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Estudios sobre los efectos de la sed.

II. Los efectos de la sed sobre el crecimiento del cuerpo y de los diversos órganos de la rata albina joven.

En ratas albinas de un mes de edad, próximamente, se mantuvo constante su peso durante varias semanas alimentándolas con una pequeña cantidad de líquido (leche) que constituye una dieta adecuada para el crecimiento. Las ratas así tratadas presentan una tolerancia progresiva de la sed, de tal modo que cada día se necesita menos leche para mantenerlas durante el experimento. La cola crece en longitud pero la longitud del cuerpo permanece constante. El peso del esqueleto aumenta marcadamente, mientras que el peso del grupo visceral aumenta ligeramente. La musculatura permanece casi constante. Aparece una ligera disminución en el tegumento y una pérdida de peso marcada en el resto del organismo. De las vísceras individuales: (1) La hipófisis, globos oculares, riñones, suprarrenales, médula espinal, esqueleto, nervios ciáticos, páncreas, estómago e intestinos, hígado y útero aumentan de peso de un modo definido. (2) El corazón, cerebro y los pulmones permanecen sensiblemente con el mismo peso. (3) El timo, ovarios, glándulas parótida y submaxilar, bazo, testículos, epidídimos y tiroides experimentan una disminución de peso más o menos marcada. La tendencia hacia el crecimiento en los diversos órganos de las ratas jóvenes durante los experimentos, corresponden en general a los encontrados en ratas de la misma edad durante experimentos sobre los efectos de una dieta deficiente, aun cuando existen algunas excepciones (testículos y riñones). Del mismo modo los resultados de los experimentos sobre la sed (también los de inanición) presentan una semejanza general con los llevados a cabo en los adultos. Existen sin embargo ciertas diferencias según la edad y también según el tipo de inanición.

STUDIES ON THE EFFECTS OF THIRST

II. EFFECTS OF THIRST UPON THE GROWTH OF THE BODY AND
OF THE VARIOUS ORGANS IN YOUNG ALBINO RATS

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It has been shown by various investigators that if young animals are underfed so as to prevent an increase in body weight, changes nevertheless occur in various parts of the body. Some organs remain nearly constant in weight, others lose, and still others show a remarkably persistent growth in spite of the underfeeding. Since for growth water is no less essential than food (as demonstrated for the human infant by Meyer, '13), it is of interest to determine whether similar changes occur in the organs of young animals in which growth is prevented by a restriction of the water in the diet. The present investigation was undertaken for this purpose.

The work was done in the Institute of Anatomy of the University of Minnesota. This opportunity is taken to express my indebtedness to Dr. C. M. Jackson, Director of the Department, for valuable aid and direction.

MATERIAL AND METHODS

The albino rat (*Mus norvegicus albinus*) was chosen as the most convenient form for experiment. Postnatal growth norms for the body and various organs are available for comparison (Donaldson, '15). The changes in the weights of the organs have also been studied in young rats during underfeeding (Jackson, '15 a; Stewart, '18, '19) and in adult rats on a dry diet (Kudo, '21).

The material used in the present experiment included fifty-six individuals in all. The forty-one survivors (from eight litters) are listed in table 1. In the first column the letter (K) indicates the series, the number preceding the decimal point designates the litter, and the number following is for the individual rat. The letter "m" signifies male; "f" female. Litters K5, K7, K8, K9, K10, K11, K12, K13, and K14 include, respectively, 4, 1, 5, 2, 8, 3, 5, 2, and 11 individuals. These include 17 males and 24 females, a total of 41. In addition 15 rats died during the test. They are excluded from the tables because the coagulated blood due to postmortem congestion might affect the weights of the organs.

In most cases the experiment began when the rats were about four weeks of age. Some of the experiments began at the age of three weeks (time of weaning), but most of these rats died.

Of the 41 rats listed, 11 were used for controls and the other 30 for the tests. The test rats were held at nearly constant body weight for varying periods as follows: for about 1 week (3 females); 2 weeks (2 males, 1 female); 3 weeks (4 males, 2 females); 4 weeks (2 males); 5 weeks (2 males, 2 females); 6 weeks (1 male, 1 female); 7 weeks (1 male, 3 females); 8 weeks (1 female); 9 weeks (1 male, 2 females); 11 weeks (1 female); and 13 weeks (1 female). Of the 30 test rats listed in table 1, one (K9.2 m.) of the 9-weeks' group was omitted, on account of its large body weight, from the corresponding group in table 2.

Eight normal controls (3 males, 5 females) were killed at the beginning of the experiment. The additional normal controls (K5.2, K 5.3, K 8.5) were killed at the end of the time periods indicated. These, and also two of the other controls (K7.1 and K9.1) are not used in table 2, because their body weights are too great for direct comparison with the test rats. A large number of observations upon normal rats previously published by Donaldson, Hatai, Jackson, Lowrey, and others are also available for comparison.

During the experiment the rats were kept each in a separate cage with wire-net bottom, allowing the feces and urine to drop through, which might otherwise be eaten. Both feces and food were carefully weighed. The rats were individually weighed daily before feeding. Those under experiment were allowed dry food *ad libitum*, together with whole milk carefully regulated in amount so as to hold them nearly constant at the initial body weight. Of course, slight fluctuations in the gross body weight were unavoidable, but they rarely exceeded 2 grams above or below the initial weight, as shown in table 1. The final gross body weight is in all cases nearly the same as the initial weight.

The temperature of the animal room was fairly constant at about 75° Fahrenheit (extreme range 65° to 80°).

Various methods of feeding were used. The eight initial controls were killed shortly after weaning (which occurs at the age of about three weeks), being subsequently fed on Graham bread and whole milk. Two control rats (K5.2, K8.5) were fed with dry 'dog-biscuit' (composition given by Kudo, '21) and water *ad*

libitum, together with 5 to 15 grams of whole milk daily. One control rat (K5.2) was fed with maize (Indian corn) with milk and water. These grew normally up to the ages indicated in table 1.

