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The Survival Period Of Salt Treated And-Salt Treated Adrenalectomized Rats Under Normal And Abnormal Conditions

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BY

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Biographical Sketch

Hubert L. Mitchell, Jr., was born July 26, 1928, in Daingerfield, Morris County, Texas. He attended both grade and high school in Daingerfield, Texas, and graduated from Rhoad's High School in May, 1946. In September, 1946, he entered Prairie View A. & M. College, where, after four years of study, he received the B. S. degree in Biology in August, 1950.

In October, 1950, he was called into the Armed Services to serve in the Korean Conflict. In September, 1952, after an honorable discharge from the Armed Services in August, 1952, he entered graduate school at Prairie View A. & M. College to pursue the M. S. degree in Biology.

His major interest is science and scientific research, which may enable science to better serve humanity.

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DEDICATION

To My Wife

(Mrs.) Robbie Jewel Mitchell

This Thesis Is Gratefully Dedicated

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INTRODUCTION

Guinevere and Oscar observed (1944) that heat production is maintained at a normal level in the absence of medullary adrenal tissue, but the effects of loss of the cortical tissue on heat production are not entirely clear. Most reports indicate that in mammals the loss of cortical hormones leads to an early decrease of the metabolic rate. It has been reported by Grollman, Brownell and Hartman that sodium salt, like other treatments (cortin, sodium factors and desoxycorticosterone), maintained adrenalectomized dogs in good condition with a normal metabolic rate (8).

Recent work in the field of biology has suggested that the inability of the adrenalectomized animal to withstand environmental stress is a consequence of impaired vascular response to stimuli from the autonomic nervous system. It was shown by the work of Goldstein that the vascular collapse, resulting from applying stress to adrenalectomized animals, is in part a result of deranged responses of the minute blood vessels in the splanchnic area to the constrictor neurohumors of the sympathetic nervous system. Stasis and damage of the minute vessels is observed following prolonged stimulation of the autonomic nervous system resulting from a variety of traumatic environmental changes (5).

Some years ago, Zewemer (1927) observed that cats with adrenal insufficiency had many symptoms that coincided with those of anhydremia. There is a rapid weight loss, the skin becomes gray, dry, wrinkled, and loses its elasticity. Along with these syndromes, there is a loss of sodium and chloride through the kidneys (23).

Schloss and Myer (1912) and Cohen (1911) have expressed the view that gain or loss of intrinsic fluid by the body is accompanied by gain or loss of total salts in molar amounts equivalent to those existing in body fluid (23).

It was finally proved by Merle and Scott (1933) that the adrenal glands are essential for life. One of the outstanding hypotheses to explain this action was that they possess a detoxifying function (13).

In 1921, however, Louis showed that the minimum lethal dose of several drugs was greatly reduced in rats after adrenalectomy. In studying the response of specific immune bodies to adrenal deficiency, Marine made the observation that adrenalectomized rabbits were often promptly killed by the injection of small doses of antigen which were harmless to normal rabbits. The adrenal cortex played an important role in a mechanism of non-specific resistance to certain types of intoxication. Working on his hypothesis, Scott proved that adrenalectomized rats had a greatly increased susceptibility to streptococcus

and staphylococcus intoxication (13).

In 1931, Hartman demonstrated a significant difference in the sensitivity of normal and adrenalectomized rats to low environmental temperatures, and showed that the resistance of adrenalectomized rats can be increased by the administration of cortical extract or salt solution (9).

Extirpation of the adrenals has been carried out by a host of workers since the pioneer work of Brown-Sequard, who demonstrated the rapidly fatal outcome of the operation in the laboratory animals. Many factors determine the period of survival of animals following adrenalectomy. This may account for the diversity of the results reported by different investigators. Certain animals (rats, frogs and goats) survive adrenalectomy much longer than others (dogs, cats and guinea pigs) due to their greater ability to withstand injuries in general. Adrenalectomized animals are extremely sensitive to trauma and hemorrhage (6).

In 1926, Marval observed that albino rats deprived of adrenals resist cold less than control normal rats (12). Experimental results obtained by Fujisawa in 1936 indicated that the epinephrine content of the adrenal decreases by being exposed to cold, but increases upon recovery.

Cutler, in 1938, observed that the general management of the animals is also of great importance in avoiding a crisis and

prolonging the life of adrenalectomized animals. Extremes of temperatures (both heat and cold) should be avoided as they tend to precipitate a crisis. The animals should avoid both mental and physical fatigue and should be shielded as much as possible from exciting factors such as pain in order to prolong the life of adrenalectomized animals (4).

