monkey were totally opposite. When heated, the animal exhibited vasodilatation and other peripheral heat loss signs, whereas cooling produced vasoconstriction, vigorous shivering and apparent agitation. Because feeding produced a similar decline in CSF flow rate, it is difficult to explain this finding on the basis of a functionally nonspecific stress due to the profound alteration in ambient temperature. It is possible that although the elaboration of CSF from the choroid plexus might have remained essentially constant, the secretion of extracellular fluid into the ventricular lumen[6] could have diminished significantly. If the ventricular lumen does act as a cellular 'sink'[7], then the physiological changes in some way could affect the release, exchange and concentration of electrolytes or other constituents of extracellular fluid. In any event, CSF flow rate at other levels of the primate's ventricles, including the lateral and 4th ventricles must, be ascertained for a more complete understanding of the fluid dynamics of the cerebral ventricular system.

Zusammenfassung. Das Flüssigkeitsvolumen des Ventrikelliquors wurde in Affen (im 3. Ventrikel kanuliert) gemessen. Die Produktion von Ventrikelliquor verringerte sich stark während 40–50 min, und zwar bei Nahrungsaufnahme, bei Erwärmung oder Abkühlung. Hernach Rückkehr des normalen Liquorvolumens.

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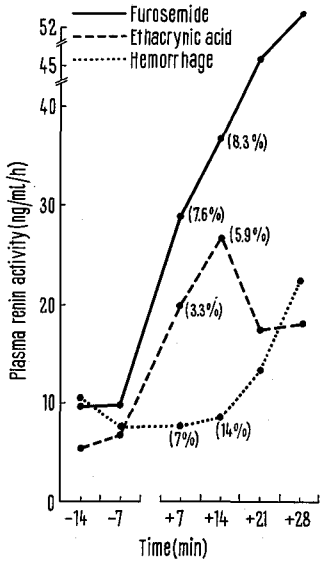
Re-Evaluation of the Role of Hypovolemia on the Release of Renin[1]

It is generally accepted that reduction of blood volume increases the release of renin[2]. It was considered of interest to study the variations of plasma renin activity (PRA) induced by blood volume reductions of similar importance but of different origins. 22 male rabbits weighing 2650 ± 150 g were anesthetized with sodium ethylmethylbutyl barbiturate (mebubarbital, Abbott 50 mg/kg, i.v.), tracheotomized, mechanically ventilated, and placed on a heating table. In a first set of 16 rabbits, reduction of blood volume was induced by i.v. injection of ethacrynic acid (Edecrin, Merck, Sharp and Dohme; 10 mg/kg, 7 rabbits) or of furosemide (Lasilix, Höchst; 10 mg/kg, 9 rabbits); these rabbits were hydrated by i.v. infusion of isotonic saline solution, given at the rate of 0.35 ml/min during the 45 min preceding the experiment. In a second set of 6 rabbits, the reduction of blood volume was accomplished by a slow arterial bleeding. In all experiments, 2 basal periods were followed by 4 experimental periods, each period being of 15 min duration. Determinations of inulin, sodium excretion, plasma volume, arterial blood pressure, and PRA were performed as already described elsewhere[3]. Central venous pressure was measured through a catheter inserted in the external jugular vein, the tip of the catheter being in the superior vena cava. Heart rate was estimated during the recording of pulse pressure with a strain gauge manometer (Telco, E.D. 26).

Results and discussion. As shown in Table I and in the Figure, ethacrynic acid significantly increased PRA, the increase being obvious in the 7th min following the injection (mid-point of the first experimental period); plasma volume was reduced by 3.3% in the first, and by 5.9% in the second experimental period. The increase of PRA observed after furosemide injection was greater than that observed after ethacrynic acid; the reduction of plasma volume seen in the first experimental period is 7%, and 8.3% in the second one. As indicated in Table II, the rate of arterial bleeding performed in the second experiment was adjusted by a screw placed on the arterial catheter so that the reduction of plasma volume was 7% for each experimental period; PRA measured on an aliquot fraction of arterial blood sampled at the mid-point of each period did not vary significantly during the 2 first experimental periods. The increase of PRA observed in the 2 last periods was significant, but inferior to that observed in the diuretic experiments (Figure). These results demonstrate that blood volume reduction



Variations of mean plasma renin activity after ethacrynic acid, furosemide and after hemorrhage. The percentage of mean plasma volume reductions observed in each experiment are indicated in brackets.

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Table I. Effect of ethacrynic acid (10 mg/kg) and of furosemide (10 mg/kg) in 16 rabbits. Diuretics are injected i.v. at the end of the second control period. Values are means ± S.E.M.

