Adrenaline Content of Adrenals in Rabbits Poisoned with Acetylcholine and its Recovery

By

Susm Satoo

(佐藤 存)

(From the Physiological Laboratory of Prof. Y. Satake,
Tohoku University, Sendai)

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The previous researches re the production of adrenaline in the adrenal gland were done to find whether the production is regulated by the nervous control and then to determine its velocity. The agencies which act to reduce the adrenaline content through the nervous route are: Diphtheria toxine on rabbits,¹⁾ cold on cats,²⁾ physostigmine on dogs³⁾ and rabbits,⁴⁾ etc.

In supplementing this series of researches, the acethylcholine was used as a means for accelerating immensely the adrenaline discharge by acting directly upon the adrenal medulla itself.⁵⁾

Method:

Rabbits, male and female without pregnancy, were used. The left splanchnicotomy was done without narcosis, and 21-68 days were then allowed to elapse until the experimentation. No food was given for 12 hours before the injection of the drug. Acetylcholine chloride (Roche) solution, prepared with saline solution, in 2.5% before the use, was hypodermically injected in a dose of 15 mg. per kg body weight. At certain intervals as 5, 12 & 24 hours after the injection the animals were killed by a blow on the neck, and the adrenals were removed out soon. The Suto-Kojima's method was used for estimating the adrenaline.

The data are given in the accompanying table.

As the control 9 rabbits were used.

On injecting the drug the animals suffered therefrom; the severe symptoms lasted ten to thirty minutes. Afterwards they looked quite normal.

As the consequence the glands taken out 5 hours after the injection were estimated extraordinarily heavy, as both glands together 341 mg. in toto and 165 mg. per kg b.w. as the average of 6 cases, against 211 mg. and 124 mg. per kg. in the 9 control cases. The glands taken out 12 hours and 24 hours respectively after the injection did not show such an increase in weight. This affords also an evidence against the use of adrenaline

TABLE

The Recovery of Adrenaline Content in the Denervated (Left) and in

No. of rabbits	Sex	L. splanchnicotomy			Interval between splanchnicotomy & experiment (days)	Experiment	
		Date	Body weight (kg.)	Route		Date (1941)	
Normal							
3	♀					12.	III.
15	♀					19.	IV.
18	♂					21.	VI.
20	♂					28.	VI.
45	♂					2.	VIII.
46	♀					4.	VIII.
47	♀					5.	VIII.
48	♂					6.	VIII.
49	♀					7.	VIII.
	Mean						
5 hours after the							
1	♂	28.	II. '41	1.76	abdominal	49	18. IV.
7	♀	5.	IV. '41	2.28	"	30	5. V.
8	♀	11.	IV. '41	1.42	"	31	12. V.
9	♂	11.	IV. '41	1.40	"	41	22. V.
12	♂	7.	V. '41	1.63	"	26	2. VI.
60	♀	8.	IX. '41	1.46	"	22	1. X.
	Mean			1.66		33	
12 hours after the							
13	♂	7.	V. '41	1.32	abdominal	66	13-14. VII.
16	♂	22.	V. '41	1.59	"	58	19-20. VII.
19	♀	28.	VI. '41	1.44	"	27	25-26. VII.
36	♂	26.	VII. '41	2.07	"	25	20-21. VIII.
41	♂	27.	VII. '41	1.45	lumbar	65	30. IX. — 1. X.
59	♂	8.	IX. '41	1.34	abdominal	21	30. IX. — 1. X.
	Mean			1.54		44	
24 hours after the							
22	♀	11.	VII. '41	2.00	abdominal	24	4-5. VIII.
24	♂	19.	VII. '41	1.90	"	21	9-10. VIII.
25	♀	19.	VII. '41	1.60	"	21	9-10. VIII.
34	♂	25.	VII. '41	1.49	lumbar	26	20-21. VIII.
50	♀	7.	VIII. '41	2.08	abdominal	21	28-29. VIII.
30	♀	21.	VII. '41	1.42	lumbar	49	8-9. IX.
	Mean			1.75		27	

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the Innervated (Right) Glands after the Exhaustion by Acetylcholine

Body weight (kg.)	Acetylcholine injection		Weight of gland (mg.)					
	Total quantity (mg.)	Duration of poisoning (min.)	L		R		L—R	
			Total	Per kg. body weight	Total	Per kg. body weight	Total	Per kg. body weight

control

1.36			97	71	111	82	208	153
1.79			170	95	135	75	170	170
2.10			106	50	104	50	100	100
1.35			63	47	61	45	92	92
1.97			117	59	104	53	112	112
2.05			199	97	172	84	181	181
1.35			97	72	79	59	130	130
1.60			68	43	71	44	87	87
1.67			74	44	72	43	87	87
1.69			110	64	101	59	211	124

administration

2.06	30.9	30	275	133	292	142	567	275
2.43	36.5	27	397	163	317	130	714	294
1.99	29.9	14	105	53	97	49	202	102
1.96	29.4	18	72	37	67	34	139	71
1.68	25.2	22	100	60	98	58	198	118
1.70	25.5	10	113	66	111	65	224	132
1.97	29.6	20	177	85	164	80	341	165

administration

2.38	35.7	40	120	50	108	45	228	96
2.10	31.5	35	146	70	121	58	267	127
1.65	24.8	15	94	57	88	53	182	110
2.15	32.3	15	133	62	119	55	252	117
1.85	27.8	21	105	57	99	54	204	110
1.74	26.1	17	124	71	118	68	242	139
1.98	29.7	24	120	61	109	56	229	117

administration

2.10	31.5	70	214	102	187	89	401	191
2.06	30.9	15	104	50	94	46	198	96
1.71	25.7	12	90	53	78	46	168	98
1.45	22.0	14	60	41	50	34	110	76
2.07	31.1	25	218	105	160	77	378	183
1.61	24.2	14	132	82	124	77	256	159
1.83	27.6	25	136	72	116	62	252	134

