Adrenaline Load of the Suprarenal Glands of Rabbits in Histamine Poisoning.

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On the glycemic action of histamine, an interesting fact was found by Satow¹⁾ in our laboratory. In rabbits, hyperglycemia is caused by the intravenous injection of histamine in a dose of 0.4–0.5 mg per kg rapidly (in 5–20 seconds). On the contrary, blood sugar decreases, when the same dose of histamine is injected slowly (in 1–1.5 minutes). This was confirmed in rabbits also by Takita²⁾ in our laboratory. Therefore it seemed to be of interest to know how acts the histamine, administered rapidly or slowly, on the adrenaline load of the suprarenals.

As regards the influence of histamine poisoning upon the adrenaline load of the suprarenal glands some papers³⁾ dealt with.

Method.

Healthy rabbits were used. Histamine phosphate ("Takeda") was injected in a following way.

(a) 0.5 mg histamine per kg of body weight was injected intravenously as a 0.1% solution in 10 seconds.

(b) Histamine in a same dose was injected intravenously in 60 seconds.

(c) 20 mg histamine per kg was injected subcutaneously as a 1% solution.

In some cases the animal died after histamine injection. In these cases the suprarenal glands were extirpated soon after the death. In other cases, 30 minutes after intravenous injection or 120 minutes after the subcutaneous injection, after killing the animal by a blow on a neck, the suprarenals were removed. For the estimation of adrenaline in the suprarenals, the corrosive sublimate method of Suto-Kojima⁴⁾ was used, taking Adrenaline chloride ("Sankyo") as a standard. The actual concentration of adrenaline was determined by the method of Kodama.⁵⁾

Results.

The adrenaline load of suprarenal glands in 9 normal rabbits was determined as a control of the present investigations. The results were

TABLE I.

Adrenaline Load in Suprarenal Glands of Normal Rabbits.

No.	Date	Body weight (kg) and sex	Weight of suprarenal gland (g)		Adrenaline load (mg)					
					total quantity		per g gland		per kg of body weight	
			R	L	R	L	R	L	R	L
1	2. X. '42	1.53 ♀	0.115	0.126	0.075	0.071	0.65	0.56	0.049	0.046
2	7. X. '42	2.11 ♂	0.177	0.198	0.071	0.074	0.40	0.37	0.034	0.035
3	22. X. '42	1.73 ♀	0.080	0.104	0.043	0.045	0.54	0.43	0.025	0.026
4	12. XI. '42	2.56 ♂	0.385	0.385	0.126	0.109	0.33	0.28	0.049	0.043
5	29. IX. '43	1.74 ♂	0.164	0.166	0.067	0.066	0.41	0.40	0.039	0.038
6	39. IX. '43	1.90 ♀	0.276	0.281	0.111	0.120	0.40	0.43	0.058	0.063
7	12. X. '43	1.65 ♀	0.091	0.104	0.061	0.063	0.67	0.61	0.037	0.038
8	22. XII. '43	1.73 ♀	0.109	0.124	0.072	0.068	0.66	0.55	0.042	0.039
9	25. XII. '43	1.26 ♀	0.103	0.109	0.050	0.050	0.49	0.46	0.040	0.040
Average		1.80	0.167	0.177	0.075	0.074	0.51	0.45	0.041	0.041

displayed in Tab. I. In these normal rabbits the adrenaline load of suprarenals per gland was in an average value 0.075 mg for the right gland and 0.074 mg for the left gland, the adrenaline load per kg of body weight was in a mean 0.041 mg for the suprarenals of each sides and adrenaline per g of gland was in a mean value 0.51 mg for the right gland and 0.45 mg for the left gland. These values coincide nearly with the value reported in the statistical studies of H. Sato on the adrenaline load of suprarenal glands of 617 normal rabbits, only the adrenaline load per g of gland of the present experiments is somewhat smaller than that of H. Sato.

The chief experiments were performed on 23 rabbits. The results were presented in Tab. II.

In 8 rabbits, histamine in a dose of 0.5 mg per kg of body weight was injected intravenously in 10 seconds. Soon after the injection the intensive convulsions took place in 4 rabbits, and 3 rabbits out of them died eventually. In other 4 rabbits the convulsions did not occur, and only the tachycardia and depression were observed. In averaging the values in these 8 rabbits, the adrenaline load per gland was 0.080 mg for the right gland and 0.079 mg for the left gland, adrenaline per kg of body weight was 0.043 mg for the suprarenals of each sides, and adrenaline per g of gland was 0.49 mg for the right suprarenals and 0.44 mg for the left suprarenals.

In other 8 rabbits the same dose of histamine was injected intravenously in 60 seconds. Only one rabbit out of them died after a occurrence of intensive convulsions. In other rabbits the convulsions were

TABLE II.
Adrenaline Load in Suprarenal Glands of Rabbits in
Histamine Poisoning.

