Table III. Variance analysis of data in Table II.

Source of variation	Sum of squares	Degree of freedom	Variance	F-test	
Between treatments	66 710	1	66 710	F[1,40] = 66 710/8 765 = 7.61	$p < 0.01$/
Between days	326 710	4	81 678	F[4.40] = 81 678/8 765 = > 9	$p < 0.005$/
Interaction	63 314	4	15 829	F[4.40] = 15 829/8 765 = < 2	$p > 0.05$/
Within treatments	356 582	40	8 764.5		
Total	813 316	49			

recorded. Results are given in Table II and evaluation with variance analysis in Table III.

Our findings provide strong evidence that the AMS administered 1 day before and 3 days after the inoculation of the antigen, caused a significant increase in the number of haemolytic plaques.

For the time being we cannot explain the mechanism of this adjuvant effect. We may presume that the enhancing effect of AMS is similar to that of endotoxin, i.e. it exerts a toxic effect on macrophages with subsequent damage of the lysosomal membrane[17].

Zusammenfassung. Beitrag zur Frage über den Einfluss des Antimakrophagenserums auf die Antikörpersynthese.

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Effect of Hypophysectomy on Sodium Excretion in Rats without Blood Dilution during Blood Volume Expansion

One of the most controversial problems of the mechanism of homeostatic increase of renal sodium excretion during extracellular fluid volume expansion is the question of the existence of a natriuretic hormone. Those who are inclined to admit its existence suggest that such a hormone could promote an increase of sodium excretion by decreasing sodium reabsorption in the renal tubules and possibly by dilating the renal vascular bed as well (for more detailed information see recent reviews[1–5]). In searching for the source of a natriuretic hormone in the organism, mostly techniques of organectomies have been used. It was found that neither decapitation, nor hepatectomy and nephrectomy (the latter in cross-circulation experiments[6]) substantially influenced natriuresis during extracellular fluid volume expansion with saline[7,8]. However, expansions with saline (or Dextran) in such experiments may have been the cause of a partial increase of sodium excretion by diluting plasma proteins and decreasing haematocrit[9–11]. Such a partial saluretic effect of diluting factors might be mistaken for an effect of a natriuretic hormone of unknown origin as the particular organectomy failed to prevent natriuresis.

On the other hand, electrolytic lesions of the posterior hypothalamus were found to have weakened the saluretic response to the expansion[12,13]; the renal extracts of saluretic dogs induced natriureris in the kidneys of non-expanded animals[14].

The discrepancies in the results of studies on the role of various organs in the mechanism of the 'volume' natriuresis induced us to reexamine the possibility of a cerebral origin of a natriuretic hormone without diluting blood during intravascular expansion.

Materials and methods. 10 male rats of Wistar strain weighing between 250–270 g were anesthetized by Inactin Promonta (100 mg per 100 g of body wt.), 3 mg of Decorton Spofa (desoxycorticosteronum aceticum, solutio oleosa) were injected subsequently i.m., then the trachea was cannulated and hypophysectomy performed through the sphenoid bone in 5 rats – the other group of 5 rats was not hypophysectomized. The surgical preparation was completed by cannulating 1 carotid artery, the jugular vein, femoral artery, femoral vein and urinary bladder with polyethylene catheters. Finally, the animals were heparinized (300 IU of Heparin Spofa i.v. and a continous infusion of Inulin-C^{14} and Vasopressin Sandoz/5 I mU per h/100 g body wt. in 1 ml of saline was started). Plasma from 2 further intact rats was pooled and administered to the experimental animal by means of an isovolemic exchanged infusion[15] in the amount of 33% of the estimated blood volume (plasma was infused into the jugular vein and the equivalent volume of blood was withdrawn from the caro-

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The influence of hypophysectomy on the urine output (V), sodium excretion ($U_{Na}V$), glomerular filtration rate (GFR) and tubular rejection fraction (TRF_{Na})

