SURVIVAL OF HYPOTHERMIA BY THE DOG * †

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THE possibility of maintaining a low body temperature for prolonged periods has been investigated as a means of reducing the metabolism in dogs. Though it was found that the dog could not be kept alive for long periods in this way, the responses of the tested animals were of such interest that experiments were carried out to learn something of the limits of endurance of the dog to low body temperatures, and better to define the limiting factors.

Although there are reports of the lowest body temperatures which various mammals can withstand, little has been found concerning the length of time they will survive at these temperatures. As early as 1862, Walther (1), using no anesthesia, lowered the temperature of rabbits to 68 F. This, he felt, was the lowest safe temperature, and even here recovery was not possible without the application of heat. He succeeded in keeping some alive, partially paralyzed by the cold, for as long as twelve hours.

Simpson (1902, 2) etherized 4 monkeys and lowered their temperatures by placing them in a cold chamber. Two animals died when they reached 54 F.; a third momentarily cooled to 57 F. survived, and was to all appearances normal during the ensuing month of observation. Simpson later reported (1905, 3) that in cats no anesthetic was necessary below 75 F., which he believed was the temperature at which the heat-regulating mechanism ceased to function. He also noted the feeble respirations that ceased before the slow heart beat when the temperature fell below 60.8 F. Britton (1922, 4) working with cats, observed that cooling induced a progressive paralysis of the central nervous system. He found 60.8 F. to be the lowest at which they could live, though animals subjected to this temperature were unable to recover spontaneously. Wiesner (1934, 5) used hypothermia as an anesthetic for the castration of newborn rats. He placed the rats in the coils of a refrigerator until their temperatures were about 35 F., and found no ill effects from this method. Hamilton (1937, 6) found that levels of 54–62 F. were lethal for rats, the variation being dependent upon the rate of cooling and the idiosyncrasies of the individual. No anesthesia was necessary for reducing the body temperature, perhaps because of the minimal shivering reaction that rats exhibit.

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METHODS

Thirteen experiments were carried out on 11 dogs. In each case the animal was given an intravenous injection of nembutal, 25 mg./Kg. of body weight. A thermocouple was then inserted 20 cm. into the rectum of males and the same distance into the horn of the uterus in females. The dog was placed in a room with constant temperature at about 40 F. Ice was packed around the animal, and the body temperature recorded at five minute intervals. When the body temperature had fallen to the desired level, the dog was removed from the ice pack, dried, and allowed to lie on a table in the temperature-regulated room. In order to keep the dog's body temperature within a certain range, the room temperature was raised or lowered as necessary. Its body temperature, pulse, respiration, and general behavior were then observed at frequent intervals.

To indicate the value of the uterine temperatures in portraying the general body temperature, thermocouples were placed at various points in a dog (no. 2) immediately after death. The results obtained were as follows: uterine temperature at death was 72 F.; subcutaneous tissues at autopsy, 71 F.; abdominal musculature, 71 F.; peritoneal cavity, 72 F.; spleen parenchyma, 70.7 F.

The intra-arterial blood pressure was continuously recorded over a period of several hours in 4 dogs (nos. 10, 11, 12, and 13). This was done by a direct mercury manometer system into which a 2½ per cent sodium citrate solution under high pressure was allowed to drip very slowly. Clotting could be avoided by admitting less than 10 cc. of citrate per hour. Oxygen consumption of 2 dogs (nos. 7 and 9) was measured by connecting an endotracheal catheter, expanded to fit tightly in the trachea, to a Benedict-Roth metabolism machine. In this way, continuous recordings were taken for two hour periods. As an indication of blood concentration changes, the specific gravity of the blood was determined at frequent intervals by the falling drop method of Barbour and Hamilton. Blood sugar determinations were made on 4 dogs (nos. 7, 8, 12, and 13) at two hour intervals by the micro method of Hagedorn and Jensen. Blood chloride and carbon dioxide determinations were also made on 4 dogs (nos. 8, 9, 10, and 13) at two hour intervals.

