Overshoot and High Equilibrium in Body Temperature Responses of Rats to Ambient Heat: Relation to Thermoregulatory Ability and Improvement in Estimation of Survival Time in a Hot Environment

Fujiya FURUYAMA, Michiko KUMAZAKI, and Hitoo NISHINO

Department of Physiology, Nagoya City University Medical School, Mizuho-ku, Nagoya 467, Japan

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ABSTRACT. Physiological significance of body temperature responses to ambient heat (BTRAH) with high overshoot or a high equilibrium phase was studied in relation to thermoregulatory ability. Subsequently, an attempt was made to predict survival time (ST) by measuring the period required to attain a colonic temperature (Tco) of 42.0°C (t42.0), whereas ST hitherto having been calculated on the basis of a period until Tco attains 42.5°C (t42.5). Tco of rat was monitored continuously with a Cu-Co thermocouple during exposure to an ambient temperature (Ta) of 42.5°C. The lower the overshoot temperature (Tos) or the equilibrium temperature (Teq), the longer the rats survived in a hot environment. The present findings further suggest that these two types of BTRAH are immature variations of the typical triphasic BTRAH which is characteristic of heat resistant individuals. A new regression line of ST (Y) as a function of the t42.0 (X) was obtained for most rats as follows: $Y=0.963X + 43.85$ (male); and $Y=0.973X + 39.10$ (female). This equation enabled to calculate ST without thermal death. However, the former approach based on t42.5 must be applied yet in small number of rats which showed the irregular BTRAHs with Tos or Teq higher than 42.0°C. Delayed influence on survival and fecundity at a Ta of 24°C were not found during one year following this hyperthermia up to 42.5°C.—**KEY WORDS:** body temperature regulation, heat, hyperthermia, rat, survival.

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BTRAH has been thought to be a complicated, unstable and uncertain phenomena on exhibiting chance variation. However, Ohara *et al.* in an attempt to analyze BTRAH in individuals, relative to a body temperature regulation system, exposed rats to a standardized high ambient heat as a step stimulation [16]. They exposed rats once a week, and found that the BTRAH for each rat was reproducible. They described three types of BTRAH; monophasic BTRAH showing a continuous rise up to the final death level, a diphasic BTRAH composed of an initial convex-shaped rise and the final rise, and a triphasic BTRAH composed of a rapid rise followed by an equilibrium phase and then further rise. Wright *et al.* also assigned BTRAH to the following three categories consisting of a linear heating pattern from resting to lethal level, an initial rapid elevation followed by a secondary lower rate of heating, and a three stage heating pattern [20]. Today the type of BTRAH is considered as a dominant indicator of thermoregulatory ability [11].

Furuyama *et al.* proposed a simple prediction method for ST on the basis of BTRAHs [4]. The method can be applied to a wide range of individuals with a variety of BTRAHs. ST was calculated with an accuracy of a few min. Tco of heat exposed rat

was monitored until Tco rise up to 42.5°C. ST was calculated as a function of t42.5 value in term of minute. Though all rats survive the Tco of 42.5°C, it is surprising that the maximum hyperthermia is only 0.6–0.8°C lower than the maximum survivable body temperature. While this exposure does not lead to thermal death, it is unclear whether any adverse effects of heat damage may be demonstrated in later life. Furthermore, if possible, a lowering of maximum hyperthermia to avoid possible heat damage in the estimation of ST would clearly be of advantage. It is benefit of rats to lower maximum hyperthermia to 42.0°C, which is 1.1–1.3°C lower than the maximum survivable body temperature. However, it is impossible to lower it sharply, because the equilibrium temperature level of the triphasic BTRAH is 40.0–42.0°C. Furthermore, it is unclear if it is possible to lower maximum hyperthermia only 0.5°C, because complicated and irregular BTRAHs are sometimes encountered besides these the basic types (See Fig. 1). For example, a high overshoot or a high plateau is often observed following the initial rise.