The test rats (held at nearly constant body weight) were variously fed as follows:

1. Twenty rats (including all the test rats except those specified below) were fed with dry 'dog-biscuit' ad libitum. They consumed an average of about 3.7 grams daily. The amount of milk fed daily decreased from about 3.5 to 4 grams at first to less than 2 grams after three or four weeks. In experiments extending more than a month, however, it was necessary to increase the amount of milk again to 2.5 or 3 grams daily. Feces averaged about 0.8 gram daily throughout the experiment.

2. Five rats (K14.5, K14.9, K10.9 K13.3 and K10.8) were fed with crushed maize. Each rat consumed daily about 3.5 grams. The amount of milk fed decreased from about 3.5 to 4 grams daily at first to about 1 gram after three or four weeks. The feces averaged 0.7 gram daily.

3. Two rats (K14.4 and K14.3) were fed with a mixture of crushed maize and 'dog-biscuit.' They ate about 3.6 grams daily of that mixture and were fed about the same amount of milk as in (2). The feces averaged about 0.8 gram daily.

4. Two rats (K11.3 and K12.1) were fed with milk powder ('Klim' brand). They consumed a daily average of about 3.4 grams of the dry powder. In addition fresh whole milk was fed, decreasing from about 5 grams at first to less than 2 grams after a month.

5. One rat (K14.2) was fed with dried polished rice. It daily ate 3.8 grams of rice throughout the experiment and passed an average of 0.7 gram of feces. At first, milk was added to the diet as follows. In the first two weeks of the test the rat was fed milk in amounts decreasing from 1.8 to 0.7 gram daily; then for about three weeks with 0.5 to 0.1 gram of milk daily. In the final period of four weeks the rat was fed with dry rice only. In that period the body weight was reduced from 33.5 grams to 27.1 grams. This rat was very active and showed no evident symptoms of vitamin deficiency.

TABLE 1
Individual data on rats used

RAT NUMBER AND SEX	FINAL GROSS BODY WEIGHT (AND RANGE)	FINAL NET BODY WEIGHT	BODY LENGTH	AGE OF RAT, DAYS	
				Initial	Final
A. Normal controls					
	<i>grams</i>	<i>grams</i>	<i>cm.</i>		
K12.3 f	22.7	20.5	8.8	25	
K12.2 f	24.0	22.6	9.4	25	
K11.0 f	25.4	23.4	9.6	31	
K 8.1 f	29.3	23.7	9.9	32	
K 5.1 m	27.8	27.2	11.1	26	
K14.0 m	28.1	26.0	9.8	30	
K 7.1 f	36.4	34.4	10.5	35	
K 9.1 m	43.5	41.2	12.0	40	
K 5.3 m	115.7	108.2	16.2	24	56
K 5.2 f	121.5	114.5	16.8	28	77
K 8.5 f	146.5	142.5	18.4	28	112
B. Test rats (held nearly at maintenance)					
K11.4 f	19.9 (19.9-26.2)	18.5	8.8	27	33
K13.2 f	21.9 (21.9-25.0)	18.9	9.0	27	33
K11.3 f	21.9 (21.9-26.8)	20.5	9.7	28	34
K14.1 f	25.4 (25.0-28.8)	22.9	9.3	30	41
K 8.2 m	29.1 (27.7-29.9)	24.5	9.5	32	47
K 8.3 m	29.6 (25.8-31.0)	26.3	9.7	32	50
K14.4 m	23.0 (23.0-30.7)	21.1	9.3	28	49
K14.7 m	23.7 (23.7-32.1)	21.6	8.7	29	49
K14.8 m	25.6 (23.2-30.7)	22.6	10.1	29	51
K14.10 f	26.8 (24.7-31.6)	23.3	10.3	32	53
K14.5 m	26.6 (25.7-30.0)	23.4	9.9	28	50
K14.9 f	26.1 (25.5-31.0)	23.7	10.4	30	50
K14.3 m	24.7 (24.2-33.9)	22.7	9.5	28	54
K10.9 m	25.6 (23.6-30.0)	23.0	10.4	29	58
K14.6 f	28.3 (24.8-31.5)	25.6	9.4	28	62
K10.6 m	23.1 (23.1-28.4)	20.1	9.1	28	65
K10.3 m	26.6 (26.6-31.8)	23.9	10.5	28	65
K13.3 f	24.9 (22.6-29.3)	22.6	8.9	32	71
K12.1 f	25.3 (23.8-30.5)	23.6	9.0	25	67
K 5.4 m	36.2 (23.1-36.8)	33.3	11.3	33	79
K10.4 m	25.4 (24.0-28.7)	23.1	10.1	28	74
K12.5 f	28.3 (26.0-29.2)	24.1	10.3	28	76
K10.1 f	28.7 (28.1-31.9)	26.8	10.7	28	77
K10.2 f	30.1 (26.6-31.8)	25.7	10.5	28	78
K10.8 f	24.6 (23.6-29.6)	22.6	8.9	28	87
K 8.4 f	30.3 (25.2-32.1)	26.8	9.8	32	95
K14.2 f	26.9 (26.9-36.7)	25.0	10.5	28	95
K 9.2 m	43.5 (38.2-49.0)	39.1	11.9	40	104
K10.5 f	26.0 (23.7-26.8)	21.9	9.7	28	104
K12.4 f	28.1 (26.3-32.0)	25.8	10.4	28	117

While no exact chemical determinations were made, it is evident that the amounts of food consumed by the rats in these thirst experiments are more than sufficient for maintenance when water is allowed *ad libitum*. Under these circumstances, Jackson ('15) found that rats of about 24 grams in body weight require for maintenance only about 5 grams daily of Graham bread soaked in whole milk; decreasing to about 3 grams later. Since a greater amount of food was consumed by my rats on the thirst experiments, it is evident that the prevention of growth is due to the lack of water rather than to inanition from inadequate food-intake.

In the inanition experiments with water (Jackson, '15 a) the amount of food required for maintenance of body weight in young rats was found to decrease as the experiment proceeds. Similarly in the present tests (as above shown) a decreasing amount of liquid (milk) is required for maintenance with dry food *ad libitum*, although the amount of dry food taken remains fairly constant.