Cleghorn (1939) made observations that in Addison's disease there is a great loss of sodium chloride and water through the kidneys, and there is a retention of potassium and urea. These observations led to the beneficial use of large doses of sodium chloride and a diet low in potassium for Addisonian patients. It was found that in crises where blood volume is reduced, intravenous injections of saline and glucose have often proved to be life saving (3).

The first extracts of cortical tissue which would maintain life in the adrenalectomized animal were prepared in 1930 by Hartman and Brownell (9).

Swingle and his associates believed that the secretions of the cortex primarily influence the distribution of electrolytes and fluids between the two great fluid reservoirs of the body, the extracellular (including the blood stream) and the intracellular fluid. In the absence of the adrenal cortex, the extracellular electrolytes are depleted, partly by renal elimination and partly

by the movement of sodium and chloride into the cells (20).

Schear (1932) obtained experimental evidence from the albino rat showing that, under low temperature, the increased heat requirement is met by mobilization of a large quantity of sugar, but this cannot be done in adrenalectomized rats because adrenal glands control carbohydrate metabolism (18).

In 1942, McPhalis observed that rats and mice are excellent experimental animals for adrenalectomy, because the glands in these species are easily extirpated and the normal period of survival is sufficiently long enough to permit complete recovery from the operation procedure (14).

Campos (1929) observed that adrenalectomized animals had a reduction in basal metabolism rate as much as 25 per cent after prolonged muscular work. Upon prolonged exposure to cold, the body temperature drops below normal. This drop of temperature is believed to be correlated with fatigued muscular reflexes and with depletion of carbohydrate stores (2).

Bourqul observed that an adrenalectomized animal is abnormally sensitive to every type of stress. Since shock may occur without excessive sodium loss through the kidneys, it is possible that cortical deprivation leads to disturbances in the vascular mechanism which make the animal unusually sensitive to stresses (1).

The problem of adrenalectomized animals' survival period on saline solution is of grave importance, as each year a great

number of diseases of the adrenal glands occur in the United States. These needless casualties could be markedly reduced if more scientific facts were uncovered, pertinent to this problem. Some of the facts now needed are methods by which adrenal disfunction of animals could be treated with a very cheap and easily acquired chemical to restore this function back to normal.

This research is concerned primarily with the survival period of adrenalectomized rats. The objectives are:

1. To determine the lethal period and inactivation period for normal control, salt treated and non-salt treated adrenalectomized rats exposed to high temperature (36 - 37 degrees C).

2. To determine the lethal period and inactivation period for normal control, salt treated and non-salt treated adrenalectomized rats exposed to low temperature (5 - 10 degrees C.).

3. To determine the lethal period and inactivation period for normal control, salt treated and non-salt treated adrenalectomized rats living under normal laboratory conditions (21 - 26 degrees C.).

4. To determine the lethal period and inactivation period for normal control, salt treated and non-salt treated adrenalectomized rats exposed to an activator machine to induce excessive muscular fatigue.

5. To determine the lethal period and inactivation period for desoxycorticosterone treated and corticosterone treated adrenalectomized rats exposed to low and high temperatures.

This work was conducted in the Research Laboratory of the Biology Department of Prairie View Agricultural and Mechanical College from May, 1953, through July, 1953.

MATERIALS AND METHODS

Throughout this research problem, Albino rats from A. and M. College of College Station, Texas were used. The age of these rats ranged from 35 to 45 days. The average weight of all rats used in this research problem was approximately 101 grams.

Rats approximately 38 days old were desired for these experiments, because adult rats would not develop adrenal deficiency as quickly as the young rats (6).

The refrigerator used in this problem was designed by the Central Scientific Company to maintain a constant temperature of -5 degrees Centigrade. However, we were only able to obtain a temperature of 5 to 10 degrees Centigrade; thus one may readily recognize the inadequacy of this refrigerator for conducting such experiments. These rats were exposed to 5 - 10 degrees Centigrade until death.

In order to expose both the control and experimental animals to a high temperature, they were placed in a Thelco incubator at a temperature of 36 to 37 degrees Centigrade where they remained until death.