In the present study, an attempt to improve the prediction equation for ST [4] was made as follows. (1) Physiological significance of high Tos or high Teq was studied in special relation to thermoregula-

Fig. 1. Graphical illustration of BTRAH types. Ordinate: Colonic temperature (T_{co}) as indicative of core temperature; Abscissa: time. (a) mono-, (b) di- and (c) triphasic BTRAH; (d): BTRAH with high overshoot; (e): BTRAH with high equilibrium level.

tory ability in terms of ST in a hot environment. The results from this experiment formed the basis for the subsequent investigations. (2) An attempt was made to estimate ST as a function of the $t_{42.0}$ value. Feasibility and applicability of this estimation was discussed thereafter. (3) Effects of hyperthermia of 42.5°C on 1 year survival and fecundity were studied prospectively. This experiment was performed, because small numbers of rats should be still subjected to heating up to a T_{co} of 42.5°C .

MATERIALS AND METHODS

Experimental animals: Rats were outbred for 5 generations for special use in Experiment 1 and 2 described later. The origins of the colony were a male ACI/N/Ncu, a male Fisher 344/DuCrj, a female Jcl: Wistar, a female WKY/NCrj and a female HOS: Wistar rat. Their ST at a T_a of 42.5°C were 90 min, 127 min, 149 min, 114 min and 101 min, respectively. Individual rats were selected on the basis of the longest ST for outbreeding. Large individual variation was observed in thermoregulatory ability in the final outbred colony. In experiment 3-A 6 strains of male rats were used—Jcl/Wistar, HOS: Donryu, Sprague-Dawley, ACI/N/Ncu, Fisher 344/DuCrj and WKY/NCrj. HOS: Donryu rats were purchased from Japan SLC, Inc., Hamamatsu. Sprague-Dawley rats were Crj: CD from Charles River Japan, Atsugi. In experiment 3-B, Jcl: Wistar rats were used.

Rats were maintained on wood shavings in poly-

carbonate cages and allowed access to pellet food and tap water ad libitum. Room temperature was maintained at $24 \pm 1^{\circ}\text{C}$ and the light-dark cycle was set 12:12.

Heat exposure: Rats were transferred to a hot climatic chamber where the T_a was controlled at $42.5^{\circ}\text{C} \pm 0.1^{\circ}\text{C}$, wind velocity was 0.3–0.7 m/s, and relative humidity was 50–60%. The lighting condition was 400–500 lux. Using this chamber, heat exposure was consistently begun between 10 and 11 a.m. to minimize possible circadian rhythm effects. T_{co} was recorded continuously using a Cu-Co thermocouple probe inserted 5–6 cm into the rectum. Although rats were able to move freely, food and water were not available during heat exposures. Stressful conditions such as restraint were avoided. Prior to the heat exposure, rats were accustomed to the climatic chamber at 24°C and to the Cu-Co thermocouple probe once a day for several days to minimize stress effects.

Selection of breeders: Rats were selected for breeders on the basis of the longest ST. Rats, 13 weeks of age, were exposed to a T_a of 42.5°C until the T_{co} attained 42.5°C . After they were transferred to a T_a of 24°C , they were immediately allowed access to hypotonic solution (0.49% NaCl, 0.005% glutamate Na, 0.0025% citrate Ca, 0.0025% carbonate Ca and 1.0% glucose) for rapid restitution from dehydration.

Hypothetical ST (Y) was calculated, on the chart of BTRAH, by applying the time (X) to attain a T_{co} of 42.5°C using the following equations; $Y = 0.976X + 30.6$ (male) and $Y = 0.968X + 31.6$ (female) [4]. The corrected coefficients of determination were 0.989 in males and 0.988 in females. This prediction method is generally applicable to each of the monophasic, diphasic or triphasic BTRAH (Fig. 1-a, b and c, respectively).

Statistical analysis: Values were expressed as mean and S.D. Regression lines were in all cases calculated by the least ordinary square method. Differences between 2 groups were tested using the Wilcoxon rank-sum and Wilcoxon signed-rank tests. Correlations between two parameters were assessed in terms of the Spearman correlation coefficient (Rho corrected for ties).

