INFORMATION TO USERS

This manuscript has been reproduced from the microfilm master. UMI films the text directly from the original or copy submitted. Thus, some thesis and dissertation copies are in typewriter face, while others may be from any type of computer printer.

The quality of this reproduction is dependent upon the quality of the copy submitted. Broken or indistinct print, colored or poor quality illustrations and photographs, print bleedthrough, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send UMI a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

Oversize materials (e.g., maps, drawings, charts) are reproduced by sectioning the original, beginning at the upper left-hand corner and continuing from left to right in equal sections with small overlaps.

ProQuest Information and Learning
300 North Zeeb Road, Ann Arbor, MI 48106-1346 USA
800-521-0600

UNIVERSITY OF CINCINNATI

May 31 1934

I hereby recommend that the thesis prepared under my supervision by Cordelia Lucille Ogle

entitled Animal Adaptation to Environmental Stimulation

be accepted as fulfilling this part of the requirements for the degree of Doctor of Philosophy

Approved by:

C C Mill

A. P Mathews

Form 668—G. S. and Ed.—1M—7-31

Animal Adaptation to Environmental Stimulation

A dissertation submitted to the

Graduate School
of the University of Cincinnati

in partial fulfillment of the
requirements for the degree of

DOCTOR OF PHILOSOPHY

1934

By

Cordelia Lucille Ogle
B.Sc. University of Cincinnati, 1930
M.Sc. University of Cincinnati, 1931

Table of Contents.

Introduction.

That climate is one of the main factors in determining the distribution of civilization has long been recognized and has recently been reemphasized by Ellsworth Huntington (1). The latter arrived at this conclusion after numerous studies of the sites of ancient civilizations and of the climatic changes accompanying their rise and downfall. From studies concerning the influence of temperature on the amount of work accomplished by factory operatives in Connecticut, Pennsylvania, Virginia, and Florida, he concluded that a mean temperature of 64°F. with frequent storms is nearest the ideal for human productivity and efficiency. He states, in his book "Civilization and Climate", that in the northern part of the United States the extremes of temperature are so great as to "place checks on the individuals." This opinion, Dr. C. A. Mills (2a) does not think tenable for the following reasons; first, because a highly variable climate stimulates man to do more work than does a monotonous one; second, residents of our northern states have a higher metabolic rate than that of the southern, and, third, it has been found that the physiological cost of work in normal individuals varies directly with the basal metabolic rate (3). As the basal metabolism increases, the energy expended in doing a given piece of

work also increases. Therefore, a too stimulating climate renders work more expensive and by constantly augmenting the demands upon the heat producing mechanism frequently leads to bodily exhaustion.

Dr. Mills (2b), accepting Huntington's evaluation of climate, sought by statistical procedures for additional evidence of its action. His work has dealt mainly with the relationship of climate to health and disease, being based on the assumption that in a given area of high stimulation some of the inhabitants would be unable to keep the pace and such inability would be evidenced in a higher incidence of, and death rate from, the over-stimulative or exhaustive diseases.

Dunwoodie (4) prepared in 1899 maps showing that the Great Lake region possesses over twice the storm frequency of any other area on the earth's surface. Dr. Mills (2c) has prepared for the United States and Canada for 1925 a map of temperature variability which was based upon both the storm frequency and the extent of temperature changes accompanying the storms of that year. The region slightly to the west and southwest of the Great Lakes had the greatest temperature variability. The areas of highest death rates from diabetes, exophthalmic goitre, Addison's disease, and pernicious anemia (diseases which are termed over-stimulative, or due to metabolic exhaustion) were found to coincide strikingly with the regions of high

temperature variability. He also found that the sex glands were influenced by temperature variability. In the northern states of the United States, women mature sooner and reach the peak of fertility at an earlier age than do women of our southern states. However, the southern women bear children over a greater span of their lives(2d).

Residents of the temperate zones who visit the tropics often have gastro-intestinal disturbances which appear directly related with the high humidity and temperature. The symptoms are: diarrhea, achlorhydria or hypochlorhydria, with impaired digestion and hypermotility of the whole tract. Frequently, there is spasticity of the cardiac, pyloric, or ileocecal sphincter. Dr. Mills found that these gastro-intestinal disturbances, which appeared to be directly related to the intense heat and high humidity in Peking, China, were usually immediately and completely relieved by the oral administration of adrenalin (2e). To quote, "It seems, therefore, that the difficulty of keeping cool in the hot humid season, whenever it occurs with sufficient intensity, serves to cause a marked suppression of suprarenal function, with the result that gastro-intestinal disturbances appear on slight provocation."

Lavoisier was the first to report that the oxygen consumption of a cooled man is greater than that of a warmed one. Eijkman (5) has been the strongest opponent to this view that man's thermal environment influences his metabolic

rate. He was the first to measure the gaseous metabolism of Europeans in Java, but he found no difference between the values obtained there and those for residents in Berlin. Nevertheless, it is fairly well established, at the present time, that residents of warm regions have a lower basal metabolism than people living in the temperate zones. De Almeida (6) has reported the basal metabolism of residents of Rio de Janeiro to be 16% lower than that for people of similar height, weight and age in New York. Sundstroem (7) obtained a heat production of 31 cal./sq.m./hr. for white men and 27.7 cal./sq.m./hr. for white women in North Queensland, Australia; the standards for residents of temperate zones being approximately 39 cal./sq.m./hr. for men and 37 cal./sq.m./hr. for women (8,9). Hafkesbring and Borgstrom state that the basal metabolic rate for natives of New Orleans is 15% lower than that of residents in our northern states (10). Berkhout repeated in 1929 the metabolic studies of Eijkman in Java and found a 10% lower rate (11). Benedict (12) in 1915 and Gessler (13) in 1925 reported a 10-11% higher respiratory exchange in winter than during the summer. These citations suffice to show that the metabolic rate of man is influenced by the environmental temperature.

But the manner and course of this alteration of the metabolism has been given scant consideration. Laboratory data warrants the assumption that environmental temperature affects in like manner the responses of man and

experimental animals. Therefore, animal experiments have been resorted to in an attempt to obtain an explanation of the above-mentioned climatic effects on the human being.

At Dr. Mills' suggestion, studies have been made on metabolic activity under conditions of continuous moist heat, of continuous cold, and of a daily change between the two. We wished, thereby, to determine why a Southerner is uncomfortable under conditions which are pleasantly tolerated by a Northerner; and, conversely, why a Northerner is exceedingly uncomfortable under conditions of heat which the Southerner easily tolerates. Also, it was desired to ascertain whether we could produce experimentally in animals the ability to adjust their physiological reactions to both hot and cold environments. Recent sutdies have shown that rats deprived of the adrenals were unable to maintain their body temperatures when exposed to cold. (14,15,16). The activity of the adrenal glands was studied under different environmental conditions, it being felt that these glands of internal secretion are the sites wherein climate exerts its influences on the human being. The results of this study are presented in Part I.

PART I. ADAPTATION OF METABOLIC ACTIVITY TO ENVIRONMENT.

A. Power of Compensating by heat production during extreme chilling of body.

Two rooms 8x8x7 ft., were constructed of steel and glass, properly insulated and provided with continuous ventilation by an exhaust fan which drew air alike from both rooms. These two rooms are located within a large laboratory. Daylight from the west was admitted to each room by a window, 46x40 inches, with two panes of glass four inches apart. An electric light bulb of 120 watts, centrally located in the ceiling, was burned for ten hours of each day in each room. Each room contained a metal rack for animal cages.

One room was kept at 88-92°F. by an electric radiant heater under control of a thermostat. Moisture in the air here was kept near 70% saturation by an electrically heated shallow pan fitted with an automatic filling device. An eleven inch fan blew an air current across the water surface constantly, aiding evaporation and providing proper air movement within the room.

The other room was maintained at a temperature range of 52°-56°F. by a Frigidaire room cooler which contained a fan to provide air movement within the room similar to that in the hot room. No record was made of the humidity in the cold room. Both rooms were equipped with recording clocks to give continuous charts of temperature, and in the hot room, of the relative humidity.

Young adult rabbits, five to six months of age and weighing three to five pounds, were the subjects in these studies. Approximately equal numbers of males and non-pregnant females were used. A constant supply of control animals was kept in out-door hutches, there being five to six animals in each hutch. The three experimental groups of rabbits were treated as follows: one group was kept in the cold room for six weeks; a second group for a similar period in the hot room; while the third group spent sixteen consecutive hours of each day in the hot room and the remaining eight hours in the cold room for the six weeks period. Two test animals were kept in each cage. Purina chow, oats, and cracked corn were used as the principal food, with an addition of green vegetables twice a week.

In order to determine an animal's resistance to chilling, the fur was moistened by pouring cold water (15°C.) over the entire body, then it was immediately placed in a large water bath (15°C.), the water was of such depth as to cover about half of the body. The rectal temperature was taken before the chilling began and at intervals thereafter until it had reached 26°C. At this point, the animal was near prostration and was removed from the bath. The survival time of an animal was taken as the exposure (in minutes) to the cold water required to bring the rectal temperature down to 26°C.

The amount of sugar in the blood of each animal was determined on samples of heart blood (17) drawn before, during, and at the conclusion of the chilling experiments. After the last sample of blood had been taken, the animal was killed by a blow on the head, an abdominal incision was made and two five gram samples of liver immediately removed for the estimation of glycogen (18). The sugar in the glycogen hydrolysates was determined by the method of Folin and Wu (17). The left adrenal gland was excised immediately following the removal of the liver tissue and weighed after being freed from the surrounding connective tissue. The adrenalin content was estimated by a modification of the Folin and Trimble method (19). The gland was rubbed to a very fine paste with a pestle in a mortar, rather than using sand as those authors suggest.

After the three groups of animals had been subjected to their different environmental conditions for six weeks, representatives were removed and tested as to their ability to produce heat and keep warm under chilling conditions.

On the assumption that environmental temperature influences the metabolic activity of an animal, one would expect to find at the end of the period of adaptation a depressed metabolism in the hot room animals and a more active metabolism in those animals which were stimulated daily by cold. Such differences in metabolic activity might be brought to light by testing the response to sudden chilling. An

animal with a sluggish metabolism, presumably, would be ill-fitted to cope with a sudden demand for increased heat production, whereas one with a highly active metabolism would be able to produce heat and keep warm much longer.

This hypothesis was tested by water bath (15°C.) experiments. Marked differences in the ability to withstand this rigorous test were, in fact, observed, the hot room animals being least able to survive this chilling emergency. Since it was found that little of the liver glycogen was used during these extremely acute experiments, less severe but more prolonged chilling tests were devised for comparing quantitatively the rate of glycogen utilization.

During the first of these studies, representatives were taken from the three groups and placed in out-of-door hutches without food for 24 hours. The mean temperature was 50°F. with a night low of 41°F. At the end of this moderate chilling, they were killed and the liver immediately removed for glycogen determination. Control animals which had not been chilled or fasted were removed from each group and killed to get the normal liver glycogen content.

Another series of animals was tested by chilling at a somewhat higher temperature. They were placed in the constant temperature room at 54°F. and kept there without food and with moistened fur for 24 hours. With these less severe chillings, the glycogen utilization was greatest for the cold room and for the third or change group animals, and least for the hot room animals.

The survival time in the water bath appeared to be closely related to the weight of the adrenal gland. These glands of control (outdoor) rabbits weighed more and the animals endured chilling longer during the late winter months than in the spring. The secretion of the cortical portion of the adrenal is intimately connected with heat production (14,16). But the medullary secretion seems less important. For the subcutaneous injection of 0.3 mg. of adrenalin, the commercial synthetic product, only slightly influenced the survival time in the water bath (15°C.) The hyperglycaemic response to the injection of adrenalin was more sustained in the hot room animals than in the controls. The ability to withstand sudden chilling is therefore dependant upon the state of activity of the cortical zone of the adrenal rather than of the medullary region.

Since these experiments were undertaken in the attempt to produce conditions comparable to summer and to winter, one would anticipate, for the above reason, differences in the adrenal weight between the three groups of animals. It was found, indeed, that the weight of these glands was greatest for the cold room animals and less for those of the hot room and change groups. The monthly variations in the response of control animals to chilling (15°C.) were studied for the last eight months of 1931 and the first month of 1932. There was much variation but, on the whole, the

winter animals were more resistant to the chilling and had heavier adrenal glands, presumably with a more highly active cortex, than the animals of the warm months.

Table I shows the results of the chilling experiments with the water bath (15°C.) The difference between the mean survival time for the hot room group and for the other two groups are definitely significant, although this is not true of the differences between the cold room and change groups. At the time the rectal temperature of the hot room animals reached 79°F. (26°C.) in the bath, the animals of the other groups were still in distinctly better condition. Actually little difference in behavior could be noticed here between the cold room and change group animals. When tested at 64.4°F. (18°C.) and left in the bath to complete prostration, however, the group changed daily gave a longer survival time than did the cold room group. Although they had spent sixteen hours of each day in the hot room, they were more resistant to prostration by chilling than were those that lived all the time in the cold room.

Table I.

Time (in minutes) required to reach rectal temperature of 77°F. (26°C.)

Bath kept at 59°F. (15°C.)

	Series I	Series II	Series III	Total No. animals used	Mean time taken to reach 26°C. rectal temp.
Hot room group	60,75,45 45,60 Average 57	60,60,60 Average 60	60,60,60,50 Average 58	12	61.17 ± 1.65
Cold room group	150,90,60, 60,75 Average 87	150,55,90 45,210 Average 110	60,120 Average 90	12	100.33 ± 6.92
Group changed daily	60,135,75 75,75,60,75 Average 79	40,150,120 150,90 Average 110	60,85 Average 73	14	91.64 ± 6.18

Survival time (in minutes) to complete exhaustion.

Bath kept at 64.4°F. (18°C.)

