EXPERIMENTAL DATA ON THE HEAT EXCHANGE IN FEVER AND DINITROPHENOL HYPERTHERMIA

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There is still a question as to the significance of increased thermogenesis in the mechanism of body temperature elevation in febrile conditions. One reason for this situation is evidently the great diversity of the changes in thermogenesis attending different febrile conditions [1]. On the other hand, the very recent theory associating thermogenesis with the character of the course of the energy exchange processes [3-6] and certain back data [2] lead one to believe that estimates of thermogenesis obtained by indirect calorimetry in febrile conditions do not always represent the actual degree of thermogenesis in the organism. Moreover, the majority of investigations concerned with the heat exchange in febrile conditions are based entirely on estimates of thermogenesis computed from the oxygen consumption. This is also true of febrile reactions induced by low-toxicity pyrogens [7].

TABLE 1. Thermogenesis in Rabbits Normally, with Fever Induced by Injection of B. mesentericus Culture and with Dinitrophenol Hyperthermia (in kg.-cal/kg per hr)

Experimental conditions	Experiment No.														Average
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Norm	4,0	3,2	4,1	3,4	4,1	4,1	2,8	4,0	4,0	4,0	4,0	3,4	3,4	3,4	3,7
Fever	3,9	3,9	3,4	4,1	5,2	3,2	4,4	—	—	—	—	—	—	—	4,0
Dinitrophenol hyperthermia	5,4	5,4	5,7	6,4	6,8	6,2	6,8	6,4	—	—	—	—	—	—	6,1

The purpose of this work was to determine the actual degree of thermogenesis in vaccinal fever uncomplicated by any significant intoxication, under which conditions the increase in oxygen consumption is slight and not stable [8, 9]. We also studied thermogenesis in dinitrophenol hyperthermia, which is known to be attended by a very sharp increase in oxygen consumption, for purposes of comparison.

EXPERIMENTAL METHODS

Thermogenesis was determined in this work with V. V. Pashutin's type of calorimeter.* The main difference in the apparatus we used was that all the mercury thermometers of the external and internal thermometric systems were replaced with sensitive thermocouples. The amounts of heat emission shown on the calorimeter are equal to the thermogenesis of the animal only if the body temperature of the latter remains constant throughout the experiment. If the body temperature became higher or lower than the original level during the period of investigation, the amount of heat retained or lost by the body in a given period was established by the formula $0{,}8 \cdot P_1 + P_2/2\,(t_1^{\circ} - t_2^{\circ})$** and the result considered as a positive or negative correction in computing the heat emission of the organism.

*A detailed description of this method can be found in E. A. Kartashevskii's monograph, "Methods of Determining Gaseous Heat Exchange in Animals Based on Academician V. V. Pashutin's Method," St. Petersburg, 1916.

**$P_1 + P_2/2$ equals the average weight at the time of calorimetric observation, 0,8, the thermal capacity of the body temperatures at the beginning and end of the observation period.

Fever was induced by subcutaneous injection of a killed Bacterium mesentericus culture in a dose of 2 ml per 1 kg weight. A 1.5% solution of dinitrophenol was administered to rabbits in a dose of 0.03 g per 1 kg weight, to dogs in a dose of 0.01 g per 1 kg weight.

EXPERIMENTAL RESULTS

A total of 41 experiments were performed on rabbits and dogs.

The 14 rabbits used in the control experiments (norm) were kept in the calorimeter for two to six hours. Thermogenesis ranged from 2.8 to 4.1 kg.-cal/kg per hour. During the 5-6 hours the animals were kept in the calorimeter in the experiments with fever, thermogenesis was 3.2-5.2 kcal/kg per hour. Under conditions of dinitrophenol hyperthermia, thermogenesis was considerably higher, averaging 6.1 kcal/kg per hour for the same experimental period (Table 1).

During the control experiments (norm), thermogenesis in the dogs was 1.8-1.9 kcal/kg per hour. No increase in the over-all heat exchange was observed in the 6-hour period during the experiments with fever. With dinitrophenol hyperthermia, thermogenesis increased in the dogs during the 5-6 hours of observation to an average of 5.24 kcal/kg per hour (Table 2).

TABLE 2. Thermogenesis in Dogs Normally, with Fever Induced by Injection of B. mesentericus Culture and with Dinitrophenol Hyperthermia (in kg.-cal/kg per hr)

Experimental conditions	Experiment No.				Average
	1	2	3	4	
Norm	1,9	1,8	1,8	2,1	1,9
Fever	2,0	2,1	1,9	1,9	1,97
Dinitrophenol hyperthermia	1,5	4,12	4,2	8,13*	

*Dinitrophenol dose 0.02 g – 0.01 g in all the other experiments.

Therefore, the experiments on the dogs brought out even more clearly the difference between the almost normal average thermogenesis level during a fever attack and the sharp increase occasioned by the administration of dinitrophenol.

The method we used does not permit dynamic determination of the heat exchange. Although the over-all heat exchange throughout the experiments with fever induced by injection of the B. mesentericus culture either equalled or only slightly exceeded the norm, there is still the possibility of its brief increase and compensatory decrease at certain stages in the febrile reaction.

Determination of the gaseous exchange during dinitrophenol hyperthermia showed the greatest increase in thermogenesis in the first two hours after dinitrophenol administration and a considerable decrease after six hours. In spite of the neutralization of the resulting values, however, there was still a great increase in the heat exchange, even in the average level determined for the whole period of the experiment.

The material presented indicates that, under conditions of fever induced in dogs and rabbits by administration of a low-toxicity B. mesentericus culture, the body temperature can increase without raising the average level of the heat exchange (for the duration of the fever attack), although a slight increase in the latter may be evoked by the mechanisms providing for the retention of heat in the body. The experiments also show that under conditions of vaccinal fever with a high body temperature, thermogenesis does not increases much more than in the case of simple overheating [10]. Preservation of the influences regulating the general level of the metabolism is the only possible explanation for this. On the basis of the experiments conducted, therefore, the following conclusions can be drawn.

Thermogenesis, as determined by the calorimeter, remains within the normal range in dogs with fever induced by the injection of a killed B. mesentericus culture. Although an increase in thermogenesis is observed under these conditions in rabbits, it is not stable and constitutes only 10-15% of the norm.

Dinitrophenol (in doses of 0.03 g for rabbits and 0.01 g for dogs) causes a sharp increase in thermogenesis.

These data, obtained by direct calorimetry, indicate the basic difference in the mechanisms responsible for the rise of body temperature in vaccinal fever and in dinitrophenol hyperthermia.

SUMMARY

In rabbits and dogs thermoproduction was studied by the method of direct calorimetry in fever provoked by killed B. mesentericus culture of low toxicity, as well as in dinitrophenol intoxication.

In fever, the length of experiment being 5-6 hours, the thermoproduction varied within the limits of the upper normal border, averaging in rabbits during the fever period 4.01 kg calories per kg per hour (the normal level being 3.7 kg calories per kg per hour) and in dogs – 1.97 kg calories per kg per hour (the normal level being 1.90 kg calories per kg per hour). In dinitrophenol intoxication the thermoproduction constituted 6.1 kg calories per kg per hour in rabbits, and from 4.1 to 8.1 kg calories per kg per hour in dogs (5-6 hours of experiment).

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