Experimental designs:

Experiment 1: T_{os} and T_{eq} of BTRAH with overshoot (Fig. 1-d) and T_{eq} of BTRAH without overshoot (Fig. 1-e) were studied in relation to thermoregulatory ability in a hot environment. Male

and female outbred rats were exposed to a T_a of 42.5°C , and T_{co} was monitored continuously. Heat exposure was stopped when T_{co} attained 42.5°C . (A): The data for individuals demonstrating overshoot in BTRAH were collected. ST values were calculated without thermal death [4] and individuals were chosen within a wide range. The T_{os} and T_{eq} values were measured and plotted against the calculated ST. (B): The data for individuals showing BTRAH without overshoot were collected. When the difference of T_{os} and T_{eq} was smaller than 0.3°C , the BTRAH was also included in this group because it was within the normal body temperature fluctuation. ST values were calculated, and individuals were chosen within a wide range of ST. T_{eq} values or the temperature level at the inflection point, when the equilibrium period was very short, were plotted against the calculated ST.

Experiment 2: In order to develop a new equation for calculation of ST as a linear function of $t_{42.0}$ in place of $t_{42.5}$, rats were first exposed to a T_a of 42.5°C and ST values were determined from the obtained BTRAH. Individuals were chosen within a wide range of ST. Then the $t_{42.0}$ values were determined from the BTRAH chart. Regression lines were obtained between ST and the $t_{42.0}$ by the least ordinary square method.

Experiment 3: Possible damage caused by hyperthermia up to 42.5°C was monitored prospectively. In this experiment saline was not given after the heat exposure. (A): Ten male rats of each of the six strains were exposed to heat until a T_{co} of 42.5°C was attained. Another ten male rats of each strain were used as control groups which were not subjected to heat exposure. Both heat exposed and control (non-heat exposed) rats were kept at 24°C and observed for 12 months. Survival was examined

at 1, 3, 6, 9 and 12 months after the heat exposure. (B): Effect of hyperthermia on fecundity was determined in terms of progeny numbers. Two pairs were chosen from each litter. They were mated at 60–75 days of age. If both pairs produced more than 7 offspring, one pair was exposed to heat until T_{co} attained 42.5°C at 110 days of age, and the other pair was used as a non-exposed control. Eight heated and eight control couples were mated 4 times at intervals of 2 months. Total offspring numbers during the following 8 months were used to calculate fecundity indices.

RESULTS

BTRAH with high overshoot in relation to survival time in a hot environment: Overshoot in BTRAH was observed 30–50 min after the start of heat exposure. A short equilibrium phase generally followed the overshoot. T_{os} and T_{eq} in males (Fig. 2-left) and in females (Fig. 2-right) were plotted against ST. In some rats that had T_{os} higher than 42.0°C , ST was shorter than 150 min and 200 min in males and females, respectively. These animals showed saliva spread on the ventral surfaces of the chin, neck, chest and a small part of the abdomen. The T_{os} values were closely associated with the ST. For instance the lower T_{os} values close to 41°C were associated with a longer ST. Saliva spreading over large surface areas of the body was present in these rats. T_{eq} also showed a clear relation to the ST. T_{eq} was lower than 42.0°C in most of the BTRAHs. Spearman correlation coefficients between T_{os} and ST were -0.857 ($p < 0.001$) and -0.738 ($p < 0.001$) in males and females, respectively. Spearman correlation coefficients between T_{eq} and ST were -0.804 ($p < 0.001$) and -0.768 ($p < 0.001$) in males and

Fig. 2. T_{os} and T_{eq} as functions of calculated ST in individual rat with overshoot. Ordinate: colonic temperature (T_{co}); Open circle: T_{os} ; closed circle: T_{eq} . Left: males; Right: females.

Fig. 3. Teq as a function of ST in individual rats without overshoot. Ordinate: colonic temperature (Tco); Left: males; Right: females.

Fig. 4. Regression line for ST as a function of time to attain Tco of 42.0°C. Ordinate: survival time (ST); Abscissa: time to attain a Tco of 42.0°C (t42.0). Left: males; Right: females.

females, respectively. These data indicated a significant negative correlation between Tos or Teq and ST.

BTRAH with high equilibrium level in relation to survival time in a hot environment: Teq values in males and females which did not demonstrate overshoot were plotted against ST in Fig. 3. With a Teq higher than 42.0°C and a small amount of saliva observed on the chin, neck and a small part of the chest, ST values shorter than 120 min were gained. In most of the others, Teq decreased to 41–40°C in accordance with an increase in ST. Saliva spread over the whole ventral surface was observed in a rat with the longest ST. Spearman correlation coefficients between Teq and ST were -0.877 ($p < 0.001$) and -0.933 ($p < 0.001$) in males and females, respectively. Thus, there was also a significant negative correlation between Teq and ST in rats in the absence of overshoot.

