DEPENDENCE OF THE TEMPERATURE DISTRIBUTION IN THE HUMAN BODY ON HOW HYPERTHERMIA IS INDUCED

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A system of equations is derived for the temperature distribution in the human body for general and deep hyperthermia. How this distribution is affected by the regimes in which the hyperthermia is induced is analyzed.

In current oncological practice there is hope that certain forms of malignant neoplasms can be cured through a complex therapy involving a controlled artificial hyperthermia and overacidity. One of the basic parts of this method is hyperthermia, i.e., the heating of the human body to a temperature on the order of 40-42°C and maintaining this temperature for a long time (150-300 min). For reasons of safety, the brain temperature should remain 1-1.5° lower than the temperature of the "core" of the body; this is arranged by a supplementary cooling of the head [1, 2].

Successful use of hyperthermia requires knowledge of the temperature distribution in the body as the torso is warmed and the head is simultaneously cooled, and it requires knowledge of how this distribution is affected by the hyperthermia regime.

To solve the problem of the temperature distribution in the human body we adopt the following model: we arbitrarily divide the body into layers (zones) and write a heat-balance equation for each layer. The number of such layers (or zones) depends on the particular conditions of the problem and the necessary solution accuracy. In our case it is sufficient to use a model of four zones (the skin, the "core," the brain, and the "shell of the head"). We also use the following assumptions:

1) The basic heat-transfer mechanism is convection, associated with blood flow [3].

2) The blood instantaneously acquires the temperature of the zone it is in.

3) The volume flow rate of the blood is a linear function of the temperature.

On the basis of these assumptions we can write the system of heat-balance equations describing the temperature distribution in the human body as

$$\dot{t}_1 = \frac{1}{m_1 c_1}\{\alpha_1 S_1 (t_5 - t_1) + G_1 c_7 (t_2 - t_1) - S_1[4/3\,(t_3 - t^*)\beta_3 + 1/3(t_1 - 33)]\},$$

$$\dot{t}_2 = \frac{1}{m_2 c_2}\{B_2 [1 + \beta_2 (t_2 - t^*)] - G_1 c_7 (t_2 - t_1) + (G_0 - G_3 - G_4)\, c_7 (\bar{t} - t_2)\},$$

$$\dot{t}_3 = \frac{1}{m_3 c_3}\{B_3 [1 + \beta_3 (t_3 - t^*)] + G_3 c_7 (\bar{t}_1 - t_3) - \frac{k S_3}{l} (t_3 - t_4)\},$$

$$\dot{t}_4 = \frac{1}{m_4 c_4}\{B_4 + G_4 c_7 (\bar{t}_1 - t_4) + \frac{k S_3}{l} (t_3 - t_4) - \alpha_4 S_4 (t_4 - t_6)\},$$

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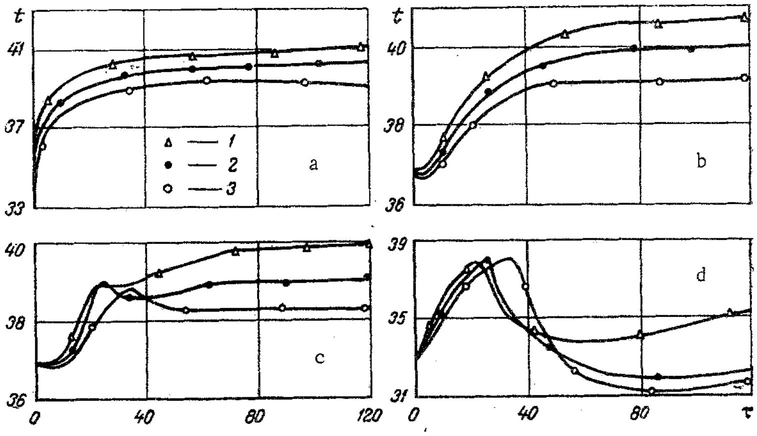

