CORTICOSTEROID PATHWAYS FROM ADRENALS TO LIVER

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Anatomical and biochemical methods demonstrate that adrenal cortical hormones enter the portal vein of the liver as well as the caudal vena cava. The mean concentration of 17-hydroxycorticosteroids in the portal vein is 65.4% of that in the caudal vena cava. Stimulation of the splanchnic nerve in three of five experiments lowered the 17-hydroxycorticosteroid concentration in the blood of the caudal vena cava and in four of five experiments it increased the content of these substances in the portal vein.

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Corticosteroids caused changes in activity of a number of enzymes in the liver taking part in protein and carbohydrate metabolism [7, 10, 11]. An increase in activity of liver enzymes under the influence of corticosteroids, it must be noted, is accompanied by an increase in the rate of synthesis of messenger RNA, which evidently determines enzyme synthesis [12, 13].

The view is still held that the corticosteroids secreted in the adrenal cortex enter the inferior (caudal) vena cava and reach the liver with the arterial blood.

It has recently been discovered [1-3] that in man and the dog the adrenal veins drain into tributaries of the portal vein of the liver, and the adrenal medullary hormone (adrenalin) has been found experimentally to enter the portal vein, in which its concentration rises considerably during stimulation of the splanchnic nerve. The blood adrenalin concentration in the inferior vena cava diminishes under these circumstances.

It has accordingly been suggested that adrenal cortical hormones (corticosteroids) may also pass directly through the adrenal veins into the portal vein and liver, by-passing the systemic circulation. The object of the present investigation was to verify this hypothesis.

EXPERIMENTAL METHOD AND RESULTS

The pathways of blood drainage from the adrenals were studied anatomically in 47 dogs.

The deep (internal) veins of the adrenal are formed from capillaries of the medulla and zona reticularis, while numerous superficial veins collect blood from the capillaries of the outer layers of the cortex and capsule of the gland. In the adrenal of the dog the deep veins form two central veins (cranial and caudal), which drain into the adreno-lumbar vein, a tributary of the caudal vena cava. Small superficial adrenal veins also drain into the adreno-lumbar vein.

Other superficial veins of the gland run directly into the caudal vena cava and its tributaries—the renal and lumbo-phrenic veins.

The cranial part of the left adrenal gives off 3-6 veins not exceeding 0.5 mm in diameter, which run medially and slightly anteriorly through the retroperitoneal cellular tissue to reach the root of the mesentery. At the base of the mesentery (between the celiac trunk and the cranial mesenteric artery) they join directly with the preaortic flexure of the splenic vein and also the veins of the tail of the pancreas, which in turn are tributaries of the splenic vein, entering the portal vein of the liver (Fig. 1).

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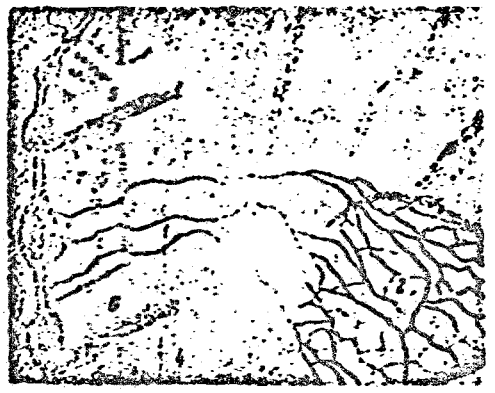

Fig. 1. Superficial veins of left adrenal of dog draining into tributaries of portal vein of the liver. 1) tributaries of portal vein; 2) venous network in dremal capsule; 3) splenic vein, preaortic flexure; 4) abdominal aorta; 5) celiac trunk; 6) superior (cranial) mesenteric artery; 7) dorsal mesentery.

