

MATERIALS AND METHODS

The present study was conducted on 15 healthy young dogs of either sex with body weights ranging between 2-4 kg. Their ages ranged from two to four months. The animals were fasted for ten hours prior to the experiment. In all the animal the rectal temperature was recorded and was found to be $38.5 \pm 0.5^\circ\text{C}$. They were anaesthetized by injecting freshly prepared solution of pentobarbital sodium (NEMBUTAL) intraperitoneally in dosage of 30 mg/kg body weight.

The blood samples were collected from inferior venacava by a thin polyethylene tube passed into it through femoral vein. Dry syringes were used for collection of blood.

The body temperature of each animal was raised by keeping them in a specially designed wooden cabinet fitted with a hot air blower and a regulator for controlling temperature. The deep body temperature was periodically recorded by a rectal thermometer.

The experimental animals were divided into two groups, where each animal served as its own control.

Group—I : Comprised of 10 young dogs weighing between 2-4 kg. After estimating control blood glucose level, each animal was subjected to hyperthermia till the rectal temperature was raised to 40.5°C and was maintained for 2 hours at this temperature. At the end of second hour two blood samples were drawn for blood glucose estimation. Then the rectal temperature was raised to 42.5°C and maintained for further two hours, at the end of which the blood samples for glucose analysis were collected.

Group—II: Consisted of 5 young dogs weighing between 2-3.5 kg. The intravenous glucose tolerance test was conducted in each animal under normothermic condition, by injecting 25% sterile solution of glucose (1 gm/kg) rapidly. On the fourth day glucose tolerance test was repeated in the same animal after inducing hyperthermia till the rectal temperature was raised to 42.5°C . In both these series of experiments, serial blood samples were withdrawn at 2, 5, 15, 30, 45, 60, 90 and 120 minutes for determination of blood glucose by the technique of Sharma *et al.* (10).

The results of intravenous glucose tolerance test were evaluated by determination of the rate of disappearance of glucose according to the first order reaction as described by Allen *et al.* (2).

$$\text{Thus, } Kt = \frac{2.303}{T_2 - T_1} \log \frac{C_1}{C_2}$$

Where C_1 is the blood glucose concentration at time T_1 , C_2 is a latter concentration at time T_2 and Kt is the fractional rate of disappearance of glucose per minute. The rate is expressed as $Kt \times 100$ rate of disappearance, percent/minute.

RESULTS

Group—I : (Table-I) The blood glucose level in ten normothermic dogs averaged 75.4 ± 2.8 mg/100 ml. This value at 40.5°C decreased significantly ($P < 0.0025$) to a mean of 62.4 ± 1.8 mg/100 ml. On raising the rectal temperature to 42.5°C , the blood glucose concentration were further decreased significantly ($P < 0.0005$) to a mean of 52.5 ± 1.7 mg/100 ml in these dogs.

Group—II : Table 2 shows the hyperglycemic responses to a rapid intravenous glucose load given at normal body temperature ($38.5 \pm 0.5^\circ\text{C}$) and at a body temperature of 42.5°C in 5 dogs.

The mean control blood glucose level in normothermic animals was 75 ± 3.2 mg/100 ml. Following the administration of glucose, it increased to a peak average value of 311 ± 15.9 mg/100 ml within 2 minutes, which slowly returned to preinjection level in about 60 minutes and remained steady at this level upto 120 minutes.

At 42.5°C the blood glucose level in these five dogs was observed to be 57 ± 2.5 mg/100 ml prior to administration of glucose. The peak value reached 241 ± 11.3 mg/100 ml at 2 minutes following the injection of intravenous glucose. After this, the blood glucose declined to preinjection level in 45 minutes. On comparison of the two responses at 38.5°C and 42.5°C respectively (Fig. 1), it was observed that blood glucose level was significantly lower in young dogs at 42.5°C ($P < 0.0025$). The peak value at 2 minutes as well as the blood glucose concentration at 5, 15, 30, 45, 60, 90 and 120 minutes after administration of intravenous glucose were also found to be lower 42.5°C as compared to those observed at 38.5°C . Moreover, it was observed that return to preinjection level was quicker (45 minutes) at 42.5°C , as compared to (60 minutes) at normal body temperature.