Hot room group	90	115	70	3
Cold room group	160	135	90	3
Group changed daily	285	155	105	3

$$\frac{\text{Difference } (100.33 - 61.17)}{\text{Probable Error of Difference}} = 5.50$$

$$\frac{\text{Difference } (91.64 - 61.17)}{\text{Probable Error of Difference}} = 4.76$$

$$\frac{\text{Difference } (100.33 - 91.64)}{\text{Probable Error of Difference}} = 0.94$$

Giaja and Gelineo (20) studied the influence of a prolonged sojourn at different temperatures on the heat producing power of the rat. They found that after one week in a thermostat at 32°C. the animals could well withstand exposure to cold air of 7°- 9°C. for 25 hours. The animals were then returned to the thermostat and kept for an additional period of twenty-five days. At the end of this time, they were removed from the thermostat and exposed to the external cold of the month of February (+3° to -4°C.). The three rats fell into a prolonged hypothermia and one succumbed. The control rat, adapted to an environmental temperature of 18°C. maintained his rectal temperature at the normal level during exposure to these chillings. This study was received for publication in the Annals de Phys. et de Biol. phys. chem. on May 27, 1931. The present writer's data concerning the influence of an animal's previous thermal environment upon his ability to endure chilling was presented in a master's thesis, May 15, 1931. The results on chilling with cold air in the laboratory at Belgrade and with cold water by the author were obviously reached at about the same date and these different lines of approach to the same general topic were being pursued without the knowledge of either worker. However, my studies of liver glycogen show that it is not a question of the animal's available fuel which accounts for the varying response to chilling, but rather a difference in the ability to metabolize the

glycogen present; this data was accepted for publication October 29, 1932.

B. Dependence of rate of glycogen utilization on the type of previous thermal environment.

The differences in carbohydrate utilization after a 24 hour fast are presented in Tables II and III along with the figures for control animals. Table II shows that the hot room animals lost 69% liver glycogen and the change group animals 96.7%. Calculated in another way, the liver glycogen percentage of the hot room group was reduced from 6.31 to 4.17, a loss of 33.9%, while for the change group the reduction was from 6.57 to 0.53, a loss of 91.9%. The glycogen utilization was less during the 24 hour fast in the cold room and with moistened fur (Table III.) However, the same relationships held as in the former experiment. The hot room animals used least, the change group animals most, while the cold room group animals fell into an intermediate position. The differences in rate of glycogen loss in these two series are sufficiently marked as to leave no room for doubt that there is a more rapid metabolism in the change group and cold room animals. The most significant feature of the results is the position assumed by the animals that endured the hot environment 16 hours of each day but were cooled the remaining 8 hours. Here, as in the previous tests, this group showed evidence of a very active metabolism, even more active than that of animals kept cooled at all times.

Table II.

Glycogen Utilization under Chilling Conditions.

Animals fasted out-of-doors

Series I. 5/1/31		Control animals not fasted or chilled			Animals fasted and chilled 24 hours.			Loss in Liver Glycogen	
		Liver			Liver				
Group	Sex	Weight gms.	Glycogen %	Glycogen gms.	Weight gms.	Glycogen %	Glycogen gms.	In weight	in percentage
Hot room	M	80.1	6.40	5.13					
	M	109.0	6.12	6.68					
	M	83.0	6.17	5.12					
	F	116.6	6.70	7.81					
	F	84.2	6.17	5.20					
Average		94.6	6.31	5.99					
Hot room	M				35.5	5.19	1.84		
	M				52.2	5.12	2.67		
	F				47.3	5.12	2.42		
	F				38.7	1.25	4.48		
Average					43.4	4.17	1.85	69.2	33.9
Changed group	F	126.2	6.99	8.82					
	M	83.1	6.22	5.17					
	F	93.5	6.50	6.08					
Average		100.9	6.57	6.69					
Changed group	F				42.5	0.19	0.08		
	F				39.3	0.88	0.35		
	M				42.5	0.52	0.22		
Average					41.4	0.53	0.22	96.7	91.9

Table III.

Glycogen Utilization Under Chilling Conditions
Animals placed in room at 54°F. with moistened fur.

Series II, 2/11/32		Control animals not fasted or chilled			Animals fasted and chilled 24 hours			Loss in Liver Glycogen	
		Liver			Liver				
Group	Sex	Weight gms.	Glycogen %	Glycogen gms.	Weight gms.	Glycogen %	Glycogen gms.	In Weight	In percentage
	M	39.1	2.92	1.14					
	M	47.5	2.56	1.22					
Hot room	F	41.2	2.75	1.13					
	F	66.5	2.85	1.90					
	F	70.1	3.71	2.60					
Average		52.9	2.96	1.60					
	M				52.0	1.20	0.62		
	F				57.4	2.88	1.65		
Average					54.7	2.04	1.14	28.7	31.1
	M	94.0	5.99	5.63					
	M	76.5	5.59	4.28					
Change	M	60.3	3.02	1.82					
	F	71.5	3.33	2.38					
	F	55.2	4.17	2.30					
Average		71.5	4.42	3.28					
	M				57.9	1.84	1.07		
Change	M				59.5	0.23	0.14		
	F				47.0	0.39	0.18		
Average					54.8	0.82	0.46	86.0	81.4
	M	123.3	2.75	3.39					
	M	108.4	0.31	0.34					
Cold room	M	137.0	2.96	4.06					
	F	137.0	6.23	8.54					
	F	86.4	0.33	0.29					
Average		118.4	2.52	3.32					
Cold room	M				59.0	1.29	0.82		
	F				66.2	0.30	0.35		
Average					62.6	0.79	0.59	82.2	68.7

C. Relation of basal metabolism to external temperatures and their variations.

In our laboratory, studies on oxygen consumption under different environmental conditions have not been made, it being felt that the studies on glycogen utilization were sufficient evidence of a difference in metabolic level between the heat adapted animals and these adjusted to the cold. Such studies have been made elsewhere and a definite difference in the level of heat production at different temperatures has been obtained. Rats kept at 26°C. have a 5% increase in the basal metabolism for each degree of drop in the environmental temperature (21). Sundstroem (7) kept rats under artificial tropical conditions and found that the heat production per square meter of body surface per hour was as follows:

Control	41.5c
Wind	36.6c
Muggies	32.3c

The "muggies" of Sundstroem's experiments were kept under stagnant air conditions, whereas the "wind" animals were in a well ventilated room. Gelineo and Giaja (22) measured the metabolic rate of rats kept at 7.5°, 18°, and 31°C. The calories produced per square meter of body surface per twenty-four hours were 859, 676, and 517 respectively. The results of these various metabolic studies check well and strengthen one another by bringing additional evidence of the influence exerted by the thermal medium on metabolism.

D. Variations in weight of the adrenals and adrenalin content due to variations in external conditions.

Table IV presents an interesting relationship between the weight of the adrenal glands and the ability to withstand chilling (15°C.) In the winter months, the control rabbits had adrenals weighing over 200 mgs. and were able to withstand the cold water for over 200 minutes. On the contrary, during the spring months, the adrenals of control animals weighed approximately 110 mgs. and these animals were near prostration from chilling within 70-80 minutes. There was likewise a seasonal variation in the adrenalin content of the left adrenal gland, which, calculated as percentage of the body weight, was about three times as high during the winter (49 x 10 − 6) as in the spring (16 x 10 − 6.)

Table IV.

Adrenalin Content of the Left Adrenal Gland of Control Animals Under Various Conditions.

Date	Body Wt. in Kgs.	Sex	Treatment	Wt. of Left Adrenal - mgs.	Survival Time in Minutes	Adrenalin in Left Adrenal as % of Body Weight
1/14/31, Winter	1.67	M	Normal	130	270	31 x 10 − 6
	2.24	M	"	234	300	39 x 10 − 6
	2.21	M	"	229	300	64 x 10 − 6
	1.99	M	"	388	195	55 x 10 − 6
Average					266.2	49 x 10 − 6
Winter	1.93	M	Injected*	160	270	36 x 10 − 6
	2.38	F	"	187	300	29 x 10 − 6
	2.38	F	"	185	90	36 x 10 − 6
	1.87	M	"	159	300	43 x 10 − 6
	2.13	M	"	275	120	65 x 10 − 6
Average				216+	216	41 x 10 − 6
4/23/31 Spring	2.64	M	Normal	150	75	Lost
	2.44	M	"	89	60	15 x 10 − 6
	1.93	M	"	111	70	16 x 10 − 6
Average					68.3	155 x 10 − 7
Spring	2.33	F	Injected*	140	120	26 x 10 − 6
	2.30	F	"	120	90	136 x 10 − 7
	2.38	F	"	118	120	309 x 10 − 7
	2.41	M	"	80	45	152 x 10 − 7
	2.27	M	"	105	60	123 x 10 − 7
	1.96	M	"	90	60	184 x 10 − 7
	2.13	M	"	98	60	142 x 10 − 7
Average				110	79.3	187 x 10 − 7

* Injected subcutaneously with 0.3 mg Adrenalin (1:1000solution, Parke, Davis & Co., 1 hr. before bath.)

There was also observed a difference in the weight of the adrenal (left) gland for the three experimental groups of rabbits (Table V.) The tendency was for these glands of the cold room animals to be heavier than those of the hot room and change group animals. Hartman and co-workers (23) observed that the exposure of rats to an environmental temperature of 4-18°C. for varying lengths of time, until a total of twenty hours was reached, lead to a 10% increase in the adrenal weight over that of the controls.

Table V.

Group	Average Body Weight - Kgs.	Average Wt. of Adrenal mgs.	Adrenalin of the left adrenal calculated as percentage of the body weight. Control	After 24 hr. fast	After exhaustion in water bath
Series I. 5/1/31.					
Hot	1.96	76.7 (9)	131 x 10 −7(5)	258 x 10 −7(4)	
Change	1.69	67.4 (6)	133 x 10 −7(3)	169 x 10 −7(3)	
Series II. 11/5/31.					
Hot	2.01	102.2 (7)*	145.5 x 10 −7(2)		138.4 x 10 −7 (5)
Cold	2.21	150.2 (7)	246.4 x 10 −7(2)		184.4 x 10 −7 (5)
Change	1.95	113.7 (10)	339.7 x 10 −7(3)		148.4 x 10 −7 (7)
Series III. 2/23/32.					
Hot	2.02	104.3 (7)	93.4 x 10 −7(2)	114 x 10 −7(2)	90 x 10 −7 (3)
Cold	2.82	146.2 (7)	64.0 x 10 −7(5)	149 x 10 −7(2)	64 x 10 −7 (5)
Change	2.29	112.4 (8)	110.0 x 10 −7(5)	134 x 10 −7(3)	110 x 10 −7 (5)

* Figures in parentheses indicate the number of cases.

The percentage of adrenalin in the left adrenal gland calculated as percentage of the body weight was generally less altered by chilling to exhaustion in the hot room animals than in those of the other groups. An increased secretion of adrenalin in cats has been obtained under the following conditions: cooling of the skin by ice, immersion in cold water or by the evaporation of water from the skin following an immersion in cold water (24). There is histological evidence of a heightened activity of the cortical region of the adrenal following exposure to cold. Mitoses in the cortical region increased over four-fold by keeping guinea pigs for eight to twenty-five days in a room with the temperature varying between 7-9°C. (25). Cramer (26) reported that in mice submitted to a high environmental temperature there was a disappearance of the cortical lipoid, conversely, there was a spreading of the cortical lipoid over the whole cortex in mice submitted to a cool environment. He concluded that the adrenal activity was proportional to the content of cortical lipoid. These results have been questioned by later workers. Miller (27) observed an age and sex relationship to a fat-free zone of the mouse adrenal. This X-zone represents the innermost part of the cortex; it develops more and persists longer in the female than in the male mouse. Miller's work has been confirmed by Whitehead (28) and Deanesley (29). The constant humid heat of the hot room in this study depressed both the activity of the adrenal cortex and of the medulla so that neither of

these mechanisms was capable of responding quickly in great emergencies but, daily stimulation by cold augmented the activity of this gland.

The month-by-month response to sudden chilling was studied in control animals. These rabbits were obtained from the same source each month, the specifications as to age and weight being the same as previously stated. Twelve animals of each sex were tested each month during the last eight months of 1931 and for the first month of 1932. The results of this study are presented in Table VI. The figures vary, but there is a definite tendency for the animals to withstand chilling longer during the winter months when, in general, the adrenal glands weigh most and contain the most adrenalin. It is my belief that if control animals were bred in out-of-door hutches over a period of years and representative numbers killed at the various seasons (the animals being comparable as to weight and age) a close parallelism would be observed between season and weight of the adrenal gland, such as has been previously shown for the thyroid (30).

Table VI.

Adrenal Weight, Percentage of Adrenalin, Survival Time in Water Bath (15°C.), and Liver Glycogen According to Time of the Year.

Month	Wt. of left Adrenal-mgs. F.	M.	Percentage of Adrenalin F	M.	Survival Time in Water Bath F.	M.	Percentage of Liver Glycogen F.	M.
					Minutes		Control	
June	85.6	85.1	193 x 10 − 7	70 x 10 − 7	62.5	80	6.41	4.73
July	58.0	78.3	95 x 10 − 7	105 x 10 − 7	45	60	5.29	7.1
Aug.	50.0	56.9	97 x 10 − 7	91 x 10 − 7	55	45	5.18	5.09
Sept.	63.7	84.2	83 x 10 − 7	105 x 10 − 7	75	80	4.42	6.6
Oct.	113.1	94.9	164 x 10 − 7	108 x 10 − 7	68.3	50	6.04	5.77
Nov.	118.3	133.2	123 x 10 − 7	153 x 10 − 7	130	145	9.39	10.80
Dec.	91.0	78.0	151 x 10 − 7	102 x 10 − 7	130	97.5	5.51	5.94
Jan.	59.0	57.5	168 x 10 − 7	106 x 10 − 7	109	95		

Hatai and Hammett (31) observed a sexual variation in the weight of the adrenal gland of albino rats, that of the female being the heavier. No sexual variation in the adrenal weight of the rabbits in this study was observed, but, in a much larger series, such as Hammett studied, such a relation might very probably be found. A seasonal variation in the muscle glycogen content of the dog, guinea pig, and carpes was reported by Maignon in 1921 (32). The maximum occurred in the summer and fall months. No significant variation was observed in the glycogen content of the large extensor muscle of the anterior aspect of the upper thigh of the hind legs of rabbits in this study.

Seidell and Fenger found approximately three times as much iodine in the thyroid gland of normal healthy hogs,

sheep, and cattle between the months of June and November as in the months between December and May (29). The probability that the seasonal variation in iodine content represented a variation in the activity of the thyroid led to an investigation of this subject by Mills (2 f). He found that rabbits kept at a high environmental temperature had an increased amount of colloid with low cuboidal epithelium. Animals kept at a cold environmental temperature had an increased thyroid activity and a small amount of colloid with high columnar epithelium. Stoland and Kinney fed 0.2 gm. dessicated thyroid per day to rats kept at 32°, 25°, and 18°C. Histological examination revealed the low cuboidal epithelium of a normal resting gland for all of the rats fed the dessicated thyroid and for all of the controls except those at 18°C. The latter animals had developed an active gland with a small amount of colloid and columnar epithelium (33).