Fig. 1. Temperature distribution in the human body for various temperatures of the hot water. a) In the skin; b) in the "core" of the body; c) in the brain; d) in the "shell of the head." 1) $t_5 = 42°C$; 2) 41; 3) 40.

$$t_5 = f_1(\tau), \quad t_6 = f_2(\tau), \text{ where } G_0 = \sum_{i=1}^{4} G_i, \tag{1}$$

$$\bar{t} = \frac{1}{G_0}[(G_0 - G_3 - G_4)\,t_2 + G_3 t_3 + G_4 t_4],$$

$$\bar{t}_1 = \bar{t} - \Delta t, \text{ where } \Delta t = \frac{\bar{t} - t_9}{G_3 + G_4}\,\alpha_8 S_3.$$

The initial conditions are $t_i = t_i^0$ at $\tau = 0$, where $i = 1, 2, \ldots, 6$. In deriving system (1) we assumed

$$G_i = G_i^0 [1 + d_i (t_i - t^*)], \quad i = 0, 3,$$

$$G_j = G_j^0 [1 + d_j (t_j - 33)], \quad j = 1, 4. \tag{2}$$

The coefficients d_i, d_j, and β_i are determined from

$$\beta_i = \begin{cases} \beta_i', & \text{if } t_i \geqslant t^* \\ \beta_i'', & \text{if } t_i < t^* \end{cases} \quad i = 1, 2, 3,$$

$$d_i = \begin{cases} d_i', & \text{if } t_i \geqslant t^* \\ d_i'', & \text{if } t_i < t^* \end{cases} \quad i = 0, 3, \tag{3}$$

$$d_j = \begin{cases} d_j', & \text{if } t_j > 33 \\ d_j'', & \text{if } t_j \leqslant 33 \end{cases} \quad j = 1, 4.$$

Equations (1) were solved on a Minsk-22 computer for concrete values of the coefficients in them. Comparison of the results with experimental data shows that the model gives a satisfactory description of the temperature distribution in the human body.

Let us examine how the temperature distribution is affected by the conditions under which the hyperthermia is induced.

1. We first examine how the temperature distribution is affected by the temperature of the hot water.

We assume that the temperature of the water cooling the head is t_6 = const; the coefficients α_1 and α_4, which are related to the rates at which the cold and hot water are supplied to the head and the rest of the body, respectively, are also constant. We consider the temperature distribution in the body for various temperatures t_5 of the hot water.

From the temperature distributions found (Fig. 1) we can draw the following conclusions:

1) The higher the temperature t_5, the higher the temperatures in the various zones of the body.

2) The higher t_5, the more slowly the entire system approaches a steady state.

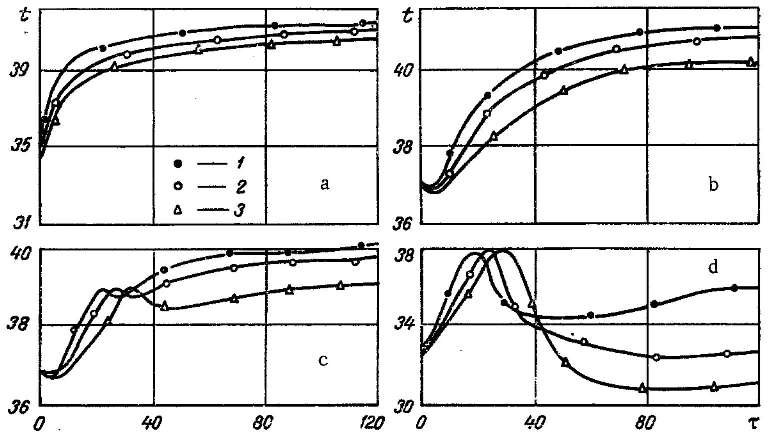

Fig. 2. Temperature distribution in the human body for various values of the coefficient α_1. a) In the skin; b) in the "core" of the body; c) in the brain; d) in the "shell of the head." 1) $\alpha_1 = 1.8$; 2) 1.2; 3) 0.8.

