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The development of the concepts of homeothermy and thermoregulation

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Abstract

The adjuncts to the existing determinations of homeothermy are made on the basis of available and new data, the principles of temperature adaptation of humans and homeothermal animals are given. The main purposes of the thermoregulation system of homeothermal animals and humans during various temperature excesses are formulated. The arguments are advanced in favor of the fact that in the thermoneutral zone the thermoregulation system goes from the principles of regulating the temperature homeostasis by one or several temperature points of a body to the regulation by the fluctuations of the total heat content of an organism, which increases the sensitivity and the accuracy of the thermoregulation system operation. The physiological mechanisms are described of determining (measuring) the total heat content of a body.

Keywords: Thermoregulation; Hypothalamus; Thermal comfort; Thermoreceptors

1. Homeothermy

The most important marker of homeothermy, which has as yet no scientific explanation, is a high level of energy exchange. It exceeds the corresponding values in vertebrate poikilothermal animals by a factor of 5–10 (given the same mass and the body temperature). Such a great difference demonstrates a profound "break", which occurred in the evolution between these two highly developed groups of animals. These differences touch upon other large problems of energetics of the living organisms, such as, for example, the differences in the energy consumption per unit of the body mass between the newborn and adult organisms, between very small and very big mammals. The elucidation of the reasons for such differences is the fundamental problem of modern energetics of the living organisms. It may lay with the changes in the efficiency of various kinds of biological work, which determines the intensity of energy consumption in an organism and its heat production. There can be other mechanisms.

Another most important marker of homeothermy consists in a constant comparatively high body temperature. For all the groups of homeothermal organisms this temperature lays in a comparatively narrow range between ~36 and 42 °C. A constant body temperature for various species (a species body temperature) is maintained under adequate conditions within even narrower ranges, comprising only several tenths of °C. The deviations from this temperature result in the thermoregulation reactions. Sometimes this gives rise to a belief that homeothermy restricts the "freedom of life". Such a simple conclusion does not reflect an important role of homeothermy in the development of the animated word. The matter is that a constant comparatively high body temperature and an intensive metabolism provide a rapid development of the central nervous system and acquisition of complex progressive forms of behavior for the homeothermal organisms (Burton and Edholm, 1955). That is why the progressive biological evolution always goes together with the development of homeothermy.

The origin of homeothermy in the biological evolution of vertebrates is associated with the tendency of maximal increase in the heat production level and of increasing the

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body temperature in various species of animals. This is necessary for the development and maintenance of complex functions of the central nervous system. In modern homeothermal animals the energy sources and the rate of the energy exchange reactions allow a continuous increase in the heat production by a factor of 1.5–2 at the expense of decreasing the efficiency of ATP resynthesis in the tissues. The existence of such biochemical mechanism is proved theoretically (Porter and Brand, 1993). We observed such an effect in a homeothermal animal as a whole and in the isolated organs (Ivanov, 1989). In such a case a question arises: why for the mammal organisms the body temperature of 37–39 °C is the upper temperature limit of life. This limit appears to depend on the protein thermal resistance. As the temperature increases, the rate of the protein denaturation increases, and the rate of their restoration decreases. When the temperature of a cell exceeds 40 °C, the cell membranes get "destroyed" and the organism dies (Bowler and Manning, 1994). The upper temperature limit of life is the most rigid biological constant. The animals do not overcome it. In any living organism the protein plays the most important role in the structure and functions of the cells. Hence the existence of a homeothermal organism near the upper temperature limit of life allows the highest level of metabolism to be achieved. Such is the special feature of homeothermy.

Another special feature of homeothermal organisms is their ability to preserve their viability during deep cooling. This is the inheritance of poikilothermal ancestors. Moreover, with the help of changing the ion composition of the blood the vital activity of a homeothermal organism can be restored without rewarming at such a low temperature, which is inherent only to poikilothermal animals (Ivanov, 1997, 2000; Ivanov et al., 2005).

2. Two purposes of thermoregulation

In humans and homeothermal animals the thermoregulation functions are distinctly divided into two parts by their physiological purposes and physiological mechanisms.

