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ADDENDUM

Out of the work presented in the thesis the following papers have been published:


Histochemical demonstration of adrenaline and nor-adrenaline in adrenal medulla of baby rabbit and pigeon exposed to higher ambient temperature - To be published in the *Journal of Histochemistry and Cytochemistry* (U.S.A.). In the press.

Thyroidal activity in higher ambient temperature - To be published in *Nature* (London). In the press.
THERMOGlyCâSMIC RESPONSE AND THE ADRENERGIC SYSTEM
IN PIGEONS. By SukHen CHAUDHURI and D. P. SADHU. From
the Department of Physiology and Nutrition, Bengal Veterinary
College, Calcutta-37, India.

(Received for publication 22nd June 1960)

Pigeons show a significant thermoglycemic response on short exposure to
high ambient temperatures. An attempt has been made to study the role of
the adrenergic system in this response of the pigeons. The birds were
controlled at 32° C. and exposed to 45° or 48° C. for 2-4 hr. Their body weight,
heart rate, plasma-cell ratio of blood, erythrocytes, leukocytes and blood
hemoglobin, specific gravity of whole blood and blood plasma concentration of
plasma proteins and blood sugar were determined. The ganglioplegic drug
"Ansolysen" and adrenergic blocking agent "Regitine" have been
found to abolish the thermoglycemic response.

Pigeons are homiothermic like the mammals, but when they and other
birds are subjected to high ambient temperature, there is a rise in their
blood sugar level. This is known as the "thermoglycemic response"
[Sturkie, 1954]. Baby rabbits and other mammals born naked without fur
show a defective thermoregulation [Gullick, 1937]. A similar increase in
blood sugar level has been observed in baby rabbits when subjected to
higher ambient temperatures, although this effect is not seen in adult mammals
on short exposure [Chaudhuri and Sadhu, 1959 and 1960]. In the course of
thermoregulatory evolution from poikilothermy to homiothermy, poikilo-
therms evolve into the heterotherms. These are poorly regulating lower
mammals, such as sloths, opossums and bats, which show some temperature
fluctuation with that of the environment and enter into a state of cold narco-
sis at low air temperature [Preser, 1952]. Some of the higher homiotherms
also show fluctuations of their body temperature with that of the environment
as a physiological adaptation, such as camels in deserts [Schmidt-Nielsen,
Schmidt-Nielsen, Houp and Jarum, 1959] and are called poikiotherms, but
these do not show cold narcois. With respect to the behaviour of oxidative
enzymes in cold ambient temperature [Sadhu, 1959], birds show homio-
thermic behaviour only in a narrow range of ambient temperature, like the
new-born mammals and it appears that this homiothermic behaviour in a
narrow range of air temperature (stenothermal behaviour) is an obligatory
phase in the evolution to full homiothermic (euthermal) behaviour of all
mammals: the birds possibly stopped at the stenothermal phase.

From the blood response to body temperature as a function of the central
nervous system Rodbard [1947] predicted an integrating role of the central
nervous system in the thermoglycemic response. However, the mechanism
by which sugar is raised in response to a rise in ambient and/or deep
body temperature in birds has not yet been investigated. In the present
study an attempt has been made to investigate the mechanism of the thermo-
glycemic response of the pigeon with the possible role of the adrenergic
system in the genesis of this response.
Thermoglycsemia in Pigeons

METHODS

Healthy pigeons weighing up to 280 g. were used. All the birds were fasted for 14 hr. before the experiments were conducted. In Series 1 thirty pigeons were housed in individual cages in a room with an average temperature of 32° C. Rectal temperatures were determined by a clinical thermometer and heart rates by an electrocardiograph of Sanborn Viso-Cardiometric type. In the blood plasma/cell—ratio was measured with a haematocrit, erythrocytes and leucocytes enumerated in a Thomas-Zeiss haemocytometer and haemoglobin determined in a Klett Summerson photoelectric colorimeter. Specific gravity of whole blood, blood plasma and the concentration of plasma proteins were determined by the copper-sulphate method (Hawk et al., 1944). Blood sugar was estimated in wing vein blood by a modification of Somogyi’s reagent No. 2 (Somogyi, 1931; Maclagan, 1940).

After some days in the controlled environment the pigeons were divided into two groups. One group was exposed to 45° C. and the other to 48° C. in a constant temperature chamber for 2½ hr. The standard error of the temperature fluctuation in the chamber was never greater than ±0·3° C. and the walls of the chamber were within ±1° C. of the air temperature. After the period of exposure was over, blood was collected and measurements made as already described.

