Adrenal Function During Bed Rest

CAPTAIN FRED H. KATZ, USAF, MC

ABSTRACT

Plasma 17-OH-CS levels as well as adrenal secretory rates of aldosterone and cortisol were measured in healthy subjects before and during periods of bed rest. The circadian rhythm of plasma 17-OH-CS was well maintained during bed rest. There was no change in adrenal cortisol secretion rates during bed rest. Aldosterone secretory rate did not change with bed rest; however, following a period out of bed, there was a diminution of aldosterone secretory rate during a subsequent bed rest period. Inactivity from bed rest therefore does not appear to change adrenal cortisol production. Conclusions cannot be drawn as yet concerning aldosterone production.

IT HAS BEEN shown by previous workers[8] that despite the maintenance of the normal diurnal rhythm of urinary 17-hydroxycorticosteroid excretion, changes in the normal day-night vertical-horizontal posture patterns abolish a normal diurnal peak and nocturnal nadir of aldosterone excretion. These studies assumed, quite justifiably, that these variations in the urinary levels of these steroids, reflected comparable changes in adrenal gland hormone production. Other workers[5] subsequently demonstrated that the urinary aldosterone output fell with only a few hours of the "weightless" state of standing in water.

The present study was undertaken to measure by more direct methods the secretion rate by the adrenal gland and the plasma level of some of the adrenocortical hormones in the hypogravic state.

MATERIAL AND METHODS

Eleven airmen, age 17 to 23, were studied prior to, and after ten days of lying supine, but unrestrained in bed. Diet was constant except for an ad lib salt intake. After the subjects had finished fourteen days of bed rest, they were divided into Groups A through F. Groups B through F participated in an organized program of exercise during the subsequent four weeks. Following this period all groups returned to bed for two more weeks. During this time, Group C had cuffs inflated to a pressure of 60 mm. Hg for one minute out of every five from 0800 to 2200 hours. Group D had the head of the bed tilted 10° from the horizontal to simulate lunar gravity. Group E had both cuffs and tilt and Group F performed standardized non-anti-gravity exercises during this second bed rest period. Only Groups A, C and F were studied.

Although the metabolic ward used for the bed rest period had its ambient temperature controlled between 75 and 81° F., the subjects were exposed to the outside temperatures of the day during control determinations, which were often in the uncomfortable, above 90° F. range. In addition, activity was not controlled during the "control" days.

Plasma 17-hydroxycorticosteroids (17-OH-CS) were measured by a modification[12] of the technique of Silber and Porter.[10]

Cortisol secretion rates were measured by a method previously outlined[6] except that 3μc. cortisol-1, 2-H^3, 50 μc./μg., obtained from the Endocrinology Study Section, National Institutes of Health, was the radioactive tracer utilized and the isolated tritiated urinary metabolites were acetylated with C^{14} labeled acetic anhydride.

Aldosterone secretory rates were determined by an unpublished method of Barlow[1] based on the isolation of the "tetrahydro metabolite" of aldosterone from urine.[11] Three microcuries d-aldosterone-1, 2-H^3, (100 μc./μg., from the Endocrinology Study Section, National Institutes of Health, and later obtained commercially, and purified chromatographically on paper in the Bush B5 and E_2B systems)[2,4] were injected in 30 ml. isotonic saline. An aliquot of urine from the subsequent 24 hours was hydrolyzed with beef liver β-glucuronidase at pH 4.7 and 37° C. for 48 hours. Ethyl acetate extracts, washed three times with 1/20 volume in NaOH and then with water were chromatographed in the B5 and E_2B systems. The urinary metabolite was detected by radioactivity. Scanning with a Model 880 Vanguard Autoscanner as well as by the R_f of concommitantly chromatographed "tetrahydroaldosterone" (first obtained through the courtesy of Dr. Seymour Lieberman, and later isolated from human urine following the oral administration of 40 mg. d-aldosterone-21-acetate supplied by Dr. C. H. Sullivan, CIBA, Inc., Summit, N. J.). The metabolite was acetylated with C^{14} labeled acetic anhydride and the resulting triacetate purified using alternating chromatography in the Bush A and B3 systems to attain radiochemical purity. This was considered attained when the tritium/carbon 14 ratio, measured as described elsewhere,[7] varied by less than 10 per cent between consecutive chromatograms. Quantitation could be obtained by acetylating crystalline cortisol with the same batch of acetic anhydride and measuring the specific activity of chromatographically purified cortisol-21-acetate with the aid of the Porter-Silber reaction.[10]