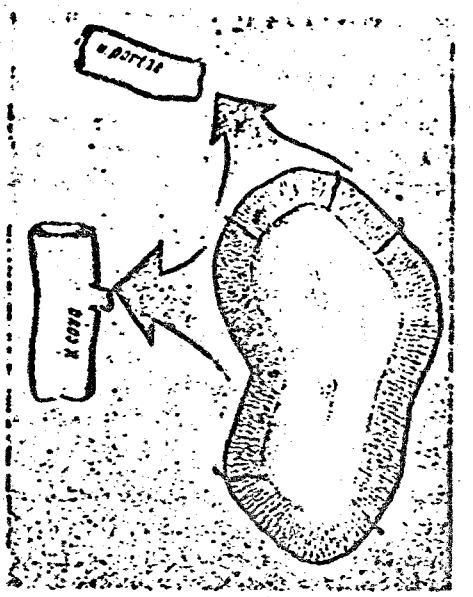

Fig. 2. Diagram showing directions of outflow of adrenal hormones in the dog into abdominal collecting veins: the inferior (caudal) vena cava and portal vein. 1) cortex; 2) medulla; 3) cranial central adrenal vein; 4) caudal central adrenal vein; 5) venous anastomosis connecting deep and superficial adrenal veins.

TABLE 1. Concentration of 17-hydroxycorticosteroids (in μg%) in Blood From Caudal Vena Cava and Portal Vein

Experiment No.	Caudal vena cava				Portal vein			
	before stimulation	after stimulation			before stimulation	after stimulation		
		10 min	30 min	60 min		10 min	30 min	60 min
1	28.0	32.0	—	—	29.6	31.25	—	—
2	20.75	—	12.0	10.0	7.5	—	17.9	14.1
3	40.0	28.7	39.0	29.0	22.5	34.4	36.0	35.0
4	52.9	40.4	37.5	29.4	32.5	33.8	44.1	40.4
5	36.0	50.0	40.0	40.0	29.0	25.0	39.0	31.0

Some superficial veins of the right adrenal join the veins of Glisson's capsule of the right lobe of the liver, bypassing tributaries of the portal vein.

Having demonstrated the existence of direct venous pathways along which blood from the left adrenal can drain into the portal vein of the liver, we next determined the concentration of 17-hydroxycorticosteroids in blood from the caudal vena cava and portal vein in seven dogs. Blood from these two veins was taken in acute experiments from animals anesthetized with sodium amytal after preliminary administration of morphine.

Blood samples were taken simultaneously from both veins. The concentration of 17-hydroxycorticosteroids in the blood was determined by the Porter–Silber method as modified by Yudaev and Pankov.

The results of these experiments showed that the 17-hydroxycorticosteroid concentration in blood from the caudal vena cava is 20-52 μg% (mean 35.12 μg%), and in blood from the portal vein 7.5-37 μg% (mean 28.3 μg%). Against the background of trauma due to the operation and under sodium amytal anesthesia the 17-hydroxycorticosteroid concentration in blood from the portal vein was between 36 and 105% (mean 65.4%) of its level for the caudal vena cava. It can be concluded that corticosteroids can pass into the caudal (inferior) vena cava and also into the portal vein of the liver via the blood stream (Fig. 2).

The 17-hydroxycorticosteroid concentration in blood from the caudal vena cava and portal vein of the dogs was also determined after stimulation of the left splanchnic nerve by interrupted electrical pulses for 1.5-2 sec (Table 1).

The results in Table 1 show that after stimulation of the left splanchnic nerve the 17-hydroxycorticosteroid concentration in the blood of the caudal vena cava fell in three of the five dogs, and rose appreciably in blood from the portal vein of four of the five animals.

At the level of the adrenal glands the caudal vena cava receives all (or nearly all) the adrenal veins. Blood taken from the caudal vena cava cranially to the right adrenal thus contains corticosteroids secreted by both adrenal glands. Meanwhile the adrenal veins of the left gland only drain into the portal vein.

Comparison of our data concerning structure of the adrenal veins of the dog and information given in the literature on human adrenal veins [1, 3, 8] shows that in man communications between the superficial veins of the left adrenal and tributaries of the portal vein are more numerous than in the dog. In addition, muscular mechanisms are present in the walls of the deep vein of the human adrenals [4-6, 9], capable of directing the flow of blood from the deep layers of the gland through deep venous anastomoses into the superficial veins with their extensive connections with tributaries of the portal vein. This suggests that in man the effect of a direct outflow of blood (and hormones along with it) from the adrenals into the liver may be greater than in dogs.

The results of anatomical and biochemical investigations thus suggest that a shorter pathway for corticosteroids to pass from the adrenals into the liver is present via the portal vein. During stress the increased demand of the liver for corticosteroids may evidently be met by their direct arrival via the caudal vein, and this factor must be taken into account when the mechanisms of development of defensive reactions of the body are being studied.

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