The intravenous injection of the active principle of the thyroid, thyroxin, produces its maximum effect several days afterward. However, adrenalin produces its maximum response within a short time after injection. It is thus clear that the adrenal gland furnishes the mechanism whereby the body responds quickly to stimulation. Therefore, since an animal requires a greater heat production under chilling conditions, it may be assumed that the adrenal gland is the chief means by which the metabolic activity can be increased. On the other hand, the activity of this gland should be depressed during the warm seasons when there are fewer demands upon it to augment the metabolic rate.

E. Adrenalin hyperglycaemia in animals exposed to various temperatures.

The hyperglycaemic response to the injection of adrenalin was slightly more pronounced in hot room group animals than in the controls. Table VII contains these data. No significant difference was found in the blood sugar level between the various groups either at rest, during the chilling tests, or after a fast. The survival time in the water bath (15°C) was increased by a very few minutes following the subcutaneous injection of 0.3 mg. adrenalin as shown by Table VIII.

Table VII.

Comparison of Hyperglycemic Response of Control and Hot Room Group Animals to Intramuscular Injection of 0.3 mg. Adrenalin.

Date	Groups	Body Weight in Kilos	Treatment	After 16 hr. fast	Blood Sugar mgs. per 100 cc Time after taking first sample 1/2 hr.	1 hr.	2 hrs.	3 hrs.
1/12/31	Control	2.27	Normal**	115	115		122	
1/16/31	"	1.87	"	132		149	134	
1/12/31	"	2.41	Injected**	115	219		220	
1/16/31	"	1.76	"	127		324	319	
1/19/31	"	2.38	"	157		351		252
1/19/31	"	1.99	"	145		455		393
1/23/31	"	1.47	"	107		327	333	
1/23/31	"	1.84	"	110		179	238	
1/23/31	"	1.39	"	113		228	262	
1/26/31	"	2.33	"	146		404	379	
1/26/31	"	2.67	"	120		356	366	
1/26/31	"	2.81	"	113		356	358	
Averages				125.3		331.1	309.4	
% Increase Over Fasting Level						164	147	
2/17/31	Hot room	1.39	Injected*	131		335	294	
2/17/31	" "	1.67	"	123		376	332	
2/18/31	" "	1.13	"	145		393	444	
2/18/31	" "	1.33	"	130		430.	515	
Averages				132		383.5	396	
% Increase Over Fasting Level						190	200	

* Animals were kept in the hot room during the experimental period.

** Animals were placed in the hot room for 1/2-3/4 hr. before the first sample of blood was drawn and kept there during the experimental period.

Table VIII.

Adrenalin Content of Hot Room and Change Group Animals Under Various Conditions.

Spring Groups	Body Weight in Kilos	Sex	Treatment	Wt. of left Adrenal mgs.	% of Body Weight Represented by the Adr. in Left Adrenal
Hot	1.59	F	Killed after 24 hr. fast	81	203 x 10 − 7
"	1.48	F	"	62	163 x 10 − 7
"	1.42	M	"	65	26 x 10 − 6
Average				69+	213 x 10 − 7
Winter Groups					
Hot	1.08	M	W. B. 15 minutes	98	19 x 10 − 6
"	1.53	F	" " 60 "	225	22 x 10 − 6
"	1.59	M	" " 90 "	140	30 x 10 − 6
Average		Survival Time 55 minutes			237 x 10 − 7
Hot	1.10	M	W. B. 30 minutes*	170	58 x 10 − 6
"	2.16	F	" " 75 " *	112	18 x 10 − 6
"	1.33	M	" " 90 " *	130	25 x 10 − 6
Average		Survival Time 65 minutes		146	34 x 10 − 6
Spring Groups					
Change	1.65	F	Killed after 24 hr. fast	62	16 x 10 − 6
"	1.73	M	" " " "	57	198 x 10 − 7
"	1.50	F	" " " "	60	29 x 10 − 6
Average				59.7	216 x 10 − 7
Winter Groups					
Change	1.47	M	W.B. 30 minutes	268	34 x 10 − 6
"	1.70	F	" " 110 "	280	22 x 10 − 6
Average		Survival Time 70 minutes			28 x 10 − 6
Change	1.56	M	W.B. 105 minutes*	223	12 x 10 − 5
Average				273	

W.B. Water Bath 15°C.

* Injected with 0.3 mg. adrenalin immediately before being placed in water bath.

F. Variations in power to result hyperthermia due to the nature of the previous environment.

In a way similar to the chilling tests described above, the animals from the three groups were also tested for their ability to withstand high temperatures. The water bath was kept at 110°F. (43°C.) and the time required for prostration noted. The time of prostration was taken as that moment when they were no longer able to hold their heads above the water.

Water Bath 110°F.

Hot room animal		survived	110 minutes
Cold "	"	"	95 "
Change "	"	"	80 "

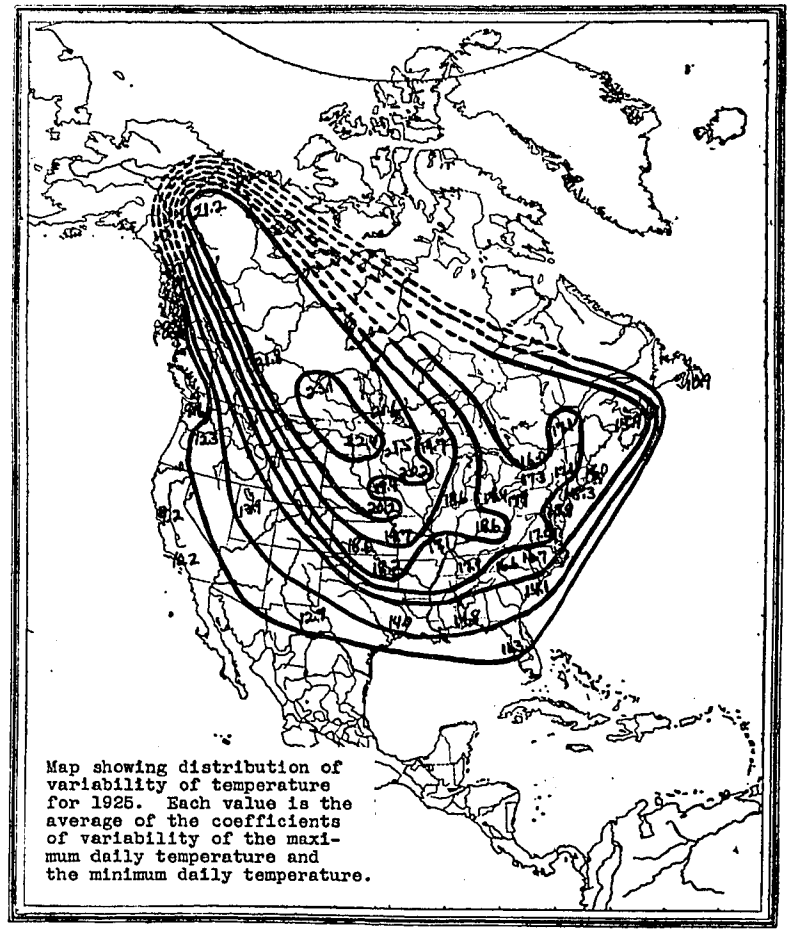
In the next series, four animals from each of the three groups were placed in the hot room and the temperature level raised up to 96°-100°F. As a result, all of the cold room and change group animals were dead within 36 hours, whereas the hot room animals survived 36, 88, 92, and 110 hours, respectively. Thus, the animals adapted to the constant heat of the hot room evidently adjusted their metabolic rate to a lowered plane better than those previously in the cold, for in the water bath there was probably no difference in the rate of heat transfer through the skin in the different groups. I believe this was accomplished mainly by the hot room animals reducing their metabolic rate, probably by suppressing the activity of the adrenal glands. The heat adapted animals were therefore better equipped to withstand higher temperatures than lower ones. On the other hand,

animals which were stimulated daily by exposure to cold had more active adrenals and when suddenly exposed to a high temperature were less able to suppress heat production and delay the exhaustion which such temperatures cause.

Strikingly, those animals, which spent sixteen hours of each day in the hot room and the remaining eight in the cold room, were the least able to withstand added temperatures, yet were the most responsive to chilling emergencies. The adrenal mechanism was thus highly active in these shifted animals, but could not be quickly suppressed when exposed to higher temperatures.

The results just reported on the susceptibility of differently adapted animals to heat were carried out by Dr. Mills. They indicated clearly a basis for the well known human susceptibility to excessive heat. Deaths and prostration from excessive heat are, in general, more frequent in those cooler portions of the temperate zones that at times must endure heat waves of several days duration. In our north central states, from the Rocky Mountains eastward to the Atlantic Ocean, and less so in west central Europe, heat prostration is most frequent. Coincidentally, the climate is most stimulating and the temperature variability highest in these two areas. Dr. Mills suggested that a statistical study of this problem for the continent of North America be undertaken. Such a study was accordingly made and there was found a fairly close agreement between the areas of greatest climatic stimulation and those of highest death rate from heat stroke.

Desk Outline Map of North America. No. 3005b



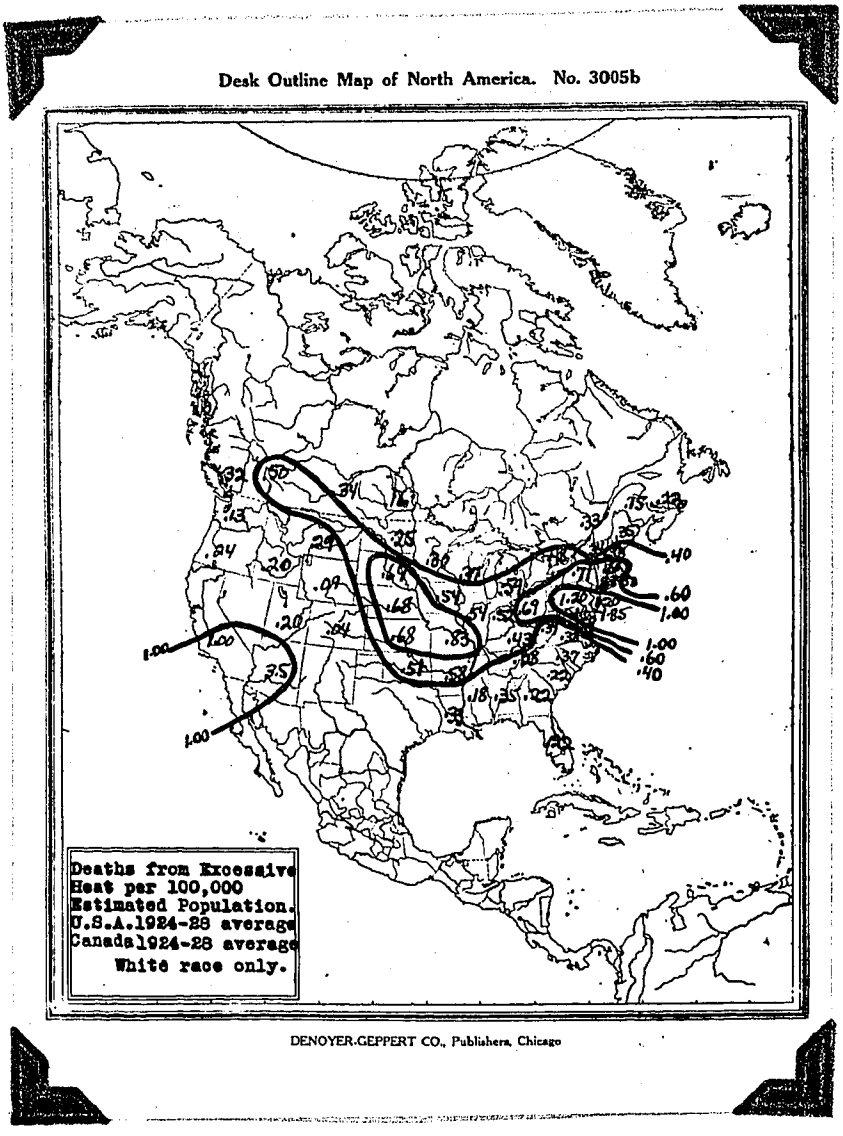
Map showing distribution of variability of temperature for 1925. Each value is the average of the coefficients of variability of the maximum daily temperature and the minimum daily temperature.

Published by DENOYER-GEPPERT CO., Chicago

MAP I

These deaths were calculated as the annual average number per 100,000 estimated population in the states of this country and provinces of Canada for the five year period of 1924-28. The results are presented in Map II with the highest rates falling in Pennsylvania, Maryland, New Jersey and Delaware. Next came New York, Connecticut and Ohio, and another area in the northern prairie states from Kansas northward. When correction is made for differences in age distribution of the population in the eastern and western high areas, however, it is found that the adjusted rate is highest in the western area. Thus, for a group of eastern states (Massachusetts, Connecticut, New York, New Jersey, Maryland and Pennsylvania) the adjusted rate for the year 1920 is 1.55 per 100,000 population; while it is found to be 1.82 in the western group (Missouri, Kansas, Nebraska, Wisconsin, Illinois and Michigan).* We may, therefore, place the entire area extending from our prairie states (from Kansas to the Dakotas) eastward across the Great Lakes area to the Atlantic coast, on a fairly uniform basis regarding susceptibility to excessive heat. The area centering around Iowa and eastern Nebraska shows perhaps the highest adjusted heat death rate. These adjusted rates were based on the total number of deaths in groups of states (in the eastern and north central portions of North America) in order to obtain a sufficiently large number of cases that could be treated mathematically. Such a

* This calculation of the adjusted rate could be carried out only for 1920, the census year, for which the age distribution of the population is obtainable.



MAP II

calculation could not be made for the south due to the scant number of cases.

The effective heat to which the people in different areas are subjected is variable and difficult of estimation. In the prairie states higher temperatures are recorded, but humidity is usually low during heat waves. In the Great Lakes region and to the eastward somewhat lower temperatures are equally as fatal because of the high humidity that accompanies them. The region of greatest temperature variability in North America (2c) extends from the northern prairie provinces eastward across the Great Lakes area to the coast, but lessening toward the New England states. The entire south possesses a much lower degree of temperature change from day to day. The Pacific northwest possesses a low temperature variability but remains always within the limits of the optimum for human activity. Excessive heat is rarely encountered in the Pacific northwest or in the Canadian provinces except those in the prairie belt. The theoretical area where, according to the climatic postulation, heat sensitivity should cause the greatest death rate thus coincides fairly closely with the actual areas of high rates.

