TECHNICAL PAPERS

Body Temperature, Blood Pressure, and Hypothalamus[1]

SIMON RODBARD

Cardiovascular Department, Michael Reese Hospital, Chicago

In the course of studies on the regulation of normal blood pressure, data were obtained which suggested a general relationship between body temperature and blood pressure. These studies were then extended to include mammals, birds, reptiles, and amphibians. It soon appeared that we were dealing with a more general principle involving adjustments of the internal environment to temperature changes, and this led to a consideration of the phylogenetic development of temperature regulation.

A comparison of data on the blood pressure of normal resting animals led us to give particular attention to the average diastolic pressure of unanesthetized mammals including dog (*2, 10*), rabbit (*5*), man, and rat which is about 80 mm Hg. These mammals have normal body temperatures approximating 38° C. The chicken (*12*), turkey, and duck (unpublished data) have diastolic pressures of 120–140 mm Hg and correspondingly higher body temperatures (about 42° C). These average normal values are represented by the circles in Fig. 1.

These findings made it appear worth while to determine if the blood pressure would change as the body temperature was changed. In the turtle the blood pressure was found to rise with increasing body temperature and to fall as the animal was cooled (*8*). For example, the pressure averaged 21/16 mm Hg at 10° C, and at 37° C it reached a maximum level of 39/33 mm Hg (Fig. 1). Similar data, not yet published, were obtained with the frog. The same relationship was elicited in mammals and birds. Cooling produced a progressive fall in blood pressure in chickens (*12*), dogs, and rabbits (unpublished data), and rewarming resulted in an equal rise in pressure *pari passu* with the body temperature (Fig. 1).

These relationships hold only within a given temperature range for each species. Warming of the mammal or bird above its normal temperature resulted in no consistent changes in pressure. At about 3° C above these normal temperatures a critical level was reached, and the blood pressure fell rapidly, leading to death. Critical thermal levels were observed in the frog at about 25° C and in the turtle at about 37° C (*8*).

At this point our interest in the mechanism of the temperature-pressure relationship was aroused. Autonomous changes in the reactivity of the blood vessels could not account for the relationship. Thus, no significant differences were observed in the pressor response to epinephrine or the depressor effects of acetylcholine in either the hypothermic or hyperthermic chicken (*9, 12*), rabbit, or the turtle. Small variations were seen in the concentration of the plasma protein and in the blood volume. Circulation time, cardiac output, and heart rate were also found to be direct functions of the body temperature. Cooling of the chicken (*9*) and the dog (unpublished data) resulted in a slowing of the circulation and a decreased cardiac output, while rewarming resulted in a speeding up of the circulation. However, the fact that the circulation rate continued to increase in severe hyperthermia even after the blood pressure had begun to fall indicated that the blood pressure changes did not depend solely on these factors.

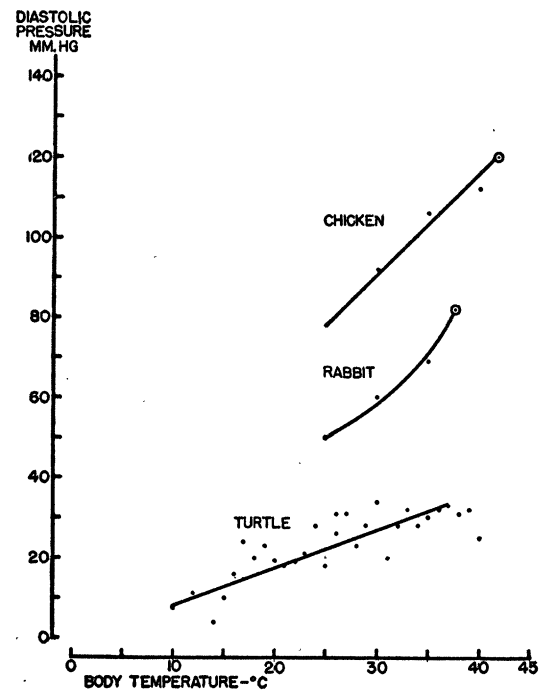

FIG. 1. Body temperature–arterial pressure relationship.

We then investigated the role of the central nervous system. Destruction of the brain or section of the cervical spinal cord eliminated the effect of body temperature on the blood pressure (*6*). In order to establish whether the temperature-pressure mechanism operated through receptors in the periphery, we tested the effect of thermal stimulation of the brain. This was accomplished by the insertion into the brain of a silver wire connected to a water reservoir. Warming the brain caused an immediate rise in arterial pressure, while cooling caused an immediate fall (*11*). Slight thermal differences caused consistent covariance when the wire was in or near the hypo-

[1] Aided by a grant from the Department of the Army to the Michael Reese Hospital.

thalamus, but not when it was in the medulla or in the olfactory or optic lobes. To our knowledge this is the first direct evidence for a temperature-sensitive center in the brain of a cold-blooded animal.

Changes were found not only in the circulation but also in the concentration of certain elements in the blood. Thus, cooling of the chicken was followed by a fall in blood sugar, and rewarming, by a return to normal levels (*7*).