No.	Date	Body weight and sex	Weight of suprarenal gland (g)		Adrenaline load (mg)						Duration after injection to death (†) or slaughter (min.)
					total quantity		per g gland		per kg of body weight		
			R	L	R	L	R	L	R	L	
<i>(A) Rapid intravenous injection of histamine (0.5 mg per kg). Duration of injection 10 sec.</i>											
1	14. IX. '42	2.53 ♂	0.296	0.297	0.074	0.070	0.25	0.24	0.029	0.028	30
2	18. IX. '42	1.67 ♂	0.199	0.174	0.094	0.083	0.47	0.48	0.056	0.050	30
3	18. IX. '42	2.06 ♂	0.182	0.184	0.054	0.050	0.30	0.27	0.026	0.024	6†
4	21. IX. '42	1.86 ♀	0.107	0.124	0.117	0.113	0.99	0.91	0.063	0.061	30
5	21. IX. '42	1.61 ♂	0.230	0.245	0.111	0.114	0.48	0.47	0.069	0.071	4†
6	25. IX. '42	1.58 ♂	0.118	0.131	0.091	0.093	0.77	0.71	0.058	0.059	30
7	28. IX. '42	1.83 ♀	0.119	0.155	0.034	0.040	0.29	0.26	0.019	0.022	5†
8	28. IX. '42	2.45 ♂	0.276	0.313	0.063	0.065	0.23	0.21	0.026	0.027	30
Average			1.95	0.191	0.203	0.080	0.079	0.49	0.44	0.043	0.043
<i>(B) Slow intravenous injection of histamine (0.5 mg per kg). Duration of injection 60 sec.</i>											
9	11. XII. '43	1.53 ♂	0.111	0.166	0.073	0.065	0.66	0.39	0.048	0.043	30
10	11. XII. '43	1.70 ♂	0.272	0.282	0.059	0.065	0.22	0.23	0.035	0.038	30
11	12. XII. '43	2.06 ♂	0.276	0.278	0.084	0.091	0.30	0.33	0.041	0.044	30
12	12. XII. '43	2.15 ♀	0.224	0.277	0.068	0.077	0.30	0.28	0.032	0.036	6†
13	22. XII. '43	1.74 ♂	0.189	0.250	0.151	0.155	0.80	0.62	0.087	0.089	30
14	24. XII. '43	1.60 ♀	0.110	0.114	0.057	0.055	0.52	0.48	0.036	0.034	30
15	24. XII. '43	1.62 ♀	0.098	0.093	0.054	0.050	0.55	0.54	0.033	0.031	30
16	25. XII. '43	1.90 ♂	0.172	0.213	0.074	0.056	0.43	0.26	0.039	0.030	30
Average			1.79	0.182	0.209	0.078	0.077	0.47	0.39	0.044	0.043
<i>(C) Subcutaneous administration of histamine (20 mg per kg).</i>											
17	25. IX. '42	1.66 ♀	0.105	0.101	0.052	0.050	0.50	0.50	0.031	0.030	120
18	22. X. '42	1.81 ♀	0.134	0.136	0.034	0.027	0.25	0.20	0.019	0.015	120
19	29. X. '42	1.77 ♂	0.116	0.126	0.062	0.061	0.53	0.48	0.035	0.034	120
20	7. X. '43	1.84 ♀	0.141	0.174	0.069	0.067	0.49	0.39	0.038	0.036	120
21	12. X. '43	1.91 ♀	0.271	0.302	0.075	0.071	0.28	0.24	0.039	0.037	120
22	18. XII. '43	2.18 ♂	0.263	0.331	0.061	0.072	0.23	0.22	0.028	0.033	120
23	25. XII. '43	1.93 ♂	0.285	0.322	0.070	0.067	0.25	0.21	0.036	0.035	120
Average			1.87	0.188	0.213	0.060	0.059	0.36	0.32	0.032	0.031

not observed. The rate of heart beat increased definitely. The mean value of the adrenaline load of the suprarenals in these rabbits was 0.078 mg and 0.077 mg per gland for the right and the left glands respectively; and 0.044 mg per kg of body weight for the right gland and 0.043 mg per kg for the left gland, and 0.47 mg per g of gland for the right suprarenals and 0.39 mg for the left.

Thus in our experiments non-effect of histamine was observed, which was injected rapidly or slowly in a dose of 0.5 mg per kg upon the adrenaline load of the suprarenal glands.

In another series of experiments, histamine was injected subcutaneously in a dose of 20 mg per kg in 7 rabbits. This dose of histamine is, according to the report of Hirano⁷⁾ in our laboratory, about double as much as the maximum non-lethal dose in rabbits and in fact 3 rabbits out of 5 in his experiment died after subcutaneous injection of histamine in a dose of 20 mg per kg. Nevertheless in the present experiments no rabbit died after application of the same dose of histamine. The rate of heart beat increased markedly. The depression and urination were often observed. The adrenaline load of the suprarenal glands in these 7 rabbits was on an average 0.060 mg for the right gland and 0.059 mg for the left gland. Reckoning the body weight or the weight of gland, they are in a mean value 0.032 mg per kg of body weight in the right gland and 0.031 mg per kg in the left gland, 0.36 mg per g of gland in the right gland and 0.32 mg per g of gland in the left gland.

Comparing these values with those of the control experiments, it is clear that the subcutaneous application of histamine in a dose of 20 mg per kg of body weight causes a reduction of adrenaline load in the suprarenal gland.

In this connection we should recall the report of Z. Kanowoka⁸⁾ on the peptone poisoning. When the animal does not die within a short period and the symptoms of poisoning continue for a certain length of time, the adrenaline load decreases. On the other hand, when the poisoning symptom is severe and the animal dies in a short period, adrenaline load of the suprarenals is not reduced.

SUMMARY.

From the evidence reported by Satow that the glycemic action of histamine is quite different in using the different manner of applications, the interest was evoked, and the present studies were undertaken to know whether the similar evidence can be found or not concerning the influence of histamine upon the adrenaline load of the suprarenal gland.

Rabbits were used. The adrenaline load of the suprarenal glands was estimated by the corrosive sublimate method of Suto-Kojima. His-

tamine was injected intravenously in a dose of 0.5 mg per kg of body weight in 10 seconds or in 60 seconds. Some rabbits died several minutes after histamine injection and others were able to recover. In the former the suprarenals were removed soon after death and in the latter it was removed 30 minutes after injection. In these experiments we could not find any definite alteration of adrenaline load after histamine. Subcutaneous injection of histamine in a dose of 20 mg per kg was also applied. In this series of experiments the reduction of adrenaline load was observed.

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