In addition to the great day to day temperature variability of our prairie states, there is also a wide diurnal fluctuation which stimulates bodily activity and renders people all the more susceptible to excessive heat, just as it did the rabbits. In the southwest, in Arizona, New Mexico, Nevada and southern California, the diurnal variation

is very great, particularly in the mountain-bound deserts, and probably helps to account for the high heat death rates observed there.

As in the animal experiments described above, the susceptibility of the human being to excessive heat depends upon the type of climate to which he has been previously adapted. Not all people in a given locality are similarly affected, any more than all such people are alike in other respects, but the character of the climate determines in large measure the general heat sensitivity of the population.

Since it had been found that environmental temperature conditions so markedly influence the energy level, it seemed worth while to determine whether our artificial "climates" would have any effect upon the functionings of the sex glands. And, if so, we desired to determine which environmental regime would support the highest level of fertility and whether the same set of conditions would be conducive to a well sustained fertility. This study is presented in Part II.

Part II. Adaptation of Sexual Activity to Environmental Stimulation.

A. The age at which maturity is reached.

Albino mice were used exclusively in this part of the investigation.

The special animal rooms described in Part I were used in this and the following experiments. A single strain of albino mice was bred in a control room (70°-80°F.) and, at the end of twenty-one days, the young were separated from the mothers and placed in the various groups for observation. Such mice, allocated to the various groups, are termed "immigrants" to the respective groups. The offspring of the "immigrants" to a group are referred to as the "descendants" of the given group.

There have been five experimental groups, namely: control room group; hot room group (88°- 92°F.); and two change groups. One change group (change group I) spent twelve consecutive hours a day in the hot room and the remaining twelve in the cold room; the second change group, like the first, spent twelve consecutive hours in the hot room, but for the remainder of the day was shifted back and forth three times between the two rooms, spending a total of sixteen hours in the hot room and eight hours in the cold room each day.

The females were mated with control males soon after the rupture of the vaginal plate. The first oestrus and the length of the oestrus cycle were determined by the usual vaginal smear method. After suckling the young twenty-one

days, the mothers were rested seven days before they were remated. Purina chow and water were given freely, and lettuce on alternate days to all animals. The mothers received, in addition, a few sunflower seeds and small amounts of lean raw beef once a week. This diet had been found amply sufficient for constant reproduction. The animals were weighed each seventh day after the day of separation from the mothers. Weighings were carried out to the nearest tenth of a gram.

The cages were of 1/4 inch mesh galvanized wire, 9x9x15 inches, with a closed food bin. Keeler (34), in his book, "The Laboratory Mouse", describes a closed food bin for mouse cages, but the type used here was described by him in a private communication. It consists of galvanized wire of 1/3 inch mesh forming a closed sloping trough near the top of the cage in the rear with food admitted to the bin through a small opening in the top of the cage.

Maternity cages suitable for mice were constructed as a definite and convenient means of determining litter size. These cages were made in the same manner as the breeding cages except for the bottoms, which were of 1/2 inch mesh wire so that the young would fall through as soon as delivered and thus prevent pedophagy. Trays, 2 inches deep, the same in length and width as the maternity cage proper and lined with paper toweling, served as the true floor or bottom for these special cages, and the young

would fall through the large meshes of the false floor to these trays. Pregnant females were placed in the maternity cages on about the second or third day prior to parturition as calculated by the date of the vaginal plug. The mother and young were removed from the maternity cage to the regular cage soon after the delivery. Paper toweling was used as the nesting material.

Dealing first with the time of onset of sexual functioning, it is seen from the data in Table IV that the vaginal plate ruptured at practically the same age for the cold room group and control room group females, whereas this phenomenon for the hot room group "immigrants" and the cold room group "descendants" occurred at a later age. The difference is slight, however, and not mathematically significant. The change group females occupied an intermediate position. It is interesting to note here that Sundstroem (7) observed the vagina of mice to open at an earlier age in a stagnant hot room than in the control room.

It has been commonly observed since Daniel's report in 1912 (35) that eating of their young [pedophagy - pais (child), phagein (eat)] by female mice is extensive under extremes of temperature or when there is marked fluctuation in the environmental temperature. In this study, it was difficult to get the hot room females to care for their young, hence the small number of hot room descendants for which only the arithmetical values of the age of plate rupture and first oestrous are given. Maturity with them was much

delayed. There was no difference observed in the length of the oestrous cycle. Prizbaum (36) also believes that a high environmental temperature has no influence on the oestrus cycle of rats.

Table I.

Mean Age of Control Room Females at Opening of Vaginal Plate and First Oestrus.

Number	Age at Plate Rupture	Age at First Oestrus	Number	Age at Plate Rupture	Age at First Oestrus
1050 – 2	28	28	238-2	31	
4	28	28	4	31	
6	28	28	1052	32	
8	28	28	103-4	32	
10	28	28	6	32	
12	28	28	8	32	
64-1006	38		10	32	
1014	31	31	12	32	
1016	33	35	122-4	31	
1018	31	31	206-2	31	
1034	32	33	-62	33	
1022	36	37	-82	31	
1024	30	33	-78	33	33
10-72	34	35	-86	33	38
6-2	30		1040	30	30
4	28		6-8-20	41	41
6	30		6-822	42	44
8	28		306-2	28	
10	30		305-32	27	
318-2	37		305-34	27	
Mean	32.04 ± 2.03	33.22 ± 0.976			

Table II.

Mean Age of Hot Room Immigrant Females at Opening of Vaginal Plate and First Oestrus.

Number	Age at Plate Rupture	Age at First Oestrus	Number	Age at Plate Rupture	Age at First Oestrus
10	37	37	76	46	46
12	31	32	78	31	32
14	37	38	80	35	36.5
16	40	46	82	35	36
18	39	39	84	33	33
20	30	35.5	86	36	36
22	33	33	88	35	36
26	31	32.5	90	34	36
28	31	31	94	35	35
32	49	50	96	42	46
34	37	37	98	50	50
38	36	38	506	38	33.5
40	38	40.5	508	33	33.5
42	32	36.5	510	38	39
44	23	25	512	23	23
46	34	37	514	35	42
48	32	32	516	31	31
50	32	33	518	31	31
52	35	36	520	32	33
54	34	35	522	37	38
56	33	35	524	31	32
58	32	36	526	33	33
60	37	37	528	32	32
62	28	28	530	41	42
64	38	38	532	34	34
66	30	34	534	43	46
68	27	27	536	24	24
70	34	36	538	29	29
72	29	29	542	34	34
74	31	31			
Mean	34.74 ± 1.04	35.7 ± 1.13			

Table III.

Mean Age of Hot Room Descendant Females at Rupture of Vaginal Plate and First Oestrus.

Number	Age at Plate Rupture	Age at First Oestrus
14 - 2	41	56
14 - 4	42	43
14 - 6	36	54
14 - 8	37	37
12 - 502	41	47
12 - 504	50	50
544	36	37
64 - 548	43	44.5
- 550	47	47
Averages	41.4	46.16

Table IV.

Mean Age of Cold Room Immigrant & Descendant Females at Rupture of Vaginal Plate and First Oestrus.

Number	Age at Plate Rupture	Age at First Oestrus	Number	Age at Plate Rupture	Age at First Oestrus
102 "I"	28	29.5	128 "I"	31	31
104	31	33.5	132	30	31
106	28	32.5	640	24	24
108	28	29	136	28	29
110	28	30	138	40	41
112	35	35	140	34	35
114	33	35.5	142	40	41
116	40	40	144	40	41
118	30	30.5	178	48	48.5
120	30	30.5	180	50	50
122	37	37	630	35	35
124	31	31	638	25	25
126	35	38			
Mean	32.82 ± 1.50	33.42 ± 1.55			
166 "D"	23	26	610	42	42
168	35	35	612	32	32
170	39	40	614	25	25
172	30	30	616	30	31
174	44	44	618	36	36
176	37	37.5	620	30	30.5
130	30	41	622	39	35
134	30	43	624	29	31
182	31	33	626	37	38
184	31	31	628	26	26
186	32	36	632	28	28
188	31	31	634	38	38
190	26	26	636	45	45
192	37	37	642	34	34
194	42	44	646	28	28
198	32	33	648	31	32
602	35	37	650	32	32
604	37	38	652	27	28
606	36	37	146	37	38
608	44	44	148	37	38
196	34	34			
Mean	34.1 ± 1.312	35.12 ± 1.116			

Table V.

Mean Age of Change Group Females at Opening of Vaginal Plate and First Oestrus.

Number	Age at Plate Rupture	Age at First Oestrus	Number	Age at Plate Rupture	Age at First Oestrus
202	46	47	312	36	36
204	44	48	316	30	31
206	38	43	318	27	30
208	42	42	320	37	38
210	41	42	322	32	35
212	37	39	324	33	33
214	38	39	326	33	33
218	41	42	328	26	27
216	26	26	330	33	34
220	29	31	332	25	25
228	31	31	334	31	34
232	35	35	336	31	31
234	40	41	338	27	28
256	26	29.5	340	25	25
302	31	42	342	25	25.5
304	30	31	346	32	33
306	32	35	348	26	26
308	43	44	314	40	40
310	39	39			
Mean	33.52 ± 1.125	35.28 ± 1.335			

Summary of Table I-V.

Mean Ages of Females at Rupture of Vaginal Membrane and First Oestrous

Group	Number of Animals	Mean Age at Plate Rupture - days	Mean Age at First Oestrous-Days
Control	40	32.04 ± 2.035	33.22 ± 0.976
Hot Room			
"Immigrant"	59	34.74 ± 1.0397	35.76 ± 1.129
"Descendant"	9	41.4*	46.16*
Cold Room			
"Immigrant"	25	32.82 ± 1.500	33.42 ± 1.553
"Descendant"	41	34.1 ±	35.12 ± 1.116
Change	37	33.52 ± 1.125	35.28 ± 1.335

*Arithmetical averages

The age at first oestrous was determined for 18 control room females.

B. Size of litters.

The first litters delivered by the females of the control and cold room groups contained practically the same number of young. The control group females, during their first five litters, brought forth about an equal number of young each time, but the cold room group females increased their litter size beyond the original figure and, at the age of 225-364 days, delivered litters averaging about eight young. The cold room descendant females were fertile at an earlier age than the females of any group. The

females of the hot room and change groups had the lowest fertility, as shown by Table VI, and gave birth to many dead young (Table VII). These results on reproduction under conditions of humid heat confirm the findings of Steinach and Kammerer (37) on the rat and Sundstroem (7) on the mouse. The former authors report that such conditions lower the fertility of female rats and the litters are small. Sundstroem, due to the difficulty of obtaining pregnancies in his hot room mice, transferred pregnant females from the control room to the hot room in order to obtain "descendant" animals.

Table VI

Average Litter Size

Litter Sequence	20 Control Room Females	45 Hot Room Females	21 "Immigrant" 23 Descendant Cold Room Females	21 Change I Groups Females	21 Change II Groups Females
1	6.8 young ‡ (20)* [84.2 da]	‡5.6 young (20) [98.5 da]** + 3.33 " (18)	6.71 young ‡ (21"I") [94.6 da] 6.91 young ‡ (23 D) [78.7 da]	2.3 young ‡ (3) [94 da]	5.25 young ‡ (8) [93.2 da]
2	6.3 young ‡ (18) [132.27 da]	5.1 young ‡ (9) [145 + da]	8.43 young ‡ (14 "I") [138.1 da]	Changed to Cold Room 4.11 young ‡ (9) [158 da]	2.66 young ‡ (3) [187 da]
3	7.1 young ‡ (15) [177.4 da]	Changed to Cold Room 7.75 young ‡ (8) [197 + da]	8.0 young ‡ (7♂) [211.6 da]	Changed to Hot Room 6.0 young ‡ (5) [179 da]	Changed to Cold Room 4.3 young ‡ (3) [308 da]
4	6.5 young ‡ (13) [234.4 da]		Changed to Hot Room 4.8 young ‡+(6♂) [178 da]		Changed to Hot Room 6.9 young ‡ (10) [187 da]
5	6.4 young ‡ (8) [265.15 da]				
Number Fertile at 100 days of age	20(100%)	38 (84.4%)	21"Immigrants" 23 Descendants (100%)	3 (14%)	8 (38%)

* Figures in parentheses indicate the number of cases.
** Figures in brackets indicate the average age of mothers at delivery of young.
‡ Females were mated with control males.
\+ Females were mated with hot room group males.

Four hot room group males were mated with hot room females (thirty-five to fifty days of age). Each male was mated with from five to seven females. There were eighteen successful pregnancies from these twenty to twenty eight matings, with an average litter size of 3.33 young (a total of sixty young in the eighteen litters). Twenty hot room group females (thirty-five to fifty days of age) were successfully mated with control males in the hot room with 112 young born, or an average litter size of 5.6 young. Thus smaller litters were born when both males and females belonged to the hot room group than when hot room females were mated with control room males.

After the delivery of their first litters, females of the hot room and change groups, although repeatedly mated with males from the control group, bore scarcely any young. In the case of the hot room females, it seemed possible that the low sexual functionings were engendered by the constant depressive conditions in the hot room, and, therefore, perhaps a sojourn in the cold room would be beneficial. To test this, eight hot room females, at an average age of 167 days, were placed in the cold room and mated with control males. Within thirty days, these females had borne litters averaging 7.75 young each, or an increase in fertility of 97% for the hot room females who had been mated with hot room males and an increase of 34% for the hot room females mated with control males in the hot room. As Table VII also

shows, six cold room females were placed in the hot room at an average age of 152 days. Three were there mated with control males and three with hot room males. These females bore young at an averate age of 178 days, i.e. 26 days after entering the hot room. The number in each litter was 4,2,7, respectively for the former matings with the control males; and 5,5,6, for the matings with hot room males. Hence, the average litter size was 4.8 young, whereas the previous average number of young delivered by these females in the cold room was 8.3. Thus by mating the cold room females in the hot room, with either hot room or control room group males, the result was a decrease of 41% in litter size. This indicates that the diminution in fertility observed when both males and females were in the hot room, must have been due chiefly to the effect in the female. And this in spite of the fact that the oestrus cycle was unaffected.

Altogether, there were forty-two females in the two change groups. Only eleven of these had borne young at ninety-four days of age, this low fertility indicating functional exhaustion of the sex glands. The sudden daily change from a hot, moist environment to a steady cool state was far too severe for the females of the change I group,as attested by the fact that only three (14%) of the twenty one were able to reproduce under these strenuous conditions. In order to determine whether the remaining 18 females, at one hundred and twenty-one days of age, had been rendered sterile by the environmental conditions, the shifting was discontinued and

they were kept in the cold room for a period of four to six weeks and mated with cold room males. Nine (42.8%) of these females then bore young with an average litter size of 4.11 young. Thus, subjection to the steady cool environment immediately after the period spent under the shifting conditions enabled more of these females to be successfully mated and to bring forth a greater number of living young in each litter. But as yet, only twelve of these change I group females had borne young. The remaining nine that had failed to reproduce at an average age of one hundred and forty-three days were mated in the hot room with control males. Five of the nine then bore young with an average litter size of six young; which was the largest litter size for change I females under any conditions.