In Series 2, twenty-four pigeons were divided into two groups and after collecting a sample of wing vein blood for sugar estimation, a ganglion-blocking agent, Ansolysen * brand pentolinium tartrate (M. & H. 2050 A), which is chemically pentamethylene 1:5-bis (1-methyl pyrrolidinium) hydrogen tartrate was injected intramuscularly into the birds of both groups. One group was then kept as a control at 32° C. and the other subjected to 48° C. for 2½ hr. The optimum dose of Ansolysen at which complete blockage of the ganglia occurs was determined previously in pigeons from the effect on the electrocardiogram to a known tachycardic response of epinephrine. Ansolysen, 0·4 mg./kg. body weight, injected intramuscularly was found to be sufficient for the complete block of the ganglia for more than 90 min. A second similar dose after this period could maintain the block for another 90 min. The blocking effect in the exposed pigeons was therefore maintained by a second dose of Ansolysen 90 min. from the time of exposure. After a period of 2½ hr. of exposure to 48° C., blood samples were taken for sugar estimation.

In Series 3, twenty pigeons were divided into two groups. After collecting a blood sample for sugar estimation, an adrenergic blocking agent, ergotamine tartrate 25 µg./kg. body weight was injected intramuscularly. One group was kept control at 32° C. and the other subjected to an ambient temperature of 48° C. and after 2½ hr. of exposure to 48° C., blood was collected and sugar determined.

RESULTS

The results are presented in Table I.

On exposure to 45° C. and 48° C. ambient temperatures, the pigeons showed a small but statistically significant increase of rectal temperature, which in general gives a good measure of average core temperature [Hardy, 1953-54]. The rise is, however, not proportional to the ambient temperature. Electrocardiograms showed a significant increase of heart rate although the tachycardia at the higher ambient temperature is out of proportion to the rectal temperature. Neither the haematocrit value nor the specific gravity of whole blood, blood plasma nor the concentration of plasma proteins

* Kindly supplied by May and Baker (India) Private Ltd.
showed any significant difference. With the high ambient temperature there was no significant shifting of plasma water. The effect of high ambient temperatures on the blood sugar level of the pigeons is shown in Table II. There was a thermoglycaemic response both at 45° C. and 48° C. ambient temperatures. A linear regression between ambient temperature in degrees centigrade and sugar level in mg. per cent shows that for each degree rise in ambient temperature there is a corresponding rise of 3.5 mg. blood sugar, and this value is also true for a similar thermoglycaemic response in baby rabbits [Chaudhuri and Sadhu, 1959].

In Series 2 the results of the ganglion-blocking agent (Ansolysen) on the thermoglycaemic response are shown in Table II. Administration of Ansolysen per se at 32° C. had no effect on the blood sugar level and exposure to 48° C. also did not increase blood sugar level. To investigate further whether the thermoglycemia could be due to increased activity of the adrenergic system in Series 3 the latter activity was blocked by ergotamine tartrate and the thermoglycemia did not appear (Table II). Temperature characteristic \( \mu \) in calories/gram, per hr., 1924 has been calculated for a difference of blood sugar from 45° C. to 48° C. and from 48° C. to 32° C., as described by Sadhu [1959].

It should, however, be noted that the temperature used in the calculation is the extrinsic ambient temperature and not the intrinsic temperature.

### Table I.—Effect of Subjecting Groups of Ten Pigeons Controlled at 32° C. to a High Ambient Temperature of 45 or 48° C. for a Period of 24 hr.

<table>
<thead>
<tr>
<th>Control 32° C.</th>
<th>Exposed to 45° C.</th>
<th>Exposed to 48° C.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight, g.</td>
<td>252-5 ±0-6</td>
<td>252-1 ±0-7</td>
</tr>
<tr>
<td>Rectal temperature °C.</td>
<td>41.0 ±0-6</td>
<td>42.3 ±0-7</td>
</tr>
<tr>
<td>Heart rate/min.</td>
<td>205 ±0-5</td>
<td>301 ±0-7</td>
</tr>
<tr>
<td>Haemoglobin g./100 ml.</td>
<td>16.3 ±0-6</td>
<td>16.2 ±0-7</td>
</tr>
<tr>
<td>Haematocrit (per cent)</td>
<td>47.3 ±0-7</td>
<td>47.7 ±0-7</td>
</tr>
<tr>
<td>Sp. gr. of whole blood</td>
<td>1-036 ±0-3</td>
<td>1-050 ±0-4</td>
</tr>
<tr>
<td>Sp. gr. of blood plasma</td>
<td>1-018 ±0-2</td>
<td>1-018 ±0-2</td>
</tr>
<tr>
<td>Plasma proteins g./100 ml.</td>
<td>4-1 ±0-2</td>
<td>4-1 ±0-2</td>
</tr>
</tbody>
</table>