First, this is thermoregulation that counteracts strong or "crude" external and internal temperature excitations, which are capable of serious disruption of temperature homeostasis of an organism and of imposing a danger for life. Under ordinary adequate conditions of homeothermal organism life such severe temperature excesses occur rarely. However, just these reactions are the main subject of thermoregulation studies up to now (Hales, 1997; Cabanac, 1997; Lomax and Schounbaum, 1997; Boulant, 1999; Griffin, 2004, etc.).

Second, this is a special type of thermoregulation, its purpose consisting of leveling comparatively small but continuously arising internal and external temperature excitations. Such fluctuations occur even in the region of thermoneutral zone (for humans in the zone of temperature comfort) and are an inherent part of the normal active life of animals and humans. Under adequate conditions in the absence of abrupt temperature excesses this is just the main function of thermoregulation system in humans and homeothermal animals. Bligh (1966) was the first to pay attention to the existence of such principal differences in the types of thermoregulation. However, the study and a detailed examination of the physiological significance of the second type of thermoregulation have started only recently. The numerical proofs in favor to this point of view will be given below.

3. The main thermoregulation reactions

During the threat of overcooling in humans and animals the skin vessels become contracted to a greatest extent and the heat production increases. There are two mechanisms of increasing the heat production. The first is the thermoregulatory muscle "tone" (Ivanov, 1989). It consists in irregular frequent contractions of separate motive units of the skeletal muscles. In the electromyogram it looks like a continuous sequence of biopotentials from 10 to 50 μV and can be registered only with the help of a highly sensitive electromyograph. This type of muscle activity increases the heat production of the whole organism by 15–50%. It is of principal significance since it goes together with all the cases of chemical thermoregulation and shows that the contractile activity of the muscles always provides the basis for the thermoregulatory increase in the heat production of an organism. If the cooling increases, the thermoregulatory tone transforms into the cold shivering, which increases the heat production of a homeothermal organism by 200–250%. For a man this is the maximal thermoregulatory increase in the heat production. The physiological protection from overheating in humans and homeothermal organisms has been much studied. Such a protection attains its greatest power on water evaporation from the surface of a body (thermal sweating) or from the mucosa of respiratory ways (thermal panting).

We emphasize that the efficiency of the above listed thermoregulatory reactions is limited. A naked man, for example, dies at the temperature of still air of +1 °C or even +2 °C (Burton and Edholm, 1955). The evaporation reactions against overheating have a large power and efficiency. However, they are not able to protect an organism against overheating for any prolonged time, since they require a large amount of energy and water. The latter is most difficult, since a high environmental temperature and an intensive insolation as a rule go together with a deficit of water in the habitat. A limited efficiency of ordinary thermoregulation reactions is of importance for understanding the mechanisms of prolonged (lifelong) temperature adaptation.

4. Mechanisms of temperature adaptation

The study of the mechanisms of human and animal adaptation to a continuous living under conditions of an increased or decreased environmental temperature is of importance for examining the general problems of thermoregulation. The attempts to clarify the mechanisms of prolonged temperature adaptation in the laboratory conditions are usually made on small animals (white mice, white rats, hamsters, guinea pigs, etc.). With the aim of elucidating the mechanisms of temperature adaptation these animals undergo the action of cold or heat in the conditions inadequate for their life. According to inadequate conditions they show inadequate reactions, such as, for example, an abrupt increase in the heat production, a decrease in the efficiency of the muscle contractions in the cold, the changes in the temperature of the ''core'' of the body. If small homeothermal animals are deprived of the possibility to protect themselves from cold with the help of their kinsmen or of special forms of behavior, they die in a short time of being exposed to cold. Small animals badly withstand also a high environmental temperature under inadequate conditions. Whereas a great number of species of various (small and large) homeothermal animals continuously inhabit the regions with a severe cold or hot climate. Of principal importance is the fact that people and various homeothermal animals almost never use physiological thermoregulatory reactions, such as cold muscle shivering (shivering thermogenesis), thermal sweating, or a continuous thermal panting for continuous adaptation to a very low or very high environmental temperature. The basal metabolic rate of people from different climatic zones of the globe and the temperature of the ''core'' of their bodies are almost the same. A similar situation exists also for identical or close species of homeothermal animals from various climatic regions. Consequently, the thermal adaptation deals only with biological measures of an organism fighting against external temperature effects (see below). There is no adaptation to an increase or decrease in the body temperature of their own for homeothermal organisms. The body temperature for homeotherms is a rigid biological constant, which cannot be stepped over without loosing the homeothermy. To the same extent a continuous (lifelong) physiological temperature adaptation is not concerned with the changes in the basal (standard) energy exchange in humans and animals.