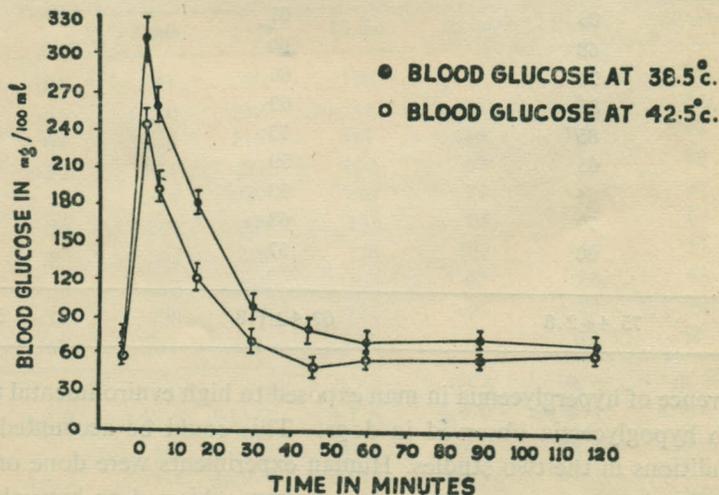


Fig. 1 : The time course of hyperglycemic response following intravenous injection of glucose (1 gm/kg) at normal (38.5°C) and at 42.5°C body temperature. The glucose injection was given at 0 time. Mean values and their standard errors of plasma glucose concentration of 5 dogs are plotted.

The calculated fractional rates of disappearance of glucose at 38.5°C and 42.5°C were 2.11 ± 0.1 percent/minute and 2.87 ± 0.3 percent/minute respectively. The rise in Kt value at 42.5°C was found to be highly significant ($P < 0.0025$).

DISCUSSION

Blood glucose concentrations decreased significantly when the anaesthetized young dogs were subjected to hyperthermia. Similar findings were reported by Kanter (6) in unanaesthetized dogs. He attributed this fall of blood glucose to an increased utilization of glucose by the respiratory muscles used in panting to regulate body temperature. In a later study Kanter (7) has reported that the fall in blood glucose level in dogs exposed to heat was not due to an insulin action which might be responsible for the increased utilization of glucose by the respiratory muscles. However, in our study two hyperthermic body temperatures were achieved viz. 40.5°C and 42.5°C. Panting was absent at 40.5°C, yet hypoglycemia was observed at this temperature (Table-I). Further, the anaesthetized animals used by us showed only mild panting at 42.5°C, but the blood glucose concentration in them fell considerably. Thus it seems likely that a generalized enhanced cell metabolism is responsible for an increased utilization of glucose during hyperthermia rather than the respiratory muscles alone.

TABLE I : Blood glucose concentrations at different body temperatures.

| S. No. | Blood glucose concentration — (mg/100 ml) | | |
|----------------|---|----------------|----------------|
| | 38.5°C | 40.5°C | 42.5°C |
| 1 | 86 | 63 | 51 |
| 2 | 86 | 61 | 56 |
| 3 | 68 | 60 | 52 |
| 4 | 73 | 66 | 50 |
| 5 | 80 | 69 | 54 |
| 6 | 85 | 73 | 61 |
| 7 | 65 | 59 | 48 |
| 8 | 64 | 53 | 44 |
| 9 | 79 | 63 | 60 |
| 10 | 68 | 57 | 49 |
| Mean \pm SEM | 75.4 \pm 2.8 | 62.4 \pm 1.8 | 52.5 \pm 1.7 |

The occurrence of hyperglycemia in man exposed to high environmental temperatures may seem contrary to hypoglycemia observed in dogs. This could be accounted for by different experimental conditions in the two studies. Human experiments were done on unanaesthetized subjects whereas the dogs were anaesthetized and then subjected to hyperthermia. Thus the factor of stress which normally would accompany heat exposure in unanaesthetized subjects would

not be operating in the dogs. Heat stress is likely to stimulate the production of adrenal corticoids and catecholamines. Both these agents will produce hyperglycemia. Adrenal glucocorticoids may not be very important in this respect during short term acute heat exposures, since they produce hyperglycemia by enhancing gluconeogenesis which is not a very quick process. However, release of catecholamines must be playing the major role in production of hyperglycemia since inhibition of glucose uptake by epinephrine has been reported (3). Moreover man shows profuse sweating due to heat whereas the dog is devoid of active sweat glands. The profuse sweating in man could result in hemoconcentration which could also contribute a little toward production of hyperglycemia.