Respiratory failure, which occurred in some dogs, was treated by artificial methods for resuscitation, including intravenous metrazol, ammonia inhalations, or dilatations of the rectal sphincter. In other dogs the heart failed and intracardiac adrenaline was used. Several dogs whose blood pressure fell to very low levels were given normal saline or 5 per cent glucose intravenously. In 2 dogs (nos. 12 and 13), oxygen was given intratracheally throughout the experiment. Two *in extremis* were given digifoline 0.2 cat units/kilo intravenously.

Dogs nos. 2 and 9 survived deep cooling and were resubmitted to the procedure two and three weeks later, respectively.

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RESULTS

Table 1 shows the temperatures to which the dogs were subjected and the duration of the experiments. In the 13 experiments performed, 8 dogs died. The survival time varied widely, the longest for any dog being twenty-six hours, and the shortest one-quarter hour, with an average of about seven hours. The lowest body temperature which an animal survived was 72 F., and all of the deaths occurred within the range of 72–78 F. It was found that the dogs began to shiver between two and four hours after the nembutal had been administered, presumably as its influence began to wear off, unless their body temperature was below 82–84 F. The shivering, once started, could not be controlled, nor could

TABLE 1

Dog No.	Sex	Hours Below 82 F.	Lowest Temperature F.	Duration of Experiment. Hours	Remarks
1	M	1¼	73.6	2	Died
2	F	2	78.2	12	Survived. Rectal temperature
2	F	¼	72.0	1¼	Died. Same dog as previous experiment
4	F	5	72.3	6	Died
5	F	13¾	74.6	14½	Died
6	F	6½	77.0	7½	Survived
7	F	26	72.5	27	Died
8	F	5	72.0	5¾	Died
9	F	7¼	77.5	7¼	Survived
9	F	5½	73.4	7¼	Died. Same dog as previous experiment
11	F	1¾	78.0	2¾	Died
12	F	10	73.8	11½	Survived
13	F	10½	73.4	13	Survived

the body temperature be lowered by ice packs unless additional nembutal was given. Four dogs died during the initial lowering of their temperature to 75 F., but two of these were undergoing the procedure for the second time. Figures 1–3 give data characteristic of 3 representative dogs, together with the blood sugar and specific gravity determinations. Figures 2 and 3 also show the blood pressure readings.

Within the body temperature range of 72–82 F., the dogs all presented a similar picture. They lay perfectly quiet, relaxed, with eyes open and pupils moderately dilated. Reflexes were difficult to elicit, and in some cases the corneal reflex was absent, although the animal later recovered. Nociceptive stimuli were ineffective, and such procedures as cutting down on an artery did not stimulate the animal. Respirations were slow, shallow, and gasping or sighing in character.

The respiratory rate, following an initial increase as the ice packs were applied, fell rapidly with decrease in the body temperature so that at 80 F. the rate averaged 9 per minute, while at 75 F. it averaged only 4½ per minute. In 3 cases the respirations were maintained at between

