EXPERIMENTAL STUDIES ON EXCESSIVE INTAKE OF NaCl I. THE EFFECT OF SALT WATER INTAKE ON THE GROWTH OF RAT

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INTRODUCTION

NaCl is an indispensable substance for human beings, but variation in the amount of intake causes ill health. In the field of pharmacology, it is classified as one of the denaturing substances. In medical literature it states that NaCl intake to an excess causes inflammation on the gastric wall, the symptoms being pain and vomiting, and further by a higher degree of stimulation, death due to shock might occur. The lethaldose for a human is 5-10 g. per 1 kg.

Sato et al. (1959)¹⁵⁾ reported that feeding a mouse with ordinary Japanese food containing salt causes bleeding on the mucous membrane of the stomach. Sasaki (1956)¹¹⁾¹²⁾ recognized the significant correlation between the NaCl intake and mortality of cerebral hemorrhage, and for the prevention of the hypertonic diseases, he pointed out the necessity for care in regulating NaCl intake¹³⁾. However, Kimura (1960)⁹⁾ did not recognize any relationship between blood pressure and the amount of NaCl intake. In addition, there are reports on favorite taste in salt³⁾, the relationship between the NaCl intake and Vitamin C¹²⁴⁾ and many reports on the correlation of high blood pressure and arteriosclerosis⁶⁾⁸⁾¹⁰⁾¹⁴⁾¹⁶⁾. At the same time, one of the authors, Miyazaki (1961)⁹⁾, made an epidemiological survey on the blood pressure of farmers in Miyaki County of Saga Prefecture and observed a meaningful correlation between the morbidity of hypertension and the amount of NaCl intake. The authors also felt certain that there are many problems to clarify experimentally as to the effect of NaCl intake.

In this paper, a report is made on the effect of salt water intake in various concentrations on the growth of rats during their maturation period.

EXPERIMENTAL METHOD

1) *Animal*

The rats used for the experiment were *Rattus norvegicus* var. *albinus* (Hatai), albino rat. Among reproduced rats from a pair of Wistar-King A originally re-

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ceived from National Institute of Heredity and the animal room of Kyushu University Medical School, the authors selected ones from the same litter, healthy, pure and with definite date of birth.

2) *The method of raising in a constant humidity and temperature room*

The animals were raised in a specially designed room of constant temperature, $21 \pm 1^\circ\text{C}$, and humidity, $60 \pm 5\%$. The temperature and humidity were automatically recorded by an automatic thermometer and hygrometer (made by Shimazu Seisakusyo) and the average value for every 6 days was recorded in dry and wet bulb temperature. Oriental Solid Food NMF (for reproduction) was administered.

3) *The method of salt water administration*

The salt was dissolved (the first class quality chemical) in concentrations of 1 %, 2 % and 3 % in the city well water. The salt water was given to rats in bottles with measurement in the condition that those rats could drink it freely any time. The remainder in each bottle was accurately measured and the amount of salt water intake was recorded every day as well as the average for 6 days which was calculated and added to the record. Administration was begun in one group on the 60th day after birth (the latter part of puberty) and in another group on the 120th day (the early part of the growth completion). 16 male and female rats from 2 litters were separated to 4 groups, including one control group.

4) *Others*

As to determining the amount of food intake, the measurement of body weight and the length of the tail, the authors followed Fujita's method²⁾ of the same department.

EXPERIMENTAL RESULT

I The group in which the start of administration was at the latter part of puberty (the 60th day after birth)

Eight rats from one litter (4 male and 4 female), born on May 1, 1960 were classified according to the following groups, and the administration was started on the 60th day after birth :

Control (city well water administered).....	♂ 200, ♀ 200
1 % salt water administered	♂ 201, ♀ 201
2 % salt water administered	♂ 202, ♀ 202
3 % salt water administered	♂ 203, ♀ 203

Figures 1 (♂) and 2 (♀) show the summarized result, comparing the control in body weight, length of the tail, the amount of food intake, the amount of salt water taken and also the variations of humidity or temperature in the animal room.

In the symbol used for female rats "MYN", Y stands for young breeding, M for the number of delivered younglings and N for the number of the alive.

In comparison with the control, the three groups which took the salt water showed less growth both in body weight and the length of the tail. The rate of growth varied inversely as the percentage of salt concentration increased; the administration of 3 % salt water, especially, caused rapid decrease in weight in both male (♂ 203) and female (♀ 203). The male died on the 36th day and the female on

Figure 1. The growth of rats when administered the salt water, the experiment starting the latter part of puberty (the 60th day after birth) (δ)

Figure 2. The growth of rats when administered the salt water, the experiment starting the latter part of puberty (the 60th day after birth) (φ)

the 72nd day.