The change II group females were rested in the hot room for a greater length of time each day than the change I group animals and, hence, were more fertile than the latter while undergoing the respective shifting routines. For this reason, when the shifting of the change II group females was discontinued and they were kept in the cold room, only three of the thirteen hitherto sterile bore young and with an average litter size of 4.3 young; This was a decrease in litter size of near twenty percent. The ten still sterile were then returned to the hot room and there mated with control room group males and all bore litters averaging 6.9 young each. The steady moist heat of the hot room was evidently quite a tonic to the reproductive processes of these over-stimulated females since both change groups were more fertile during

their sojourn in the hot room than under any other environmental conditions to which they were subjected.

C. Viability of young.

Fewer dead young were delivered by the offspring of the cold room females (cold room "descendants"), when living in the cold room, than by any other group of females (Table VII.) However, the female offspring of control room females which, at 21 days of age, were separated from their mothers and placed in the cold room ("immigrants" to the cold room), after their first litters, approached the low figure set by their "descendants." It seems, therefore, that after approximately 100 days in the cold room the generative system of the "immigrant" females had become better suited for the reproduction of healthy young. Near fifteen per cent or more of the young from the hot room and change group females were still-births, many of these being abnormally large when the litter size was small. Only one change I group female and three change II group females bore more than one litter while in the shifting groups. There were six of such litters with a total of eighteen young, six or 33.3%, of which were dead. The reproduction by all females is given in detail in Tables VIII - XIII.

Table VII.

Control Room (70°-80°F.) group Females

20	- 1st litters	- total of	136	young with	15	or	11.0%	dead
17	- 2nd "	- " "	108	" "	13	"	12.0%	"
38-3-6th	"	- " "	257	" "	13	"	5.0%	"

Hot Room (88°-92°F.) Group Females

37	- 1st litters	-total of	169	young with	25	of	14.8%	dead
9	- 2nd "	- " "	46	" "	8	"	17.8%	"
9-3 to 5th	"	- " "	49	" "	8	"	16.3%	"

Cold Room (60°- 68°F.) "Immigrant" Females

21-1 st litters		- total of	143	young with	10	or	6.9%	dead
14-2 nd	"	- " "	118	" "	5	"	4.2%	"
10-3 to 5th	"	- " "	82	" "	4	"	4.9%	"

Cold Room Group "Descendant" Females

27-1 st litters - total of 190 young with 8 or 4.2% dead

Change Group Females

18 - 1 st litters - total of 73 young with 13 or 17.8% dead

Table VIII.

Litter Size According to Age of Control Room Females.

Number	Age in Days	Litter Size	Number	Age in Days	Litter Size	Number	Age in Days	Litter Size
6 - 2	105	6	238 - 4	57	4	306 - 2	78	9
	155	9		88	5		121	5
	209	7		118	9		172	11
6 - 4	76	9		169	10		229	8
	145	5		211	2		280	6
	191	9		244	7	23 - 62	84	8
	248	6	103 - 2	81	7		152	7
	308	5		131	5		219	10
6 - 6	69	5		166	6		273	9
	95	6		247	7	23 - 64	112	9
	143	6	-4	66	6		151	5
	211	4		128	6	3 - 84	94	7
	274	5		210	9	305 - 32	103	8
6 - 8	68	5		269	3		147	9
6 - 10	68	7	-12	69	6		179	4
	105	6		115	8		229	9
	154	6		147	8		260	10
	196	3	122 - 4	111	8	- 34	82	8
	258	8		137	7		147	3
	295	7		200	7		240	8
318 - 2	60	2		272	7	10 - 2	116	8
238 - 2	60	6	206 - 2	125	8		157	8
	105	7		150	7		212	4
	168	7		173	3			
	225	7		213	5			
	278	9		252	6			

Table IX.

Litter Size According to Age of Cold Room Immigrants.

Number	Location	Age in Days	Litter
	Cold room	78	3?
	" "	105	9
	" "	226	7
	" "	287	10
120	" "	364	8
	Cold Room	71	5
	" "	112	10
	" "	241	9
123	" "	303	8
	Cold Room	83	8
	" "	145	11
102	Hot Room	201	5
	Cold Room	82	6
	" "	134	7
	Hot "	195	7
106	Cold "	236	5
	Cold Room	106	5
	" "	150	10
110	" "	224	10
	Cold Room	79	6
	" "	102	8
112	" "	169	7
	Hot Room	202	5
	Cold "	95	7
114	" "	158	8
	Cold Room	117	5
	" "	152	9
116	Hot "	209	6
	Cold Room	129	8
	" "	163	9
120	" "	225	8
	" "		
	Cold Room	88	7
	" "	144	8
122	" "	197	8
	Cold Room	103	8
	" "	150	6
126	" "	199	7
	Cold Room	97	6
124	" "	154	10
	Cold Room	98	4
128	" "	146	4
	" "	110	9
140	" "	154	9
125	Cold Room	75	9
152	Cold Room	104	7
162	Cold Room	103	7
164	Cold Room	85	9
178	Cold Room	75	7
180	Cold Room	76	6
604	Cold Room	78	7
608	Cold Room	90	5

Table X.

Litter Size According to Age of Cold Room Descendants.

Number	Location	Age in Days	Litter	Number	Location	Age in Days	Litter
	Cold Room	87	8	188	Cold Room	70	5
	" "	131	8				
132	" "	202	7	184	Cold Room	68	7
	Cold Room	75	8	192	Cold Room	68	5
136	" "	109	8				
				196	Cold Room	64	7
	Cold Room	101	10				
	Hot Room	155	4	198	Cold Room	63	6
138	Cold Room	192	8				
				612	Cold Room	68	8
	Cold Room	62	6				
	Hot Room	105	2	620	Cold Room	71	9
144	Cold Room	150	3				
				624	Cold Room	82	8
154	Cold Room	100	8				
				632	Cold Room	71	4
156	Cold Room	91	7				
				614	Cold Room	69	7
166	Cold Room	108	7				
				616	Cold Room	81	8
168	Cold Room	80	7				
170	Cold Room	78	6				
174	Cold Room	97	6				
176	Cold Room	90	6				
186	Cold Room	66	6				

Table XI.

Litter Size According to Age of Hot Room Females.

Number	Location	Age at Delivery	Litter Size
	Hot Room	85 da.	5
	" "	121 "	7
	" "	200	6
	" "	234	5
0	" "	342	3
	" "		
	Hot Room	93	5
10	" "	160	7
	Hot Room	97	6
	" "	155	5
	" "	179	6
	" "	215	5
12	Cold Room	295	8
	Hot Room	74	9
	" "	221	4
14	" "	274	7
	Hot Room	101	2
	" "	126	7
	" "	160	7
14-4	" "	199	8
	Hot Room	100	4
		169	2
14-8	Cold Room	223	?4
	Hot Room	91	5
	" "	117	6
20	Cold Room	194	7
	Hot Room	168	3
22	Cold Room	206	8
	Hot Room	91	2
26	" "	120	3
	Hot Room	85	2
	" "	118	5
	" "	166	2
28	Cold Room	203	9
	Hot Room	162	2
14	Cold Room	238	8
16	Hot Room	175	4
12	Hot Room	149	1
18	Hot Room	123	1
50	Hot Room	107	1
52	Hot Room	111	5
54	Hot Room	101	6
	Cold Room	149	6
56	Hot Room	113	7
516	Hot Room	86	3
60	Hot Room	108	6
64	Hot Room	81	6
	Hot Room	79	6
62	Cold Room	140	8
74	Hot Room	102	2
76	Hot Room	91	7
80	Hot Room	97	10
82	Hot Room	96	4
84	Hot Room	96	8
86	Hot Room	72	3
88	Hot Room	69	6
90	Hot Room	69	6

?—Females were not in maternity cages at time of delivery.

Table XI. Continued.

Litter Size According to Age of Hot Room Females.

Number	Location	Age at Delivery	Litter Size
96	Hot Room	69 da.	6
98	Hot Room	86	3
	Hot Room	69	2
502	Cold Room	130	8
504	Hot Room	85	3
32	Hot Room	101	6
506	Hot Room	70	6
510	Hot Room	64	6

Table XII.

Litter Size According to Age of Change I Group Females.

Number	Location	Age in Days	Litter Size	Number	Location	Age in Days	Litter Size
	Ch. I Group	77	2		Cold Room	*140	
	Ch. I Group	98	6	218	" "	170	1
212	Ch. I Group	175	2				
	Ch. I Group	238	2		Hot Room	*140	
				228	" "	160	7
	Hot Room	*163					
202	" "	199	5		Cold Room	*104	
				232	" "	129	3
	Ch. I Group	103	4				
	Hot Room	*181			Cold Room	*95	
206		231	8	234	" "	132	5
	Hot Room	*142			Cold Room	*93	
208	Hot Room	177	5	236	" "	133	2
210	Ch. I. Group	132	4		Cold Room	*104	
				238	" "	147	3
	Ch. I. Group	102	1				
	Cold Room	*140			Cold Room	*88	
212	Cold Room	176	1	240	" "	139	8
	Cold Room	*140			Hot Room	*90	
214	Cold Room	188	7	256	" "	126	5
	Cold Room	*182					
216	" "	206	7				

* Age in days when removed from Change Group I.

Table XIII.

Litter Size According to Age of Change II Group Females.

Number	Location	Age in Days	Litter Size	Number	Location	Age in Days	Litter Size
	Ch.II Group	89	7	306	Hot Room	231(*-209)	8
	" " "	169	4				
310	Cold Room	308*	2		Ch.II Group	88	3
				310	Hot Room	206(*-184)	3
	Ch.II Group	81	4				
	" " "	195	2		Hot Room	189	3
312	Cold Room	303(*-277)	7	320	" "	162*	
314	Ch.II Group	84	6				
	" " "	90	5		Hot Room	181	8
	" " "	196	2	324	" "	158*	
316	Hot Room	303(*-277)	6		" "	180	9
				328	" "	158*	
318	Cold Room	314 (*-277)	4				
					Ch.II Group	81	3
302	Ch.II Group	112	6	330	Hot Room	203(*-184)	10
306	" " "	121	8	338	Hot Room	124(*-103)	8

D. Age of cessation of fertility.
Female mice, generally, cease to be fertile between the ages of ten to twelve months, but males keep their fertility much longer.

In order to obtain an approximation for the cessation of ovarian activity, older females of the cold room and hot room groups were mated in their respective rooms with control males. Nine of the most fertile cold room females at the age of eleven to thirteen months were mated for six weeks to two months. At the end of this time, five of the females had borne an average litter of six young. On the other hand, seven of the ten most fertile hot room group females similarly mated with control males between the age of thirteen to eighteen months, bore an average litter of 3.86 young during this period. This indicates that the fertility of the hot room females lasts longer than that of the cold room. It will be recalled that there was no difference in the onset of maturity.

E. Discussion of results.

Thus we have data on laboratory animals which bear out the observations on human beings to the effect that climatic stimulation markedly influences the activity of the sex glands. The steady coolness of the cold room produced an increase in the fertility of the females there, but shortened somewhat the length of the span of fertility; whereas the constant heat and high humidity of the hot room were conducive to small litters with most of the young born dead but fertility persisted longer. The fertility

of the cold room females was markedly decreased by mating them in the hot room and keeping them there during the gestation period, while a sojourn of equal duration in the cold room brought about a pronounced increase in litter size for hot room group females.

The shifting environmental conditions tested during this experiment were most unfavorable to reproduction. However, either constant moist heat or a steady cool environment enabled these change group animals, in most cases, to increase their fertility, the former condition being decidedly more beneficial that the latter. In time, the conditions prevailing in the hot room would very probably bring about a reduction in the newly acquired fertility of these females (originally of the change groups) down to that of the regular hot room group females. There seemed to be a definite reproductive exhaustion in these mice submitted to the most changeable and excessive stimulation.

Many observations point toward a very intimate relationship between the adrenal glands and the ovaries, but the fine points of such inter-relationships are by no means clear. Riddle (38) observed an hypertrophy of the adrenal cortex coincident with ovulation in birds. Similar results have been obtained with the guinea pig (39), frog (40), mole (41), and rat (42). Adrenalectomy leads to a suppression of the oestrous cycle in the experimental animal but the injection of cortin restores the cycle to normal(43), (44), (45). Cortical injection also leads to an earlier maturity of female

rodents (45). The temperature of the room in which rabbits are housed influences the length of time consumed for the response by ovulation following the injection of pregnancy urine (46). The sexual functionings under the various conditions here described are believed to be dependant on changes in the inter-relationships between the adrenals and the ovaries, with the adrenals probably initiating the responses to changes in environmental stimulation.

F. Effects on the males.

As stated above, fertility was high in the cold room and control room group males, but lower in the hot room males, However, the change group males evidenced a most marked loss of fecundity. Eight of these males (50 days of age) were mated with control females in the control room and normal litters resulted. Matings of these same males with females of the change group, while undergoing the shifting regime, rarely resulted in pregnancy. There was noted a most interesting behavior of the male mice in regard to the use of their scrotal sacs. It is commonly considered that retention of the testes within the body cavity leads to sterility, but here the testes of the cold room group males remained in the abdominal cavity as long as the mice were kept in the cold room without producing sterility. Those of the hot room and change group males rested in scrotal sacs which depended farther than in control mice. However, the cold room group males which were mated in the hot room developed far depending scrotal sacs within

three days after their admission to the hot room; but upon return to the cold room the testes moved back to their former abdominal position. The testes of the control room group males rested in scrotal sacs which did not depend as far as those of either the hot room group or change group males. Although retaining their testes within the abdominal cavity, the males in the cold room were fully as fertile as the controls, and more fertile than those in the hot room with well descended testes.

The testes of these males were studied histologically after fixation in 4% formaldehyde. The sections (5u) were stained with haemotoxylin and eosin. The results of this study are presented in table XIV. The histological picture of a normal tubule was obtained only in the control room males kept constantly in the control room and examined at 6 months of age. In all other cases, the cytoplasm of the germinating epithelium took little of the eosin stain and the nuclear material was pyknotic, a condition which was observed in the control room males at 9/1/2 months of age, the only other age at which the control males were examined.

Table XIV.