The difference in the amount of milk required for maintenance of body weight with the different kinds of food probably depends (at least in part) upon the amount of water contained in the food. In all cases, however, there is a decrease in the milk required as the experiment proceeds. Jackson ('15 a) thought that in young rats held at maintenance by underfeeding the amount of living protoplasm is greatly decreased, thereby decreasing the basal rate of metabolism, with a corresponding decrease in the necessary food-intake. Possibly a similar explanation may hold in the case of the present thirst experiments. The metabolism may be altered in some way so as to require less water for maintenance of constant body weight.

Both test rats and controls were killed by chloroform and dissected according to the technique described by Donaldson ('15), with a few modifications. The submaxillary gland and thyroid gland were removed first. The parts and organs upon removal were placed in a closed jar upon glass plates resting on moist filter-paper. After weighing, the organs were dried to constant weight in an oven at about 95°C. in order to determine their water content (not included in this paper).

Percentage losses in the various organs were calculated as follows. The average weight (table 2) for each organ or part in the test rats was compared with the corresponding average for the normal controls of similar body weight. The data in the column 'Difference' express the apparent percentage changes (+ or -) as the result of the experiment. In table 2 the average gross body weight and net body weight (gross body weight minus intestinal contents) are seen to differ but slightly (usually less than 5 per cent) in the various test groups, as compared with the normal controls. These differences have been ignored in calculating the percentage changes for the various parts.

In view of the comparatively small number of observations and the known variability, especially of some of the organs (Jackson, '13), the conclusions reached in the present paper are by no means to be considered as final. It is believed, however, that they are sufficient to give an approximate idea of some of the more obvious and important changes, so as to make possible a comparison of the effects of a relatively dry diet (water deficiency) with other forms of inanition.

GENERAL OBSERVATIONS

In general the test rats remained active and apparently healthy, although many died during the course of the experiment, as above stated. The skin becomes somewhat roughened, but the hair is not easily detached (as occurs in adults during thirst). Dryness and desquamation were observed on the plantar surfaces. The claws become much elongated, especially in the later test periods. The fecal material is usually hard, never diarrheal in character. The urine is scanty. Haemorrhage from the conjunctiva or nose was not observed, although it sometimes occurred in the stomach or intestines. In the rats dying during the experiments (not included in the tables) hemorrhage and ulceration of the stomach were often observed. Dryness of the external genital organs, especially in females, was observed, and eczematous conditions often occurred in the longer experiments. Paralysis of the legs or other parts was never found in the young rats (as noted occasionally in adults by Kudo, '21). In some young rats the

TABLE 2
Average data for controls and test rats, with percentage of change in the various test groups, as compared with normal controls.
Weights are given in grams, lengths in centimeters

	NORMAL CONTROLS (2m; 4f) AGE 25 TO 30 DAYS AVERAGE	TEST RATS ON DRY DIET HELD AT CONSTANT BODY WEIGHT FOR PERIODS INDICATED				
		1 to 2 weeks (2m; 4f) Average and percentage difference	3 to 4 weeks (6m; 2f, 4f) Average and percentage difference	5 to 6 weeks (3m; 3f) Average and percentage difference	7 to 8 weeks (1m; 4f) Average and percentage difference	9 to 13 weeks (6m; 4f) Average and percentage difference
Gross body weight.....	26.2	24.6 (-6.1)	25.3 (-3.4)	27.4 (+4.6)	27.4 (+4.6)	27.8 (+4.6)
Net body weight.....	23.7	22.4 (-5.5)	22.7 (-4.2)	24.9 (+5.1)	24.4 (+3.0)	24.9 (+5.1)
Body length.....	9.8	9.3 (-5.1)	9.8 (0)	9.9 (+1.0)	10.1 (+3.1)	10.1 (+3.1)
Tail length.....	7.0	7.4 (+5.7)	8.7 (+24.3)	8.4 (+20.0)	8.8 (+25.7)	9.0 (+28.6)
Integument.....	4.35	3.74 (-14.0)	3.91 (-10.2)	3.48 (-10.0)	3.97 (-8.7)	3.98 (-7.5)
Musculature.....	7.32	6.81 (-7.0)	6.98 (-4.7)	7.38 (+0.8)	6.82 (-6.8)	6.97 (-4.8)
Lig. skeleton.....	3.73	4.26 (+14.2)	4.59 (+23.1)	5.09 (+36.5)	5.22 (+40.0)	5.06 (+35.7)
Cart. skeleton.....	2.79	3.80 (+36.2)	3.42 (+22.6)	4.17 (+49.5)	4.29 (+53.8)	4.42 (+58.4)
Humeri and femurs...	0.3355	0.3856 (+14.9)	0.4026 (+20.0)	0.4540 (+35.3)	0.4152 (+23.7)	0.4439 (+32.3)
Visceral group.....	5.1912	5.3501 (+3.1)	5.4883 (+5.7)	5.6224 (+8.3)	6.1769 (+19.0)	6.2578 (+20.6)
Remainder.....	1.10	0.51 (-37.3)	0.58 (-47.3)	0.64 (-41.9)	0.59 (-46.4)	0.54 (-50.9)
Brain.....	1.2424	1.1894 (-4.3)	1.3088 (+5.4)	1.2583 (+1.3)	1.2636 (+1.7)	1.3493 (+8.6)
Spinal cord.....	0.1565	0.1891 (+20.8)	0.2107 (+34.6)	0.2165 (+38.2)	0.2389 (+52.5)	0.2398 (+53.1)
Nn. ischiadici.....	0.0087	0.0090 (+3.5)	0.0119 (+36.8)	0.0111 (+27.6)	0.0123 (+41.4)	0.0129 (+48.3)
Eyeballs.....	0.1054	0.1152 (+9.3)	0.1456 (+38.3)	0.1448 (+37.5)	0.1719 (+63.3)	0.1797 (+70.8)
Heart.....	0.1696	0.1557 (-8.2)	0.1547 (-8.8)	0.1695 (+0.06)	0.1963 (+15.8)	0.1873 (+10.4)
Spleen.....	0.0838	0.0432 (-48.4)	0.0474 (-43.5)	0.0436 (-48.0)	0.0762 (-9.1)	0.1136 (+36.6)
Lungs.....	0.2369	0.2145 (-9.5)	0.2310 (-2.5)	0.2452 (+3.5)	0.2363 (-0.25)	0.0523 (-37.6)
Parotid glands.....	0.0284	0.0149 (-47.6)	0.0152 (-46.5)	0.0115 (-59.6)	0.0160 (-43.7)	0.2294 (-2.8)
Submaxillary glands..	0.1010	0.0759 (-24.9)	0.0573 (-43.3)	0.0415 (-59.0)	0.0512 (-49.3)	0.0155 (-45.4)
Liver.....	1.1636	1.3244 (+13.8)	1.2313 (+5.8)	1.3045 (+12.1)	1.2363 (+6.3)	0.0598 (-40.8)
Pancreas.....	0.1389	0.1610 (+15.9)	0.1795 (+29.2)	0.1722 (+24.0)	0.1846 (+32.9)	1.5522 (+33.5)
						0.2032 (+46.3)