The possible mechanism involved in production of hypoglycemia during hyperthermia be an increased secretion of insulin and/or enhanced sensitivity of tissues to insulin.

Our results indicate the possibility of an increase in release of insulin during high body temperature, resulting in an increased over all utilization of glucose by the peripheral tissues. This is supported by the calculated Kt values (fractional rate of disappearance of glucose/minute) which were significantly higher ($P < 0.0025$) in animals subjected to hyperthermia. Since the increased rate of uptake of glucose by the peripheral tissues to a great extent is mediated by an increased insulin secretion, the Kt value may be taken as an index of insulin secretion. Thus hypoglycemia would result in dogs exposed to hyperthermia due to increased insulin action.

Further, the results of intravenous glucose tolerance tests performed at normal and high temperature also favour the possibility of an elevated insulin secretion in the latter condition.

TABLE II : Blood glucose concentration (mg/100 ml) before and after glucose administration (1 gm/kg).

| S. No. | Body Temp. °C | Control | Blood glucose concentrations at specific times post injection | | | | | | | |
|-------------|---------------|---------|---|--------|---------|---------|---------|---------|---------|----------|
| | | | 2 min | 5 min. | 15 min. | 30 min. | 45 min. | 60 min. | 90 min. | 120 min. |
| 1 | 38.5 | 84 | 344 | 288 | 186 | 87 | 67 | 63 | 68 | 83 |
| | 42.5 | 65 | 280 | 218 | 141 | 52 | 31 | 32 | 48 | 51 |
| 2 | 38.5 | 67 | 256 | 216 | 167 | 118 | 100 | 78 | 55 | 50 |
| | 42.5 | 54 | 224 | 174 | 110 | 60 | 44 | 69 | 66 | 69 |
| 3 | 38.5 | 75 | 314 | 267 | 210 | 84 | 50 | 50 | 63 | 58 |
| | 42.5 | 59 | 247 | 206 | 131 | 83 | 54 | 57 | 60 | 63 |
| 4 | 38.5 | 80 | 343 | 278 | 178 | 100 | 108 | 91 | 100 | 95 |
| | 42.5 | 50 | 217 | 201 | 103 | 87 | 74 | 69 | 61 | 58 |
| 5 | 38.5 | 69 | 298 | 239 | 171 | 97 | 73 | 70 | 68 | 60 |
| | 42.5 | 57 | 237 | 161 | 123 | 75 | 61 | 65 | 57 | 55 |
| Mean 38.5°C | | 75 | 311 | 257 | 182.4 | 97.2 | 79.6 | 70.4 | 70.8 | 69.2 |
| ±SEM | | ±3.2 | ±15.9 | ±13.2 | ±7.6 | ±6.0 | ±10.7 | ±6.9 | ±7.6 | ±8.4 |
| 42.5 °C | | 57 | 241 | 192 | 121.6 | 71.4 | 52.8 | 58.4 | 58.4 | 59.8 |
| | | ±2.5 | ±11.3 | ±10.4 | ±6.8 | ±6.6 | ±6.1 | ±5.2 | ±2.9 | ±3.1 |

A higher rate of disposal of exogenous glucose was observed in animals subjected to hyperthermia (Fig. 1). Also, the maximum increment in blood glucose level following an intravenous injection of glucose was significantly less in dogs subjected to hyperthermia than that observed in them during normothermia. The return of plasma glucose concentration to control level was also faster being 45 minutes in hyperthermic dogs as compared to 60 minutes in normothermic animals. Thus faster rate of disposal of glucose evidenced by high Kt values suggests an increased output of insulin in hyperthermic dogs.

However, the possibility of an increased sensitivity to insulin acquired by the peripheral tissues under the effect of heat, though unlikely, cannot be ruled out completely and is worth investigating.

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