RESULTS

Plasma 17-OH-CS:—Figure 1 indicates that the diurnal variation of plasma unconjugated 17-OH-CS per-

From the USAF School of Aerospace Medicine Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas.

The address of Dr. Katz is University of Chicago, 950 East 59th Street, Chicago, Illinois 60637.

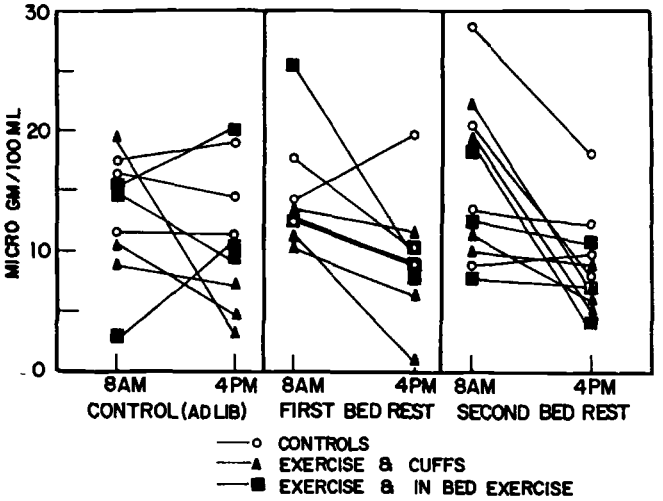

Fig. 1. Persistence of diurnal plasma free 17-hydroxycorticoid variation after 10 days of recumbency.

sisted generally during the two bed rest periods in Groups A, C, and F following ten days of recumbency. The circadian rhythm, with its morning peak, was better established during the bed rest periods than during the period of ad lib activity.

Cortisol Secretory Rate:—The results of the adrenal secretion rate determinations for cortisol are shown in Figure 2. Although there was a good deal of variation

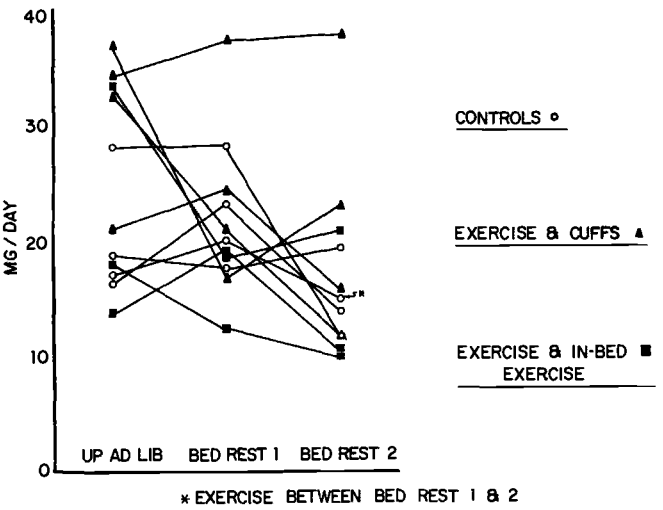

Fig. 2. Cortisol secretory rate.

in some of the subjects from one period to the next, statistical analysis revealed these differences not to be significant even at the 10 per cent level, for either Group A, C, or F, the only groups tested.

Aldosterone Secretory Rate:—The results for this parameter are shown in Table I. It can be seen that the subjects who were tested during bed rest period 1 showed no difference in aldosterone production compared to the control period. During bed rest period 2 the mean aldosterone secretory rate for the subjects examined was markedly lower than during the other periods.

