Hormonal Body Temperature Regulation in Passive and Active Hyperthermia

Passive hyperthermia means a continuous and significant rise of body temperature above the normal level conditioned by an abnormally hot environment. High relative humidity is often the decisive factor in bringing about passive hyperthermia, because it renders the evaporation of water—the only means of heat loss in a hot surrounding—impossible. The body temperature regulating mechanism proper is not damaged, it is only overcharged. All available measures for reducing heat production and raising heat loss are employed, but above a certain limit even the best regulation fails, and heat stagnation leading to passive hyperthermia develops.

Active hyperthermia (active pyrexia, fever) is a rise of body temperature produced by increased heat production or reduced heat loss (in most cases by both) due to a (pathological) change in the mechanism regulating body temperature, independently of environmental conditions. The function of the temperature regulating centre is modified and maintains an abnormal heat balance characterized by heat retention. Representatives of this type of hyperthermia are fevers of quite different origin.

In passive hyperthermia—as is known—the rise of body temperature elicits a hormonal reaction of the thyroid (MANSFELD[1]). A substance—called thermothyrin A—is poured into the blood stream, which is able to reduce the oxidation processes, i.e. the heat production of normal animals. The physiological bearing of this mechanism on heat tolerance could be demonstrated (BERDE[2]). The presence of this hormone in the blood can be easily detected[1]:— A rabbit is overheated in a thermostat at 34–35°C for 4–5 hours. Blood is taken from the jugular vein. If, after elimination of proteins and lipids, a few cc of this preparation are injected into normal albino rats, a decrease of O_2-consumption and CO_2-production can be observed. Sera of thyroidectomized overheated blood donors are ineffective.

As the mechanism of active hyperthermia (fever) differs distinctly from that of passive pyrexia, it seemed worth while to investigate *whether the secretion of thermothyrin A can be demonstrated in active hyperthermia or not?* It is of interest to remember that fever is generally regarded as a result of a change of the function of the nervous center regulating the body temperature; furthermore, that one of us (BERDE[3]) has recently demonstrated that the secretion of thermothyrin A is directed by the vegetative nervous system.

In our experiments fever was produced by heat puncture (Wärmestich) according to the method of ARONSOHN and SACHS[4] in 21 rabbits. Blood was taken from the jugular vein in one group of the animals (11 rabbits) during the period of continuous high fever (stadium acmes), in the other group (10 rabbits) in the period of defervescence, when the temperature was approaching, but had not yet reached the normal level (lysis).

The clotted blood was centrifuged. The serum was treated with 4 volumes of alcohol to precipitate proteins. After removing the alcohol by vacuum distillation at 40°C, lipids were eliminated by ethereal extraction. 2·5 cc. of this preparation were injected into normal male albino rats to test its effect on the basal metabolic rate.

The effect of serum preparations of rabbits with fever on the basal metabolic rate of rats. (Maximal deviations expressed in per cent.)

Blood was taken	
during continuous high fever (acmes) (11 rabbits)	during diminishing fever (lysis) (10 rabbits)
− 4	− 3	− 5	− 2
+ 3	−14	− 2	0
− 6	− 9	− 1	0
+10	+10	0	− 3
− 3	− 7	+ 2	− 3
+ 3	0	− 1	− 1
+ 4	− 5	− 3	−12
−12	−20	−14	− 6
− 1	+ 3	−12	− 9
+ 9	+ 2	− 9	+ 5
+17	− 2		
Mean: −1,5 (s = 8,66)		Mean: −7,6 (s = 6,32)	

s = Medium square deviation.

The sera of 21 rabbits were tested in 42 respiratory exchange experiments in an apparatus of BELÁK and ILLÉNYI[1]. Determinations were carried out 2, 5, 7 (sometimes also 9), and 24 hours after injection, always at 28°C, the indifferent environmental temperature of the rodent.

The maximal changes in the respiratory metabolism of the rats—expressed in per cent of the basal metabolic rate ascertained in numerous preliminary experiments—following the administration of serum preparations of rabbits with fever are tabulated below. Apart from a few exceptions nearly all data are inside the limits of error of the applied method. *The presence of thermothyrin A in the blood during active hyperthermia could not be demonstrated,* neither during the high fever period nor in the lytic phase.

Passive and active hyperthermia differ therefore distinctly regarding hormonal thermoregulation. This observation throws some light on the background of the mechanism involved in the changes of body temperature regulation in the course of active hyperthermia.

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Zusammenfassung

Geraten Tiere durch abnorm hohe Umgebungstemperatur in eine *passive Hyperthermie*, so kann, wie man weiß, in ihrem Blutserum das oxydationshemmende Schilddrüsenhormon (Thermothyrin A) nachgewiesen werden. Wird dagegen durch Wärmestich eine *aktive Hyperthermie* hervorgerufen, dann läßt sich in den Seren der fiebernden Tiere keine stoffwechseldämpfende Substanz nachweisen. Dieser Befund ist ein weiterer, in das Kapitel «hormonale Wärmeregulierung» gehörender Beitrag zur Frage der Verschiedenheit von aktiver und passiver Hyperthermie.

[1] G. MANSFELD, *Die Hormone der Schilddrüse und ihre Wirkungen* (B. Schwabe & Co., Basel 1943); Exper. *3*, 352, 398 (1947).

[2] B. BERDE, Hungarica acta physiologica *1*, 52 (1947); Schweiz. med. Wschr. *77*, 1367 (1947).

[3] B. BERDE, Exper. *4*, 231 (1948).

[4] E. ARONSOHN and J. SACHS, Pflügers Arch. *37*, 232 (1885).

[1] S. BELÁK and A. ILLÉNYI, Biochem. Z. *281*, 27 (1935).