overline{F} + F_1, m = \overline{m} + m_1$. The determinant of the corresponding linear system has the following form:

$$(\lambda + rn\Delta e^{-\lambda})(\beta - \gamma F_1 - \lambda)(\mu_c + \lambda)(\mu_f + \lambda)(\mu_m + \lambda) = 0.$$

From condition (2) and the positivity of the coefficients in the system (3), a theorem is derived:

Theorem 2. *If condition (2) and conditions*

$$\beta - \gamma F_1 < 0, C^*\mu_c > \varepsilon_c E^*, \varepsilon_m E^* \leq \mu_m m^*$$

are satisfied, then solution (4) is locally asymptotically stable.

Corollary 2.1. *When the conditions of Theorem 2 are met and $V_0 = V^*$, the disease will not occur. In this case, the stability depends on the delay Δ and is independent of the time $\tau > 0$ – formation of plasma cells. An estimate for V^* has been constructed.*

The system of equations (1), (3) may have another stationary solution that corresponds to the state of a chronic disease:

$$\begin{aligned} E_2 &= E^*, F_2 = \frac{\beta}{\gamma}, \\ V_2 &= \frac{\mu_c\mu_f\beta - \rho\gamma\mu_c C^* + \rho\gamma\varepsilon_c E^*}{\beta(\alpha\rho - \mu_c\eta\gamma)}, \\ C_2 &= \frac{\alpha\beta\mu_f - \eta\gamma^2\mu_c C^* + \eta\gamma^2\varepsilon_c E^*}{\gamma(\alpha\rho - \mu_c\eta\gamma)}, \\ m_2 &= \frac{\delta V_2 + E_2}{\mu_m}. \end{aligned} \tag{5}$$

A stationary solution (5) exists if either

$$\alpha\rho > \mu_c\eta\gamma, \quad \rho\gamma\mu_c C^* < \mu_c\mu_f\beta + \rho\gamma\varepsilon_c E^*$$

or the inequality with the opposite sign is satisfied.

From the analysis of the roots of the characteristic equation of the linearized system, conditions for the asymptotic stability and instability of solution (5) have been found. Therefore, sufficient conditions for either maintaining a chronic disease state or transitioning from a chronic condition to an acute form have been obtained.

Numerical simulations of the dynamics of the mathematical model (3) have been conducted.

References

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