TABLE I. ALDOSTERONE SECRETORY RATE—μg/24 HOURS

Group	Subject number	I Up ad lib	II Bed rest 1	III Bed rest 2
A	1		155	148
	2	277	259*	88
	3	221	119	66
	4		116	111
C	1	173	255	146
	2	103		139
	3	273	109	93
	4	162	126	72
F	1	172	210	175
	2	151	168	144
	3	87	98	89
Mean of all groups		180	162	115

Comparison of means	t value	p value
I and II	.618	N.S.
I and III	2.80	< 0.025

* Exercised between rest periods

DISCUSSION

As far as cortisol production by the adrenal gland is concerned, these studies have confirmed the work of previous authors[9] that this parameter is independent of body position, as shown by plasma 17-OH-CS levels. In addition, direct measurements of the cortisol secretory rate have now established that there is no significant change in the hypodynamic state.

There is no evidence that comparable periods of hypodynamic states would have an adverse effect on the body levels of cortisol.

The results for aldosterone secretory rate do not lend themselves to straightforward interpretation. Although there was no change during the first bed rest period, the diminution in the mean value during the second bed rest period was significant at the 2.5 per cent level. It can be seen from Table I that this change could not be attributed to either of the maneuvers imposed on Groups C and F during bed rest period 2.

To further complicate the interpretation of this data, it may be noted that the lack of change between the control and first bed rest period could hide an *increased* aldosterone production with bed rest, since the hotter environmental temperatures during the control period might be expected to increase aldosterone production.[3]

The fact that all subjects had already experienced a previous bed rest period might in some way be responsible for the diminution during bed rest period 2.

ACKNOWLEDGMENT

Airman Second Class Joseph C. Perry rendered valuable technical assistance.

REFERENCES

1. BARLOW, J. J.: Boston Lying-In Hospital, Boston, Mass. Unpublished communication.
2. BUSH, I. E.: Methods of paper chromatography or steroids applicable to the study of steroids in mammalian blood and tissues. *Biochem. J.*, 50:370, 1952.
3. CONN, J. W.: Aldosteronism in man. Clinical and climatological aspects. *J.A.M.A.*, 183:775, 1963.
4. EBERLEIN, W. R., and BONGIOVANNI, A. M.: New solvent systems for the resolution of corticosteroids by paper chromatography. *Arch. Biochem. & Biophy.*, 59:90, 1955.
5. GOWENLOCK, A. H., MILLS, J. N., and THOMAS, S.: Acute postural changes in aldosterone and electrolyte excretion in man. *J. Physiol.*, 146:133, 1959.
6. KATZ, F. H., LIPMAN, M. N., FRANTZ, A. G., and JAILER, J. W.: The physiologic significance of 6β-hydroxycortisol in human corticoid metabolism. *J. Clin. Endocrinol. & Metab.*, 22:71, 1962.
7. KATZ, F. H., and SHANNON, I. L.: Identification and significance of parotid fluid corticosteroids. *Acta Endocrinol.* In press.
8. MULLER, A. F., MANNING, E. L., and RONDEL, A. M.: Influence of position and activity on the secretion of aldosterone. *Lancet*, 1:711, 1958.
9. PERKOFF, G. T., EIK-NESS, K., NUGENT, C. A., FRED, H. L., NIMER, R. A., SAMUELS, L. T., and TYLER, F. H.: Studies of the diurnal variation of plasma 17-hydroxycorticosteroids in man. *J. Clin. Endocrinol. & Metab.*, 19:432, 1959.
10. SILBER, R. H., and PORTER, C. C.: The determination of 17, 21-dihydroxy-20-ketosteroids in urine and plasma. *J. Biol. Chem.*, 21:923, 1954.
11. ULICK, S., LARAGH, J. H., and LIEBERMAN, S.: The isolation of a urinary metabolite of aldosterone and its use to measure the rate of secretion of aldosterone by the adrenal cortex in man. *Tr. Ass. Am. Physicians*, 71:225, 1958.
12. WALLACE, E. Z., CHRISTY, N. P., and JAILER, J. W.: Clinical application of the simplified Silber-Porter method for determining plasma 17-OH-corticosteroids. *J. Clin. Endocrinol. & Metab.*, 15:1073, 1955.