The Activity of the Hypothalamo-Hypophysial Antidiuretic System in Conscious Dogs
I. The Influence of Isoosmotic Blood Volume Changes

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Summary. The influence of isoosmotic changes of blood volume on the plasma vasopressin level, osmotic reactivity of the antidiuretic system, arterial blood pressure, central venous pressure and heart rate was examined in 13 conscious intact dogs. The rate of disappearance of exogenous vasopressin under control conditions and during hypovolemia was also investigated. A moderate decrease of blood volume produced a clear cut and persistent increase of the plasma vasopressin level, and a fall of central venous pressure. The same blood loss did not change the rate of disappearance of vasopressin from the plasma.

Moderate blood volume expansion produced a decrease of plasma ADH level and of the osmotic reactivity of the antidiuretic system. Hypervolemia produced a marked increase of central venous pressure and central blood volume.

The result suggest that moderate changes of blood volume modify the activity of the hypothalamo-hypophysial antidiuretic system and support the hypothesis of Gauer and Henry (see [7]) that impulses influencing the activity of the hypothalamo-hypophysial antidiuretic system arise in the central low-pressure part of the circulatory system.

Key words: Vasopressin — Hypothalamo-Hypophysial Antidiuretic System — Blood Volume.

There is much data to suggest that the activity of the hypothalamo-hypophysial antidiuretic system (HHAS) may be modified by isoosmotic changes of the blood volume [2,7,8,10]. Isoosmotic expansion of the blood volume of the central part of the circulatory system is accompanied by an increase of urine output and a rise of free water clearance [2, 16—18,21] as well as by a decrease of plasma vasopressin (ADH) levels [2]. On the other hand, isoosmotic diminution of the total blood volume or displacement of the blood within the vascular bed with a concomitant decrease of the blood volume in the central part of the low-pressure system is accompanied by a decrease of the diuresis [1,2, 13] increased plasma ADH levels [2,13]. Unfortunately in most of the experiments reported in the literature acute, anaesthetized preparations were used to study this problem. As anaesthesia and surgical trauma are known to activate the HHAS [3,4,9] there is no way of being sure
that these procedures have not influenced the reactivity of the latter and the resulting plasma ADH levels. There are only few reports on experiments carried out with conscious animals [11,12]. Moreover is not known whether the changes of plasma ADH concentrations in hypovolemia is due to an activation of the HHAS because the rate of disappearance of the ADH from blood has been never examined under these conditions.

The present study was performed on unanaesthetized dogs to check whether a moderate isoosmotic changes of blood volume, which does not modify mean arterial pressure and pulse pressure influences the activity of the HHAS.

**Materials and Methods**

*Animals.* Thirteen male mongrel dogs weighing 16—20 kg were used. They were accustomed to a partial restraint on a stand and to the experimental situation.

*Series of Experiments.* Four series of experiments were made. In series I plasma ADH level, central venous pressure (CVP), mean blood pressure (MBP), pulse pressure (PP) and heart rate (HR) were measured after an isoosmotic decrease of blood volume and compared to those obtained under control conditions. Course of experiments: the dog was laid down on one side so that the femoral artery could be approached. The skin was incised under local anaesthesia, the artery was punctured and 1.4 mm polyethylene catheter was introduced reaching to the thoracic aorta, according to a method of Saldinger. Then the dog resumed a standing position and another polyethylene catheter was introduced into the saphenous vein until it reached the vicinity of the right atrium. One and one half hours elapsed before control measurements were made (after this time plasma ADH level did not exceed average levels found in animals which were not submitted to the procedure of catheterization). The total blood volume was then decreased 15% of its initial value (as determined prior to the experiments) by an arterial haemorrhage at a rate of 15 ml/min. A blood sample for ADH determination was taken at the end of the haemorrhage and immediately thereafter arterial and venous pressure and heart rate were measured. These measurements were repeated every 5 min following the haemorrhage.

In series II the rate of disappearance of exogenous vasopressin was studied in the same dogs after a decrease of the blood volume by 15% and compared to those obtained under control conditions. Course of the experiments: Pitressin (Parke, Davis and Co.) at a dose of 50 mU/kg of body weight was injected intravenously within 3 sec. Blood samples for plasma ADH determination were taken 4, 8 and 12 min later. The disappearance curve was plotted and plasma ADH level at \( t_0 \) was calculated by extrapolation. The biological half life \( (T_{1/2}) \) was calculated from following equations:

\[
T_{1/2} = \log_e \frac{2V_d}{C} \tag{1}
\]

\[
\ln \left( \frac{P}{P_0} \right) = \frac{C}{V_d} t \tag{2}
\]

where \( V_d \) = distribution space of the hormone,
\( C \) = total clearance,
\( P_0 \) = plasma concentration of hormone at \( t_0 \) (time of injection),
\( P \) = plasma concentration of the hormone at time \( t \) after injection.