There were no significant differences in ST between males with a Teq higher than 42.0°C and those with a Tos higher than 42.0°C. However, it is noteworthy that females with a Tos higher than 42.0°C had longer ST values than those with a Teq

of 42.0°C ($p < 0.02$).

Lowering the maximum hyperthermia for estimation of thermoregulatory ability: ST values were calculated as a function of the t42.0 values in males (Fig. 4-left) and females (Fig. 4-right). Regression lines between ST (Y) and t42.0 (X) were calculated for males and females as follows: $Y = 0.963X + 43.85$ (adjusted R-squared = 0.978, $p < 0.0001$); and $Y = 0.973X + 39.10$ (adjusted R-squared = 0.989, $p < 0.0001$). Thus, ST could be expressed as a function of t42.0 with a high degree of fitness.

Delayed heat damage assessed by long term survival and fecundity: During the heat exposure most rats, especially those demonstrating long ST, were at rest and looked comfortable. They sometimes seemed to be sleeping during the equilibrium phase. When the Tco was approaching 42.5°C the rats moved around more actively, but no rats showed symptoms of heat exhaustion or critical thermal maximum [18].

Survival of rats after heat exposure is shown in Fig. 5-left. There was no statistically significant decrease in survivors at 1, 3, 6, 9, and 12 months after hyperthermia in comparison to non-exposed

Fig. 5. Prospective study on delayed effects of 42.5°C hyperthermia. *Left*: Number of survivors during the 12 months after the heat exposure. Open column: controls; Closed column: heat survivors. *Right*: Number of babies born after the heat exposure.

controls. The average progeny of control pairs resulting from 4 mating periods was 29.38 ± 11.84 (Fig. 5-right), while that of heat survivors was 25.75 ± 11.29 . There was thus no significant decrease in fecundity attributable to hyperthermia up to 42.5°C.

DISCUSSION

It is difficult to find a rat strain which demonstrates a wide range of variation of ST, although there are discrete differences in ST among different strains [3, 5]. We therefore bred an outbred colony with large individual variation in ST for particular use in the present study. In our outbred colony the majority of animals demonstrated ST values of 1–2 hr, whereas some were 2–3 hr and a few were longer than 3 hr. These values were comparable with the range of differences among strains [3, 5], and it can be considered that the variation of individual ST reflects the general distribution of ST in the rat, *Rattus norvegicus*.

In the present study Teq higher than 42.0°C was comparable with high overshoot. In such case, Tco increased to over 42.0°C within 30 min after the start of heat exposure. This might be due to only a small amount of saliva secreted. In other rats overshoot was followed by transient decrease in Tco which might have been brought about by effective salivation. Thermal salivation is well known to be induced by a hot environment [1, 6, 9, 10], producing the long plateau in cases of typical three-phasic BTRAH. There were many intermittent variations between the two types of BTRAH investigated in the present study and triphasic

BTRAH. Rats which showed BTRAH with high Tos or high Teq demonstrated poor salivation and therefore shorter ST than triphasic BTRAH. Rats with high Tos or high Teq survived heat longer than those with mono- or di-phasic BTRAH [3]. BTRAH with high Tos or high Teq might be considered as immature types of triphasic BTRAH. While no significant difference in ST was observed between the two typically irregular BTRAH in males, females with overshoot higher than 42.0°C survived heat longer than those with Teq higher than 42.0°C ($p < 0.02$). It is a problem if rats with high overshoot had an advantage in thermoregulation in a hot environment over those with only high Teq.

The thermoregulation system is disturbed during stressful conditions. For instance, lethal body temperature and ST in restrained rats was found to be lowered and shortened [2]. ST values at a Ta of 40 or 45°C were remarkably shorter in exercising rats than in resting rats [17]. We determined that the maximum survivable body temperature was 43.1–43.3°C in freely moving rats in a hot environment [3]. However, the lowest value reported as maximum survivable body temperature was 40.4°C in running and restrained rats [12]. It was also reported that Teq decreases in heat acclimated man [8]. It is well known that the activities of the central nervous system, endocrine system and immune system are easily changed by stress [13]. BTRAH can also be altered by stress and adaptation. This is one of reasons why BTRAH was not thought to be stable and reproducible in early days. In the present study rats were therefore not restrained, but able to move freely, and animals with inserted thermocouples were also transferred into the climatic chamber

at 24°C for several days preceding the heat exposure to minimize possible stresses other than heat itself.

