

surviving irradiated vaccinees and nonirradiated vaccinees.

We wish to acknowledge the collaboration of Lt. Colonel Joshua Henderson in the X-irradiation procedures and of Dr. Joseph V. Jemski in the aerogenic vaccination exposures.

1. Shechmeister, I. L., *Radiation Res.*, 1954, v1, 401.
2. Taliaferro, W. H., Taliaferro, L. G., *J. Immunol.*, 1951, v66, 181.
3. Benacerraf, B., *Bact. Rev.*, 1960, v24, 35.
4. Eigelsbach, H. T., Downs, C. M., *J. Immunol.*, 1961, v87, 415.
5. Eigelsbach, H. T., Braun, W., Herring, R. D., *J. Bact.*, 1951, v61, 556.

6. Mills, R. C., Berthelsen, H., Donaldson, E., Wilhelm, P. L., *Bact. Proc.*, 1949, 37.

7. Brigham, G. C., *Diagnostic Procedures and Reagents*, Am. Public Health Assn., Inc., New York, 1950, 262.

8. Wolfe, E. K., *Bact. Rev.*, 1961, v25, 194.

9. Downs, C. M., Coriell, L. L., Chapman, S. S., Klauber, A., *J. Bact.*, 1947, v53, 89.

10. Nutter, J. E., Guss, M. L., *Bact. Proc.*, 1963, 79.

11. Shevelev, A. S., Prudnikova, M. N., *Bull. Exp. Biol. and Med.*, 1960, v49, 504.

12. Shevelev, A. S., Zhur, *Mikrobiol., Epidemiol., Immunobiol.*, 1964, v4, 107.

Received December 19, 1966. P.S.E.B.M., 1967, v124.

Effect of a Low Sodium Diet on Aldosterone-Stimulating Activity Of Angiotensin II in Dogs. (31973)

W. F. GANONG AND A. T. BORYCZKA

Department of Physiology, School of Medicine, San Francisco Medical Center, University of California, San Francisco

In dogs(1) and humans(2) fed a low sodium diet, ACTH produces a greater increase in aldosterone secretion than it does in control subjects. Since angiotensin II also stimulates aldosterone secretion we have studied the effect of a low sodium diet on the adrenocortical response to angiotensin II.

Methods. Male mongrel dogs weighing approximately 12 kg were fed a diet providing less than 1 mEq of sodium per day for 14 days. They were then anesthetized with pentobarbital, subjected to cannulation of the right lumboadrenal vein, bilateral nephrectomy and hypophysectomy *via* the transbuccal route. Using methods described in detail previously(1,3), the increases in 17-hydroxycorticoid and aldosterone secretion produced in these dogs by angiotensin II and ACTH were determined. The doses of angiotensin II infused were 0.017, 0.042, 0.167 and 1.67 $\mu\text{g}/\text{min}$, and the doses of ACTH 10 and 50 mU. Seventeen-hydroxycorticoids in adrenal venous plasma were measured by the method of Silber and Porter (4), and aldosterone by the method of Kliman and Peterson(5). Control dogs fed a diet containing about 40 mEq of sodium and

about the same amount of potassium as the low sodium diet were also studied. The results obtained in these control dogs have been published(3).

Results and discussion. The increments in aldosterone and 17-hydroxycorticoid output produced by angiotensin II and ACTH are summarized in Tables I and II, and the pressor response to angiotensin II in Table III. Angiotensin II in doses of 0.017 and 0.04 $\mu\text{g}/\text{min}$ produced increases in aldosterone secretion in the dogs fed the low sodium diet, but 0.04 $\mu\text{g}/\text{min}$ failed to produce any increase in the control dogs. Larger doses of angiotensin II also produced greater increases in aldosterone secretion in dogs fed the low sodium diet, although the differences between these and the increments in the control dogs were not statistically significant. ACTH produced a greater increase in aldosterone secretion in the dogs fed the low sodium diet, confirming results previously reported from this laboratory(1). On the other hand, 17-hydroxycorticoid responses to angiotensin II and ACTH were unaffected by restricting dietary sodium intake.

The pressor activity of angiotensin II in

TABLE I. Increments in Aldosterone Secretion Produced by Angiotensin II and ACTH.