	Sodium excretion μEq/kg/min	Clearance of inulin ml/kg/min/kidney	Hematocrit %	Plasma volume ml/kg	Central venous pressure cm H20	Mean arterial pressure mm Hg	Heart rate (per min)	Plasma renin activity ng/ml/h
Control periods	3.7 ± 0.5	1.7 ± 0.1	39.0	–	4.8 ± 0.6	110 ± 15	349 ± 13	5.1 ± 0.9
	3.4 ± 0.5	1.5 ± 0.1	39.3	33.5 ± 1.3	4.8 ± 0.6	106.7 ± 7.7	347 ± 14	6.7 ± 1.6
Ethacrynic acid	77.2 ± 15.7	3.2 ± 0.7	39.7	32.5 ± 7.5	4.8 ± 0.6	107.2 ± 12.2	353 ± 16	19.6 ± 6.9
	30.4 ± 10.2	1.2 ± 0.3	40.1	31.4 ± 1.7	3.9 ± 0.4	99.4 ± 9.5	356 ± 13	26.6 ± 11.0
	4.1 ± 2.4	0.3 ± 0.1	39.5	31.5 ± 1.3	3.8 ± 0.6	88.2 ± 10.1	350 ± 14	17.4 ± 1.2
	1.6 ± 2.5	0.2 ± 0.1	37.0	32.6 ± 1.6	3.4 ± 0.5	87.0 ± 8.5	354 ± 13	17.9 ± 2.6
Control periods	5.5 ± 1.7	2.2 ± 0.1	38.0	–		100.8 ± 3.3		9.9 ± 1.5
	7.9 ± 4.3	2.2 ± 0.3	38.0	30.1 ± 1.3		100.3 ± 4.9		9.9 ± 2.2
Furosemide	100.6 ± 22.2	4.2 ± 0.7	39.5	27.8 ± 1.3		96.6 ± 4.0		28.8 ± 3.6
	73.2 ± 15.1	3.0 ± 0.6	39.0	27.6 ± 1.2		95.4 ± 5.8		36.8 ± 7.0
	48.9 ± 13.4	2.1 ± 0.5	38.0	28.1 ± 1.3		90.9 ± 7.3		46.8 ± 8.8
	35.7 ± 8.6	2.0 ± 0.5	38.0	28.2 ± 1.6		91.3 ± 6.5		53.8 ± 15.1

Table II. Effect of arterial bleeding in 6 rabbits. Hemorrhage is started at the end of the second control period, and is regulated so that 7% of plasma volume is lost in each experimental period. Values are means ± S.E.M.

	Hematocrit %	Plasma volume ml/kg	Central venous pressure cm H20	Mean arterial pressure mm Hg	Heart rate (per min)	Plasma renin activity ng/ml/h
Control periods	40.0	–	6.0 ± 0.9	96.2 ± 4.3	345 ± 16	10.0 ± 2.0
	40.0	32.5 ± 0.5	5.8 ± 0.9	98.7 ± 3.6	342 ± 15	7.5 ± 1.0
Hemorrhage	40.0	29.2 ± 0.5	4.6 ± 1.5	97.5 ± 1.6	362 ± 17	7.5 ± 1.0
	38.8	26.9 ± 0.5	4.5 ± 1.9	88.7 ± 3.6	373 ± 14	8.5 ± 2.0
	36.8	24.6 ± 0.5	4.1 ± 1.2	85.0 ± 4.9	376 ± 12	13.2 ± 2.0
	36.3	22.3 ± 0.5	3.4 ± 1.1	72.7 ± 9.1	369 ± 13	22.2 ± 4.0

cannot be considered as a stimulus of renin release: for blood volume reductions of similar importance and rapidity, renin release is far greater when the volume reduction is induced by a renal loss of sodium than when it is secondary to an arterial hemorrhage (Figure). Since arterial bleeding reduces primarily the intravascular volume, and since the diuretics reduce the whole extracellular compartment, one cannot exclude the hypothesis that the release of renin is mediated through extravascular voloreceptors. Our data suggest however that the increase of PRA during diuretic induced hypovolemia as well as in hypovolemia resulting from hemorrhage, is due to some intrarenal mechanism. In a previous study[3], we have shown that PRA was increased by furosemide, even if volume losses were prevented; this observation led to the conclusion that renin release was stimulated by some intrarenal change brought about by the diuretic, possibly by the increase of intratubular sodium concentration. The moderate increase of PRA observed after ethacrynic acid in this study, supports this possibility since ethacrynic acid was less natriuretic than furosemide.

The lack of release of renin during progressive hemorrhage has been previously observed by others[4] and contrast with the clear-cut increase of PRA following a severe hypotensive hemorrhage[5]. The increase of PRA observed in this circumstance has been attributed either to the activation of the autonomic nervous system[6], or to the direct lowering of renal arterial perfusion pressure. In our experiments, the neural component manifested by tachycardia and steady arterial pressure was present without increased PRA. We conclude, therefore, that the increase of PRA induced by hemorrhage also results from a direct intrarenal mechanism.

Résumé. Les auteurs ont comparé l'effet d'hémorragies progressives et de diurétiques (acide éthacrynique, furosémide) sur l'activité rénine plasmatique. Pour des déplétions volémiques comparables, l'élévation de l'activité rénine plasmatique est plus grande après diurétiques qu'après hémorragie. Le rôle stimulant d'une hypovolémie sur la sécrétion de la rénine est de ce fait critiqué.

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