Fujita and Yamanouchi have described that 52% of pregnant rats died between the 18th and 20th day of gestation under continuous exposure to a warm environment (33°C) because of disorders in blood pressure regulation [7]. However, it has been reported that hyperthermia up to 42.5°C does not result in delayed heat damage assessed during the following 8 weeks [4], and in the present study no effect was evident in rats kept under observation for up to 12 months after heat exposure. These findings suggest that acute exposure to high temperatures is safer than chronic exposure for many generations to moderate heat.

It is desirable that a method to estimate precisely ST before heat death can occur is developed. Ohara *et al.* first predicted ST on the basis of BTRAH [16], the main parameter used for the method being the slope of Tco increase during the period following the initial rise. However, one problem was that an irregular high Tos or high Teq appeared occasionally in the same period. Wright and Knecht [19] reported that it was rather difficult to estimate ST in rats with a long plateau by the method of Ohara *et al.* [16] because of similar slopes despite marked variation in length of plateau. We therefore presented a simple approach to prediction which could be applied even to rats surviving heat for more than 150 min [4]. In this case ST was principally calculated as a simple function of the t42.5 value. Although it is 1–2°C higher than Teq in typical triphasic BTRAH which is a specific characteristic of relatively heat resistant individuals, this is also close to the maximum survivable body temperature (43.1–43.3°C) [3]. It is desirable to lower the maximum hyperthermia during heat exposure, because 42.5°C is only 0.6–0.8°C lower than the 43.1–43.3°C. In the new method, the maximum hyperthermia is 1.1–1.3°C lower than the 43.1–43.3°C. This method enabled to predict ST safely prior to breeding and experiments.

Feasibility and applicability of the former method and new prediction method developed in the present study was examined and confirmed. It is relatively simple to determine t42.0 values for cases of mono-, di- and triphasic BTRAH. In triphasic BTRAH, body temperature rises first within 30 min after the beginning of exposure up to the plateau which is lower than 42.0°C. The t42.0 value was determined in the course of the final rise. Thus we attempted to

stop heat exposure in the course of Tco monitoring when Tco had attained 42.0°C and predicted ST based on the t42.0 value. However, it is not easy to lower the maximum hyperthermia. The main obstacle for applying this new method is the occasional existence of irregular BTRAH with Teq or Tos values higher than 42.0°C and large individual variation in the latter part of the BTRAHs. Sometimes it is difficult to discriminate between irregular BTRAH and diphasic BTRAH within the first 30 min after the start of heat exposure, 30–40 min being required for BTRAH with Tos and Teq higher than 42.0°C to become evident. If the Tco increases above 42.0°C within 40 min and this indicates an irregular response, the method developed by us earlier [4] should therefore be applied. If Tco increased above 42.0°C after 40 min, Tco always decreased thereafter in our experience of cases, allowing ST to be calculated by the new method based on the t42.0 value of the final rise. A Tco of 42.0–42.5 was found in the present study to be only one narrow body temperature range available for prediction of ST without thermal death. Thus our new prediction method is generally applicable for most rats other than a small number of those with irregular BTRAH with Tos or Teq higher than 42.0°C.

Although a new prediction method for ST based on t42.0 value has been developed in the present study, the t42.5 value also has to be applied to a small number of rats. We therefore examined prospectively the effects of 42.5°C hyperthermia on 1 year survival and fecundity. There was no significant differences in 1 year survival or fecundity between the control group and heat survivors. Thus, the method formerly used can be also applied, although the possibility of slight heat injury may remain.

Hyperthermia induces dehydration *via* evaporative heat loss system. If rats are allowed access to water, they drink actively, but stop before rehydration is complete. This phenomenon, called voluntary dehydration, results from Na deficiency in the brain [14, 15]. Rats were therefore allowed access to a hypotonic solution, which does not cause Na deficiency in the brain, so that dehydration was completely recovered. This would be expected to have diminished a possible delayed cellular damage.

