Conditions Required to Produce a Prolonged Hypothermia in the Mouse*

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Four papers (1-4) have appeared describing the influence of lowered body temperature, or the influence of the attempt to produce lowered body temperature, upon the growth of sarcoma 180. It is the purpose of this note to clarify the interpretation of the data recorded and to submit additional data dealing with hypothermia in the mouse.

The conditions necessary to produce a state of continuous hypothermia in the mouse were reported from this laboratory (1-3) as follows:

Hypothermia is not produced at environmental temperatures of 10 to 15° C. below room temperature maintained for 10- to 15-day periods. Hypothermia is produced by subjecting mice to sudden low environmental temperatures, --2 to --5° C. Shivering occurs down to a skin temperature of about 20° C. In the range of skin temperature (inguinal) 15 to 20° C., the animals lose consciousness, respiration is considerably lessened and erratic, and the heart beat is reduced to about one-half normal. About 2 hours are required to arrive at this stage. When the hypothermic state is reached the mice may be maintained in it for 24 hours (body temperature below 20° C.) by placing them in an environmental temperature of approximately 15° C. The variation in temperature that might be expected in different parts of the body is not observed (Example: inguinal 19.4° C., peritoneal 17.9° C., thoracic 18.1° C., heart 19.2° C.). A considerable number of animals do not survive the treatment, and the success of the venture depends on constant vigilance during the hypothermic state as well as during the cooling period.

The conditions used by Goldfeder (4) follow: A temperature (environmental) of about 5 to 7° C. for a period of 8 to 24--and in a few instances 48--hours was found to be the limit of endurance. The rectal temperatures of the mice were determined before exposure to cold and immediately after their removal from the refrigerator. When a mouse was shivering intensely or was almost motionless, apparently near death, it was removed from the refrigerator and the refrigeration was resumed when the behavior appeared normal. The rectal temperature of mice varied from 29 to 31° C. The mice consumed a certain amount of food.

Our experience would indicate that the temperatures of 29 to 31° C. reported by Goldfeder were not attained for sustained periods of time and probably only at the end of the refrigeration period. It is stated that the mice were removed when shivering intensely or when motionless; viz., Goldfeder's experiment terminated at the point where experiments in this laboratory began. In our experience, mice maintained at an environmental temperature of 5 to 7° C., as was done in the experiments of Goldfeder, are able to maintain body temperature only slightly below normal for considerable periods. This adjustment occurs at expense of endogenous calorie-supplying deposits and by increase in caloric intake. We believe that Goldfeder's experiment is in reality a study of the influence of the effect of low environmental temperature in increasing metabolism. Such a study was reported from this laboratory (1) and the Goldfeder experiments on tumor growth should be interpreted in this light, rather than on the basis of a prolonged hypothermia. When such an interpretation is made the anomalies in respect to respiratory quotients disappear.

EXPERIMENTAL

The experimental conditions described by Goldfeder were followed. Temperature was measured by means of a specially constructed rectal thermocouple, for which we are indebted to Dr. A. E. Koehler. The only difference in procedure was that the mice were removed from the container at intervals (2 to 4 hours) to record rectal temperature. The rectal temperatures of 4 mice weighing 25 to 27 gm. at the beginning of the experiment were 37.8, 38.2, 35.5, and 36.7° C. respectively. In two of the mice, the temperatures fell to 32.8° C. only after 36 hours' exposure to an environmental temperature of 5 to 7° C. for 24 hours, were 35.4 and 36.1° C. After 48 hours' exposure the temperature of one of these mice fell to 34.0° C. In two other mice the temperatures fell to 32.8° C. only after 36 hours' exposure, but rose to 35.4 and 35.1° C. in the ensuing 12-hour period of exposure. The mice consumed 9 gm. of calf meal (1 gm. = 3.3 calories) per mouse in 24 hours. This is just double the average food consumption at room temperature. In the experiments, reported from this laboratory, in which a continuous hypothermia was produced, no food was consumed as the mice were unconscious during the period of hypothermia.

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SUMMARY AND CONCLUSIONS

The rectal temperature of mice, which are maintained at an environmental temperature of 5 to 7°C and which have access to an adequate supply of foodstuffs, does not fall immediately to temperatures below 33°C but may be maintained in the lower limits of the normal range for 24 to 48 hours. This adjustment occurs at expense of endogenous caloric-supplying depots and by means of increase (about double) in caloric intake. The influence of these experimental conditions upon tumor growth should be interpreted on the basis of a profound increase in metabolism, without losing sight of the derangement of the metabolic and catabolic processes which obviously ensue. To ascertain the immediate effects of hypothermia on tumor growth the period of increased metabolism can be reduced to 2 hours or less by using an environmental temperature —2 to —5°C, entailing a loss of body heat which exceeds the capacity for adjustment.

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REFERENCES

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