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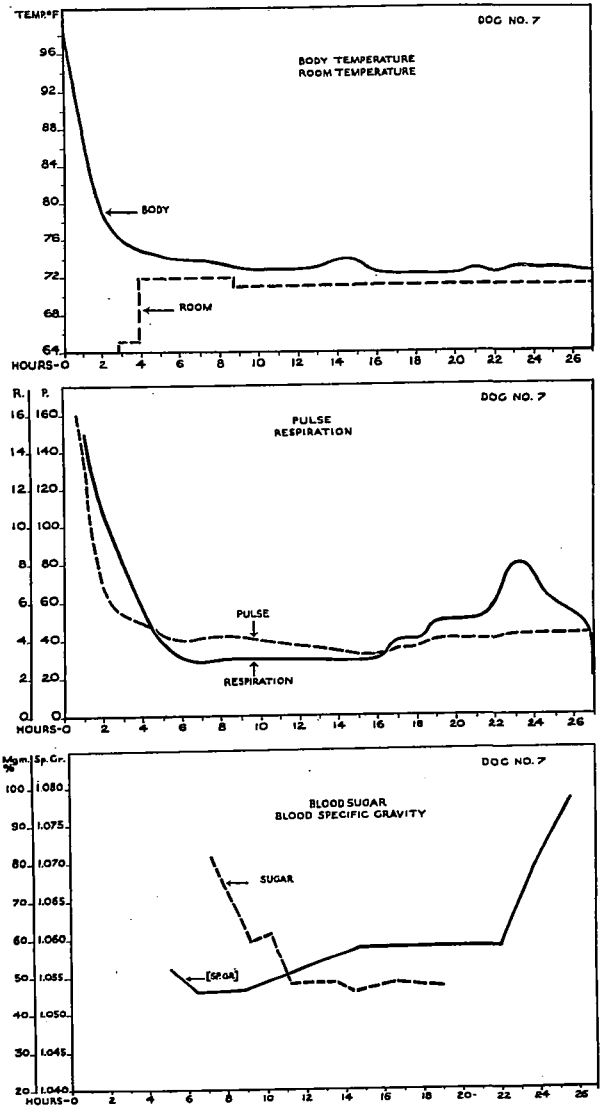

FIG. 1. Effects of hypothermia on a nembutalized dog.

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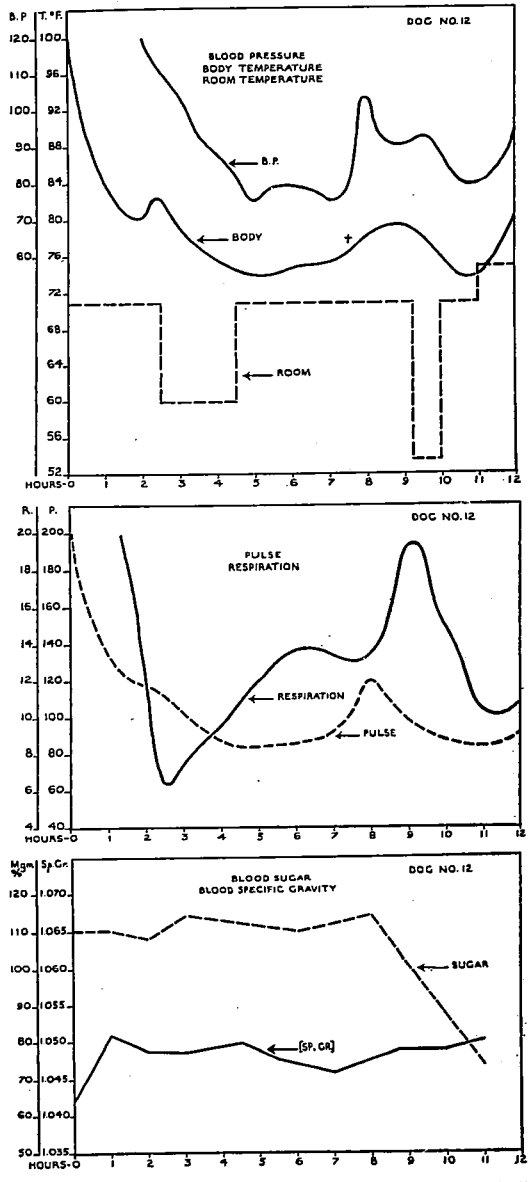

FIG. 2. Effects of hypothermia on a nembutalized dog. † digifoline.