II The group in which the start of administration was at the early part of growth completion (the 120th day after birth)

Eight rats from one litter (4 male and 4 female) born on May 30, 1960 were classified to the following groups, and the administration was started on the 120th day after birth :

Control (city well water administered).....	♂ 240, ♀ 240
1 % salt water administered	♂ 241, ♀ 241
2 % salt water administered	♂ 242, ♀ 242
3 % salt water administered	♂ 243, ♀ 243

Figures 3 (♂) and 4 (♀) show the summarized results, comparing the control in body weight, length of the tail, the amount of food intake, the amount of salt water taken and also the variations of temperature or humidity in the animal room. In comparison with the control, the three groups which took the salt water showed less growth both in body weight and length of tail. The rate of growth varied inversely as the percentage of salt concentration increased; the administration of 3 % salt water particularly, causing a rapid decrease both in male (♂ 243) and female (♀ 243). The male died on the 97th day and the female on the 123rd day.

III Comparative Discussion as to the Starting Period of the Experiment

A comparative discussion was made concerning the onset of the experiment between the latter part of puberty (abbreviated as LPP) and the early part of growth completion (abbreviated as EGC). The authors observed the difference in body weight, length of the tail, the amount of food intake and the amount of total salt intake. (See Table 1—4)

(1) Body Weight

Considering the body weight of both male and female control rats on the 180th day as 100, the following results were observed :

LPP	1 % salt water administered	♂ 68
		♀ 80
	2 % salt water administered	♂ 49
		♀ 69

Generally speaking, male rats grew less than female rats.

On the other hand :

EGC	1 % salt water administered	♂ 91
		♀ 86
	2 % salt water administered	♂ 81
		♀ 73

Contrary to LPP, female rats grew less than the male rats in EGC. From these results, we can tell that LPP is more affected by the administration of salt water than EGC, the growth in body weight being less. At the administration of 3 % salt water, the male in LPP died on the 36th day (the decreasing rate compared with the body weight at the start of the experiment was 27.8 %) and female on the 72nd day (the decreasing rate compared with the body weight at the start of the experiment was 44.8 %). The male in EGC died on the 97th day (59.6 %) and female on the 123rd day (51.8 %). Those in LPP died earlier than EGC, and it was confirmed that LPP was more affected by the salt water

Figure 3. The growth of rats when administered the salt water, the experiment starting the early part of growth completion (the 120th day after birth) (♂).

Figure 4. The growth of rats when administered the salt water, the experiment starting the early part of growth completion (the 120th day after birth) (♀).

TABLE 1

The growth in body weight of rats (the experiment starting at different stage)

Starting period of the experiment	Sex	The days	The starting day of the experiment				The 60th day				The 120th day				The 180th day				The 240th day			
		Concentration of salt water	Control	1 %	2 %	3 %	Control	1 %	2 %	3 %	Control	1 %	2 %	3 %	Control	1 %	2 %	3 %	Control	1 %	2 %	3 %
The group in which the start of administration was at the latter part of puberty (the 60th day after birth)	♂	Body weight (g)	190	171	181	180	331	291	221	130	381	283	215	—	398	271	195	—	408	278	200	—
		Comparison with the control (100)	100	90	95	95	100	88	67	(1) 44	100	74	56	—	100	68	49	—	100	68	49	—
	♀	Body weight (g)	150	158	145	145	218	200	162	111	240	197	156	80	232	186	160	—	246	192	164	—
		Comparison with the control (100)	100	105	97	97	100	91	74	51	100	82	65	(2) 34	100	80	69	—	100	78	67	—
The group in which the start of administration was at the early part of growth completion (the 120th day after birth)	♂	Body weight (g)	340	326	306	334	380	346	316	176	402	366	342	135	408	372	335	—				
		Comparison with the control (100)	100	96	90	98	100	91	83	46	100	91	85	(3) 34	100	91	81	—				
	♀	Body weight (g)	220	216	214	197	250	212	190	132	274	235	196	106	281	242	202	95				
		Comparison with the control (100)	100	98	97	90	100	85	76	53	100	86	83	39	100	86	73	(4) 35				

Remarks :

- 1) The compared ratio with the control 295 g on the 96th day in body weight at the time of death.
- 2) The compared ratio with the control 236 g on the 132nd day in the same as 1).
- 3) The compared ratio with the control 392 g on the 217th day in the same as 1).
- 4) The compared ratio with the control 275 g on the 243rd day in the same as 1).