Stomach-intestines (with contents).....	3.60	3.65 (+1.4)	3.94 (+9.4)	4.00 (+11.1)	4.65 (+29.2)	4.70 (+30.6)
Stomach-intestines (empty).....	1.30	1.38 (+6.2)	1.36 (+4.6)	1.44 (+10.8)	1.68 (+29.3)	1.75 (+34.6)
Kidneys.....	0.2988	0.4034 (+35.0)	0.4451 (+48.4)	0.4797 (+60.5)	0.4940 (+65.3)	0.4435 (+48.4)
Testes.....	0.1427	0.0962 (-32.5)	0.0748 (-47.5)	0.1005 (-29.5)	0.0450 (-68.3)	
Epididymides.....	0.0190	0.0144 (-24.2)	0.0147 (-22.6)	0.0128 (-32.6)	0.0132 (-30.5)	
Ovaries.....	0.0114	0.0077 (-32.5)	0.0061 (-46.5)	0.0041 (-64.0)	0.0043 (-62.3)	0.0038 (-66.7)
Uterus.....	0.0161	0.0138 (-14.3)	0.0174 (+8.1)	0.0136 (-15.5)	0.0204 (+26.7)	0.0217 (+34.8)
Thyroid.....	0.0038	0.0033 (-13.1)	0.0035 (-7.9)	0.0032 (-15.8)	0.0028 (-26.3)	0.0039 (+2.6)
Thymus.....	0.0771	0.0240 (-68.9)	0.0094 (-87.8)	0.0134 (-82.6)	0.0109 (-85.9)	0.0067 (-91.3)
Suprarenals (m).....	0.0077	{0.0124 (+61.0)			0.0132 (+71.4)	
Suprarenals (f).....		{0.0106 (+37.7)			0.0128 (+66.2)	
Hypophysis (m).....	0.0016	{0.0017 (+6.3)			0.0023 (+43.8)	
Hypophysis (f).....		{0.0015 (-6.3)			0.0022 (+37.5)	

penis was extruded, possibly from attempts to get the urine. It is to be noted that the specific symptoms generally found associated with various vitamin deficiencies are either slight or entirely absent in survivors of these thirst experiments.

The general condition observed at autopsy are as follows: There is extreme general emaciation, especially in the longer periods. The skin and muscles appear somewhat dry and difficult to separate. The blood is thick. The fat has usually almost disappeared from the subcutaneous and muscular tissues; but in some cases it remains in relatively large amount. The orbital and interscapular fat persists in small amount even in the longer experiments. There is no appreciable change in amount of serous fluid in the pericardial, pleural, and peritoneal cavities. The viscera generally appear normal. The liver is often congested and occasionally yellowish in color (fatty change?). The kidneys are often congested, and their surfaces appear rough in a few cases. Marked congestion of the brain, kidneys, suprarenals, spleen, and lungs was sometimes found. In general, however, the effects of thirst on young rats, as shown by observations and autopsy, appear slighter than in adult rats.

LENGTH OF BODY AND TAIL

The body length is measured from the tip of the nose to the anus and the tail length from the anus to the tip of the tail. The measurements were taken immediately after death, the body and tail being extended by very slight tension. Measurements during life are not very accurate, although they might be obtained by the use of anesthetics. Some measurements were made on the living animals, however, which show changes in the lengths of body and tail similar to the changes indicated by the measurements at autopsy.

In the groups of rats held at constant body weight for the five periods (table 2) the percentage changes in average body length are insignificant, usually corresponding to the slight differences in body weight between test rats and controls. It is evident that the body length remains nearly constant. The tail length, however, shows a marked and progressive increase, indicating for the

five periods gains of 5.7, 24.3, 20.0, 25.7, and 28.6 per cent, respectively (table 2).

Thus the rats held at constant body weight by thirst become relatively long-tailed, as found likewise by Jackson ('15 a) in young rats held at maintenance by underfeeding. Some data indicating an opposite result were reported by Hatai ('08).

In adult rats during thirst the body length in the acute series shows an average loss of 11.4 per cent and in the chronic-thirst series a loss of 14.7 per cent. The tail, however, has nearly the same average length in controls and test rats (Kudo, '21).

INTEGUMENT

The general changes in the integument were mentioned above under 'General Observations.' In the young rats held at constant body weight in five test series (table 2) there is a slight apparent loss varying from 7.5 to 14 per cent in weight of the integument (which includes the skin and appendages, hair and claws). It would appear that this slight loss occurs early, and is not progressive during the course of the experiment.

In adult rats during thirst the loss of the integument is very nearly proportional to that of the whole body (Kudo, '21).

In inanition (with water) a much greater loss of 36 per cent or more was found in the weight of the integument of young rats by Jackson ('15 a).

SKELETON

The bones, together with the cartilages, periosteum, and ligaments, constitute the 'ligamentous skeleton.' The bones and cartilages, after removal of the periosteum and ligaments by immersion for about one hour in 1 per cent aqueous 'Gold Dust' (a commercial soap powder) solution at 90°C., constitute the 'cartilaginous skeleton.' Donaldson and Conrow ('19) have shown that while such a maceration in hot 'Gold Dust' solution causes only a slight loss (less than 5 per cent) in the skeleton of adult rats, in young rats the loss in skeletal weight is considerably greater, amounting to about 15 per cent in the new born. The humerus and femur (of both sides) were therefore cleaned sepa-

rately without maceration, and their weights are recorded separately in table 2, though also included in the weights of the whole skeleton.