Continued on the back

No. of rabbits	Adrenaline content (mg.)									Room temperature (c)
	Total quantity			Per gr. of gland			Per kg. of body weight			
	L	R	L+R	L	R	L+R	L	R	L+R	
Normal control										
3	0.078	0.080	0.158	0.80	0.72	0.76	0.057	0.059	0.116	11
15	0.064	0.059	0.123	0.38	0.44	0.40	0.036	0.033	0.069	10
18	0.084	0.080	0.164	0.79	0.77	0.78	0.040	0.038	0.078	20
20	0.054	0.051	0.105	0.86	0.84	0.85	0.040	0.038	0.078	23
45	0.080	0.080	0.160	0.68	0.77	0.72	0.041	0.041	0.081	22
46	0.174	0.160	0.334	0.87	0.93	0.90	0.085	0.078	0.162	22
47	0.058	0.048	0.106	0.60	0.61	0.60	0.043	0.036	0.078	27
48	0.048	0.050	0.098	0.71	0.70	0.71	0.030	0.031	0.061	24
49	0.070	0.070	0.140	0.95	0.97	0.96	0.042	0.042	0.084	27
	0.079	0.075	0.154	0.74	0.75	0.74	0.046	0.044	0.090	
5 hours after the administration										
1	0.090	0.082	0.172	0.33	0.28	0.30	0.044	0.040	0.083	10
7	0.068	0.072	0.140	0.17	0.23	0.20	0.028	0.030	0.058	17
8	0.040	0.042	0.082	0.38	0.43	0.41	0.020	0.021	0.041	16
9	0.044	0.044	0.088	0.61	0.66	0.63	0.022	0.022	0.045	19
12	0.068	0.072	0.140	0.68	0.73	0.71	0.040	0.043	0.083	20
60	0.052	0.058	0.110	0.46	0.52	0.49	0.031	0.034	0.065	18
	0.060	0.062	0.122	0.44	0.48	0.46	0.031	0.032	0.063	
12 hours after the administration										
13	0.054	0.058	0.112	0.45	0.54	0.49	0.023	0.024	0.047	18
16	0.045	0.041	0.086	0.31	0.34	0.32	0.021	0.020	0.041	23
19	0.062	0.058	0.120	0.66	0.66	0.66	0.038	0.035	0.073	20
36	0.080	0.082	0.162	0.60	0.69	0.64	0.037	0.038	0.075	25
41	0.036	0.058	0.094	0.34	0.59	0.46	0.019	0.031	0.051	18
59	0.058	0.044	0.102	0.47	0.37	0.42	0.033	0.025	0.059	18
	0.056	0.057	0.113	0.47	0.53	0.50	0.029	0.029	0.058	
24 hours after the administration										
22	0.088	0.080	0.168	0.41	0.43	0.42	0.042	0.038	0.080	22
24	0.042	0.040	0.082	0.40	0.43	0.41	0.020	0.019	0.040	19
25	0.074	0.070	0.144	0.82	0.90	0.86	0.043	0.041	0.084	21
34	0.058	0.060	0.118	0.97	1.20	1.07	0.040	0.041	0.081	24
50	0.128	0.130	0.258	0.59	0.81	0.68	0.062	0.063	0.125	23
30	0.052	0.070	0.122	0.39	0.56	0.48	0.032	0.043	0.076	25
	0.074	0.075	0.149	0.60	0.72	0.65	0.040	0.041	0.081	

to the weight of gland as the adrenaline content in the case of rabbits.⁶⁾

Then in consulting the figures of the total amount of adrenaline and the amount per kg. of b.w. on the table, the general outcome will be extracted in the following paragraphs:

In all the series of experiments the amount of adrenaline in toto and per kg. b. w. as well was almost same in the fellow glands, i.e. in the left denervated and the right intactly innervated. The loss of innervation has no influence upon either the decrease of adrenaline store by acetylcholine or its recovery.

Secondary the adrenaline content was smaller in the series of 12 hours after the injection than in that of 5 hours. This proves that the gland is still losing adrenaline at that period. It is however obscure when namely before or after 12 hours after the injection the adrenaline load diminishes at most. Safely can it be said that the gland restores one fourth of the normal store of adrenaline in first 12 hours.

In short, the adrenaline store of adrenals in rabbits is reduced by acetylcholine, without regard to whether the innervation of glands interfered with or not. The drug is fully proved to attack the adrenal medulla directly as reported by previous investigators.

The gland is able to recover the adrenaline load at the rate of one-fourth of the normal value in the second 12 hours after the injection of acetylcholine. The recovery process takes place independently of the innervation.

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