Of course, a question arises in such a case: what are the principles and mechanisms of continuous, ''lifelong'' thermal adaptation, which occurs without the loss of homeothermy. The matter is that adaptation to cold, for example, in polar animals consists of an increased heat resistance of the body coating (fur, subcutaneous fat, and feathers). Complex forms of behavior are also used (building of warm nests, closed shelters, deep burrows; mass seasonal migration of the animals from cold to warmer regions, etc.). Continuous adaptation of the animals to a high environmental temperature also occurs at the expense of complex forms of behavior (the use of ponds, building of deep burrows, the change of the habitat, a sharp decrease in the heat production at the expense of limiting the muscle activity). There are special adjustments for increasing the convective heat removal, for increasing the heat conductivity of the body coatings, and a number of other biological measures of protecting against overheating. A man in the polar regions protects himself against cold first of all by clothes and building the dwellings. Nowadays in the polar settlements the air conditioning is in use. Modern clothes are exploited, the specimens of which have a great heat resistance given a small weight. A man uses dwellings, special clothes, and air conditioning to protect himself against high environmental temperature. These measures do not require any increase in the energy expenditure of an organism. As well as in the animals a continuous thermal adaptation in humans is accomplished without common physiological protective reactions, which arise on strong temperature excesses.

Owing to biological and behavioral methods of protection against the temperature influences of the environment the homeothermal organisms in both cold and hot climate are under the conditions of thermoneutral zone for the most part of their life. In such a case a natural question arises—what is the purpose and what are the mechanisms of thermoregulation in the homeothermal organisms in the thermoneutral zone.

5. Thermoregulation in the thermoneutral (comfort) zone

Scientific investigations of thermoregulation have been carried out for many tens of the years in various animals and humans. Constant and short time temperature actions on an organism were studied and also corresponding thermoregulatory physiological reactions, which prevented overcooling or overheating of the body (Bazett, 1927; Hardy, 1961; Benzinger, 1969; Bligh, 1973, 1998; Hensel, 1981; Simon et al., 1986; Cabanac, 1997; Lomax and Schounbaum, 1997; etc). Paradoxically enough, but after a great number of such studies nowadays there is reason to make a conclusion that the main purpose of physiological thermoregulation in humans and animals during their whole life consists in maintaining temperature homeostasis in the thermoneutral zone rather than fighting against dangerous temperature excesses. Let us illustrate this seeming paradox with an example. The energy expenses of a man of average age and weight, when he lies quietly under conditions of thermoneutral (comfort) zone, are approximately 35 kcal/h m^2. In the sitting position as the result of a slight tension of some groups of muscles the metabolic rate increases to 50 kcal (i.e. by 43%), in the standing position—to 60 kcal (i.e. by 71%), and on quiet walking along the room—to 100 kcal (i.e. by 285%) (Fanger, 1970). A calculation shows that in a theoretical case of complete absence of thermoregulation in a human organism after passing from the lying position to the sitting position the body temperature will increase on average by 0.51 °C in an hour as the result of increasing the heat production. In the standing position the temperature will increase by 0.85 °C in an hour. During a slow walking along the room the body temperature in an hour will increase by ~3.4 °C and approach the temperature limit of the thermal death. These examples conveniently explain why even in the thermoneutral zone the thermoregulation system of humans and homeothermal animals is continuously operating (Ivanov and Webb, 2003). In the thermoneutral zone the heat balance is maintained mostly at the expense of vessel control. In a man the tone of the vessels of wrists and feet is regulated. In rabbits these are the vessels of the ear skin. The vessel control of the heat loss is the most precise mechanism of thermoregulation. In humans in the thermoneutral zone during a complete muscle rest an occasional increase in the hypothalamus temperature by 0.1 °C or even by 0.07–0.08 °C results in a statistically reliable dilatation of the wrist skin vessels. The temperature of these sites of the skin with a very intensive circulation increases by 2–2.5 °C, which results in an increase in the heat loss and a slow return of the hypothalamus temperature to the starting level. In a rabbit an occasional increase in the hypothalamus temperature by 0.1–0.2 °C results in a rather abrupt dilatation of the ear vessels and a sufficiently rapid return of the hypothalamus temperature to the starting value. Near the upper temperature limit of the thermoneutral zone owing to an abrupt increase in the thermal sensitivity of the thermoregulation system in humans and animals the deviations of the hypothalamus temperature from the starting level and its return to the starting level acquire a continuous oscillating character. The amplitude of these oscillations is 0.1–0.15 °C. We described these phenomena earlier (Ivanov, 1997).