As shown by table 2, while the body weight is held constant during the thirst experiments, the ligamentous skeleton continues to increase in weight to a marked degree. The increase is progressive from 14.2 per cent at one to two weeks up to 40 per cent at seven to eight weeks (slightly less at nine to thirteen weeks). For the cartilaginous skeleton the apparent increase in weight is still greater, ranging from 22.6 to 58.4 per cent. It is possible that these large percentages (especially that of 36.2 per cent at one to two weeks) may be erroneous, due to abnormalities or to errors in technique.

The humerus and femur (weighed separately in the moist cartilaginous state, after removal of periosteum and ligaments without immersion in the hot soap solution), as shown in table 2, show percentage increases which are very close to those of the ligamentous skeleton, and these probably form a more accurate index of the actual changes in the weight of the cartilaginous skeleton.

In an underfeeding experiment, Jackson ('15 a) found that the increase in young rats held at constant body weight from three to ten weeks of age forms 28 per cent in the weight of the ligamentous skeleton, and 21.5 per cent in the weight of the cartilaginous skeleton which is somewhat lower than that obtained in the present thirst experiments. This may be because less water is required for the growth of bone, so that its growth is less retarded on a relatively dry diet.

In the inanition experiment on young rats, Jackson ('15 a) noted that the skeletal growth tends to proceed along the lines of normal development, as indicated by decrease in the water content, by formation and union of various epiphyses, etc. Very similar phenomena were noted in the skeleton during the present thirst experiments (epiphyses of vertebrae and humerus, appearance of third molars, etc.).

Data cited by Jackson from other investigators (Waters, Aron, Variot) indicate that a persistent growth of the skeleton during

inanutition likewise occurs in the young of other species (calves, puppies, human infants). Jackson and Stewart have shown that the growth of the skeleton in underfed rats appears less intensive in very young (newborn) rats and in older rats (approaching maturity).

MUSCULATURE

As shown in table 2, the various groups of tests rat show apparent slight decreases (4.7 to 7 per cent) in weight, excepting the third group, which is nearly constant. These differences are insignificant, especially when the slight differences in body weight between controls and test rats are taken into account, but there is perhaps a slight tendency to decrease in the later periods.

In young rats held at constant body weight by inanition (simple underfeeding) the musculature, as in thirst, also remains nearly constant, but with a very slight tendency to increase in weight (Jackson, '15 a).

During thirst in adult rats the musculature loses approximately in proportion to the entire body (Kudo, '21).

VISCERA AND 'REMAINDER'

The visceral group includes the brain, spinal cord, hypophysis, and eyeballs, as well as thoracic and abdominal viscera. In the animals held at constant body weight (table 2) the visceral group shows a progressive increase in weight of 3.1 to 20.6 per cent in the five test series.

The weight of the visceral group depends essentially upon that of the larger organs. As will be seen later, however the individual viscera differ greatly in their changes in weight during the thirst experiments.

In the maintenance of the body weight by simple inanition, Jackson ('15 a), in young albino rats, and Aron ('11), in young dogs, found that the visceral group undergoes but little change in weight.

The 'remainder' is that part of the body which remains after removing the skin, skeleton, musculature, and visceral group. It includes the adipose and interstitial connective tissue, mesen-

terium, larger peripheral nerves, and blood-vessels, etc. The escaped fluids and the loss by evaporation are not included. As shown in table 2, the 'remainder' in the various tests undergoes a loss in weight increasing from 37.3 per cent in the one to two weeks' test to 50.9 per cent in nine to thirteen weeks. This loss is probably chiefly due to that of the fat, which largely disappears, as mentioned under 'General Observations.'

BRAIN

The brain weight of the control rats (table 2) corresponds closely to the data of Donaldson ('15) and Jackson ('15a). In the rats at the various test periods the average brain weight shows slight apparent changes, varying from -4.3 per cent to +8.6 per cent. It will be noted, however, that (with one exception) these apparent changes are in the same direction as the corresponding slight differences between test rats and controls in average body weight. The apparent differences in brain weight are therefore insignificant, considering the small number of observations, and it seems probable that the brain undergoes no appreciable change in weight during these thirst experiments.

Hatai ('04) found a slight apparent loss (average about 4.7 per cent) in the weight of the brain in young albino rats fed with starch, beef fat, and water, the body weight being reduced about 30 per cent (average). In a later experiment, however, Hatai ('08) found that the growth in brain weight was retarded in the same proportion as the whole body weight. In albino rats with retarded growth on a lipoid-free ration, the brain was apparently about 2 per cent subnormal in weight (Hatai, '15).

In underfed young rats (with water), Donaldson ('11) found an apparent slight increase (3.6 per cent) in the brain weight, while Jackson ('15 a) found no significant change. It is evident that the age at which the inanition occurs is important, as Stewart ('18, '19) found a marked increase (125 per cent) in the brain of newborn rats held at constant body weight by underfeeding for sixteen days. Variot and Lassabliere ('09) observed a tendency to persistent growth in brain weight in human infants whose body weight was retarded by malnutrition. The brain

weight of the adult rats subjected to thirst showed no significant change in weight (Kudo, '21). The constancy of the brain weight in adults under various forms of inanition has been repeatedly observed by numerous investigators. McCarrison ('19), however, finds an apparent increase of one-seventh in the brain weight of monkeys on various diets deficient in vitamins.

SPINAL CORD

The spinal cord shows a marked and progressive increase (20.8 to 53.1 per cent) in weight in the various test periods (table 2).

Jackson ('15 a) found an increase of 36 per cent in the spinal cord of rats held at constant body weight by underfeeding from three to ten weeks of age, and a smaller increase was obtained by Donaldson ('11). In newborn rats, held at maintenance by underfeeding from sixteen days, Stewart ('19) found an increase of 83 per cent in the weight of the spinal cord. In the thirst experiments on adult rats, the spinal cord shows but little change in weight (Kudo, '21).