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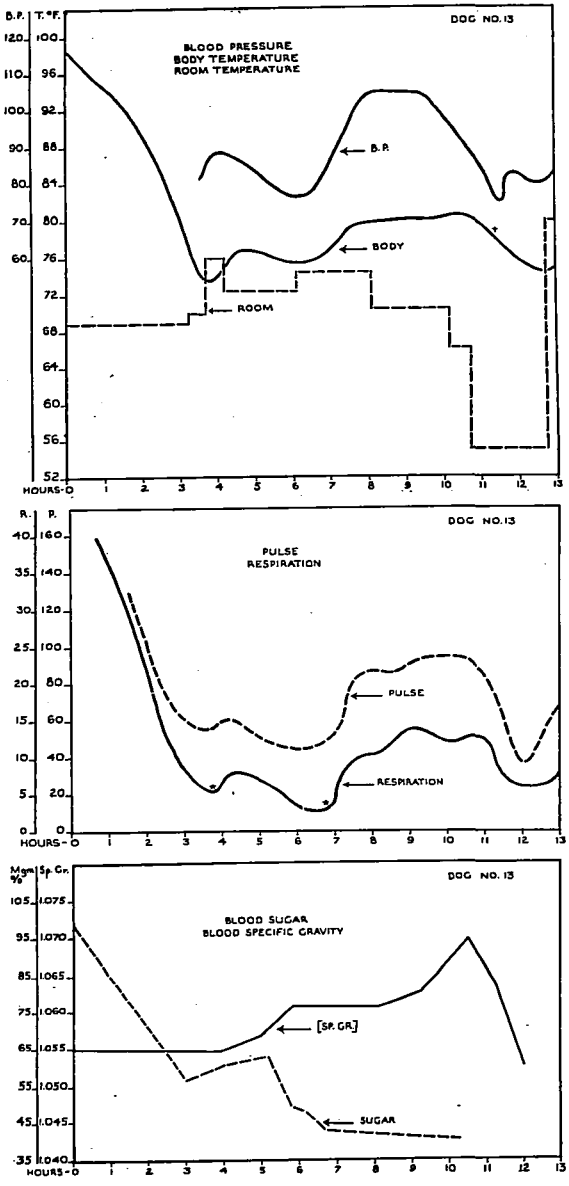

FIG. 3. Effects of hypothermia on a nembutalized dog. †Digifoline. * Respiratory failure.

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2 and 3 per minute for more than four hours. At the same time, the volume of each respiration and the tidal air fell, being recorded at 12.5 cc./kilo at a body temperature of 82 F., and at 11 cc./kilo at 73 F. On nine occasions respirations ceased quite suddenly, but in most instances could be started again by artificial methods and would then continue for several hours. When the respirations were 3 per minute or less, the blood usually became dark in color and the mucous membranes cyanotic. As this often preceded the respiratory failure, it was thought that anoxia of the respiratory centers might be responsible. Accordingly, oxygen was administered to 2 dogs throughout the procedure, but without effect since two respiratory arrests occurred.

The pulse and blood pressure decreased rapidly with the fall in body temperature and remained at low levels while the dog was inactive. Any increase in the body temperature was quickly and markedly reflected in an increased pulse and blood pressure. Though the pressure might remain at less than 75 mm. Hg for several hours, the pulse, with one exception (dog no. 13) remained slow with a good pressure. If then the animal's body temperature rose to normal levels, its blood pressure and pulse also returned to normal.

In certain dogs the blood pressure failed to level off as the low body temperature was reached, and continued to fall until it reached extremely low values. In one instance (dog no. 10) it was recorded at the astonishingly low pressure of 40 mm. of water, with a slow, steady pulse. It was found that these dogs, if untreated, would die after a short period; accordingly digifoline (.2 cat units/kilo) was given to 2 animals that appeared *in extremis*, with pressure dropping rapidly. Prompt, definite recovery occurred in each case, with a rise in blood pressure and improvement of the peripheral circulation, going on to complete recovery although the room temperature was not raised.