6. Mechanisms of thermoregulation in the thermoneutral zone

The dilatation of the ear vessels can be triggered in an unanaesthetized rabbit and other animals at the room temperature of 12–15 °C only when with the help of a miniature thermode chronically inserted into the hypothalamus the region of the thermoregulation center is heated by 1.0–1.5 °C. In the thermoneutral zone, i.e. at the air temperature of 25–26 °C, the same thermoregulation reaction arises on increasing the hypothalamus temperature by 0.1–0.2 °C only. Consequently, in the thermoneutral zone the thermal sensitivity of the thermoregulation system is increased by at least a factor of 4–10 (Hellstrom and Hammel, 1967; Kruck and Davidov, 1977; Ivanov, 1990a, b). In humans the temperature sensitivity of the thermoregulation system also increases in the zone of thermal comfort. As has been pointed above, an occasional increase in the temperature of the tympanic membrane under these conditions by only 0.07–0.08 °C can result in the dilatation of the wrist skin vessels of a man (Ivanov, 1990a, b). What is the mechanism of increasing the temperature sensitivity? We suggested that under the conditions of thermoneutral zone the thermoregulation system uses a special highly sensitive mechanism of maintaining the temperature homeostasis. The subject of thermoregulation becomes the fluctuations of the total heat content of an organism and not the temperature of one or several points of a body (Ivanov, 1999). With the help of a special soft thermode chronically implanted into the abdominal cavity of a rabbit we "introduced" a particular "dose" of heat into the animal body. We found that the animal did not react to the increase in the temperature of the abdominal tissues touching the thermode (within the limits of 1.5–2 °C), but distinctly reacted to a certain threshold amount of heat "introduced" into the organism via the thermode and the blood vessels of the organs and tissues of the abdominal cavity. We showed that in the thermoneutral zone the reaction of ear skin vessel dilatation begins in a rabbit when the amount of "introduced" heat was from 100 to 300 cal/1 kg of the body mass. Given the average heat capacity of the living tissues of 0.83 cal/g °C, this resulted in an increase in the mean temperature of the animal body by ~0.12–0.30 °C. In humans, by our data, the vessel reaction in the wrist skin occurred after increasing the total heat content of the body by 50–60 cal/kg. The mean body temperature was increased in such a case (according to the calculation) by ~0.08–0.09 °C only. We carried out all these studies in the beginning of 1970s and described them in detail later (Ivanov, 1985, 1997). There are reasons to believe that the accuracy of thermoregulation increases, if it occurs by the fluctuations of the total heat content of the body, since in this case the thermoregulation system integrates and takes into account all the temperature shifts in an organism. We emphasize that an increase in the body heat content increases the local thermal sensitivity of the thermoregulation center in the hypothalamus (we have noted this effect above). However, in the thermoneutral zone the temperature relationships between the blood and the tissues are very complicated. A minimal quantity of heat introduced via the thermode is distributed in the blood and tissues in a different way (see Table 1). As can be seen from the Table 1, in a number of experiments with animals during a minimal increase in the heat content of the body the dilatation of skin vessels occurs without any increase in the hypothalamus temperature. The same was found in our observations in humans. This means that in the thermoneutral zone the thermoregulation center reacts to an increase in the body heat content even in the absence of its own temperature changes. Of course the question arises, what is the mechanism of determining (measuring) the fluctuations of the total heat content of the body by the thermoregulation system. In the coats of gradient calorimeters, which are used by the physicists, the thermosensors are located in two levels. One level is in the outer layer of the coat of the calorimeter, the other is in the inner layer. The heat flow from a heated physical body inserted into the calorimeter passes through the coat of the calorimeter and makes a temperature gradient. The two layered (or multilayered) location of the thermosensors makes possible the measurements of the heat flow, passing through the coat and of its fluctuations.