Blood sugar mg. per cent = 3.5 times ambient temperature in °C., + 4-4 (valid from 32 to 48° C.).
Thermoglycæmia in Pigeons

DISCUSSION

The chick is potentially homoiothermic at hatching, but upon exposure to temperature extremes reverts to a poikilothermic state [Randall, 1943]. Pigeons were subjected to short exposures of high ambient temperature in chambers sufficiently ventilated to exclude much changes in humidity and their rise of body temperature and of blood sugar level was similar to that of new-born mammals [Chaudhuri and Sadhu, 1960]; under these conditions there is neither any change in body temperature nor in blood sugar level in the adult pigeon. This similarity of behaviour in the ability to regulate body temperature over a narrow range of air temperature between the birds and the baby mammals shows that the birds, although homiothermal, are so only in a narrow range (stenothermal) and not in a wide range (not eu-thermal) as in the adult mammals. It appears that in the gradual evolution of stages from poikilotherm, heterothermal and (stenothermal and eu-thermal phases of homoiothermal), the stenothermal phase is an obligatory one in the ontogenetic evolution of thermoregulation, at which stage the birds have stopped, while the mammals have evolved into the final eu-thermal phase of homoiothermal stage.

Rodbard [1947], and 1951) demonstrated that the blood pressure response to body temperature change is mediated directly by the central nervous system, while blood sugar response is dependent upon a more complex, slowly mobilized mechanism and predicted an integrating role of the central nervous system in this response. In our present experiments and those on baby rabbits [Chaudhuri and Sadhu, 1960], there is a greater correlation of the thermoglycæmic response with the rise of ambient rather than of the rectal temperature, as shown by greater slopes of the former and this indicates that the hypothalamus is stimulated more effectively by the peripheral thermoreceptors than by the blood temperature. The hyperglycæmia is not due to haemoconcentration, as the hematocrit value and specific gravity of the blood remain relatively constant. The effect is not likely to be due wholly to disturbance in the utilization of sugar within the short periods of 2 hr., although this point has not been clarified by studies on the arterio-venous sugar difference. The hyperglycæmia is also not likely to be due to sampling as the wing veins of the birds were exposed by clipping of the feathers on the day previous to the experiment and the birds are handled gently at the time of exposure and of drawing of blood samples so as to prevent the development of any abnormal emotional state.

Most of the adrenergic blocking agents diminish or block many of the excitatory effects of epinephrine by being adsorbed onto liver cells and thus prevent epinephrine from stimulating glycoegenolysis. Ergot alkaloids are quite active in preventing epinephrine-induced hyperglycæmia [Komrad and Lowe, 1951]. From the results obtained after treatment with Ansolysen and ergotamine tartrate, it is clear that there is a greater mobilization of glucose from the liver as a result of increased adrenergic activity at the high ambient temperature. There is no appreciable thermal tachycardia after
these blocking agents. The thermoglycaemic response, tachycardia and hyperthermia may be interpreted to be mediated by the adrenergic system.

The temperature characteristic $\mu$ in calories is studied at two different temperatures to investigate if there are different "master reactions" at these points and also to find out if the proposition that changes of ambient temperature may affect the $\mu$ value as in vivo experiments [Brody, 1945]. The similarity of the two $\mu$ values does not indicate different master reactions and from the low values of the temperature characteristic, it cannot be concluded that ambient temperature affects these master reactions in the same way as in the in vitro tissue slice experiments [Sadhu, 1945].

ACKNOWLEDGMENTS

The authors are grateful to Lt.-Col. J. M. Lahiri, Director of Veterinary Services and Animal Husbandry, West Bengal and to Principal S. C. Mukherjee for their interest and advice.

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Role of adrenergic system in thermoglycemic response in baby rabbits

SUKHEN CHAUDHURI AND D. P. SADHU
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Pigeons are homeothermic under conditions of small changes in the ambient temperature but when subjected to higher room temperature, the body temperature rises, with an increase of blood sugar level (1). A similar increase in blood sugar has been observed in other birds and is called thermoglycemic response (2). Baby rabbits show a defective regulation of body temperature (3). In view of the defective thermoregulation in birds and baby rabbits and of the current interest in hypothermia (4) it was thought desirable to investigate whether the latter animals also show a thermoglycemic response and, if so, the mechanism of this response. An attempt has been made in the present investigation to study the mechanism of the thermoglycemic response and some aspects of the role of the adrenergic system in this response in baby rabbits.