In Experiment III an activator machine was used in this research problem to induce death from muscular fatigue in the adrenalectomized rats. The time of inactivation and death was noted. This activator machine is an apparatus mounted on a

table stand with a cage that is kept moving in a circular direction by a one-fourth horsepower electric motor. The revolving cage, which made 1/7 of a revolution every second, remained still for three seconds out of ten. By this method, all rats were made to keep walking unless the machine was stopped by the observer.

The preparation prior to adrenalectomy was as follows: hair was removed from the mid-dorsal surface on the back by plucking, then ether was used to anesthetize the animals.

Bilateral adrenalectomy was accomplished through two lumbar incisions. When sufficiently exposed, the fascia and root structures of the glands were firmly grasped with fine forceps and dissected away with the glands.

All rats used in this research problem were given 48 hours to recover from the operation prior to being exposed to any abnormal conditions.

In this problem, all salt treated adrenalectomized rats were given only physiological saline solution to drink from the time of adrenalectomy until the time of death. These animals were considered as being salt treated adrenalectomized rats. Non-salt treated animals were adrenalectomized rats which were given only tap water to drink from the time of adrenalectomy until death. Observations were made on all rats every hour in this research problem.

In Experiment I, seven rats were used, each being weighed before being placed in the refrigerator where they were exposed to 5 to 10 degrees Centigrade until death. These rats were listed as A_1. A_2, A_3, A_4, A_5, A_6 and A_7, in order to make direct and strict observations of every animal exposed to a low temperature, whereby the inactivation time and lethal temperature time could be recorded for the normal rat and compared with the adrenalectomized salt treated and non-salt treated rats. Animals A_3 and A_4 were the non-salt treated: A_5, A_6 and A_7 were the salt treated. Three cages were placed in the refrigerator which contained the animals in the following order: normal control, non-salt treated, and salt treated. Throughout these experiments, all rats were never denied food and water, or food and physiological saline solution.

Seven rats were used in Experiment II in order to determine the lethal temperature time and the time of inactivation of two normal controls and five adrenalectomized rats exposed to higher temperature of 36 to 37 degrees Centigrade. The rats were numbered respectively B_1, B_2, B_3, B_4, B_5, B_6 and B_7. All rats were weighed before being placed in cages in the incubator. B_1 and B_2 were the normal control animals; B_3 and B_4 were the adrenalectomized non-salt treated animals; whereas, B_5 , B_6 and B_7 were the salt treated adrenalectomized rats.

In Experiment III, seven rats were used to determine the time of inactivation and lethal time of normal and adrenalectomized animals after being exposed to excessive muscular fatigue induced by the activator machine. All rats were numbered respectively: C_1, C_2, C_3, C_4, C_5, C_6, and C_7. Each rat was weighed and placed in the activator machine with observations being made every hour until death. C_1 and C_2 were normal control rats; C_3 and C_4 were the adrenalectomized non-salt treated animals; C_5, C_6 and C_7 were salt treated adrenalectomized animals. The activator machine was stopped every two hours to give all rats twenty minutes to eat and drink water or saline solution.

Seven rats were used in Experiment IV to determine the survival period of adrenalectomized rats in hours under normal laboratory conditions. These animals were numbered respectively as : D_1, D_2, D_3, D_4, D_5, D_6 and D_7. The temperature in the laboratory was from 21 to 26 degrees Centigrade while performing these experiments. D_1 and D_2 were normal control rats used to make observation while living under normal conditions: D_3 and D_4 were non-salt treated adrenalectomized rats; rats D_5, D_6 and D_7 were adrenalectomized slat treated animals. Observations were made every hour from time of adrenalectomy until the time of death.

In Experiment V, sixteen adrenalectomized rats were used to determine the effects of desoxycorticosterone and corticosterone upon the lethal temperature time and the inactivation

time of adrenalectomized rats subjected to extreme heat or cold. For this study the rats were divided into two groups designated as Group E and Group F. Group E consisted of two adrenalectomized non-hormone treated control rats (E_1 and E_2), three adrenalectomized corticosterone treated rats (E_3, E_4 and E_5), and three adrenalectomized desoxycorticosterone treated rats (E_6, E_7 and E_8). After weighing these animals, they were placed in a refrigerator at 5 to 10 degrees Centigrade, and observed for lethal temperature time and inactivation time. Rats of Group F were similar to Group E with the exception that they were exposed to a temperature to 36 to 37 degrees Centigrade. The rats of Group F consisted of two adrenalectomized non - hormone treated controls (F_1 and F_2), three adrenalectomized corticosterone treated rats (F_3 , F_4 and F_5) and three adrenalectomized desoxycorticosterone treated rats (F_6 , F_7 and F_8).