Summary of Histological Study of Testes.

Age in Weeks	Group: Control Room	Cold Room	Hot Room	Change Groups
8		1) P.V. (13)* 2) Pyknosis 3) Sperm present 4) Many very active tubules	1) P.V. (12) 2) Lumina large 3) Pyknosis 4) G.C. rare 5) Sperm present	
12		Same as at 8 weeks (13)	1) P.V. (15) 2) Varying stages of activity 3) G.C. more frequent	
16		1) Pyknosis (9) 2) Fairly active but thin epithelium 3) G.C. rare	1) P.V. (3) extensive 2) Many thin walled tubules 3) Increase in G.C.	1) P.V. (8) 2) Varying stages of activity 3) Occassional G.C. 4) Sperm present
20			1) More advanced degeneration (9) 2) G.C. numerous	1) P.V. (10) 2) Large lumina 3) Varying stages of proliferation 4) Some G.C. 5) Sperm present
25	1) Tubules normal and highly active (6)		1) Interstitial tissue prominent (5) 2) Some moderately active tubules	1) P.V. (10) 2) Few Sperm 3) G.C. frequent
31				1) Tubules very small (9) 2) Extensive degeneration 3) G.C. frequent

* Figures in parentheses indicate the number of cases.
P.V. Peripheral tubules vacuolated.
G.C. Giant cells

The hot room and cold room group males presented similar testicular tubules up to the age of twelve weeks; most of the peripheral tubules were vacuolated with pyknotic nuclear material and varying degrees of proliferation. From this age on, the hot room males showed more extensive vacuolization with thin tubular linings and an increasing number of giant cells. Between the age of eight to twelve months, giant cells were not so abundant yet many tubules were bare, the interstitial tissue very prominent and the degree of activity quite variable. Sperm were present in some tubules but not usually where there was extensive vacuolization.

The germinating epithelium of the cold room group males was usually thin, but many sperm were present. Giant cells were rarely observed. Nine cold room group males (five months of age) were mated in the hot room, kept there for varying periods and then killed. Those animals which were killed after being in the hot room for one month presented a highly degenerated germ tissue with extensive vacuolization, many giant cells and few, if any, sperm. After a sojourn of two months in the hot room there were fewer giant cells and an increase in all types of germ cells save sperm. One cold room male was placed in the hot room for twenty-six days. At the end of this period he was returned to the cold room for one week before being killed. The testes showed a fairly thick tubular epithelium, almost devoid of sperm and with few giant cells. A second cold

room male was placed in the hot room for two months. During this time the right testicle descended and weighed 56.3 mg. However, the left gland remained intra-abdominal and weighed 18.3 mg. The right testis presented a histol0-gical picture quite like that of hot room males at the same age- peripheral tubules highly vacuolated, many tubules with no sperm and some giant cells. The left testicle presented a typical picture of cryptorchidism.

The control room group males which were mated in the hot room reacted similarly to those of the cold room group so treated. Ten days in the hot room was the shortest exposure of the control room or cold room group males to the humid heat. At the end of this time the germ tissue was extensively degenerated, contained a great number of giant cells and was devoid of sperm. The testes of the change group males showed various degrees of activity with occasional giant cells up until the age of approximately 23-25 weeks. At this time, most of the tubules showed much degeneration with few sperm, many giant cells and prominent interstitial tissue.

It seems that humid heat leads to the destruction of germinating tissue very soon after the exposure of the cold room and control room group males to same. However, after six to eight weeks in the hot room, these animals became adapted to their new environment and had many of all types of germ cells save sperm, but the regeneration occurred

sooner if the animals were returned to their native habitat. Males of the hot room and change groups possessed the least active germinating tissue. Even though the testes of the hot room males depended far, the environmental temperature was sufficiently high and the body metabolism so depressed that an intensely active germinating tissue could not be maintained.

Sundstroem (7) placed rats, one month old, in a hot humid room and kept them there for six months. At the end of this time, the testes presented a picture indicative of sterility for the animals kept under stagnant conditions. Litter brothers which were fanned had normal testes but were less willing to mate than the controls. These hot room animals had large scrotal sacs which he considered as accessory cooling organs.

Moore (47) found that the scrotal temperature was 1 to 1.5°C. lower than the abdominal temperature for normal rats, guinea pigs, and rabbits. Forced retention of the testes in the peritoneal cavity gave rise to progressive degeneration of the entire generative portion of the guinea pig within five to seven days, but, a few months after the return of the testes to the scrotum, regeneration occurred. Also, the insulation of the pendant scrotum of the ram leads to an early degeneration of all seminiferous tubules of the testes (48). Application of heat to the scrotum by warm water, electric light or stove, hot air or the sun's rays leads to severe testicular injury (49,50). Moore and his co-workers

concluded that the function of the scrotum is that of a heat regulator for the production of sperm.

The depressive temperature and humidity of the hot room, in the experiment here reported, permitted only a very low fertility even though the males had very large bare scrotal sacs. On the other hand, the testes of the cold room males remained in the abdominal cavity and these animals were equally as fertile as the control room group males. The testes of males of all the other groups rested in scrotal sacs, which for the hot room males depended most. Fukui (50b) observed that forced retention of the testes in the abdominal cavity of a dog did not produce extensive destruction of the germ tissue if that part of the abdomen where the testes resided was cooled. Thus, it seems that retention of the testes intra-abdominally is not necessarily harmful, unless over-heating occurs.

Coincidentally with the observations on fertility under different environmental conditions, it was also noted that body weight and length were greatly influenced. Conditions of moist heat, by affecting the general metabolic level, were found to produce definite alterations in weight and length relations of body and tail. The results of these studies are taken up in Part III.

Part III. Climatic Influence on the Growth of the Male Albino Mouse.

The conditions of this experiment were the same as those described in Part II. A comparable number of animals from each group was sacrificed at similar ages and body measurements immediately made. The animals were killed quickly by either a blow on the head or ether. The total body length in cms. was obtained by measuring from the tip of the nose to the end of the tail, then the tail length was ascertained by measuring from the anus to the tip of the tail. The difference between these two measurements represented the body length. Weighings were made each week as described in Part II.

A. Growth in weight under different environments.

The weight curves for the males of the control room and cold room groups fall very close together, with the cold room "immigrants" remaining slightly but consistently below the other two groups. The hot room males made their greatest increase in body weight during their first week of residence in the hot room. Thereafter, they gained but slowly, soon reaching a plateau and, by eighteen weeks of age, had begun to decline. The growth curve of the change II group males closely followed that of the hot room males until the point where the latter reached their plateau, from this point on the change II group males surpassed

the hot room males. The change I group males grew at a slower rate than any of the other males, but their growth was steady, so that, near eighteen weeks of age, they surpassed the hot room males. The mean weekly weights for the various groups are presented in Table I, and chart I was constructed from these data.

TABLE 1

Weekly weights in grams of males

AGE	CONTROL	HOT ROOM GROUP	COLD ROOM GROUP		CHANGE I GROUP	CHANGE II GROUP
			"Immigrants"	Descendants		
weeks						
3	8.16±0.409*(50)	8.64±0.312(48)	8.35±0.492(24)	8.31±0.347(40)	7.71±0.410(24)	8.43±0.607(22)
4	12.44±0.434 (50)	12.46±0.430(48)	11.10±0.568(24)	10.60±0.382(40)	9.87±0.477(24)	12.0 ±0.773(24)
5	17.1 ±0.368 (50)	14.41±0.438(48)	14.67±0.940(24)	15.56±0.573(40)	12.12±0.589(24)	14.44±0.198(29)
6	19.56±0.453 (50)	15.78±0.154(48)	18.6 ±0.873(24)	19.20±0.554(39)	13.69±0.615(24)	15.56±0.540(27)
7	21.06±0.529 (50)	16.45±0.488(45)	19.37±0.774(24)	21.50±0.591(39)	14.91±0.640(24)	16.92±0.534(28)
8	22.22±0.633 (50)	16.88±0.480(45)	21.39±0.484(24)	21.93±0.561(40)	16.00±0.623(24)	17.06±0.817(23)
9	23.08±0.546 (50)	17.89±0.714(33)	22.7 ±0.666(24)	22.76±0.768(27)	16.10±0.676(24)	17.41±0.879(23)
10	23.68±0.474 (50)	19.26±0.545(32)	23.6 ±0.663(24)	24.54±0.963(27)	17.41±0.662(24)	18.41±0.926(22)
11	24.32±0.518 (50)	19.88±0.679(31)	24.2 ±0.761(24)	24.62±0.707(27)	18.02±0.532(24)	19.13±0.539(22)
12	25.27±0.537 (43)	19.75±0.682(32)	25.1 ±0.757(24)	25.60±0.688(27)	18.87±0.568(24)	20.43±0.539(22)
13	25.64±0.689 (43)	20.16±0.765(22)	25.6 ±0.728(20)	25.39±0.658(18)	19.58±0.523(23)	21.45±0.723(22)
14	26.12±0.734 (42)	20.59±0.483(22)	25.9 ±0.765(20)	26.41±0.784(18)	19.81±0.614(23)	21.86±0.511(22)
15	26.98±0.533 (42)	20.91±0.596(22)	26.0 ±1.067(20)	26.58±0.645(18)	19.92±0.559(23)	22.47±0.586(22)
16	27.19±0.745 (42)	20.51±0.720(19)	26.9 ±1.027(20)	26.83±0.713(18)	20.42±0.639(23)	21.54±0.455(22)
17	27.28±0.458 (42)	21.17±0.946(13)	26.39±0.674(17)		21.16±0.596(18)	22.02±0.629(18)
18	27.47±0.569 (42)	20.58±0.914(12)	26.87±0.690(16)		21.47±0.662(18)	22.83±0.577(18)
19	27.29±0.657 (42)	21.04±0.874(12)	27.37±0.678(16)		21.66±0.545(18)	22.80±0.697(18)
20	27.81±0.708 (42)	20.79±0.820(12)	27.62±0.718(16)		22.12±0.682(16)	23.97±0.664(17)
21	28.14±0.539 (42)				21.46±0.642(12)	
22	27.5 ±0.622 (38)				22.29±0.863(12)	
23	27.95±0.649 (38)				22.25±0.976(12)	
24	27.58±0.612 (38)				22.7 ±0.837(12)	
25	29.09±0.617 (27)					
26	28.58±0.747 (26)					
27	28.54±0.772 (24)					
28	28.04±0.828 (24)					
29	28.08±1.029 (24)					
30	29.25±0.739 (24)					
31	29.13±0.801 (23)					
32	29.36±0.566 (22)					

* Figures in parentheses indicate the number of cases.
The steady diminution in group numbers was due to killing off for length measurements.

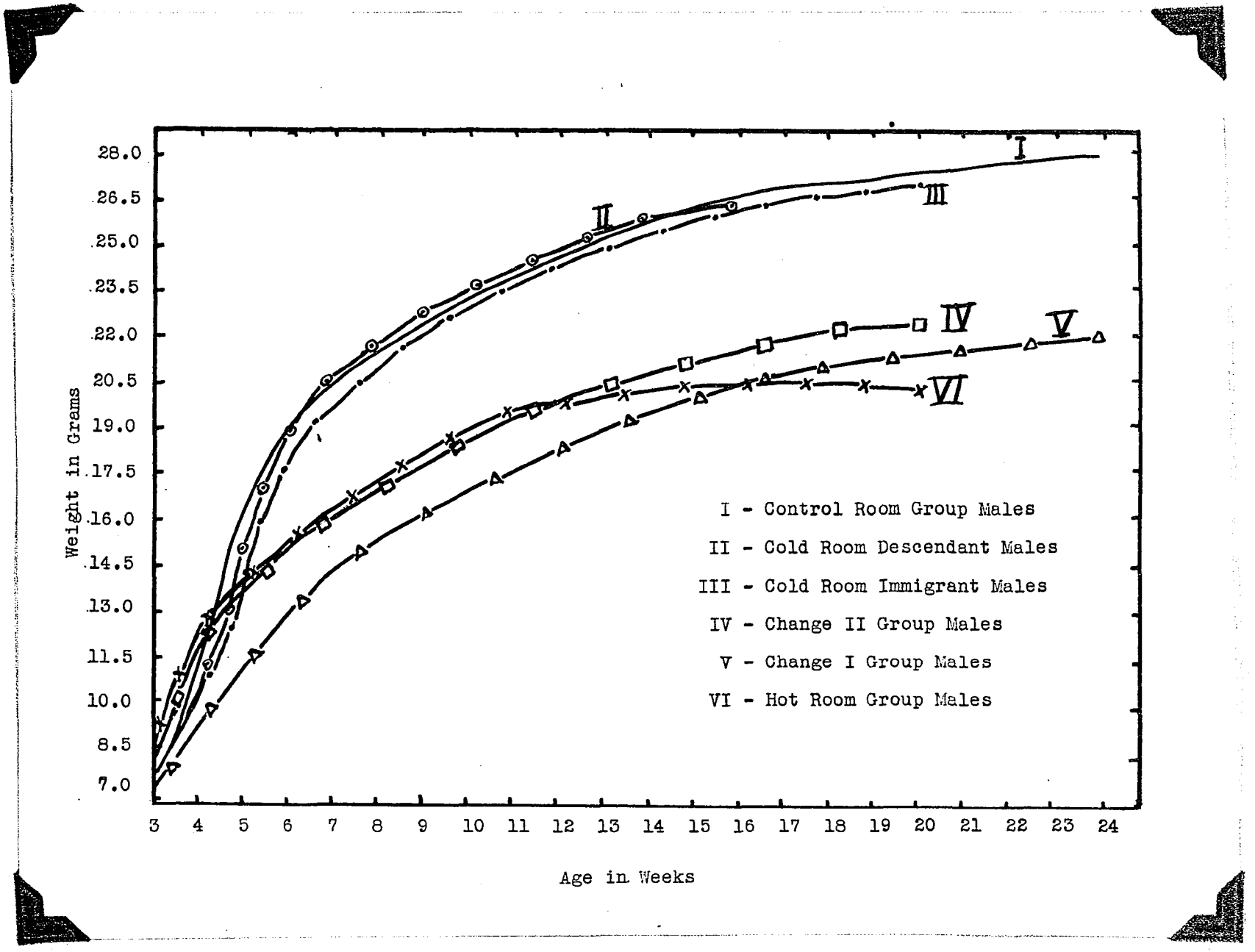


Chart I

B. Variations in type of growth according to environment.

Concomitant with these different rates of increase in body weight there were found significant differences in the growth of the body skeleton of the mice from the various groups. Tables II-V shows that all males, except those of the change groups, had reached their mature body form by twelve weeks of age. The hot room group males exhibited the shortest bodies and longest tails of any group; the tails were always 1 cm. longer than their bodies whereas the converse applied to the cold room males. From the twelfth to the twenty-fourth week of age, the bodies of the control room males had increased in length approximately 1 cm. but the tail length remained unaltered during this period. The body and tail lengths of the change groups males, during their early growth, approximated those of the hot room males, but the former continued to grow steadily and, at thirty-two weeks of age, both their body and tail lengths were near the maximum recorded during this experiment for animals of any group. The measurements for individual animals are next presented.