SCIATIC NERVES

The sciatic nerves (nn. ischiadici) in the test rats showed an increase in weight which is similar to that of the spinal cord, excepting the first period (table 2). This indicates that the continued growth of the spinal cord is correlated with that of the peripheral nerves, as might be expected. In the thirst experiments on adult albino rats, however, the sciatic nerves lost in weight, while the spinal cord did not. No further data on the changes in weight of peripheral nerves during inanition have been found in the literature.

EYEBALLS

The eyeballs likewise show a marked and progressive increase in average weight during the various test periods (table 2), varying from 9.3 to 70.8 per cent. The apparent increase of 70.8 per cent in weight of the eyeballs during the thirst experiments is greater than that observed in any other organ or system.

In the adult rats the eyeballs lose nearly 10 per cent during thirst (Kudo, '21). In young rats underfed (with water) from three to ten weeks of age, Jackson ('15 a) found an increase of nearly 50 per cent in the weight of the eyeballs. A still greater increase (146 per cent) was found by Stewart ('19) in similar experiments on newborn rats.

Jackson ('15 a) thought the striking growth capacity of the eyeballs during inanition might depend upon their large water absorption, as the eyeballs are known to have a very high water content. The present thirst experiments, however, indicate that the remarkably persistent growth of the eyeballs continues even when the water supply to the organism is greatly restricted.

Notwithstanding the great increase in the size of the eyeballs in the test rats, they do not protrude abnormally. More space is doubtless provided for them, partly by actual growth of the skeletal orbit and partly by atrophy of the orbital fat.

HEART AND AORTA

The heart (table 2) in the test rats shows an apparent slight decrease in weight in the earlier periods with a small increase in the later periods of thirst. It will be noted, however, that these changes do not greatly exceed the differences between test rats and controls in body weight, which are in the same direction. The apparent changes in heart weight are therefore of doubtful significance.

In rats underfed from three weeks of age, Jackson ('15 a) likewise found no significant change of weight, although in underfed newborn rats Stewart ('19) noted an increase of 26 per cent.

During thirst in adult rats the heart likewise maintains its relative weight, losing in absolute weight nearly in proportion to the entire body (Kudo, '21).

Aorta. The aorta was cut proximally at the heart and distally at the origin of the iliac branches. All branches of the aorta were clipped close to the vessel. All blood content was removed. The following observations are too few (especially on controls) to warrant conclusions, but would seem to indicate an increase in the weight of the aorta during the thirst experiments.

LENGTH OF TEST	NUMBER OF RATS	AVERAGE NET BODY WEIGHT	AVERAGE WEIGHT OF AORTA
		<i>grams</i>	<i>gram</i>
(Control)	1	26.0	0.0187
1-2 weeks	2	20.9	0.0159
3-4 weeks	7	22.6	0.0212
5-6 weeks	3	23.9	0.0246
7-8 weeks	4	24.8	0.0232
9-13 weeks	3	24.2	0.0234

SPLEEN

The spleen (table 2) shows a marked loss in average weight (36.6 to 48.4 per cent) in all the test groups but one, in which the loss appears much smaller (9.1 per cent). The very small apparent loss in this test group is due to an abnormally large spleen which weighed 0.2 gram, which brought up the average for the group. If this abnormal spleen were excluded, the loss in this group would appear as 46.5 per cent. Similarly in the last group, the inclusion of an abnormally large spleen gives an apparent average increase of 36.6 per cent; omitting this spleen, there is an average loss of 37.6 per cent. Although the spleen is normally one of the most variable organs in the body (Jackson, '13), requiring caution in drawing conclusions, it is evident that it usually undergoes a great loss in weight in young rats held at constant body weight by thirst.

In adult albino rats during thirst, both acute and chronic, the spleen similarly loses relatively much more in weight than does the body as a whole (Kudo, '21). Jackson ('15 a) found that in young rats held at maintenance by underfeeding beginning at the age of three weeks there is a marked tendency to decrease in weight of the spleen, while at later (and longer) periods the spleen appears to undergo no material change in weight. In the underfed newborn rats, Stewart ('19) found an increase of 33 per cent in the spleen.

LUNGS

The lung infections frequently found in older rats rarely occur before the age of ten weeks (Jackson, '15 a) and did not occur in the rats shown in tables 1 and 2. The average weight of the lungs in the test groups shows slight changes, varying from -9.5 to $+3.5$ per cent. These changes are usually in the same direction as the differences in average body weight, however, and are too small to be significant. It is therefore evident that there is but slight if any change in the weight of the lungs during the present thirst experiments.

During thirst in adult rats the percentage loss in the weight of the lungs appears slightly greater than that of the whole body (Kudo, '21). In young rats held at constant body weight by underfeeding, Jackson ('15 a) found a slight decrease in the early periods, but not in the later. There is no appreciable increase in the lungs of the underfed newborn rats (Stewart, '19).

SALIVARY GLANDS

Parotid glands. The parotid glands (table 2) show a marked decrease in average weight, varying from 43.7 to 59.6 per cent in the various test groups. This loss apparently occurs early and remains fairly uniform throughout the various test periods. In adult albino rats during thirst, both in acute and chronic, the percentage loss in weight of the parotid glands is likewise much larger than that of the entire body (Kudo, '21).

Submaxillary glands. A striking decrease in weight similar to that of the parotid glands is apparent in the submaxillary glands (table 2) in all except the first test group, where the loss (24.9 per cent) is somewhat smaller. In adult albino rats during thirst, both acute and chronic, the submaxillary glands likewise decrease in weight relatively much more than does the body as a whole (Kudo, '21).

LIVER

The liver shows somewhat irregular increases in average weight (table 2), varying from 5.8 to 33.5 per cent in the different test periods. While the liver thus shows a definite tendency to

increase, caution must be observed in drawing conclusions, on account of the great variability in the weight of the normal liver (Jackson, '13).

In the adult rats during thirst the liver loses weight in about the same proportion as the whole body (Kudo, '21). In young rats underfed from three weeks of age the liver is variable, showing a definite increase in weight in the earlier periods, but a decrease later (Jackson, '15 a). Stewart ('19) found a marked loss in the liver weight of underfed newborn rats.