Intramuscular injections of corticosterone in .2 cc. doses per day (24 hours) were administered to rats E_3, E_4 , E_5 , F_4 and F_5 ; whereas, intramuscular injections of desoxycorticosterone of the same dosage were administered to rats E_6, E_7 , E_8 , F_6 , F_7 and F_8 from the time of adrenalectomy until death.

EXPERIMENTS AND RESULTS

Experiment I deals with the determination of the lethal temperature time and inactivation time of normal control rats, non-salt treated and salt treated adrenalectomized rats exposed to low temperature of 5 to 10 degrees Centigrade. Lethal temperature time may be defined as the length of time required for rats to die after being placed in the refrigerator at a temperature of 5 to 10 degrees Centigrade. Inactivation time is the length of time required for these rats to become inactive. The syndromes pointing to inactivation were fallen body temperature, and the animal lay prostrate. Seven rats (three females and four males) were used in this experiment, five adrenalectomized rats and two normal control rats. These rats were 38 days old and their weights are shown in Table I.

Results: In Table I, it is observed that the normal control rats (A_1 and A_2) had a lethal temperature time of 90 and 88, and an inactivation time of 85 and 83 hours, whereas, the adrenalectomized non-salt treated rats (A_3 and A_4) had a lethal temperature time of 43 to 40 hours, and an inactivation time of 40 and 38 hours as contrasted with a lethal temperature time of 52, 54 and 60 hours, and an inactivation

time of 48, 51 and 58 hours for the adrenalectomized salt treated rats listed as A_5 , A_6 and A_7.

TABLE I. THE INACTIVATION TIME AND LETHAL TEMPERATURE TIME OF RATS EXPOSED TO LOW TEMPERATURE OF 5 TO 10 DEGREES CENTIGRADE

RAT NO.	WT.	SEX	TYPE OF RAT	TREATMENT	INACTIVATION TIME	LETHAL TEMP. TIME
A_1	101 gm.	M	Normal Control	None	85 Hours	90 Hours
A_2	100 gm.	F	Normal Control	None	83 Hours	88 Hours
A_3	101 gm.	F	Adrenalectomized	None	40 Hours	43 Hours
A_4	102 gm.	M	Adrenalectomized	None	38 Hours	40 Hours
A_5	102 gm.	M	Adrenalectomized	Physiological Saline Solution	48 Hours	52 Hours
A_6	101 gm.	F	Adrenalectomized	Physiological Saline Solution	51 Hours	54 Hours
A_7	103 gm.	M	Adrenalectomized	Physiological Saline Solution	58 Hours	60 Hours

Experiment II deals with the determination of the lethal temperature time and inactivation time of adrenalectomized non-salt treated, salt treated and normal control rats exposed to high temperature of 36 to 37 degrees Centigrade in an incubator. Lethal temperature time is the length of time required for rats to die after being exposed to 36 to 37 degrees Centigrade. Inactivation time is the number of hours required for rats to become inactive. The syndromes indicating inactivation were a fall in body temperature, and the animal lay prostrate. Seven rats (four males and three females) were used in Experiment II, five adrenalectomized rats and two normal controls. The average weight was 101 grams and their age was approximately 38 days.

Results: In determining the inactivation time and lethal temperature time for rats exposed to 36 to 37 degrees Centigrade, it may be observed from Table II that B_1 and B_2, the controls, survived indefinitely. Rats B_3 and B_4 were adrenalectomized non-salt treated animals and showed an inactivation time of 50 and 53 hours and a lethal temperature time of 54 and 58 hours, respectively. The salt treated adrenalectomized rats, B_5, B_6 and B_7, showed a markedly higher tolerance as their inactivation times were 70, 73 and 65 hours and the lethal temperature times were 73, 75 and 70 hours, respectively.