A review of the phylogenetic development of the circulation suggested further approaches to the understanding of the general problem. For example, the development of homeothermism undoubtedly placed great stresses on the circulatory system if the rapidly metabolizing tissues were to receive adequate substrate and oxygen for prolonged activity. At optimal body temperatures, poikilotherms are capable of high degrees of activity for brief periods only. This limitation is probably due in part to the low-resistance pulmonary shunt, which does not permit the development of high pressures in the systemic circulation. The evolutionary separation of the low-resistance pulmonary shunt made possible an increase in the systemic pressure and opened the way for the maintenance of a blood flow adequate to nourish the more active tissues of the homeotherm. The temperature-pressure relationship of the ancestral poikilotherm appears to have persisted in the systemic circulation, even though the diastolic pressure is at the higher levels of 80 or 120 mm Hg, while the pulmonary pressure continues at the more primitive level. Our data showing the pulmonary pressures of dogs (*3*) and chickens to be about 25/10 mm Hg support this concept.

A consideration of the temperature ranges which various vertebrates could withstand without obvious injury indicates an evolutionary increase in the ability to tolerate rapid changes in body temperature, which has had important bearing on the development of warm-blooded animals (Fig. 2). For example, for fish living in large bodies of water, the ability to adjust to rapid temperature changes is not essential for survival, since such changes do not occur. However, shallow-water fish may be exposed to variations of several degrees during the course of the day and hence must be able to withstand such changes.

This process continued with the evolution of the air-breathing vertebrates. When the fish left the water and lived on the land as amphibians, they were exposed to far greater diurnal temperature changes than occurred under cover of the high specific heat of the protecting water. Within the next 60,000,000 years some amphibians had developed the capacity to tolerate still greater diurnal changes in temperature and were able to leave the water completely, giving rise to the reptiles.

These diurnal environmental temperature changes play an important role in the normal cycles of activity of the terrestrial poikilotherm. It is apparent that early in the morning in temperate climates poikilotherms living on the land have a low body temperature and are at low metabolic and activity levels. Absorption of solar energy during the day raises the body temperature and increases the metabolic activity, as indicated by oxygen consumption, general activity, respiratory and heart rates, blood pressure, and circulation rate. Optimal body temperatures may be regulated by locomotor responses. During

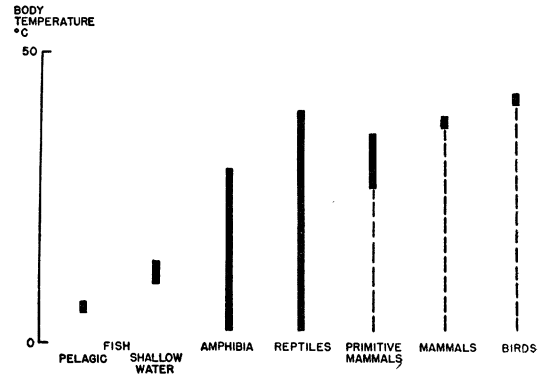

FIG. 2. A schematic representation of the diurnal variations in body temperature of vertebrates. Heavy lines suggest the variations in body temperature which may occur during a single day. Dotted lines indicate the potential temperature changes normally prevented by temperature-regulating mechanisms.

this period the nutritive, defensive, and reproductive activities which result in individual and species survival are performed. With evening, the poikilotherm loses heat. This leads to a decline in metabolism, activity, circulation rate, and blood pressure, and the animal may fall into a sleep-like torpor. Each day this cycle of warming and activity, cooling and torpidity, is repeated.

In the Triassic period, the theriodont reptiles, which may already have developed the ability to withstand large temperature changes, gave rise to the early mammals. Thirty million years later, in the Jurassic, another group of reptiles, which may have increased their diurnal temperature range still more, gave rise to the ancestors of the modern birds. Thus, the birds may have adjusted their normal body temperature at their optimal level, higher than that of the earlier evolving mammals. Hair or feathers conserved the warmth gained during the day and kept metabolism relatively high during the early night, compared with the cold, torpid poikilotherms. Further evolution brought the development of heat-conservation mechanisms, such as the pilomotor function and the ability to shift blood from the skin, and thermogenic mechanisms evolved which came into play whenever the body temperature began to fall. When the increasing efficiency of heat conservation and thermogenic mechanisms brought the danger of raising the body temperature above the critical level, heat-loss mechanisms began to have survival value. Similar patterns of development of temperature regulation have been suggested by observations on newborn mammals and birds (*4*) which show that, ontogenetically, heat-conservation mechanisms precede thermolytic mechanisms.

