SECRETION AND UTILIZATION OF ADRENAL CORTICOSTEROIDS IN EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS

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In the period of clinical manifestations of experimental allergic encephalomyelitis no increase is observed in the blood levels of hydrocortisone, cortisone, and corticosterone from the lumboadrenal vein of dogs. The peripheral blood level of these hormones was several times higher than normal, due to slowing of the metabolism and disturbance of the utilization of corticosteroids by tissues of the CNS.

The development of the clinical picture of experimental allergic encephalomyelitis (EAE)—a model of inflammatory-demyelinating lesions of the brain and spinal cord—is accompanied by an increase in the peripheral blood glucocorticoid level [1, 5, 7].

The object of this investigation was to study the secretion of corticosteroids by the adrenal cortex and to examine some aspects of their utilization by the tissues in dogs with EAE.

EXPERIMENTAL METHOD

Experiments were carried out on 120 mongrel female dogs weighing 10-16 kg. EAE was produced by immunization with a single dose of encephalitogenic material [2]. Pareses, paralyses, tremor, and trophic disturbances developed in the animals on the 9th-14th day after immunization. Histologically, characteristic inflammatory-demyelinating lesions were observed in the brain and spinal cord. Depending on the clinical picture, groups of dogs with severe and mild forms of EAE were distinguished.

Using the method of thin-layer chromatography [4] the corticosteroid level was determined in the peripheral blood (lateral subcutaneous vein of the leg) and the lumboadrenal vein. In the latter case, under careful local anesthesia a skin incision was made and a catheter introduced into the inferior vena cava at the level where it receives the lumboadrenal vein. In some experiments, 17-hydroxycorticosteroids (17-HCS) were determined in the same blood samples by the method of Porter and Silber [8].

During the period of clinical manifestations of EAE, hydrocortisone was administered in a dose of 1 mg/kg body weight intravenously.

The level of 11-hydroxycorticosteroids (11-HCS) was determined by a fluorimetric method [9], with certain modifications [3], in the white matter and cortex of the brain, hypothalamus, pituitary gland, spinal cord, adrenal cortex, liver, and spleen.

Before immunization the animals were kept in the animal house and adapted to the experimental situation. Healthy dogs, having undergone adaptation, were used as the control.

EXPERIMENTAL RESULTS

The results given in Table 1 show that the corticosteroid level in blood from the lumboadrenal vein of healthy dogs was higher than in peripheral blood, in agreement with results obtained by other workers

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TABLE 1. Corticosteroid Level in Blood from the Lumboadrenal and Peripheral Veins of Dogs with EAE

Index studied (in μg %)	Vein from which blood was taken	Healthy dogs	Dogs with EAE		
		control	severe form	mild form	mild and severe forms together
Hydrocortisone*					
	Lumboadrenal	4,68±0,68 $n=15$	3,45±0,63 $n=20$ $P>0,1$	4,50±0,67 $n=15$ $P>0,1$	3,94±0,46 $n=35$ $P>0,1$
	Peripheral	1,80±0,32 $n=10$ $P_1<0,001$	—	—	3,86±0,40 $n=12$ $P<0,001$
Cortisone					
	Lumboadrenal	2,07±0,50 $n=15$	2,30±0,24 $n=20$ $P>0,5$	2,54±0,35 $n=15$ $P>0,1$	2,41±0,20 $n=35$ $P>0,5$
	Peripheral	1,22±0,30 $n=10$ $P_1>0,1$	—	—	2,75±0,50 $n=12$ $P<0,05$
Corticosterone					
	Lumboadrenal	2,14±0,35 $n=18$	2,13±0,29 $n=20$ $P>0,5$	1,80±0,30 $n=15$ $P>0,1$	1,94±0,21 $n=35$ $P>0,5$
	Peripheral	0,38±0,14 $n=10$ $P_1<0,001$	—	—	2,63±1,20 $n=12$ $P<0,1$
17-HCS†					
	Lumboadrenal	12,04±1,38 $n=10$	13,3±1,44 $n=10$ $P>0,5$	14,42±1,36 $n=10$ $P>0,2$	13,86±0,95 $n=20$ $P>0,2$
	Peripheral	2,29±0,21 $n=35$ $P_1<0,001$	—	—	11,70±1,02 $n=35$ $P<0,01$

*Results of chromatographic determination.
†Results of determination by the method of Porter and Silber.
Legend: P) significance of differences between experiment and control; P_1) the same between values for lumboadrenal and peripheral veins.

[10, 11]. During the development of the clinical picture of EAE no significant changes in the concentrations of hydrocortisone, cortisone, and corticosterone were found in blood from the lumboadrenal vein. A considerable increase in the hormone level, practically indistinguishable from the level in blood from the lumboadrenal vein, was observed in the peripheral blood on animals with EAE.

It will be noted that in EAE the secretory activity of the adrenal cortex was not increased but, on the contrary, the mean values actually showed some tendency for the hydrocortisone level in the blood of the lumboadrenal vein to fall, especially in dogs with a severe form of EAE. The 17-HCS concentration in blood from the lumboadrenal vein also differed only slightly from the control.

The half-excretion period for exogenous hydrocortisone, as these experiments showed, was delayed in EAE even 4 h after loading, 80.8 ± 13.6% of the dose injected was still circulating in the blood stream, whereas in healthy dogs under the same conditions only 46.4 ± 5.6% remained ($P < 0.05$). These results indicate a disturbance of hydrocortisone metabolism probably attributable primarily to depression of the metabolic function of the liver in EAE [6].

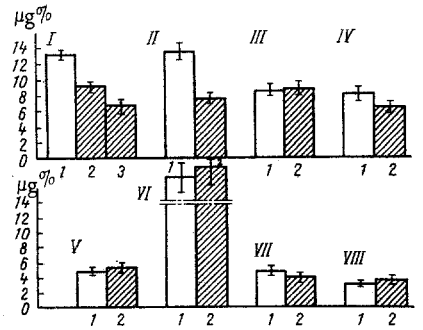

Fig. 1. 11-HCS concentration in tissues of dogs with EAE: I) white matter of cerebral hemispheres; II) spinal cord; III) cerebral cortex; IV) hypothalamus; V) pituitary; VI) adrenal cortex; VII) liver; VIII) spleen; 1) healthy dogs; 2) dogs with clinical manifestations of EAE; 3) white matter of brain with macroscopically visible lesions. Values of M ± m given.

The 11-HCS level in the white matter of the brain, the hypothalamus, and the spinal cord was below normal in EAE (Fig. 1; $P < 0.001$, < 0.05 and < 0.001 respectively). It fell particularly sharply in areas of white matter with macroscopically visible lesions. In other tissues studied, no significant changes were found.

The decrease in the corticosteroid concentration in the brain structures with inflammatory-demyelinating lesions, associated with the high circulating blood level of the hormones, suggests a disturbance of their utilization. On the other hand, these results also explain the discrepancy between the low level of corticosteroids in the lumboadrenal vein, i.e., by absence of their increased secretion and by the accumulation of large quantities of the hormones in the peripheral blood. The high peripheral blood level is thus not proof of activation of the adrenal cortex during clinical manifestations of EAE, but it reflects delay in the metabolism and disturbance of the utilization of corticosteroids in the tissues of the CNS where the inflammatory-demyelinating process develops.

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