PANCREAS

The pancreas (table 2) in the various test periods shows a progressive increase in average weight (15.9 to 46.2 per cent). It may be noted that the average weight of the pancreas in my controls (0.1389 gram) is considerably below the corresponding weight found by Hatai ('18) (0.206 gram); but, as Hatai remarks, it is difficult to dissect out the gland with uniform accuracy.

In adult rats a decrease in weight of the pancreas during thirst is relatively much greater than that of the whole body. Thus the loss in the weight of the pancreas resembles that of the salivary glands.

STOMACH AND INTESTINES

The stomach and intestines were separated from mesentery and pancreas. The digestive tube with contents (table 2) shows a progressive increase in average weight, varying from 1.4 to 30.6 per cent. The increase is not significant until after six weeks. The data for the empty stomach and intestines show a very similar progressive increase in average weight, varying from 4.6 to 34.6 per cent. Thus both the alimentary canal and the intestinal contents appear to increase in weight, especially in the thirst experiments extending beyond six weeks in length. The intestinal contents in the test rats are watery or mucous in character in the small intestine, becoming usually very hard in the fecal material of the large intestine.

In rats underfed from three weeks of age Jackson ('15 a) likewise found an increase in the weight of the intestinal canal (plus

mesentery and pancreas), which continued up to the age of six weeks, but appeared to decrease later. In adult albino rats during thirst there is a marked decrease (relatively slightly less than that of the entire body) in the weight of the stomach and intestines (Kudo, '21).

KIDNEYS

The kidneys (table 2) in the test groups show a marked apparent increase in average weight, progressing from 35 to 65.3 per cent in the first four groups, but decreasing to a gain of only 48.4 per cent in the longest test (nine to thirteen weeks). It is possible, however, that the large apparent increase may be due in part to an abnormally low kidney weight in my controls, which is somewhat below the normals of Jackson ('15 a) and Donaldson ('15). In young rats underfed beginning at three weeks of age Jackson ('15 a) found a slight increase in the weight of the kidney, but little or no change at later periods. Stewart ('19) found a great increase (90 per cent) in the kidney weight of underfed newborn rats.

In adult rats during acute and chronic thirst the kidneys lose in weight relatively slightly less than the body as a whole (Kudo, '20).

TESTES

The average net body weights of the males in the various groups of table 2 are as follows: controls (2), 26.6 grams; 1-2 weeks (2), 26.7 grams; 3-4 weeks (6), 22.4 grams; 5-6 weeks (3), 25.8 grams; 7-8 weeks (1), 23.1. It is thus evident that the average body weights of the various test groups differ somewhat from the controls, which partly accounts for the greater apparent losses in the groups at three to four weeks and seven to eight weeks. Making allowance for this difference in body weight, the tests would show an average decrease of something over 30 per cent.

On the other hand, Jackson ('15 a) found an apparent increase of 34 per cent in the weight of the testis in rats underfed beginning at three weeks of age, and Stewart ('19) obtained an enormous increase (average 374 per cent) in the testes of newborn rats held at maintenance by underfeeding for about sixteen days.

In adult rats the testes during acute thirst lose about 15 per cent in their weight and during chronic thirst they lose 52.7 per cent, while the loss of the whole body is respectively 36.1 per cent and 52.4 per cent (Kudo, '21). Hatai ('15) found that the testes of young albino rats show an actual loss in weight (23 per cent) as a result of six months on the lipoid free-diet.

EPIDIDYMIDES

The apparent losses in the average weight of the epididymis (table 2) are, of course, subject to the same corrections as those of the testis, on account of differences in body weight between test rats and controls. The actual losses are therefore somewhat lower than those indicated in the table and below those of the testis.

In adult rats during thirst the epididymides lose weight roughly in proportion to the body weight (Kudo, '21).

OVARIES

The average body weight of the female rats in the control group (table 2) is slightly lower than that in all the test groups, excepting the first. But the maximum difference in body weight is only about 10 per cent, so the relatively large apparent losses in the average weight of the ovaries, increasing progressively from 32.5 to 66.7 per cent, would not be materially affected by the required corrections.

This loss in the weight of the ovaries during thirst is materially greater than that (27 per cent) found by Jackson ('15 a) in rats underfed beginning at three weeks of age. Stewart ('19) found practically no change in the weight of the ovaries in underfed newborn rats. Hatai ('15) found in young albino rats fed with lipoid-free diet a loss of 17.4 per cent in the weight of the ovaries.

UTERUS

The uterus (including tubes) is subject to considerable variation in weight, as appears in the various test groups in table 2. While the tendency during the earlier test periods is somewhat fluctuating and doubtful, there appears to be a definite increase in

average weight (26.7 to 34.8 per cent) in the two longest tests. Its change in weight therefore appears quite different from that of the ovaries.

THYROID GLAND

The thyroid gland shows an apparent loss in average weight in all but the last test group (table 2). In most cases the difference is too small to be significant, however, especially when the individual variation in the weight of the thyroid gland and also the great difficulty in dissecting it out in a uniform manner are considered. Jackson ('15 a), however, found an apparent loss of about 24 per cent in the thyroid of rats underfed from three weeks of age.

In adult albino rats during thirst, both acute and chronic, the thyroid glands lose markedly in weight (Kudo, '21).

THYMUS

The loss of 68.9 to 91.3 per cent in the average weight of the thymus in the various test groups (table 2) is greater than that in any other organ. According to Hatai ('14), the thymus should reach its maximum absolute weight (0.29 gram) at about eighty-five days of age, after which it normally undergoes a slow age involution. As is well known, the thymus is especially liable to a rapid involution under various unfavorable circumstances ('accidental involution' of Hammar). This was found by Jackson ('15 a) in rats underfed at three weeks of age and later, and also by Stewart ('19) in newborn rats. In adult rats during thirst the involution of thymus is likewise very marked, with loss of about 90 per cent in weight (Kudo, '21).