Our discovery of the thermal sensitivity of the hypothalamic region in the cold-blooded animal (*11*) made it possible to correlate our work with a number of hitherto

uncorrelated data. This miniscule portion of the brain has been deluged with responsibility for a large number of apparently unrelated functions (*1*); it has been considered the head-ganglion of the autonomic nervous system, responsible for the regulation of body temperature, blood pressure, respiration, appetite, the diurnal rhythm of sleep and wakefulness, the sexual cycle, and the control of the metabolism of sugar, fat, and water. On the basis of the approach presented above, these functions may be considered as parts of an integrative mechanism. Thus, it is apparent that as the neo-amphibian leaves the water and is exposed to large changes in body temperature, immense variations may occur in the metabolic rates of the numerous tissue and organ systems which might lead to maladjustments of the internal economy. An internal environment optimal for 5° C might be wholly unsuitable for survival at 30° C. Since temperature variations of such magnitude may occur rapidly in terrestrial poikilotherms under natural conditions, the development of a coordination center for metabolic adjustment would provide survival value for its possessor. In such poikilotherms this center would be charged, not with the maintenance of the constancy of the internal environment (homeostasis) but with the coordination of changes in the internal environment (homeodynamics) to meet the demands placed by other changes such as temperature. Such a rapidly reacting center for homeodynamic control appears to have been developed in the hypothalamus. The rich vascularity of this organ makes it eminently suitable for such a role.

Our studies suggest that some homeodynamic regulations depend upon the independent variable, the temperature of the temperature-sensitive center in the brain. In the course of time, heat conservation, thermogenic and thermolytic mechanisms apparently were laid down proximal to the homeodynamic center, introducing a new factor: the relative constancy of body temperature. Under these conditions, the homeodynamic adjustments became minimal during the diurnal cycle, although the adjusting mechanisms persisted. Patterns of behavior of warm-blooded animals suggest retentions of some elements of the diurnal cycle of the poikilotherms, such as the diurnal variations in body temperatures and the period of torpor (sleep). Phenological functions, such as the reproductive cycle, which previously depended in part upon the diurnal variations and their annual precession, may escape and establish a reproductive calendar independent of the solar year.

Although begun as an analysis of a relationship between body temperatures and blood pressure, our studies have not only indicated that the relationship depends on the central nervous system, but have suggested that it may be but a portion of a more general integration. Some of these integrating mechanisms may be approached experimentally in the poikilotherm by producing variations in body temperature. In homeotherms, the superimposition of a relatively constant body temperature serves to mask the basic integrative mechanisms, but induced hypothermia causes the animal to revert to a more primitive condition and thus exposes the homeodynamic apparatus to experimental analysis.

References

1. Ingram, W. R. *Psychosom. Med.*, 1939, **1**, 48.
2. Katz, L. N., Friedman, M., Rodbard, S., and Weinstein, W. *Amer. Heart J.*, 1939, **17**, 334.
3. Katz, L. N., and Steinitz, F. S. *Amer. J. Physiol.*, 1940, **128**, 433.
4. Randall, W. C. *Amer. J. Physiol.*, 1943, **139**, 56.
5. Rodbard, S. *Amer. J. Physiol.*, 1940, **129**, 448.
6. Rodbard, S. *Fed. Proc.*, 1947, **6**, 191.
7. Rodbard, S. *Amer. J. Physiol.*, 1947, **150**, 67.
8. Rodbard, S., and Feldman, D. *Proc. Soc. exp. Biol. Med.*, 1946, **63**, 43.
9. Rodbard, S., and Fink, A. *Amer. J. Physiol.*, 1948, **152**, 383.
10. Rodbard, S., and Katz, L. N. *Amer. Heart J.*, 1943, **26**, 114.
11. Rodbard, S., and Samson, F. *Fed. Proc.*, 1948, **7**, 104.
12. Rodbard, S., and Tolpin, M. *Amer. J. Physiol.*, 1947, **151**, 509.

Indole-3-Acetic Acid and Flowering

Marion Green and Harry J. Fuller

Department of Botany, University of Illinois

The experiments described briefly in this paper were conducted to test the assumption by Thurlow and Bonner (*2*) that, since a marked decrease in the auxin content of plants at the time of their flowering has been demonstrated (*1*), it might be possible to delay flowering by externally supplying plants with auxin. Thurlow and Bonner sprayed soybean and *Xanthium* plants, grown under flower-inducing short photoperiods, with indole acetic and naphthalene acetic acid solutions (500 ppm) and observed inhibition of production of flower primordia, a result which lends support to Bonner's assumption. Since the leaves of the treated plants showed pronounced epinasty and other growth deformities and since the inhibitory effect of the spray might thus be an indirect leaf-injury effect, it was thought desirable to treat plants with indole acetic acid by immersing their roots or the cut ends of their stems in water solutions of this auxin in order to avoid direct auxin contact with leaves.

In the first set of experiments the roots of petunia plants (var. Topaz Queen) which were 7 weeks old and which were approaching flowering time, though still without flower primordia, were immersed for 24 hrs in water solutions of indole-3-acetic acid (200 ppm). The plants were then potted in rich loam soil. The first visible flower buds appeared in these treated plants 23 days after the first flower buds were visible on the control plants, roots of which were treated for 24 hrs with water. Thus, the indole acetic acid treatment distinctly delayed flowering, a result which agrees with that of Thurlow and Bonner. No signs of leaf epinasty or other types of deformity appeared in the leaves of the treated plants, nor was there any apparent difference in root development between treated plants and controls.

This experiment was repeated on Lincoln soybeans,