TABLE II. THE INACTIVATION TIME AND LETHAL TEMPERATURE TIME OF RATS EXPOSED TO HIGH TEMPERATURE OF 36 TO 37 DEGREES CENTIGRADE

RAT NO.	WT.	SEX	TYPE OF RAT	TREATMENT	INACTIVATION TIME	LETHAL TEMP. TIME
B_1	102 gm.	F	Normal Control	None	None	None
B_2	103 gm.	M	Normal Control	None	None	None
B_3	102 gm.	M	Adrenalectomized	None	50 Hours	54 Hours
B_4	101 gm.	F	Adrenalectomized	None	53 Hours	58 Hours
B_5	101 gm.	M	Adrenalectomized	Physiological Saline Solution	70 Hours	73 Hours
B_6	102 gm.	F	Adrenalectomized	Physiological Saline Solution	73 Hours	75 Hours
B_7	101 gm.	M	Adrenalectomized	Physiological Saline Solution	65 Hours	70 Hours

Experiment III deals with the determination of the lethal time and inactivation time of salt treated, non-salt treated adrenalectomized rats and normal control rats after being exposed to excessive muscular fatigue induced by the activator machine. In this experiment, the lethal time is the length of time required for rats to die after being placed in the activator machine. Inactivation time is the length of time required for these rats to become inactive. The syndromes pointing to inactivation were the animal lay prostrate, and the body temperature had fallen. Seven rats (three females and four males) were used in this experiment, five adrenalectomized rats and two normal controls. The average weight of the rats was 101 grams and the age approximately 38 days.

Results: A study of the data in Table III shows the effects of muscular exercise upon adrenalectomized rats when placed in an inactivator machine. This table reveals that normal non-adrenalectomized rats C_1 and C_2, the controls become inactive at the end of 90 and 93 hours and died at the end of the 96 and 98 hour, after being placed in the inactivator machine. On the other hand, the adrenalectomized non-salt treated group rats (C_3 and C_4) showed a low tolerance to fatigue. The animals of this group had an inactivation time of 70 and 68 hours and a lethal time of 74 and 71 hours, respectively. However, it was observed that the salt treated

adrenalectomized rats showed an increased tolerance to the state of fatigue, as compared with the non-salt treated rats. The inactivation time for salt treated adrenalectomized rats, C_5, C_6, and C_7 was 78, 80 and 83 hours while their lethal time was 81, 84 and 87 hours, respectively.

TABLE III. THE INACTIVATION TIME AND LETHAL TEMPERATURE TIME OF SALT TREATED AND NON-SALT TREATED ADRENALECTOMIZED RATS EXPOSED TO MUSCULAR FATIGUE

RAT NO.	WT.	SEX	TYPE OF RAT	TREATMENT	INACTIVATION TIME	LETHAL TIME
C_1	101 gm.	F	Normal Control	None	90 Hours	96 Hours
C_2	102 gm.	M	Normal Control	None	93 Hours	98 Hours
C_3	101 gm.	M	Adrenalectomized	None	70 Hours	74 Hours
C_4	100gm.	F	Adrenalectomized	None	68 Hours	71 Hours
C_5	101 gm.	M	Adrenalectomized	Physiological Saline Solution	78 Hours	81 Hours
C_6	100 gm.	F	Adrenalectomized	Physiological Saline Solution	80 Hours	84 Hours
C_7	102 gm.	M	Adrenalectomized	Physiological Saline Solution	83 Hours	87 Hours

Experiment IV deals with the determination of the lethal time and time of inactivation of adrenalectomized salt treated, non-salt treated and normal control animals under normal laboratory conditions. In this experiment the lethal time (death time) is the length of time that adrenalectomized rats can survive under normal laboratory conditions. Inactivation time is the length of time required for these rats to become inactive under normal laboratory conditions. The syndromes indicating inactivation were a fall in body temperature, and the animal lay prostrate. Seven rats (three females and four males) approximately 38 days old, were used in this experiment, five adrenalectomized rats and two normal control rats.

Results: It was observed in this experiment, as may be seen in Table IV, that the normal control animals (D_1 and D_2) survived indefinitely under normal laboratory conditions. But in contrast, the adrenalectomized non-salt treated animals, rats $D_3$and D_4, had an inactivation time of 192 and 198 hours and a lethal time of 194 and 201 hours, respectively. The salt treated adrenalectomized rats, D_5 , D_6 and D_7, however, showed a markedly higher tolerance to laboratory conditions as their inactivation times were 260, 270 and 265 hours and their lethal times were 265, 274 and 268 hours, respectively.