In conclusion, the two irregular BTRAHs characterized by high overshoot or equilibrium were suggested to be immature types of triphasic BTRAH

and attributable to a shortage in thermal salivation. The new estimation method for ST based on time spent until the T_{co} attains 42.0°C might warrant application in most rats. The estimation method based on $t_{42.5}$ values can be applied to the remaining small number of rats, because a hyperthermia of 42.5°C has no obvious delayed influence on death or fecundity within one year.

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REFERENCES

1. Elmer, M. and Ohlin, P. 1971. Salivary secretion in the rat in a hot environment. *Acta Physiol. Scand.* 83: 174–178.
2. Frankel, H. M. 1959. Effects of restraint on rat exposed to high temperature. *J. Appl. Physiol.* 14: 997–999.
3. Furuyama, F. 1982. Strain difference in thermoregulation of rats surviving extreme heat. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 52: 410–415.
4. Furuyama, F., Ohara, K., and Ota, A. 1984. Estimation of rat thermoregulatory ability based on body temperature response to heat. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 57: 1271–1275.
5. Furuyama, F., Yoshida, T., Kumazaki, M., and Ohara, K. 1988. Thermal salivation and body water economics among Wistar rat strains. *Jpn. J. Vet. Sci.* 50: 415–423.
6. Furuyama, F., Ishida, Y., Furuyama, M., Hashitani, T., Isobe, Y., Sato, H., and Nishino, H. 1989. Thermal salivation in rats anesthetized with barbiturates, chloralose, urethane and ketamine. *Comp. Biochem. Physiol.* 94C: 133–138.
7. Fujita, S. and Yamanouchi, C. 1984. Influence of hot environment on body temperature, heart rate and blood pressure in pregnant rats. *Exp. Anim. (Tokyo)* 33: 61–67.
8. Givoni, B. and Goldman, R. F. 1973. Predicting effects of heat acclimatization on heart rate and rectal temperature. *J. Appl. Physiol.* 35: 875–879.
9. Hainsworth, F. R. and Epstein, A. N. 1966. Severe impairment of heat-induced saliva-spreading in rats recovered from lateral hypothalamic lesions. *Science* 9: 1255–1257.
10. Hainsworth, F. R. and Stricker, E. M. 1970. Salivary cooling by rats in the heat. pp. 611–626. *In: Physiological and Behavioral Temperature Regulation* (Hardy, J. D., Gagge, A. P., and Stolwijk, J. A. J., eds.), Charles C. Thomas-Publisher, Springfield, U.S.A.
11. Horowitz, M. 1989. Heat acclimation: a continuum of processes. 1989. pp. 445–450. *In: Thermal Physiology* (Mercer, J. B. ed.), Elsevier Science Publishers B. V., Amsterdam.
12. Hubbard, R. W., Bowers, W. D., Mattew, W. T., Curtis, F. C., Criss, R. E. L., Sheldon, G. M., and Rattree, J. W. 1977. Rat model of acute heatstroke mortality. *J. Appl. Physiol.* 42: 809–816.
13. McCubbin, J. A., Kaufmann, P. G., and Nemeroff, C. B. 1991. Stress, neuropeptides, and systemic disease, Academic Press, Inc., San Diego, U.S.A.
14. Morimoto, T. 1990. Thermoregulation and body fluids: role of blood volume and central venous pressure. *Jpn. J. Physiol.* 40: 165–179.
15. Nose, H., Yahata, T., and Morimoto, T. 1985. Osmotic factors in restitution from thermal dehydration in rats. *Am. J. Physiol.* 249: R166–R171.
16. Ohara, K., Isobe, Y., and Furuyama, F. 1975. Prediction of survival time of rats in severe heat. *J. Appl. Physiol.* 38: 724–729.
17. Robinson, S. M. and William, F. B. 1968. Heat tolerance of the resting and exercising rat. *Can. J. Physiol. Pharmacol.* 46: 189–194.
18. Wright, G. L. 1976. Critical thermal maximum in mice. *J. Appl. Physiol.* 40: 683–687.
19. Wright, G. and Knecht, E. 1977. Prediction of survival time of rats in hot environment. *Ohio J. Sci.* 77: 199–206.
20. Wright, G., Knecht, E., and Wasserman, D. 1977. Colonic heating patterns and the variation of thermal resistance among rats. *J. Appl. Physiol.: Respirat. Environ. Exercise Physiol.* 43: 59–64.