	Change in aldosterone output (m μ g/min)		
	Low sodium diet 14 days	Control	p value, low sodium vs control
Angiotensin II			
.017 μ g/min	3.6 \pm 1.7 (9)	1 (1)	—
.04 "	5.6 \pm 1.5 (8)	.5 \pm 1.3 (5)	<.05
.17 "	18.6 \pm 4.1 (9)	11.4 \pm 3.3 (8)	NS
1.67 "	27.6 \pm 4.2 (6)	24.0 \pm 5.0 (7)	NS
ACTH			
10 mU	9.0 \pm 6.9 (4)	-2.7 \pm 3.4 (6)	NS
50 "	38.5 \pm 6.2 (4)	5.4 \pm 1.1 (5)	<.01

Values are means \pm standard errors at each dose of the adrenal venous outputs during the 4th to the 14th minute after injection of ACTH or after start of infusion of angiotensin II minus the outputs immediately before administration of ACTH or angiotensin II. Figures in parentheses are number of dogs.

NS: p > 0.05.

the dogs fed a low sodium diet was not significantly different from that in the control dogs. Davis and associates(6) reported diminished pressor activity of angiotensin II in sodium depleted dogs. However, their animals were fed a low sodium diet for 2-3 weeks and given mercurial diuretics in addition. It is possible that a fairly large loss of sodium is necessary before pressor activity

of angiotensin II is significantly diminished, and the low sodium diet alone did not produce a sodium loss of this magnitude.

Summary. The effect of various doses of angiotensin II on adrenocortical secretion of aldosterone and 17-hydroxycorticoids was determined in dogs fed a low sodium diet for 14 days and in control dogs. The increments in aldosterone secretion produced by angiotensin II in the animals fed the low sodium diet were greater than the corresponding increments in controls. No changes in the increments in 17-hydroxycorticoids or blood pressure were observed.

TABLE II. Increments in 17-Hydroxycorticoid Secretion Produced by Angiotensin II and ACTH.

	Changes in 17-hydroxycorticoid output (μ g/min)	
	Low sodium diet 14 days	Control
Angiotensin II		
.017 μ g/min	0 \pm .1 (9)	.4 (1)
.04 "	0 \pm 0 (7)	.1 \pm .4 (5)
.17 "	.2 \pm .1 (9)	.3 \pm .4 (8)
1.67 "	3.2 \pm .7 (6)	3.9 \pm .8 (7)
ACTH		
10 mU	6.8 \pm .7 (4)	7.9 \pm 2.0 (5)
50 "	8.2 \pm .7 (4)	7.0 \pm 1.1 (5)

See legend for Table I. Figures in parentheses are number of dogs.

TABLE III. Increments in Systolic Blood Pressure Produced by Angiotensin II. Values are means \pm standard errors of means.

	Change in systolic blood pressure (mm Hg)	
	Low sodium diet 14 days	Control
Angiotensin II		
.017 μ g/min	8 \pm 1.7 (9)	0 (1)
.04 "	9 \pm 3.2 (8)	12 \pm 5.6 (5)
.17 "	26 \pm 2.5 (9)	26 \pm 3.4 (8)
1.67 "	68 \pm 11.9 (6)	77 \pm 8.5 (7)

Angiotensin II (1-L-asparaginyl-5-L-valyl angiotensin octapeptide) was provided by Ciba Pharmaceutical Co., Summit, N. J. ACTH was provided by Upjohn Co., and Lonalac for preparation of low sodium diets by Mead Johnson Co. We wish to thank Mr. Roy Shackelford and Miss Margaret Saari for technical assistance.

1. Ganong, W. F., Boryczka, A. T., Shackelford, R., Clark, R. M., Converse, R. P., Proc. Soc. Exp. Biol. and Med., 1965, v118, 792.
2. Venning, E. H., Dyrenfurth, I., Dosseter, J. B., Beck, J. C., Metabolism, 1962, v11, 254.
3. Mulrow, P. J., Ganong, W. F., Cera, G., Kuljian, A., J. Clin. Invest., 1962, v41, 505.
4. Silber, R. H., Porter, C. C., J. Biol. Chem., 1954, v210, 928.
5. Kliman, B., Peterson, R. E., *ibid.*, 1960, v235, 1639.
6. Davis, J. O., Hartroft, P. M., Titus, E. O., Carpenter, C. C. J., Ayers, C. R., Spiegel, H. E., J. Clin. Invest., 1962, v41, 378.

Received December 21, 1966. P.S.E.B.M., 1967, v124.