TABLE IV. THE INACTIVATION TIME AND LETHAL TIME OF ADRENALECTOMIZED RATS UNDER NORMAL LABORATORY CONDITIONS

RAT NO.	WT.	SEX	TYPE OF RAT	TREATMENT	INACTIVATION TIME	LETHAL TIME
D_1	101 gm.	M	Normal Control	None	None	None
D_2	100 gm.	F	Normal Control	None	None	None
D_3	102 gm.	M	Adrenalectomized	None	192 Hours	194 Hours
D_4	101 gm.	F	Adrenalectomized	None	198 Hours	201 Hours
D_5	102 gm.	M	Adrenalectomized	Physiological Saline Solution	260 Hours	265 Hours
D_6	102 gm.	F	Adrenalectomized	Physiological Saline Solution	270 Hours	274 Hours
D_7	103 gm.	M	Adrenalectomized	Physiological Saline Solution	265 Hours	268 Hours

Sixteen adrenalectomized rats, approximately 38 days old, were used in Experiment V. These rats were divided into two groups. Group E was exposed to a high temperature of 36 to 37 degrees Centigrade, three being corticosterone treated, whereas, the other three were desoxycorticosterone treated.

The experimental animals of Group F received the same hormonal treatment as Group E, but were exposed to a low temperature of 5 to 10 degrees Centigrade. In both groups (E and F) two adrenalectomized rats were used as controls.

Results: The effects of the cortical hormones (corticosterone and desoxycorticosterone) upon the survival time of adrenalectomized rats, exposed to high and low temperatures, can be seen in Table V and Table VI. When a careful observation is made of Table V, it is observed that both the lethal temperature time and the inactivation time of the adrenalectomized desoxycorticosterone treated rats were longer than both the adrenalectomized corticosterone treated and the adrenalectomized control animals when these rats were exposed to a high temperature. But when the animals similarly treated with corticosterone hormone were exposed to a low temperature, Table VI shows that the adrenalectomized corticosterone treated rats had the longest inactivation time and lethal temperature time of the three groups.

TABLE V. SHOWING THE LETHAL TEMPERATURE TIME AND INACTIVATION TIME OF DESOXYCORTICOSTERONE AND CORTICOSTERONE TREATED ADRENALECTOMIZED RATS EXPOSED TO A HIGH TEMPERATURE (36 TO 37 DEGREES C.)

RAT NO.	WT.	SEX	TYPE OF RAT	TREATMENT	INACTIVATION TIME	LETHAL TIME
E_1	90 gm.	F	Adrenalectomized Control	None	51 Hours	54 Hours
E_2	92 gm.	F	Adrenalectomized Control	None	49 Hours	51 Hours
E_3	91 gm.	F	Adrenalectomized Experimental	Desoxycorticosterone	78 Hours	81 Hours
E_4	91 gm.	F	Adrenalectomized Experimental	Desoxycorticosterone	79 Hours	82 Hours
E_5	92 gm.	F	Adrenalectomized Experimental	Desoxycorticosterone	75 Hours	79 Hours
E_6	93 gm.	F	Adrenalectomized Experimental	Corticosterone	68 Hours	70 Hours
E_7	90 gm.	F	Adrenalectomized Experimental	Corticosterone	70 Hours	72 Hours
E_8	92 gm.	F	Adrenalectomized Experimental	Corticosterone	72 Hours	73 Hours

TABLE VI. THE LETHAL TEMPERATURE TIME AND INACTIVATION TIME OF DESOXYCORTICOSTERONE AND CORTICOSTERONE TREATED ADRENALECTOMIZED RATS EXPOSED TO LOW TEMPERATURE (5 - 10 DEGREES C.)

RAT NO.	WT.	SEX	TYPE OF RAT	TREATMENT	INACTIVATION TIME	LETHAL TIME
F_1	93 gm.	F	Adrenalectomized Control	None	36 Hours	38 Hours
F_2	94 gm.	F	Adrenalectomized Control	None	37 Hours	39 Hours
F_3	91 gm.	F	Adrenalectomized Experimental	Desoxycorticosterone	67 Hours	70 Hours
F_4	90 gm.	F	Adrenalectomized Experimental	Desoxycorticosterone	73 Hours	75 Hours
F_5	92 gm.	F	Adrenalectomized Experimental	Desoxycorticosterone	68 Hours	69 Hours
F_6	93 gm.	F	Adrenalectomized Experimental	Corticosterone	78 Hours	81 Hours
F_7	92 gm.	F	Adrenalectomized Experimental	Corticosterone	75 Hours	78 Hours
F_8	91 gm.	F	Adrenalectomized Experimental	Corticosterone	71 Hours	74 Hours

DISCUSSION AND RESULTS

To maintain the life of a warm-blooded animal, it is necessary to keep the body temperature fairly constant, notwithstanding the external and internal conditions which tend to raise or lower it. When the human body temperature falls to about 24 degrees Centigrade, and this temperature is maintained for several hours, death usually occurs. On the other hand, a temperature higher than 44 or 45 degrees Centigrade, maintained for more than a brief length of time, is also fatal (22).

