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CORRELATION BETWEEN PLASMA LEVELS OF ACTH AND CORTISOL IN BASAL STATES AND DURING THE CRH TEST IN NORMAL SUBJECTS AND PATIENTS WITH HYPOTHALAMO-PITUITARY DISORDERS

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Using a new ACTH-immunoradiometric assay (IRMA), we measured plasma ACTH levels in the basal states and during CRH test in normal subjects and the patients with hypothalamo-pituitary disorders. The basal levels of plasma ACTH in 76 normal young (25–45 yr) and 140 elderly (60–85 yr) subjects were 23.1±13.6, and 17.5±11.2 pg/m*l*, respectively. The plasma ACTH levels were less than detection limit (5 pg/m*l*) in 3 patients with isolated ACTH deficiency, and less than 10 pg/m*l* in 6 of 7 patients with hypopituitarism. A significant correlation was observed between the basal levels of plasma ACTH and of cortisol in two age groups, with almost the same regression line, showing no age-related decline in the plasma levels of ACTH and cortisol. In 2 normal subjects and 2 patients with Cushing's disease, synchronized secretions of ACTH and cortisol were observed between 0800h and 1800h. In normal subjects and the patients with pituitary disorders, a significant correlation was observed between the Area Under the Curve's for plasma ACTH and cortisol during the CRH test. The correlation constant was higher in normal subjects, but lower in the patients with acromegaly, non-functioning pituitary tumor, and Cushing's disease in this order, suggesting low sensitivity of the pituitary-adrenal axis in these patients. These results suggest that the ACTH-IRMA kit provide reliable data for clinical investigation, and that the secretions of ACTH and cortisol correlate each other in basal states and during the CRH test in the patients with pituitary disorders as well as in normal subjects.

Key words: CRH—ACTH—Cortisol—Aging—Cushing's disease—Immunoradiometric assay (IRMA)

ACTH and cortisol play important roles in the pathophysiology of the pituitary-adrenal axis in normal and diseased states. The plasma concentration of ACTH has been measured by radioimmunoassay (RIA)[2,4,19], but it has not always given satisfactory results by non-specific interference of the plasma and the assay sensitivity. In addition, there has been contraversy concerning age-related changes in the plasma levels of ACTH and cortisol[1,5,9,18,23,24]. Recently, the immunoradiometric assay (IRMA) for ACTH has been developed by Ratter *et al.* [20], and followed by providing the ACTH-IRMA kit [10,27]. The ACTH-IRMA kit "Mitsubishiyuka" developed recently, showed high sensitivity, specificity and precision as reported previously[11]. Using this kit, we monitored the changes in the plasma ACTH levels in basal states and during the CRH test in normal and diseased states, and evaluated the correlation between the plasma levels of ACTH and cortisol.

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Materials and Methods

Subjects

Seventy-six young subjects aged 20–45 years and 140 elderly subjects aged 60–85 years who were nothing particular in physical, biochemical and hormonal examination, were examined as normal controls. The patients with hypothalamo-pituitary disorders (Table 1) were diagnosed by clinical manifestations and hormonal and morphological examinations. The study was approved by the Human Subjects Protection Commitee, School of Medicine, the University of Tokushima, and the informed consent for the study was obtained from all volunteers and patients.

To measure the basal levels of plasma ACTH and cortisol, the blood was with-

Table 1.
Responses of plasma ACTH and cortisol during CRH test

	Case No.	age (yr)	sex M/F	plasma ACTH basal (pg/ml)	plasma ACTH peak (pg/ml)	plasma ACTH AUC (pg·hr/ml)	plasma cortisol basal (pg/ml)	plasma cortisol peak (pg/ml)	plasma cortisol AUC (pg·hr/ml)
normal	1	24	M	46.3	84.7	36.0	11.3	17.8	9.2
	2	20	M	17.2	59.4	45.4	20.5	36.4	20.7
	3	21	M	35.3	75.0	30.4	15.7	19.4	3.2
	4	20	M	10.3	47.8	58.4	5.2	23.0	24.8
	5	22	M	5.1	23.3	17.5	17.2	21.1	4.2
	6	23	M	26.9	60.0	46.1	10.0	22.3	14.9
Cushing's disease	7	26	F	89.9	142.2	41.1	30.0	51.4	29.9
	8	42	F	70.2	93.5	26.7	21.0	35.5	12.2
	9	43	F	97.7	189.1	39.0	18.8	40.3	21.0
	10	36	F	41.8	139.6	67.6	15.1	32.4	21.9
	11	34	F	146.9	264.9	26.7	37.1	56.5	21.4
	12	36	F	115.0	232.0	68.0	35.6	57.6	15.5
	13	48	F	60.0	129.0	58.9	23.5	43.8	25.7
	14	52	M	29.0	182.0	133.5	23.8	35.6	11.6
acromegaly	15	58	F	7.5	32.3	24.2	11.7	32.9	24.9
	16	33	F	20.0	28.8	4.4	8.0	18.6	13.2
	17	71	F	23.0	47.6	27.3	19.5	32.9	13.4
	18	45	M	9.5	18.2	4.8	17.0	25.0	4.0
	19	35	F	24.5	64.8	48.0	13.2	17.4	3.7
	20	61	F	29.1	53.5	30.6	14.8	19.6	9.1
	21	31	F	31.5	59.0	13.2	11.0	19.1	9.0
non-functioning	22	49	M	23.2	38.5	27.6	8.2	18.8	14.2
pituitary tumor	23	52	M	26.9	81.9	46.3	11.0	22.5	6.6
	24	47	M	20.4	55.8	34.5	10.8	22.5	11.6
	25	47	M	17.1	65.9	41.3	9.5	15.0	7.2
	26	62	F	29.0	29.7	0.2	19.2	21.3	1.9
	27	29	M	16.3	29.9	6.7	15.9	18.9	2.1
	28	59	F	31.4	80.3	46.1	9.3	28.9	20.9
hypopituitarism	29	53	F	8.2	8.8	0.5	1.0	1.8	0.7
	30	42	M	8.7	9.5	0.2	3.1	3.5	0.2
	31	33	F	4.0	14.3	8.8	1.0	1.3	0.3
	32	16	M	7.0	16.2	11.2	1.8	3.3	0.8
	33	21	M	3.4	3.5	0.1	1.1	1.1	0.1
	34	37	F	5.5	6.8	0.3	1.0	1.3	0.2