3) In the steady state, for any temperature t_5, we have the inequalities $t_4 < t_3 < t_2 < t_1 < t_5$.

4) The temperature difference between the different zones (at large values of τ) is extremely insensitive to the value of t_5.

Accordingly, by adjusting the hot-water temperature t_5 we change only the absolute values of the temperatures in the various zones, leaving the relations between the temperatures of the various zones essentially unchanged.

2. Let us now examine the temperature distribution in the body for various values of the coefficient α_1.

We assume t_5 = const, t_6 = const, and α_4 = const. We consider how the temperature distribution is affected by the value of α_1, which is related to the rate at which the hot water is supplied to the surface of the body (Fig. 2).

We see from Fig. 2 that as the value of α_1 is raised this model system approaches a steady state more rapidly, and the temperatures of the resulting steady state become higher. Since the head is cooled only at $t_3 \geq 39$, the curves in Figs. 2c and 2d shift to the right. This is a completely understandable result, since as the value of α_1 is raised the temperature increases more rapidly in these zones.

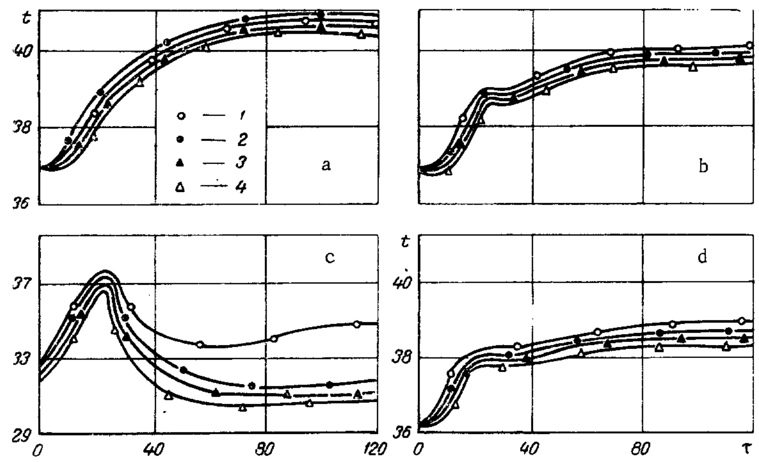

Fig. 3. Temperature distribution in the human body for various temperatures of the water cooling the head. a) In the "core" of the body; b) in the brain; c) in the "shell of the head," d) in the eardrum region. 1) $t_6 = 6°$; 2) 4; 3) 2; 4) 0.5.

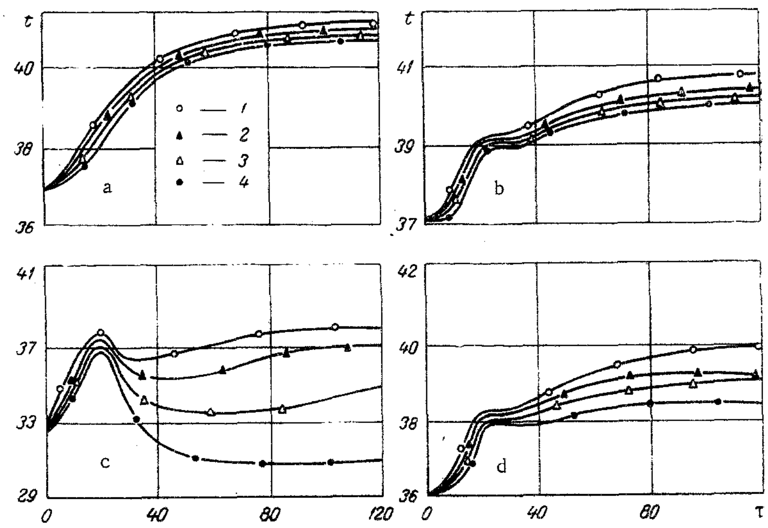

Fig. 4. Temperature distribution in the human body for various values of the coefficient α_4. a) In the "core" of the body; b) in the brain; c) in the "shell of the head"; d) near the eardrum. 1) $\alpha_4 = 0.6$; 2) 0.8; 3) 1.0; 4) 1.2.