Experiment I deals with the determination of the lethal temperature time and inactivation time of adrenalectomized non-salt treated, salt treated and normal control rats.

A_1 and A_2, the normal control rats, had an inactivation time of 85 and 83 hours, and a lethal temperature time of 90 and 88 hours. This difference in time, however, may be explained by the fact that animals of the same age group and species may have varying susceptibility to low temperature. Rats A_3 and A_4 were adrenalectomized non-salt treated animals which showed a markedly lower tolerance to low temperature as compared with the salt treated adrenalectomized rats, which had an average lethal time of 53 hours and an average inactivation time of 49 hours. The above observations are in agreement with Harvath (1938) who demonstrated the

sensitivity of normal and adrenalectomized rats after the animals had been exposed to low environmental temperatures. He showed that the resistance of adrenalectomized rats can be increased by the administration of salt solution (10). Early in the course of cortical insufficiency, there is an increased excretion of sodium through the kidneys, and as a result, the concentration of this ion in the blood is lowered. The progressive loss of water and salt leads to hemoconcentration and a decrease in volume of blood plasma with the progressive loss of body fluids. The blood pressure is diminished and the rate of blood flow is decreased. But by giving salt, these conditions may be minimized, because salt will aid in preventing fluid shifts in the body and proplong the life of adrenalectomized rats being exposed to low temperature.

Experiment II was concerned with determining the lethal temperature time and inactivation time of adrenalectomized non-salt treated, salt treated and normal control rats exposed to high temperature of 36 to 37 degrees Centigrade. The normal control rats (B_1 and B_2) were not affected by being exposed to 36 to 37 degrees Centigrade, as shown in Table II. It was observed by Long(1940) that one of the functions of the adrenal cortex is concerned with the maintenance of normal rats in good condition in high environmental temperatures for a long period of time (11).

It is believed that sodium chloride prevents hemoconcentration and dehydration of tissues, thereby prolonging the life of adren-

alectomized animals exposed to high environmental temperatures. Rats B_3 and B_4 (adrenalectomized non-salt treated animals) had an average lethal temperature time of 56 hours, and an average inactivation time of 51 hours. The average lethal and inactivation time for the salt treated rats were 73 and 69 hours, respectively. As can be readily seen here, there is quite a difference existing between the lethal temperature time and the inactivation time of non-salt treated and salt treated rats exposed to a high temperature of 36 to 37 degrees Centigrade.

The results obtained show that salt treatments may prolong the life of adrenalectomized rats exposed to high environmental temperatures. This is in agreement with Swingle (1940) who observed that hemoconcentration is correlated with the excessive loss of sodium, thereby causing a reduction in blood circulation and a low tolerance to heat (20).

A study of the data in Table III shows the effects of muscular fatigue on normal controls, non-salt treated and salt treated adrenalectomized rats exposed to an activator machine. This table reveals that the control rats, C_1 and C_2, had an average lethal time of 97 hours and an average inactivation time of 91 hours. The non-salt treated adrenatectomized rats, C_3 and C_4, had an average inactivation time of 69 hours and an average lethal time of 72 hours as compared with the salt treated adrenalectomized

rats, C_5, C_6 and C_7, which had an average lethal time of 84 hours and an average inactivation time of 80 hours. It was observed that the salt treated adrenalectomized rats had a high tolerance to muscular fatigue as compared with the non-salt treated adrenalectomized rat. The results obtained from Experiment III are in agreement with Ingle, (1940), who observed that the ability of maintaining the work capacity of adrenalectomized rats may be controlled by giving saline solution to these animals (11). Adrenal decortication renders an animal apathetic and diminishes its capacity for sustained muscular work. Such animals are hesitant in moving about and take little interest in their surroundings. Their gait is spastic, and as insufficiency progresses, the limbs may become so weakened that they cannot support the weight of the body. The results of this experiment may be explained on the basis that cortical insufficiency leads to involvement of the nervous system. There is the probability that some of the mental impairment, characteristic of Addisan's disease, results from decreased cerebral circulation. It may be that cortical insufficiency indirectly impairs the nervous system by influencing the distribution of electrolytes, thereby preventing the proper reflexes and muscular coordination of adrenalectomized animals.