The specific gravity of the blood was followed in 6 dogs. It was found in general to rise sharply for the first few minutes and reach a plateau which was maintained, except for a terminal rise. This blood concentration indicates the persistence, in spite of cooling, of a reflex which has been shown (7) to be mediated by the central nervous system, more particularly by the hypothalamus. One animal (no. 13) went into shock after ten hours and showed a second sharp increase in concentration beyond the initial rise.

The blood sugar was determined at intervals in 4 dogs. In two (nos. 7 and 13) the sugar fell from above 100 mg. per cent to about 45 mg. per cent, one (no. 13) reaching this level in seven hours, while the other reached it only after eleven hours. However, no hypoglycemic convulsions were observed. In another dog (no. 12) the control level of 100 mg. per cent persisted unchanged until the eleventh hour, when it fell to 72 mg. per cent. This dog recovered shortly afterwards. The fourth (no. 8) dog's blood sugar dropped sharply during the fifth hour to reach 78 mg. per cent just before death.

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The blood chloride and carbon dioxide determinations (Table 2) made on 4 dogs showed no abnormal variations.

The oxygen consumption was measured on 2 dogs (nos. 7 and 9). Dog no. 9, while its body temperature remained between 82–83 F., consumed 1,630 cc. of oxygen in one hour. If an R.Q. of .83 is assumed and the Meeh formula for surface area is used, with Rubner's constant (.112) for the dog, the metabolism is computed at 10.8 cal./sq.m./hr. Dog no. 7, while maintained at a body temperature ten degrees lower, i.e., 73 F., consumed only 850 cc. of oxygen in one hour. Calculated in the same manner, this represents a metabolism of 6.5 cal./sq.m./hr.

TABLE 2

Dog No.	Blood Chlorides mg. Cl/100 cc.	Blood CO_2 Vol. %	Hours below 82 F.
8	385	46	Normal
	425	47	5
9	380	48	Normal
	364	52	1
	385	54	6
	380	50	7¼
9(2)	405	40	1½
	402	42	2½
	402	43	3½
13	394	48	Normal
	373	50	1
	349	52	3¼
	349	52	5½
	373	48	7¼

Since this is a difference of 5.5 C. between these observations, the temperature coefficient of change in this range is quite consistent with the coefficient (for 10 C. rises) of 2 to 3 required by van't Hoff's law. It also accords with results in curarized dogs as well as for cold blooded animals. The protective reflexes mediated normally by the central nervous system (especially the hypothalamus) thus become quite ineffective or absent, as a result of the depressant action of nembutal, reenforced and perhaps substituted entirely by cooling of the nerve cells.

Marked dilatation and flabbiness of the heart was characteristic of the 8 dogs that succumbed during refrigeration. The dilatation was evident when, on incising the confining pericardium, the heart quickly expanded to almost half again its usual size. No changes other than edema were seen in the histological sections. One dog (no. 5) showed evidence of acute pulmonary edema. The lymphatic trunks of the abdominal cavity in all dogs dying during the experiments showed engorgement, which was very marked in three instances. Two dogs (nos. 6 and 12) were kept alive for two weeks following the procedure, and in

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these no pathological changes were demonstrated. The brain was examined in 5 cases and showed no gross or histological changes, either in those dying acutely or in those who were autopsied two weeks after the experiment. These findings may be reasonably interpreted as representing an acute failure of the myocardium, the edema and engorgement of the abdominal lymphatics resulting from increased venous pressure.

COMMENTS

Lowering the body temperature of dogs without the use of anesthetics is presumably impossible by ice packs until the dog has exhausted itself by shivering, but it was found that if the animal was anesthetized until the body temperature fell below 78–82 F., shivering did not occur, even after many hours, and the animal remained in a deeply anesthetized state, due finally to cold alone. If, however, the body temperature was allowed to exceed 78–82 F. three hours or more after nembutal had been given, the animal would start to shiver and bring his body temperature to normal within a few hours, despite added ice packs. Thus, an internal temperature of about 80 F. appears to be critical for the function of heat regulation.

