11392 P

Effect of Tyrosinase on Blood Pressure of Hypertensive Rats.

HENRY A. SCHROEDER. (Introduced by A. E. Cohn.)

From the Hospital of the Rockefeller Institute for Medical Research, New York.

Recent studies on the action of pressor substances in experimental arterial hypertension make it probable that some pressor material liberated by diseased kidneys is responsible for the elevation of blood pressure. Because this pressor substance may be a relatively simple amine, an attempt has been made to learn the action of enzymes capable of altering certain amines, upon the blood pressure of hypertensive and of normal animals. Rats were made hypertensive (1) by partial constriction of one renal artery, (2) by unilateral hydronephrosis, and (3) by unilateral renal injury, the other kidney remaining healthy. Tyrosinase, obtained from Professor J. M. Nelson of Columbia University, was injected intravenously into 37 animals. Blood pressure was measured by a Hamilton manometer, the needle of which was inserted into the femoral artery, and records made for 40 to 60 minutes thereafter. In a few instances another measurement of blood pressure was made several days later.

In every case the diastolic pressure of the *hypertensive* animals fell 30 mm Hg or more (Table I), and in no case did it return to the initial level. Indeed in only one animal (Rat G 104) did it subse-

TABLE I (Abnormal Animals).
Diastolic Blood Pressure mm Hg. Before and After the Injection of Tyrosinase.

Rat No.	Dose, cc	Control	15 min after injection	30 min after injection	Change at 30 min	Subsequent level
H 93	0.5	120	50	70	—50	85—24 hr later
H 94	1.0	110	81	65	—45	82—70 min "
H 95	0.4	102	50	65	—37	70— 2 wks "
H 97	1.0	126	93	85	—41	
H 100	0.5	112	52	82	—30	60— 5 days "
G 104	0.8	134	86	100	—34	92— 2 wks "
G 113	0.5	110	65	69	—41	82—98 min "
G 115	1.0	120	102	74	—46	
G 117	0.8	132	86	92	—40	82—75 " "
G 121	0.5	110	104	80	—30	72—80 " "
G 122	0.5	110	100	72	—38	62—75 " "
G 123	0.6	128	90	88	—40	100—17 days "
G 140	1.0	128	75	68	—60	85—75 min "
I 19	0.75	112	60	60	—52	
I 22	0.4	138	108	96	—42	80—70 " "
		M = 120	M = 80	M = 78	M = —42 σ = 7.8	

quently rise above 100 mm Hg, falling later to lower levels; in 2 others it rose for a short time above 90. Changes comparable in magnitude occurred in the systolic pressure. No effect was noticed until the injection had been given 5 to 15 minutes, when a spontaneous fall was seen. The blood pressure of five rats followed 1, 5 and 14 days remained low. An inactive preparation of the enzyme gave no effect.

Variable results were seen in *normal* rats. In 2, the diastolic pressure fell significantly. In the remainder the change was of smaller magnitude or a distinct rise was noticed (Table II).

Five animals operated upon failed to develop hypertension, and injection of the enzyme into them gave inconsistent results similar to those found in normal rats.

Injection of the enzyme appeared to have no toxic effect upon the animals.

The fact that this enzyme acts consistently as a depressor in hypertensive rats and has a variable effect in normal ones suggests that some substance common to the former is changed. It is possible, from the specificity of the enzyme for phenolic configurations, that the substance contains one or more of these chemical groups. No adequate interpretation of these results can, however, be made now,

TABLE II (Normal Animals).
Diastolic Blood Pressure mm Hg. Before and After the Injection of Tyrosinase.

Rat No.	Dose, cc	Control	15 min after injection	30 min after injection	Change at 30 min	Subsequent level
22	0.5	90	121	110	+20	102—45 min later
23	0.5	60	70	60	0	60—61 " "
24	0.5	75	70	79	+ 4	79—64 " "
26	0.8	115	95	80	—35	
27	0.5	100	100	100	0	
28	0.75	70	50	52	—18	55—55 " "
29	0.7	94	70	60	—34	
31	1.0	114	100	100	—14	
32	0.8	85	118	114	+29	
33	0.5	108	110	87	—21	112—17 days "
34	0.5	80	86	92	+12	106— 9 " "
35	0.5	105	126	120	+15	110—60 min later
36	0.5	100	112	112	+12	120—45 " "
37	0.5	136	144	136	0	
40	0.5	80	65	65	—15	
41	0.5	122	126	122	0	
42	0.5	102	104	98	— 4	98—45 " "
43	0.5	102	110	114	+12	110—60 " "
45	0.5	85	86	82	— 3	
80	1.0	80	65	87	+ 7	
		M = 95	M = 96	M = 93	M = —2 σ = 52.4	

nor can consideration of these effects be applied to any animals save rats with unilateral renal disease until further studies, now in progress, indicate that similar action upon blood pressure takes place on the use of such enzymes in other mammals.

Summary. The injection of tyrosinase into hypertensive rats consistently and markedly lowered the blood pressure, this effect appearing 5 to 15 minutes after intravenous administration. The use of this material in normal animals gave variable results.

11393

Effect of Two Steroid Compounds on Weight of Thymus of Adrenalectomized Rats.*

DWIGHT J. INGLE. (Introduced by F. D. W. Lukens.)

From the George S. Cox Medical Research Institute, University of Pennsylvania, Philadelphia.

The thymus gland of rats can be made to regress rapidly by the administration of extracts of the adrenal cortex or by the administration of some of the steroid compounds occurring in the extracts. In studies of the biologic effects of 11-desoxy-corticosterone acetate and 17-hydroxy-11-dehydro-corticosterone acetate it was noted that the latter substance was the more active of the two in producing thymus atrophy.

Male rats of the Sprague-Dawley strain each having an initial body-weight of approximately 180 g were used. The diet was Purina Dog Chow. The test substances were dissolved in sesame oil and administered twice daily by subcutaneous injection. Ten normal rats were killed in order to obtain control data on thymus weights; 10 adrenalectomized rats were maintained for 7 days without treatment; 5 adrenalectomized rats were treated with 2 mg daily of 17-hydroxy-11-dehydro-corticosterone acetate; 5 adrenalectomized rats were treated with 2 mg of 11-desoxy-corticosterone; and 5 adrenalectomized rats were treated with 10.0 mg daily of 11-desoxy-corticosterone. Necropsy was performed on the 7th day. The data on body weights and thymus weights are summarized in Table I.

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