It was observed in Experiment IV, as may be seen in Table IV, that normal control rats, D_1 and D_2 , survived indefinitely under

normal laboratory conditions. But in contrast, the adrenalectomized non-salt treated animals, D_3 and D_4, had an average lethal time of 197 hours and an average inactivation time of 195 hours, whereas, the salt treated adrenalectomized rats, D_5, D_6 and D_7, showed a markedly higher tolerance to laboratory conditions as their average inactivation time was 265 hours and the average lethal time was 269 hours. The results obtained in this experiment are supported by the researches of Cleghorn (3) who in 1939 observed that the life span of decorticated animals is lengthened greatly from 7 to 8 days to 12 or 13 days by the administration of sodium salts, whereas, potassium salt aggravates the conditions and is sufficient to cause the death of the animal. If totally adrenalectomized animals are maintained on low potassium rations and are given sodium chloride, sodium citrate or sodium bicarbonate, they will remain in good health after the injections of cortical extracts for a period of three or four years.

The effects of the hormones of the adrenal cortices (corticosterone and desoxycorticosterone) upon the survival time of adrenalectomized rats exposed to high and low temperatures can be seen in Tables V and Vi. These animals are divided into Group E and Group F.

Group E was exposed to a high temperature of 36 to 37 degrees Centigrade. The average lethal temperature time of E_1 and E_2

(control adrenalectomized rats) was 52 hours and the average inactivation time was 50 hours, whereas the adrenalectomized desoxycorticosterone treated rats' lethal temperature time and inactivation time were longer than both the adrenalectomized corticosterone treated rats, E_6 , E_7 and E_8 , and the adrenalectomized control animals. These results are in accord with Gardon's (7), who observed that steroids, belonging to the desoxycorticosterone series have the ability to prolong the life of adrenalectomized rats exposed to high environmental temperatures. During cortical insufficiencies, profound circulatory inadequacies become apparent. There is reason to believe that certain fluids and electrolytes shift within the body. Since sodium is the principl cation in the extracellular fluid and potassium the chief ion of the intracellular fluid, the movement of water will be conditioned to a large extent by the distribution of sodium chloride, and the loss of sodium will cause hemoconcentration which results in subsequent fall in blood pressure and eventual death from dehydration shock. Desoxycorticosterone will prolong the survival period of adrenalectomized rats by controlling the electrolytic metabolism of these animals.

Group F was exposed to low temperature. Table VI shows that the adrenalectomized controls, F_1 and F_2 , had an average inactivation time of 36 hours, and lethal temperature time of 38 hours whereas the desoxycorticosterone treated adrenalectomized

rats, F_3, F_4 and F_5, had an average inactivation time of 68 hours, but the corticosterone treated rats, F_6, F_7 and F_8, had a high tolerance to low temperature as compared with the other two groups. Hartman and Brownell (9) made observations in 1943 on the ability of corticosterone treated adrenalectomized rats to tolerate low temperatures. They believed that corticosterone increased the carbohydrate content of the body, indicating that the new carbohydrate is formed from some non-carbohydrate precursor. Evidence for this was proved by using slices of liver removed from normal rats treated with compounds of the corticosterone series. These hormones were found capable of converting lactic and pyruvic acids into carbohydrate to a greater extent than similar slices from untreated animals. By increasing the carbohydrate metabolism, more heat and energy will be liberated, thereby causing the adrenalectomized corticosterone treated animals to have a higher tolerance to low temperature.

SUMMARY

This research problem has revealed that adrenalectomized rats of the same general age group, weight and species of any specific group will have a varying susceptibility to normal and abnormal conditions.

From observation made through experimentation, it was noted that adrenalectomized salt treated rats had a higher tolerance to normal and abnormal environmental conditions as compared to the non-salt treated adrenalectomized rats exposed to the same conditions.

It was observed that male and female adrenalectomized rats showed no observable difference in the average length of survival time, providing they were exposed to the same types of conditions.

The desoxycorticosterone treated adrenalectomized rats had a longer survival time while being exposed to high temperatures as compared to the normal adrenalectomized and corticosterone treated adrenalectomized rats.

The corticosterone treated adrenalectomized rats had a longer survival time while being exposed to low temperature as compared to the adrenalectomized controls and desoxycorticosterone treated adrenalectomized rats.

Adrenalectomized animals live longer when maintained at constant temperatures which are not excessively high or low. Excitement, excessive muscular work and other conditions demanding an increase in metabolic response usually prove injurious to adrenalectomized animals.

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