TABLE 2
The growth in tail-length of rats (the experiment starting at different stage)

Starting period of the experiment	Sex	The days	The starting day of the experiment				The 60th day				The 120th day				The 180th day				The 240th day			
		Concentration of salt water	Control	1 %	2 %	3 %	Control	1 %	2 %	3 %	Control	1 %	2 %	3 %	Control	1 %	2 %	3 %	Control	1 %	2 %	3 %
The group in which the start of administration was at the latter part of puberty (the 60th day after birth)	♂	Tail-length (cm)	14.9	15.5	14.4	14.2	18.1	17.8	17.6	14.6	19.9	18.3	18.1	—	20.3	18.7	18.3	—	20.9	19.0	18.3	—
		Comparison with the control (100)	100	104	97	95	100	98	97	(1) 86	100	92	91	—	100	92	90	—	100	91	88	—
	♀	Tail-length (cm)	15.6	14.2	15.0	14.7	18.2	16.5	16.3	15.0	19.0	17.0	16.7	15.0	19.7	17.3	17.1	—	20.4	17.6	17.4	—
		Comparison with the control (100)	100	91	96	94	100	91	90	82	100	89	88	(2) 81	100	88	87	—	100	86	85	—
The group in which the start of administration was at the early part of growth completion (the 120th day after birth)	♂	Tail-length (cm)	19.7	19.9	19.7	19.6	20.6	20.2	20.0	19.6	21.2	20.4	20.1	19.7	21.5	20.4	20.1	—				
		Comparison with the control (100)	100	101	100	99	100	98	97	95	100	96	95	(3) 94	100	95	93	—				
	♀	Tail-length (cm)	17.8	17.0	16.9	17.2	18.9	17.9	17.6	17.4	19.1	18.1	17.9	17.4	19.6	18.2	18.0	17.4				
		Comparison with the control (100)	100	96	95	97	100	95	93	92	100	95	94	91	100	93	92	(4) 91				

Remarks :

- 1) The compared ratio with the control 17.0cm on the 96th day in tail-length at the time of death.
- 2) The compared ratio with the control 18.5cm on the 132nd day as in the 1).
- 3) The compared ratio with the control 21.0cm on the 217th day as in the 1).
- 4) The compared ratio with the control 19.2cm on the 243rd day as in the 1).

TABLE 3

The food intake of rats (the experiment starting at different stage) (The averaged amount per a rat per day for 6 days)

Starting period of the experiment	Sex	The days	The starting day of the experiment				The 60th day				The 120th day				The 180th day				The 240th day			
		Concentration of salt water	Control	1 %	2 %	3 %	Control	1 %	2 %	3 %	Control	1 %	2 %	3 %	Control	1 %	2 %	3 %	Control	1 %	2 %	3 %
The group in which the start of administration was at the latter part of puberty (the 60th day after birth)	♂	The amount of intake (g)	15.0	14.6	18.5	16.5	14.0	13.3	14.3	(1) 4.5	20.7	13.0	8.2	—	22.2	15.6	12.5	—	24.0	20.0	16.0	—
		Calory/kg	283	307	367	329	152	164	232	124	196	165	137	—	200	207	230	—	211	258	287	—
		N amount (g/kg)	3.31	3.58	4.28	3.84	1.77	1.91	2.71	1.45	2.28	1.92	1.60	—	2.34	2.41	2.69	—	2.46	3.01	3.35	—
		The amount of salt intake (g/kg)	0.51	0.56	0.66	0.60	0.28	0.30	0.37	0.22	0.35	0.30	0.25	—	0.36	0.37	0.42	—	0.38	0.47	0.52	—
	♀	The amount of intake (g)	13.5	12.8	11.3	11.2	17.5	12.7	9.0	3.6	15.8	15.3	8.8	(2) 2.0	18.2	13.2	12.8	—	17.2	13.0	9.5	—
		Calory/kg	323	291	280	277	288	228	199	116	237	280	203	90	282	255	287	—	251	243	208	—
		N amount (g/kg)	3.77	3.39	3.27	3.24	3.36	2.66	2.33	1.36	2.76	3.25	2.36	1.05	3.29	2.97	3.35	—	2.93	2.84	2.43	—
		The amount of salt intake (g/kg)	0.58	0.53	0.51	0.50	0.52	0.41	0.36	0.21	0.43	0.51	0.37	0.16	0.51	0.46	0.52	—	0.45	0.44	0.38	—
The group in which the start of administration was at the early part of growth completion (the 120th day after birth)	♂	The amount of intake (g)	20.0	22.1	19.2	21.7	18.0	18.7	13.7	6.9	19.0	15.0	15.0	(3) 3.3	21.5	19.0	14.5	—				
		Calory/kg	211	243	230	233	171	195	156	141	170	147	157	88	189	183	155	—				
		N amount (g/kg)	2.46	2.84	2.68	2.72	1.98	2.27	1.82	1.64	1.98	1.72	1.84	1.02	2.21	2.14	1.81	—				
		The amount of salt intake (g/kg)	0.38	0.44	0.42	0.42	0.31	0.35	0.28	0.26	0.31	0.27	0.28	0.16	0.34	0.33	0.28	—				
	♀	The amount of intake (g)	19.8	14.6	13.9	15.8	15.5	11.3	9.0	8.0	15.7	13.5	11.0	4.3	20.0	19.0	11.5	(4) 3.0				
		Calory/kg	323	243	233	292	223	192	171	218	206	206	201	146	256	282	204	113				
		N amount (g/kg)	3.77	2.83	2.72	3.41	2.60	2.23	1.98	2.54	2.40	2.41	2.35	1.70	2.98	3.29	2.39	1.32				
		The amount of salt intake (g/kg)	0.58	0.44	0.42	0.53	0.40	0.35	0.31	0.39	0.37	0.37	0.36	0.26	0.46	0.51	0.37	0.20				