Every method of supportive therapy which seemed indicated was employed, but the average time the dogs lived during the experiments was only seven hours, with a maximum of twenty-six hours. To keep dogs at body temperatures between 72 and 82 F. for very extended periods, therefore, seems impossible. The fall of pulse, respiration, and blood pressure, and the flabby heart found at autopsy, all militate against such an outcome.

The anoxemia which occurs with the fall of pulse and respiratory rate to very low levels is not the only deciding factor in the short survival time of the dog, because continuous oxygen administration, though it prevents the cyanosis, causes no appreciable change in the general course. The respiratory failure which plays such a prominent role, occurring nine times in the 13 experiments, also is not due directly to anoxia.

Although the blood pressure remained at 75 mm. of mercury for several hours at a time, only one of 11 dogs went into shock. Usually there was a slow, steady pulse, good peripheral circulation, and with any increase in body temperature, a prompt, rapid rise in blood pressure occurred.

When a terminal fall in blood pressure seemed in progress, intravenous 5 per cent glucose or normal saline caused no more than a very temporary improvement, and if the cold was continued the dogs died, either of respiratory or heart failure. Guided by the previous autopsy findings of a flabby dilated heart, pulmonary edema, and dilated lymphatics, digifoline was administered intravenously in two instances. A marked beneficial effect was noted with a rapid rise in blood pressure and pulse pressure, and improvement in the peripheral circulation.

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The initial rise in blood specific gravity results reflexly from the shift of fluid to within the cells as a part of the physical attempt at heat regulation. In spite of progressive cooling of the nervous tissue, the resulting increase in concentration of the blood is maintained. The terminal superimposed rise is probably a result chiefly of a new fall in the circulating blood volume (8) from water loss to the tissues, due perhaps in large part to increased capillary permeability throughout the body.

The fall in blood sugar in each of 4 animals could hardly represent depletion of the glycogen stores in such short periods. All the evidence points rather to a marked reduction in the glucose requirements of the tissues associated with retardation of glucose mobilization.

The metabolism was strikingly reduced, as shown by the very low oxygen consumption. Since this could be followed continuously up to two hours at a constant body temperature, and the animals had had an opportunity to become stabilized for long periods before readings were taken, the temperature of all the organs must have been close to the recorded temperature. The readings must, therefore, represent a close approximation to the true metabolic rate of uncontrolled cells at the temperatures observed. The small difference in temperature between the room and the animal was confirmatory of the low metabolic activity. Thus one dog (no. 7) was maintained for twelve hours at 73 F. by a room temperature which was only two degrees lower than his body temperature.

SUMMARY

From data derived from a series of experiments involving the subjection of dogs to low temperatures for prolonged periods, the following points may be summarized:

1. Dogs are unable to survive hypothermia sufficiently long to make protracted metabolic studies feasible.
2. The lowest body temperature at which a dog survived was 72 F., all of the animals dying between this point and 78 F. Between these limits the survival time varied from one-quarter hour to twenty-six hours and averaged about seven hours.
3. Respiratory failure was a frequent cause of death and could not be prevented by oxygen therapy.
4. Circulatory failure occurred in all dogs that avoided respiratory failure. It was associated with cardiac dilatation, loss of tone, and anhydremia.
5. Digitalis apparently was effective for some hours in preventing circulatory failure and, in fact, appeared to be the most effective of any procedure in prolonging life.
6. Even at very low temperatures, no significant changes were found in the blood content of chloride or CO_2. A trend toward hypoglycemia was, however, apparent.

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7. The metabolic rates observed in 2 dogs showed the direct effects of internal cooling and suggested the complete loss of protective heat producing reflexes.

8. Blood concentration showed two marked increases, initial and terminal, attributable respectively to normal protective reflexes and to increased capillary permeability, as in shock.

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