3. Let us now examine the temperature distribution as a function of the temperature of the water cooling the head.

We assume t_5 = const, and we assume that the coefficients α_1 and α_4 are also constant. We examine the changes in the temperature distribution in the body as a function of the temperature t_6 of the water cooling the head (Fig. 3).

We see from Fig. 3 that changes in t_6 have almost no effect on the dynamics of the temperature of the "core" (Fig. 3a) and the skin (not shown in this figure). Furthermore, judging from the results found on the basis of this mathematical model, changes in t_6 under conditions of general hyperthermia have no Gosénergoizdat on the temperature of the inner part of the brain (Fig. 3b), affecting primarily the temperature of the more superficial layers of the brain (the "shell of the head").* These results are of practical importance: firstly, in practice the brain temperature is inferred primarily from the temperature near the eardrum. It can be shown that this temperature, $\bar{\bar{t}}$, is the resultant temperature determined by the brain temperature, t_3, and the temperature t_4 of the "shell of the head"; i.e., $\bar{\bar{t}} = n_1 t_3 + n_2 t_4$ where $n_1 < 1$, $n_2 < 1$.

Consequently, a certain temperature decrease near the eardrum (Fig. 3d) apparently does not imply an equal temperature decrease in the brain.

Secondly, the relative insensitivity of the brain temperature to the temperature of the water cooling the head makes it unnecessary to employ extreme cooling and the corresponding complicated apparatus. Thirdly, serious attention should be paid to the development of methods permitting a higher temperature gradient between the "core" of the body and the brain in the hyperthermia (e.g., cooling of the neck).

4. We turn now to the temperature distribution in the body for various values of the coefficient α_4.

We assume t_5 = const, t_6 = const, and α_1 = const. We consider the temperature distribution in the body as a function of the coefficient α_4, which is related to the rate at which the water cooling the head is supplied (Fig. 4).

We see from Fig. 4 that changes in α_4 have essentially no effect on the temperature of the "core" of the body (Fig. 4a) or of the skin (not shown in this figure). There are important changes in the brain temperature, but even so these changes are less than would be inferred from the temperature changes near the eardrum.

*The zones referred to here as the "brain" and the "shell of the head" are chosen extremely arbitrarily. Accordingly, these results require a more detailed study and experimental verification.

Comparison of the results in Secs. 3 and 4 shows that adjustment of the coefficient α_4, i.e., of the rate at which the cold water is supplied to the surface of the head, is a more effective method for reducing the brain temperature than a decrease in the temperature of the water cooling the head. Since the temperature of the "core" (for sufficiently large values of the coefficient α_1) remains essentially constant, the temperature difference $\Delta t = t_2 - t_3$ increases; this result is of considerable practical importance.

Accordingly, by adjusting t_5 we are primarily setting the height of the steady-state level of our system. By changing α_1, we strongly influence the time required for the system to reach this level, and by changing α_4 we set the temperature difference between the different zones.

NOTATION

$\dot{t} = dt/d\tau$, t	is the temperature, °C;
t^*	is the reference temperature, °C;
m	is the mass, kg;
c	is the specific heat, J/(kg·deg);
G	is the mass flow rate of blood, kg/sec;
α	is the heat-transfer coefficient for heat transfer between the surface and the heat-transfer fluid, W/(m^2·deg);
k	is the thermal conductivity, W/(m·deg);
B	is the basic metabolism, W;
S	is the surface area, m^2;
l	is the thickness of the "shell of the head."

Subscripts 1-9 refer to the skin, the "core" of the body, the brain, the "shell of the head," the hot water, the cold water, the blood, the neck, and the air, respectively.

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