Remarks: 1) The amount of food intake per a rat per day for the 6 days before death (died on the 96th day. 2) The same as 1). (died on the 132nd day). 3) The same as 1). (died on the 217th day). 4) The same as 1). (died on the 243rd day).

TABLE 4
The total salt intake of rats (the experiment starting at different stage) (The averaged amount per a rat per day for 6 days)

Starting period of the experi- ment	Sex	Concentration of salt water The days	Control			1 % salt water admi- nistered			2 % salt water admi- nistered			3 % salt water admi- nistered		
			The amount of water taken (cc)	The salt intake from the food (g)	The total salt intake per kg (g)	The amount of salt water intake (cc)	The salt intake from the food(g)	The total salt intake per kg (g)	The amount of salt water intake (cc)	The salt intake from the food(g)	The total salt intake per kg (g)	The amount of salt water intake (cc)	The salt intake from the food(g)	The total salt intake per kg (g)
The group in which the start of admi- nistration was at the latter part of puberty (the 60th day after birth)	♂	The starting day of the experiment	34	0.01	0.51	35 *	0.10	0.56	47 *	0.12	0.66	39 *	0.11	0.60
		The 60th day	30	0.09	0.27	62	0.09	2.43	47	0.09	4.63	5	0.03	1.38(1)
		The 120th day	47	0.14	0.35	58	0.09	2.35	33	0.05	3.32	—	—	—
		The 180th day	55	0.15	0.36	62	0.10	2.66	63	0.08	6.88	—	—	—
		The 240th day	50	0.16	0.38	57	0.13	2.52	60	0.10	3.50	—	—	—
		The averaged ** amount of experi- mental period	44	0.12	0.34	54	0.11	2.42	49	0.09	5.23	38	0.05	7.84
	♀	The starting day of the experiment	23	0.09	0.58	35 *	0.08	0.53	35 *	0.07	0.51	25 *	0.07	0.50
		The 60th day	25	0.11	0.52	55	0.08	3.17	35	0.06	4.69	7	0.02	2.11
		The 120th day	38	0.11	0.46	44	0.10	2.74	31	0.06	4.34	6	0.02	2.48
		The 180th day	38	0.12	0.51	60	0.09	3.69	57	0.08	7.65	5	0.01	2.04(2)
		The 240th day	46	0.11	0.40	57	0.09	3.41	61	0.06	7.70	—	—	—
The group in which the start of admi- nistration was at the early part of growth completion (the 120th day after birth)	♂	The starting day of the experiment	36	0.13	0.38	47 *	0.14	0.44	40 *	0.13	0.42	48 *	0.14	0.42
		The 60th day	40	0.12	0.31	57	0.12	2.00	60	0.09	4.08	33	0.05	5.88
		The 120th day	55	0.17	0.41	60	0.11	1.93	62	0.09	3.89	7	0.04	1.81(3)
		The 180th day	44	0.14	0.34	56	0.12	1.84	51	0.10	3.48	6	—	—
		The averaged ** amount of experi- mental period	43	0.13	0.33	56	0.11	1.91	52	0.10	3.69	38	0.07	5.34
	♀	The starting day of the experiment	50	0.13	0.58	33 *	0.10	0.44	43 *	0.09	0.42	39 *	0.10	0.53
		The 60th day	50	0.10	0.40	60	0.07	3.18	60	0.06	6.63	20	0.05	4.94
		The 120th day	48	0.10	0.38	50	0.09	2.50	49	0.07	5.37	8	0.03	2.53
		The 180th day	50	0.13	0.47	58	0.12	2.91	53	0.08	5.62	7	0.02	2.42(4)
		The averaged ** amount of experi- mental period	47	0.12	0.47	53	0.09	2.82	53	0.07	5.78	35	0.06	7.32

Remarks: 1. The averaged salt intake per a rat per day for 6 days before death (died on the 96th day) 2. The same as above (died on the 132nd day) 3. The same as above (died on the 217th day) 4. The same as above (died on the 243rd day) * The city well water intake as same with the control. ** The averaged total salt intake per a rat per day for the whole period of the experiment.

administration. It was a notable fact that in both groups female rats lived longer than male rats.