Arithmetical values for the relationship between the body length and body weight of these males are expressed in table VI. Ordinarily, as an animal ages, the value of this ratio declines due to the continued deposition of adipose tissue long after the bony skeleton has stopped growing. Thus, we see that the ratio for the control room

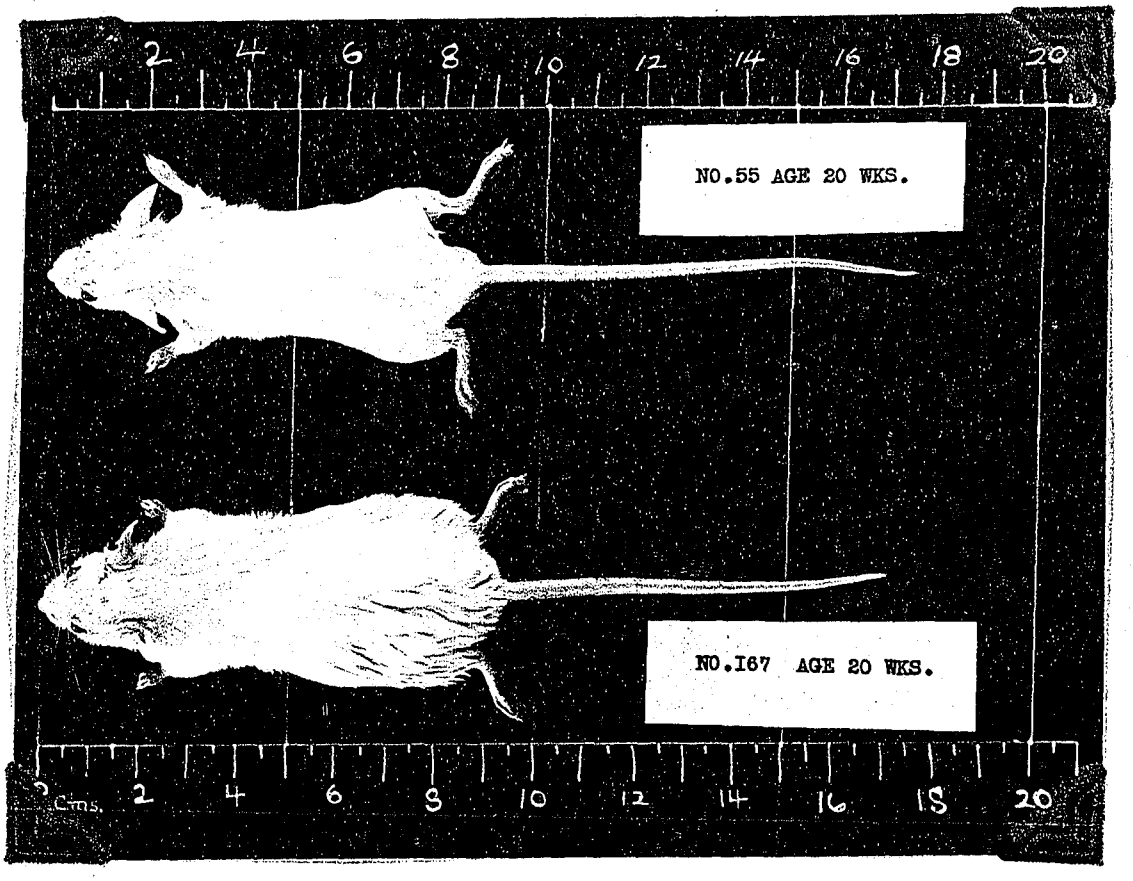


Plate I. Comparison of representative hot and cold room males at 20 weeks of age.

Males 55 and I67 were born in the control room. At 3 weeks of age,no.55 was placed in the hot room to remain there until 20 weeks of age, and no. I67 was placed in the cold room for an equal period of time.

Table II.

Body Measurements of Control Room Males at Different Ages.

Number	Age in Weeks	Body Weight Gms.	Body Length Cms.	Tail Length Cms.	Body Length Body Weight
1031	24	27.7	9.7	9.5	0.35
1033	"	27.5	9.2	10.1	0.33
1035	"	29.0	9.5	10.3	0.33
6115	"	26.2	9.7	9.4	0.37
C - 1	"	25.5	9.3	8.8	0.36
C - 3	"	25.9	9.4	8.8	0.36
C - 5	"	25.1	9.2	8.0	0.36
C - 7	"	26.0	9.1	8.5	0.35
C - 9	"	26.5	9.3	8.9	0.35
C - 11	"	23.6	8.8	8.4	0.37
Averages			9.32	9.07	0.349
1029	12	15.8	7.8		0.49
1039	"	20.0	8.6	9.0	0.43
1041	"	19.8	8.3	9.0	0.42
1045	"	21.7	8.0	9.2	0.36
1001	"	19.2	8.1	9.0	0.42
1003	"	22.3	9.0	9.5	0.40
1007	"	20.6	8.5	9.0	0.41
1009	"	22.0	8.9	9.4	0.40
1011	"	22.2	8.6	9.3	0.39
1013	"	18.9	8.1	8.7	0.43
1017	"	22.2	9.1	9.3	0.41
			8.45	9.14	0.418

Table III.

Cold Room Animals at Different Ages.

Number	Age in Weeks	Body Weight Gms.	Body Length Cms.	Tail Length Cms.	Body Length Body Weight
621	8	23.3	8.5	7.4	0.36
623	"	24.2	8.9	8.0	0136
625	"	21.3	8.7	Stub	0.40
627	"	22.4	8.6	7.7	0.38
629	"	23.3	8.7	8.0	0.37
631	"	19.9	8.1	7.7	0.40
633	"	22.3	8.9	7.9	0.39
635	"	22.1	8.7	7.8	0.39
637	"	23.3	8.4	7.8	0.36
639	"	19.8	8.2	7.3	0.41
641	"	20.7	8.6	7.9	0.41
643	"	20.3	8.3	7.0	0.40
645	"	21.3	8.3	7.6	0.38
Average			8.58	7.67	0.389
191	12	20.9	8.4	7.4	0.40
193	"	24.1	9.2	7.4	0.38
195	"	27.1	9.1	8.5	0.33
197	"	31.0	9.7	8.6	0.31
199	"	28.0	9.0	8.4	0.32
601	"	25.3	9.2	7.3	0.36
603	"	23.3	8.7	8.3	0.37
605	"	28.7	9.3	8.7	0.32
607	"	27.3	9.2	8.6	0.34
609	"	28.5	8.5	8.4	0.30
611	"	28.8	9.3	8.4	0.32
613	"	28.0	9.1	8.4	0.32
615	"	26.5	9.4	8.0	0.35
Average			9.08	8.17	0.341

Table III Continued.

Cold Room Animals at Different Ages.

Number	Age in Weeks	Body Weight Gms.	Body Length Cms.	Tail Length Cms.	Body Length / Body Weight
103	16	30.4	9.1	7.8	0.29
105	"	30.2	9.3	8.8	0.30
107	"	27.1	9.2	8.2	0.33
177	"	26.8	8.7	Stub	0.32
181	"	23.1	8.7	7.4	0.37
183	"	27.0	9.0	7.8	0.33
185	"	25.5	9.1	8.3	0.35
187	"	27.6	9.3	8.5	0.33
189	"	25.8	9.2	8.6	0.35
Averages			9.06	8.175	0.336
149	20	23.9	8.4	8.2	0.35
151	"	26.2	8.9	8.1	0.33
159	"	29.8	8.7	7.5	0.29
161	"	30.4	9.3	7.6	0.30
163	"	28.6	9.3	7.3	0.32
165	"	27.9	8.6	7.3	0.30
167	"	29.0	8.8	8.4	0.30
169	"	26.7	8.9	8.6	0.33
171	"	30.3	9.4	8.4	0.31
153	"	25.3	9.0	8.0	0.35
155	"	26.3	8.9	8.2	0.33
173	"	29.6	9.5	Stub	0.32
175	"	28.1	9.2	8.6	0.32
Average			8.99	8.01	0.324

Table IV.

Body Measurements of Hot Room Animals at Different Ages.

Number	Age in Weeks	Body Weight Gms.	Body Length Cms.	Tail Length Cms.	Body Length Body Weight
99	8	17.7	8.0	8.8	0.45
501	"	16.0	6.9	8.6	0.43
503	"	19.5	8.5	9.8	0.44
505	"	19.5	8.5	8.9	0.44
507	"	18.7	8.5	9.5	0.45
509	"	19.5	8.3	10.0	0.43
511	"	16.1	8.3	9.1	0.52
513	"	17.5	7.9	9.0	0.45
515	"	19.2	8.7	9.4	0.45
517	"	17.9	8.0	9.2	0.45
519	"	16.4	7.9	Stub	0.48
521	"	17.5	8.0	9.1	0.46
Averages			8.2	9.3	0.453
67	12	20.8	8.7	8.4	0.42
69	"	20.5	8.8	8.2	0.43
71	"	18.8	8.4	9.0	0.44
77	"	17.6	8.3	8.9	0.47
79	"	19.9	8.3	9.0	0.42
81	"	24.5	9.2	10.1	0.38
83	"	23.3	9.1	9.6	0.39
85	"	20.3	8.7	9.2	0.42
87	"	22.3	9.2	9.1	0.41
89	"	18.6	8.6	8.8	0.46
91	"	20.6	8.4	9.4	0.41
93	"	19.7	8.7	9.3	0.44
95	"	19.9	8.6	8.9	0.43
97	"	18.5	8.4	8.9	0.45
Averages			8.67	9.77	0.426

Table IV Continued.

Body Measurements of Hot Room Animals at Different Ages.

Number	Age in Weeks	Body Weight Gms.	Body Length Cms.	Tail Length Cms.	Body Weight Body Length
7	16	14.9	8.0	9.1	0.54
9	"	14.2	7.1	8.7	0.50
11	"	15.8	8.9	9.2	0.56
13	"	19.0	9.1	9.2	0.47
15	"	17.9	8.5	9.6	0.48
19	"	17.0	8.0	9.4	0.47
25	"	21.7	9.0	9.6	0.41
29	"	13.9	8.2	9.7	0.59
57	"	19.5	8.3	9.5	0.43
59	"	21.1	8.8	9.6	0.42
61	"	19.5	8.3	9.3	0.43
Averages			8.38	9.35	0.480
35	20	21.0	8.8	8.5	0.42
37	"	19.4	8.5	8.8	0.44
1	"	20.8	9.0	9.7	0.43
43	"	17.0	8.4	8.9	0.49
45	"	18.7	8.5	9.4	0.45
47	"	18.7	8.7	9.3	0.47
49	"	17.2	8.4	Stub	0.49
51	"	20.4	8.3	8.6	0.41
53	"	21.6	8.5	9.8	0.39
63	"	20.4	8.4	9.5	0.41
65	"	24.3	8.3	9.1	0.35
Averages			8.52	9.16	0.432

Table V.

Body Measurements of Change Group Animals at Different Ages.

Number	Age in Weeks	Body Weight Gms.	Body Length Cms.	Tail Length Cms.	Body Length Body Weight
245	16	16.4	8.2	8.7	0.50
247	"	18.6	8.5	8.7	0.46
249	"	20.8	8.7	9.3	0.42
251	"	20.3	8.9	9.5	0.44
349	"	18.8	8.6	9.2	0.41
351	"	21.9	8.7	10.1	0.40
353	"	21.7	8.6	9.4	0.40
355	"	22.0	8.9	9.5	0.41
Averages			8.64	9.30	0.427
235	20	25.8	8.7	Stub	0.34
237	"	21.6	8.5	"	0.39
239	"	21.2	8.9	9.3	0.42
241	"	22.5	8.4	9.1	0.37
243	"	20.0	8.5	9.0	0.43
339	"	24.0	9.1	8.8	0.38
341	"	22.3	8.6	9.0	0.39
343	"	23.4	8.6	9.4	0.37
345	"	25.5	8.9	9.5	0.35
347	"	23.7	8.9	8.9	0.38
Averages			8.71	9.12	0.380
225	24	24.1	8.9	9.2	0.37
227	"	20.1	8.4	8.1	0.42
229	"	25.2	8.8	9.6	0.35
231	"	18.6	8.5	9.0	0.46
233	"	24.6	9.2	9.2	0.37
331	"	29.9	9.2	10.0	0.31
333	"	24.2	9.0	9.3	0.37
335	"	25.9	9.0	10.4	0.35
337	"	27.8	9.5	10.4	0.34
Averages			8.94	9.46	0.370

Table V Continued.

Body Measurements of Change Group Animals at Different Ages.

Number	Age in Weeks	Body Weight Gms.	Body Length Cms.	Tail Length Cms.	Body Length Body Weight
219	28	17.8	9.2	9.1	0.52
221	"	19.6	9.1	9.2	0.46
223	"	20.5	8.8	9.2	0.43
317	"	17.1	8.6	9.3	0.50
319	"	23.7	9.2	9.4	0.39
321	"	22.8	8.9	9.5	0.39
323	"	22.9	8.9	10.2	0.39
325	"	22.9	9.0	9.7	0.39
327	"	24.2	9.1	9.9	0.38
Averages			8.98	9.50	0.427
205	32	24.0	8.9	9.8	0.37
207	"	20.2	9.0	9.7	0.45
209	"	21.2	8.9	9.6	0.42
211	"	26.6	9.1	9.6	0.34
213	"	27.7	9.1	9.2	0.33
215	"	21.4	8.8	9.3	0.41
301	"	26.7	9.4	10.3	0.35
303	"	27.4	9.6	Stub	0.35
3141	"	22.4	8.9	9.1	0.40
307	"	21.9	8.7	9.7	0.40
309	"	24.0	9.1	10.2	0.38
Averages			9.04	9.65	0.381

Summary of Tables II-V.

Average

Body and Tail Lengths of Males According to Age and Group.