EXPERIMENTAL METHODS

Baby rabbits, each weighing 300-400 gm, were housed in individual cages in a room with an average ambient temperature of 32°C. Body weight was measured, rectal temperature determined by clinical thermometer and heart rate by an electrocardiograph. Plasma cell ratio of blood was measured by hematocrit, erythrocytes and leucocytes enumerated by Thoma-Zeiss hemocytometer, blood hemoglobin determined in a Klett-Summerson photoelectric colorimeter, specific gravity of whole blood, plasma and the concentration of plasma proteins determined by copper sulfate method (5). Sugar was estimated from ear vein blood by a modification of the Somogyi's reagent no. 2 and by the use of a

<table>
<thead>
<tr>
<th>TABLE 1. Physiological Effects of Subjecting Baby Rabbits Housed at 32°C to a High Ambient Temperature of 42°C or 45°C for a Period of 2¼ Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
</tr>
<tr>
<td>Body weight, gm</td>
</tr>
<tr>
<td>Rectal temperature</td>
</tr>
<tr>
<td>Heart rate/min.</td>
</tr>
<tr>
<td>Erythrocyte, million/cm³</td>
</tr>
<tr>
<td>Leucocyte, thousands/cm³</td>
</tr>
<tr>
<td>Hemoglobin, gm/100 ml blood</td>
</tr>
<tr>
<td>Hematocrit</td>
</tr>
<tr>
<td>Specific gravity of blood</td>
</tr>
<tr>
<td>Plasma proteins, gm/100 ml</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE 2. Glucose Levels of Baby Rabbits Housed at 32°C and Exposed to High Ambient Temperature of 42°C or 45°C for a Period of 2¾ Hours*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambient temperature</td>
</tr>
<tr>
<td>Control</td>
</tr>
<tr>
<td>Ansolysen</td>
</tr>
<tr>
<td>Ergotamine</td>
</tr>
</tbody>
</table>

Blood sugar mg % = 3.4 times ambient temperature in °C. * With and without treatment with the ganglion-blocking agent Ansolysen (M.B.) at 0.4 mg/kg b.wt. or the adrenergic-blocking agent ergotamine tartrate, 0.4 mg/kg b.wt.
weaker (0.002 n) thiosulfate solution which resulted in an increased sensitivity of the method (6, 7). In series 1, 40 rabbits were used and the enumerated data collected; then they were divided into two groups, one being placed at 42°C and the other at 45° for 2½ hours and all data were collected again. In series 2 a ganglion-blocking agent, Ansolysen brand pentolinium tartrate (M & B 2050A) which is pentamethylene-1,5-bis(1-methyl-pyrrolidinium) hydrogen tartrate, and in series 3 an adrenergic blocking agent, ergotamine tartrate, 50 µg/kg body weight were used and their effects on blood sugar were studied in rabbits, both at normal and higher ambient temperatures. The optimum dose of Ansolysen at which complete blockade of ganglia occurs was determined from the effect on the electrocardiogram to a known tachycardiac dose of epinephrine. A 0.4-mg dose of Ansolysen, injected intramuscularly per kilogram body weight, made complete blockade for 1½ hours and a second similar dose after this period maintained the block for another period of 1½ hours.

RESULTS AND DISCUSSION

In series 1 the results of subjecting the baby rabbits to 42° to 45°C on their body weight, rectal temperature, heart rate and blood composition are presented in table 1. There was a slight increase in rectal temperature of the rabbits at higher ambient temperature, although the rise was not proportional to the ambient temperature, while tachycardia at the higher temperature was out of proportion to the hyperthermia. The hematocrit value did not show any significant difference, nor the specific gravity of whole blood, of blood plasma or the concentration of blood proteins. With this high ambient temperature on the nervous system, the thermoregulatory response, and these effects, along with the biochemical evidences on tissue respiration (4), might possibly be due to defective thermoregulation in baby rabbits.

The authors express their thanks to Lt. Col. J. M. Lahiri, Director of Veterinary Services and Animal Husbandry, West Bengal, and to Dr. K. C. Mukerjee, Principal of the Bengal Veterinary College for their interest. Thanks are also due to May & Baker (India) Ltd., for supply of Ansolysen used in this investigation.

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