Period		Time (min)	Non-hypophysectomized ($n = 5$) means ± S.E.	Hypophysectomized ($n = 5$) means ± S.E.	P
			V µl/min		
Control	1	0– 20	10.42±2.24	3.75±0.64	ns
Exp.	2	20– 40	38.21±5.37 [b]	7.43±1.86	<0.001
	3	40– 60	103.12±8.28 [c]	18.52±2.74 [b]	<0.001
	4	60– 80	34.32±6.65 [a]	10.67±2.91	<0.02
	5	80–100	16.32±2.84	7.14±2.71	ns
			$U_{Na}V$ µEq/min		
Control	1	0– 20	2.12±0.69	0.07±0.04	<0.02
Exp.	2	20– 40	7.23±0.94 [a]	0.41±0.26	<0.01
	3	40– 60	16.51±1.54 [b]	2.31±0.65 [a]	<0.001
	4	60– 80	6.60±1.19 [c]	1.38±0.69	<0.01
	5	80–100	3.81±0.75	0.86±0.64	<0.002
			GFR ml/min		
Control	1	0– 20	2.02±0.39	1.18±0.21	ns
Exp.	2	20– 40	2.59±0.20	1.88±0.24	ns
	3	40– 60	3.12±0.38	1.70±0.27	<0.02
	4	60– 80	1.98±0.20	1.03±0.13	<0.01
	5	80–100	1.70±0.33	0.91±0.12	ns
			TRF_{Na} (%)		
Control	1	0– 20	0.59±0.16	0.05±0.01	<0.01
Exp.	2	20– 40	1.90±0.18 [b]	0.15±0.08	<0.001
	3	40– 60	3.84±0.27 [c]	1.11±0.39	<0.001
	4	60– 80	2.21±0.29 [b]	0.81±0.29	<0.01
	5	80–100	1.39±0.13 [a]	0.57±0.31	<0.05

All values calculated per 1 g of the kidney weight. Control, preexpansion period. Exp., blood volume expansion. Letters indicate the statistical significance of the values in the periods 2–5 as compared to the control values (period 1): [a] $P < 0{,}05$; [b] $P < 0.01$; [c] $P < 0.001$. P, statistical significance of the difference of respective values found in non-hypophysectomized and hypophysectomized groups of animals.

tid artery). This exchanged infusion decreased the haematocrit to approximately 30% and thus urine output was slightly increased. The procedure permitted us to take 20-min urine samples for chemical analysis without any sort of prehydration of the rats. The exchanged infusion was followed by 1 h of equilibration. Then the control urine sample was taken and during the next period the intravascular volume of the experimental animal was expanded by reinfusion of the previously exchanged blood, which had a slightly higher haematocrit than the circulating blood in the animal. The volume expansion was followed by another 3 urine sampling periods of 20 min each. – Sodium plasma and urine was determined by flamephotometry (Unicam S.P. 900), glomerular filtration rate (GFR) was calculated on the basis of Inulin-C^{14} clearence. – The results were tested statistically by means of the Student t-criterion.

Results and discussion. The results are summarized in the Table. In both the hypophysectomized and non-hypophysectomized animals, urine and sodium output as well as tubular sodium rejection fraction and glomerular filtration rate increased during blood volume expansion. However, the peaks of changes in non-hypophysectomized rats were approximately 5-fold higher for urine output, 7-fold higher for sodium excretion, doubled for glomerular filtration rate and tripled for the sodium tubular rejection fraction. All these differences were of high statistical significance.

It is understood that the effect of hypophysectomy on any function in the organism is of a very complex nature. Even the operating stress – apparently more pronounced in the hypophysectomized animals – might have played a role in the decreased glomerular filtration rate. However, as a result of the work by DEWARDENER, MILLS et al.[16], it has been almost generally accepted that the increase of glomerular filtration rate is not the critical natriuretic factor in 'volume' natriuresis. Thus a more specific role of the pituitary in the mechanism of sodium excretion during blood volume expansion is suggested. In the light of our present and earlier findings, and in agreement with LOKKETT's[17] results, we presume that the posterior hypothalamus and the pituitary might participate in the renal mechanism of theextracellular fluid volume regulation and that this involvement might be of a humoral nature fitting the frame of the still undefined 'natriuretic hormone'.

Zusammenfassung. Experimentell wurde an hypophysektomierten Ratten, im Vergleich mit intakten Tieren, eine signifikant verminderte diuretische und natriuretische Reaktion auf die isoonkotische Expansion des Blutvolumens festgestellt.

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