SUPRARENAL GLANDS

In the suprarenal glands of the rat there is normally a sexual difference in weight, observable from the age of about six weeks (Jackson, '13, Hatai, '13). Before this age the sexes may safely be grouped together, as in my controls. In the test groups the sexes are separated, although on account of the small numbers and the irregularity of the data they are combined into only two

age groups, one to four weeks and five to thirteen weeks. All four groups show a marked apparent increase in weight, which is about 60 per cent in all except the younger group of females (37.7 per cent). This difference is not on account of the appearance of the normal sex difference, however, for normally the suprarenals become larger in the female. As a matter of fact, the tendency to sexual difference in weight does not appear in these thirst experiments, (contrary to the observations of Jackson) ('15 a) in underfeeding).

In the rats underfed beginning at three weeks of age Jackson ('15 a) found an apparent increase of 12 to 39 per cent in the weight of the suprarenals. A much smaller increase (5 per cent) was found by Stewart (19) in underfed newborn rats.

In adult rats during thirst there is a relatively small loss in weight of the suprarenal glands (Kudo, '21).

HYPOPHYSIS

The hypophysis in rats above 50 grams in body weight must be considered separately in the sexes, since it then normally becomes relatively heavier in the female. This does not affect my controls (grouped together in table 2), and it is evident from table 2 that there likewise appears no sexual differentiation in weight in the test rats during the thirst experiments (in agreement with the inanition experiments of Jackson, '15 a). There is evidently no significant change in the average weight of the hypophysis in the one to four weeks' group, but a marked increase (37.5 to 43.8 per cent) in the five to thirteen weeks' group.

Jackson ('15 a) found a smaller increase (18 to 19 per cent) in the rats underfed from three weeks of age, while Stewart ('19) found a slightly larger increase in the underfed newborn rats.

In adult rats during thirst the hypophysis changes but little in absolute weight (Kudo, '21).

DISCUSSION

The changes in the average weights of the various organs and parts in rats held at constant body weight for the various periods are summarized in table 2. While no great emphasis can be laid

upon the exact accuracy of the figures shown in table 2, it is evident that, with respect to the changes in weight during the thirst experiments, the organs may be divided into three groups. In the first group, which includes hypophysis, eyeballs, kidneys, suprarenals, spinal cord, skeleton, sciatic nerves, pancreas, alimentary canal, liver, humerus and femur, visceral group and uterus, there is a well-marked increase in weight during the maintenance of constant body weight by thirst in young rats. As shown in table 2, the rate of increase in the weight of the organs, in general, is progressively greater in the longer periods.

In the second group, which includes heart, brain, musculature, and lungs, the organs remain nearly constant in weight.

In the third group, including the thymus, ovaries, parotid and submaxillary glands, 'remainder,' spleen, testes, epididymides, thyroid, and integument, there is a marked loss in weight. This loss appears in most of the organs already in the earlier test periods and in some cases (thymus, thyroid) appears more or less progressive in character.

If we compare the changes in weight, as a measure of their relative resistance to thirst, in young growing rats with those observed in adult rats during acute and chronic thirst (Kudo, '21), it is found that in general there is in many cases a considerable degree of correspondence. The hypophysis, eyeballs, skeleton, and spinal cord increase in weight in the young rats and also show marked resistance (slight loss in weight) in adults during acute and chronic thirst. The brain in all cases remains nearly constant in weight.

The heart weight is nearly constant in the young rats and loses nearly in proportion to the body during adult thirst. The thymus, 'remainder,' salivary glands, spleen, testes, and epididymides lose weight markedly during thirst in both young and adult rats.

In many other cases, however, the changes in organ weight in the young differ materially in tendency from those in adult. Thus the pancreas and liver have a marked growth tendency in the young test rats, but lose heavily during adult thirst. Lesser degrees of difference are observed in many other organs.

Comparing my results in young rats on thirst tests with those of Jackson ('15 a) in young rats of similar age held at constant body weight by underfeeding (with water allowed), there is found a remarkable similarity between them. Thus, in both cases there is a marked growth in the brain, spinal cord, eyeballs, hypophysis, skeleton, suprarenals, and alimentary canal. In both series the brain, musculature, and heart remained nearly constant, and the thymus, ovaries, spleen, thyroid, and integument decreased greatly in weight. There are some differences between the results of the thirst and the inanition tests, however. The kidneys appear to gain markedly during thirst, but remain constant during inanition. The testes lose heavily in weight during thirst, but gain markedly during inanition. Other forms of partial inanition give results differing more or less from the foregoing, as shown by the experiments of Hatai, Osborne and Mendel, McCarrison, and others on diets defective in various respects, including vitamine deficiencies (cf. Jackson and Stewart, '19, and Kudo, '21).

It has also been shown by Jackson and Stewart that the changes in organ weight during inanition differ greatly according to the age of the animals. Thus, the changes during underfeeding in the newborn are very different from those in adolescent rats and these in turn differ from those in older animals. The age factor is doubtless equally important in the effects of thirst upon the weight of the various organs.

SUMMARY

The principal results of the present investigation may be briefly summarized as follows.

Albino rats about one month old may be held at constant body weight for several weeks by a restricted amount of liquid (milk) in a diet otherwise adequate for growth. The rats show a progressive tolerance of thirst, so that less liquid milk is daily required for maintenance as the experiment proceeds.

The tail becomes elongated while the body length remains constant.

There is in general a marked increase in the weight of the skeleton and a slight increase in the visceral group.

The musculature remains nearly constant in weight. There is a slight decrease in the integument and a marked loss in the 'reminder.' Of the individual viscera:

1. The hypophysis, eyeballs, kidneys, suprarenals, spinal cord, skeleton, sciatic nerves, pancreas, stomach-intestines, liver, and uterus show a definite increase in weight.

2. The heart, brain, and lungs remain nearly constant in weight.

3. The thymus, ovaries, parotid and submaxillary glands, spleen, testes, epididymides, and thyroid suffer more or less well-marked decrease in weight.

The growth tendencies of the various organs in the young rats during the thirst experiments correspond in general to those found in rats of similar age during underfeeding, although certain exceptions occur (testes and kidneys).

Likewise the results of the thirst tests (also those of the inanition experiments) show a general resemblance to those of similar character in adults. There are certain differences according to age, however, as well as according to the type of inanition employed.

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