(2) The Length of the Tail

Considering the length of the tail of both male and female control rats on the 180th day as 100, the authors observed the following results :

LPP	1 % salt water administered	♂ 92
		♀ 88
	2 % salt water administered	♂ 90
		♂ 87
EGC	1 % salt water administered	♂ 95
		♀ 93
	2 % salt water administered	♂ 93
		♂ 92

There was no significant difference between the sexes at the time of death caused by 3 % salt water administration. The growing rate of the tail at the time of the death was as follows :

LPP	♂ 2.8 %	EGC	♂ 0.5 %
	♀ 2.0 %		♀ 1.2 %

The administration of salt water did not affect the growth of the tail as much as the body weight.

(3) The Amount of Calory Intake

The average calory intake per kg. per day was :

LPP	Control	♂ 200 Cal
		♀ 282 Cal
	1 % salt water administered.....	♂ 207 Cal
		♀ 255 Cal
	2 % salt water administered.....	♂ 230 Cal
		♀ 287 Cal

This shows that the averaged total calory intake in female per kg. per day was considerably more than in male.

EGC	Control	♂ 189 Cal
		♀ 256 Cal
	1 % salt water administered.....	♂ 183 Cal
		♀ 282 Cal
	2 % salt water administered.....	♂ 155 Cal
		♀ 204 Cal

In this group, the averaged total calory intake in female per kg. per day was also more than in male. There was not a significant difference between those two groups although in the 3 % salt water administered, a remarkable decrease was observed in the total calory intake per kg. per day. The averaged total calory intake for the 6 days before the death was : LPP male.....124 Cal, female.....90 Cal, and EGC male.....88 Cal, female.....113 Cal.

(4) The Amount of Total Salt Intake

The averaged total salt intake per kg. per day was :

LPP	Control	♂ 0.34 g
		♀ 0.52 g

EGC	1 % salt water administered	♂ 2.42 g
		♀ 3.45 g
	2 % salt water administered	♂ 5.23 g
		♀ 6.84 g
	3 % salt water administered	♂ 7.84 g
		♀ 11.28 g
	Control	♂ 0.33 g
		♀ 0.47 g
	1 % salt water administered	♂ 1.91 g
		♀ 2.82 g
	2 % salt water administered	♂ 3.69 g
		♀ 5.78 g
	3 % salt water administered	♂ 5.34 g
		♀ 7.32 g

The averaged amount of total salt intake per kg. per day was much more in LPP than in EGC, and in both groups it was interesting to note that the total amount was greater in female than male.

SUMMARY

16 rats from two litters (8 male and 8 female) were administered 1 %, 2 % and 3 % of salt water freely, starting at the latter part of puberty (the 60th day after birth) and early part of growth completion (the 120th day after birth). The effect of salt water intake on the growth of those rats in the two different growing stages was observed.

1. The increase of body weight in the group which started taking the salt water at the latter part of puberty was inverse as the concentration increased. The growth in male was rather less than in female.

2. The increase of body weight in the group which started taking the salt water at the early part of growth completion was also inverse as the concentration increased. In comparison with the former group, however, the degree of ill effects was much less and female growth was somewhat less than male.

3. The administration of the 3 % salt water caused death in all 4 rats. The period up to death was prolonged in the female about twice as in the male. Comparing the two groups, the group starting the experiment at the latter part of puberty died much earlier than the other.

4. Growth of the tail was affected relatively as the concentration increased although there was not much difference in two groups in body weight. Also there was no significant difference between the sexes.

5. Generally speaking, the averaged calory intake per kg. per day was more in the female than the male; but the authors did not observe a meaningful difference between the two groups. The group administered 3 % salt water took particularly fewer calories.

6. The total salt intake per kg. per day was the most in the 3 % salt water administered group and decreased as the concentration was lowered. The LPP group and the female sex took remarkably more salt in comparison.

The authors will make another report in the near future as to the biochemical, ecological and pathohistological observations of the studied rats.

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