Table 1
Mean temperatures in the different parts of rabbit body under the conditions of thermoneutral zone and their changes at the moment of the starting of thermoregulation reaction of the ear vessel dilatation resulting from a gradual increase in the body heat content (the "introduction" of heat amounting to 100–250 cal/kg via a thermode chronically implanted into the animal abdomen)

Site of temperature measurement	Temperature (°C)		P	Percent of cases of reaction starting without temperature increase
	At the beginning of heat introduction	At the moment of starting thermoregulation dilatation of ear vessels		
Back skin	33.50±0.20	33.50±0.20	>0.05	53
Under the back skin	37.98±0.14	38.09±0.15	>0.05	44
Back muscles	38.06±0.13	38.20±0.16	>0.05	45
Brain cortex	38.39±0.05	38.56±0.04	<0.05	20
Hypothalamus	39.18±0.05	39.33±0.05	<0.05	23
Carotide	39.29±0.05	39.42±0.05	>0.05	31
Abdominal aorta	39.09±0.13	39.37±0.03	<0.05	27
Vena cava posterior	39.36±0.06	39.45±0.05	>0.05	33
Rectum	39.07±0.06	39.14±0.05	>0.05	42

Three rabbits. Thirty-six separate measurements in each animal ($\bar{x} \pm m$).

By these data it is easy to calculate the values of the oscillations of the heat content and of the mean temperature of the physical body under study. Let us note specially that all these physical values can be obtained by this method without immediate measurements of the temperature in various points of the body under study. The thermoregulation system of humans and animals is operating in a similar manner.

Skin thermoreceptors are believed to be located only in the surface layer of the skin under the epidermis (Hensel, 1981). Thorough electrophysilogical studies of separate thermoreceptors of a rabbit skin showed that about 60% of cold thermoreceptors are really located immediately under the epidermis at a distance of 100–300 μm from the skin surface. However about 15% of thermoreceptors are located deep within the skin between the derma and the subcutaneous fat. Other ~25% of thermoreceptors are between these two layers (Ivanov et al., 1986). The electrophysiological studies of the communications between separate neurons of the thermoregulation center and surface and deep skin thermoreceptors allowed justified assumptions to be made that there are neurological mechanisms in the thermoregulation center for comparing the intensities of the temperature signals from surface and deep skin thermoreceptors (Ivanov et al., 1987; Ivanov, 1990a). A multilayered location of the skin thermoreceptors suggests that the physiological system of thermoregulation is capable of measuring the fluctuations of the heat content and of the mean temperature of the whole organism by the fluctuations of the intensity of the heat flow passing through the skin, i.e. without direct measurements of the temperature by the thermoreceptors in various points of a body. These facts formed the basis of Webb's conception about the thermoregulation being performed in some cases by the heat rather than by the temperature of separate points of the body (Webb, 1995, 1997). Later on we were able to show that such a method of thermoregulation takes place only in the thermoneutral zone, i.e. under the conditions, when the thermoregulation system attains its highest temperature sensitivity and accuracy in maintaining the temperature homeostasis (Ivanov and Webb, 2003).

7. Conclusions

The examination of available and new data presented in this paper allowed principal conclusions on the main problems of homeothermy and thermoregulation. A consecutive consideration of modern data on the thermoregulation reactions, the principles of temperature adaptation, purposes and mechanisms of maintaining the temperature homeostasis leads us to the conclusion that the most important function of the system of physiological thermoregulation in humans and animals during their whole life consists of continuous accurate maintaining of the temperature homeostasis under adequate temperature conditions rather than in counteracting comparatively rare and occasional temperature excesses in the environment or organism. We bear in mind the thermoneutral zone and the environmental temperatures close to it. We have proved that in this very temperature region the thermoregulation system attains its highest temperature sensitivity and the accuracy of regulation owing to the transfer from regulation by the temperature (i.e. by the temperature of one or several points of the body) to the regulation by the heat (i.e. by the fluctuations of the total heat content). The proofs are given of the existence of physiological mechanisms of percepting (measuring) the minimal fluctuations of the heat content in a human or animal organism. These materials and conclusions, as seems to the author, change the paradigm in the field of the energetics of homeothermal organisms and in the field of the mechanisms and purposes of thermoregulation.

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