Age Weeks	Control Group		Hot Room Group		Cold Room Group		Change Group	
	Body L. cms.	Tail L. cms.	Body L. cms.	Tail L. cms.	Body L. cms.	Tail L. cms.	Body L. cms.	Tail L. cms.
8			8.2 (13)	9.3	8.5 (13)	7.7		
12	8.45 (11)	9.1	8.7 (14)	9.8	9.1 (13)	8.2		
16			8.4 (11)	9.4	9.1 (9)	8.2	8.6 (8)	9.3
20			8.5 (11)	9.2	9.0 (13)	8.0	8.7 (10)	9.1
24	9.3 (10)	9.1					8.9 (9)	9.5
28							8.98(9)	9.5
32							9.0 (11)	9.6

Figures in parentheses indicate the number of cases.

Table VI.

Male Body Length: Body Weight Ratio.

Age Weeks	Control Group cm./gm.	Hot Room Group cm./gm.	Cold Room Group cm./gm.	Change Groups cm./gm.
8		0.453 (12)*	0.381 (13)	
12	0.418 (11)	0.426 (14)	0.341 (13)	
16		0.480 (11)	0.336 (9)	0.427 (8)
20		0.432 (11)	0.324 (13)	0.380 (10)
24	0.349 (10)			0.370 (9)
28				0.427 (9)
32				0.381 (11)

* Figures in parentheses indicate the number of cases.

males, at twenty-four weeks of age, is numerically less than when they were twelve weeks of age. Due to the fact that the hot room males had exceedingly light and short bodies, their ratio had the highest numerical value and varied little from one age to another. There was a steady but slow decline in the body length: body weight ratio for the cold room males, since they, like the control males, had heavy bodies. The change group males possessed relatively light but long bodies, hence this relationship is expressed by a fairly high figure which gradually decreased as the animals grew older.

These differences in growth are possibly due to changes in the thyroid-pituitary activities, which are, in turn instigated by the environmental temperature and humidity. The steady coolness of the cold room and the environmental conditions of the control room stimulated the occupants of these rooms to make increments in weight and body length at a more rapid rate than did any other set of environmental conditions here reported.

In 1886, Malling-Hansen reported accurately recorded observations on seasonal growth in height and weight of school children (51). These studies were carried out over a period of three years and showed a maximum increase in weight from mid-September to mid-December. Similar results were obtained by Cramerer in Germany (52), Porter in Boston (53), and by Orr and Clark in Aberdeen (54). The period of greatest increase in height was associated with a minimum

increase in weight and vice versa. Such results are comparable to the seasonal growth of plants. The latter also grow in height in the spring but add weight during the fall by storing food for the winter.

Gelineo and Giaja reported in 1933 their studies of growth in rats at the environmental temperatures of 7°-10°C. and 30°C. (55). At the end of ninety days, the females kept at 30°C. weighed 27% less than those kept at the lower temperature and the males showed a 25% decrease. Allen (56) has likewise written that in the northern hemisphere, in nearly all types of birds and mammals of obviously northern origin, there is a gradual decrease in general size from the north southward in the representatives of a specific group.

Sumner (57) has studied the effects of heat and cold on the growth of white mice. His warm room was kept at a temperature range of 75°-80°F. and the cold room at 43°-48°F. At the temperature of the cold room he did not observe any definite effect upon body length, probably because it was quite below the optimal temperature, but he did discover that the cold room mice had distinctly shorter tails than the warm room mice. His data on mouse growth agrees with that of Table II-V of this paper, both of which indicate that comparisons of earlier and later measurements upon the same animals show a distinct tendency toward the reduction of these experimentally produced differences during subsequent growth, even when the conditions remain unchanged. This statement applies only to the cold room and hot room group

males, since the change group males were still showing increases in body and tail lengths at thirty-two weeks of age. The change II group males responded better in body weight than did the change I group as the regime imposed upon the former was less strenuous than that for the latter group. However, the environmental conditions for both groups were so severe that growth was delayed, but, at a comparatively late age, these animals possessed body and tail lengths near the maximal values in this experiment.

Sundstroem (7) found that much of the depressing action of humid heat was overcome by fanning. The tail, ears, and scrotal sac were larger in his hot room mice than in the controls. He considered these organs as accessories for the radiation of heat. The tails of the cold room mice in this study were very short, but proximally were larger in diameter than those of any other animals in the experiment; this phenomenon appears as an adaptive measure in order to check the loss of heat by radiation. Conversely, perhaps as an adaptive device, the hot room animals had very long spindle-like tails so as to increase their surface for cooling. Likewise, the slight bodies of the hot room mice would seem to be an adaptation in order that they might avoid overheating. The cold room males had more and longer vibrissae than did the hot room animals, but the significance of this modification is obscure.

Summary.

Rabbits adapted to constant heat have a lowered ability to produce heat and keep warm under chilling emergencies. Those adapted to a cooler environment are more capable of meeting chilling conditions by increased heat production, but are less tolerant of excessive heat than those adapted to the constant heat.

A few hours exposure to cold each day completely offsets the depressive effects of heat and renders the metabolism as responsive to chilling as does a constantly cool environment. Animals adapted to a cold or a changeable environment rapidly exhaust their glycogen supplies when chilled, whereas glycogen utilization is much slower in those adapted to the heat alone. It seems altogether likely, therefore, that a few hours cooling each day would markedly offset the debilitating effects of excessive heat on human energy. The productivity and wealth of the warmer regions of the world would be greatly augmented by such procedure.

White mice submitted to a warm humid environment evidence a low fertility in three ways, namely; a low percentage of matings that result in pregnancy, small litter size, and low viability of young.

Most efficient sex functioning comes with a steady cool environment. There the greatest number of matings

result in conception, large litters of lusty offspring are born, and the onset of sexual life and fertility in the young come earlier than in the moist heat. However, the span of fertility is shorter in these cold adapted animals than in those adapted to the constant heat.

Mice seem poorly adapted to a changeable envrionment, and suffer a severe loss of sexual function when thus over stimulated. This loss is not permanent, however, but is replaced by normal fertility when they are relieved of the exhausting stimulation. Comparable results have been observed in the human being. Childless women of our highly stimulating zones who visit the south during its depressive seasons frequently conceive.

Male mice, kept continuously in a cold room, retain their testes within the abdomen, but when exposed to humid heat they descent in large, loose scrotal sacs. Great destruction of the germinating epithelium occurs soon after the exposure of highly active males to humid heat. Many giant cells arise due either to fusion of the spermatids (58) or to sudden suppression of cytoplasmic activity. With fertility high in the cold room mice it is evident that failure of the testes to descend from the abdomen does not in itself produce sterility. This difference between the hot and cold room males is more likely a matter of adaptation to keep the testes nearest the optimal temperature for proper function. Constant or intermittent exposure to humid

heat is not conducive to a highly active germ tissue in this species.

Mice adapted to a cool environment grow much more in weight and body size than animals under humid heat. Nevertheless, the tails of the former are one cm. shorter than their bodies, presumably to diminish heat ratiation. On the other hand, animals kept constantly under hot humid conditions have a longer total body length, including the tail; this long tail, large bare scrotal sac, and large ears aid in the radiation of heat and help to keep the animal comfortable under the moist heat. These data on the high fertility and the type and rate of growth under a cool environment are highly suggestive and worthy of trial in the breeding of livestock and furred animals.

Thus, if man's climatic environment is unsuited to his most favorable development, he has a means at hand whereby his indoor climate can be regulated as he chooses. His energy level can be increased in the warm regions by night-time cooling, the fertility of his breeding animals can be brought to a high level, and the rate and type of growth of his livestock can be greatly augmented. However, due consideration should be given to physiological limitations such as the susceptibility of a person with a highly active metabolism to excessive heat and functional exhaustion due to over simulation. When these limitations become generally recognized, a saner use of the world's variety of

climates and an intelligent application of the means for varying the indoor environment will be reached, all for the betterment of mankind.

Bibliography.

1) Huntington, E., Civilization and Climate, Yale University Press, New Haven, Third Edition, 1924.

2) a - Mills, C. A., Personal communication.
b - Ohio Journ. Sci., 1930, 30, No. 4.
c - Amer. Jour. Hyg., 1932, 15, 573
d - Archives of Int. Med., 1930, 46, 921.
e - Archives of Int. Med., 1928, 42, 390.
f - Am. Jour. Phys., 1918, 46, 329.

3) McClintock, J. I., and S. Paisley, Proc. Soc. Exper. Biol. and Med., 1932, 30, 162.

4) Dunwoodie, H.H. C., Bartholomew's Physical Atlas, Vol. 3, Archibald Constable and Co., Westminster, 1899.

5) Eijkman, C., Pflüger's Archiv. F.D.ges. Phys., 1896,64,56.

6) De Almeida, O., Jour. Phys. et Path. Gén., 1919,18,958
1924,22,12
Compt. Rendu, 1924, 91, 1124

7) Sundstroem, E. S., Amer. Jour. Phys., 1922, 60, 397.
Jour Biol. Chem., 1925, 63, 41 (proc.)
Phys. Rev., 1927, 7, 320.

8) Harris, J.A., and F. G. Benedict, Carnegie Inst. of Wash. Publ. No. 279, 1919, p. 241.

9) Du Bois, E. F., Basal Metabolism in Health and Disease, Lea and Febiger, Philadelphia, 1927.

10) Hafkesbring, R., and P. Borgstrom, Amer. Jour. Phys., 1926-27, 79, 221.

11) Berkhout, reviewed in Lancet, 1930, 2, 617.

12) Benedict, F. G., Jour. Biol. Chem., 1915, 20, 263.

13) Gessler, H., Pflüger's Arch., 1925, 207, 376.

14) Wyman, L. C., and C. Tum Suden, Amer. Jour. Phys., 1929, 89, 362.

15) Hartman, F. A., Endocrinology, 1930, 14, 229.
" , K.A. Bronnell, and W. E. Hartman, Amer. Jour. Physiol., 1930, 95, 670

16) Swingle, W. W., and J. J. Pfiffner, Amer. J. Physiol., 1931, 96, 153
Proc. Soc. Exper. Biol. & Med., 1931,28, 510.

17) Folin, O., and H. Wu,J.Biol. Chem., 1920, 41, 367.

18) Pflüger, E., Arch. ges. Physiol., 1904, 103, 169.

19) Folin, O., and H. Trimble, Jour. Biol. Chem., 1924, 60, 472.

20) Giaja, J., and S. Gelineo, Ann. de Phys. et de Biol. phys. chem., 1931, 7, 163.

21) Horst, K., F. Benedict, and Mendel, L., Jour. Nutr. Sept.,1930.

22) Gelineo, S., and J. Giaja, Bulletin, Academie Royale Serbe, Belgrade, 1933.

23) Hartman, F. A., K. A. Bronnell and A.A. Crosby, Amer. Jour. Phys., 1931, 98, 674.

24) Hartman, W. E., and F. A. Hartman, Amer. Jour. Phys., 1923, 65, 612.

25) Schmeckebier, M.M., Proc. Soc. Exp. Biol., and Med., 1934,31, 770.

26) Cramer, W., Brit. Jour. Exper. Path., 1926, 7, 88.

27) Miller, E. H., Amer. Jour. Anat., 1927, 40, 251.

28) Whitehead, R., Brit. Jour. Exp. Path., 1931, 12, 305;14,149.

29) Deanesley, R., Proc. Roy. Soc. B., 1928, 103, 523.

30) Seidell, A., and F. Fenger, Jour. Biol. Chem., 1913, 13, 517.

31) Hammett, F. S., Jour. Metab. Res., 1926, 7, 8, 91.
Hatai, S., Am. J. Anat., 1913, 15, 87.

32) Maignon, F., Jour. Phys. et Path. Gén, 1921, 19, 13.

33) Stoland, O.O., and M. Kinney, Amer. Jour. Phys., 1919, 49, 135.

34) Keeler, C. E., The Laboratory Mouse, Harvard Univ. Press, 1931, Cambridge, Mass.

35) Daniel, J. F., Jour. Exp. Zool., 1912, 9, 865.
Amer. Nat., 1912, 46, 591.

36) Prizbaum, H., Akad. Wissenschaft., Wien, Akad. Anz. no. 18, 1919
(reviewed by E. S. Sundstroem, Phys. Rev., 1927, 7, 320).

37) Steinach, E., and P. Kammerer, Arch. Entwickl. mechanik. der Org., 1920, 46, 391.
(reviewed by Sundstroem, Phys. Rev., 1927, 7, 320).

38) Riddle, O., Amer. J. Phys., 1923, 66, 322.

39) Guieyesse, C. R., Soc. Biol., 1899, 51, 898.

40) Stilling, H., Arch. mikr. Anat., 1898, 52, 176.
(reviewed by Andersen in Jour. Physiol., 1932, 76, 247.)

41) Koliner, W., Arch., Mikr. Anat., 1919, 91, 1.
(reviewed by Andersen in Jour. Physiol., 1932, 76, 247.)

42) Andersen, D. H., and H. S. Kennedy, Jour. Physiol., 1932, 76, 247.

43) Wyman, L. C., Amer. Jour. Phys., 1929, 86, 528.

44) Martin, S. J., Amer. Jour. Phys., 1932, 100, 180.

45) Corey, E. L., and S. W. Britton, Proc. Soc. Exp. Biol. and Med., 1933, 30, No. 5.

46) Dr. E. B. Teitz, Personal communication.

47) Moore, C. R., Amer. Jour. Anat., 1924-25, 34, 337.

48) Moore, C. R., and R. M. Oslund, Amer. Jour. Phys., 1924, 67, 595.

49) Moore, C. R., and H. D. Chase, Anat Rec., 1923, 26, 344.

50)a Fukui, N., Japan Med. World, 1923, 3, 27

b 1923, 3, 160

(50 a and b were reviewed by C. R. Moore in Amer. J. Anat., 1924-25, 34, 337.

51) Malling-Hansen, R., Jahrb. für Kinderh., 1886, 24, 84.
(reviewed by Orr and Clark, Lancet, 1930, 2, 365).

52) Cramerer, W., Jahrb. Für Kinderh., 1893, 36, 249.
(reviewed by Orr and Clark, Lancet, 1930, 2, 365.)

53) Proter, W. L., Amer. Jour. Phys., 1920, 52, 121

54) Orr, J. B., and M. L., Clark, Lancet, 1930, 2, 365.

55) Giaja, J., and S. Gelineo, Ext. du Bulletin de l'Acad. des Sciences Math. et Nat., 1933., 1, 103.

56) Allen, J. A., Science, 1905, 22, 661.

57) Sumner, F. B., Jour. Exp. Zool., 1909, 7, 97.
1915, 18, 325.

58) Maximow, A. A., Text-Book of Histology, 1931, W. B. Saunders Co.