

Zusammenfassung

Die Vorbehandlung mit Thenalidin (Sandosten) führt zur Verminderung der mit Serotonin hervorgerufenen hämorrhagischen Erosionen im Magen der Ratten. Thenalidin zeigt einen Effekt auf das mit Reserpin bewirkte Magengeschwür und verstärkt die Vormagengeschwürbildung bei den Ratten.

Effect of the Non-Protein Fraction of Rabbit Hypothalamic Extract on the Function of Adenohypophysial Autografts in the Anterior Chamber of the Eye of Hypophysectomized Rats

It was found in previous experiments<sup>1</sup> that the non-protein fraction of aqueous extract of rabbit hypothalami increased acid phosphatase activity in rat pituitary homogenates. Evidence was also submitted indicating the existence of a relationship between pituitary acid phosphatase activity and the formation of thyrotrophic hormone (TSH), and suggesting that the hypothetical hypothalamic factor activating pituitary acid phosphatases may be a hypothalamic TSH-hypophysiotrophic factor<sup>2</sup>.

Experiments were carried out *in vivo* to verify this assumption. Since the systemic (intravenous) administration of even relatively high doses of extract does not significantly influence thyroid function in intact rats<sup>3</sup>, evidently because this method does not give a sufficiently high concentration of the factor in the hypophysial portal vessel blood, the problem was approached by the local administration of the non-protein fraction of hypothalamic extract to adenohypophysial autografts in the anterior chamber of the eye of hypophysectomized rats.

Male rats (descendants of the Wistar strain, Velaz, Prague) acclimatized at 25 ± 2°C and fed on a standard Larsen diet with water *ad libitum*, were hypophysectomized by the parapharyngeal route. About one third of the pituitary (adenohypophysis) was aspirated into a No. 24 intramuscular needle with blunted point. An incision of about 2 mm was made with a fine scalpel in the cornea of the upper half of the left eye. The aspirated adenohypophysial tissue was then introduced into the

with autografts the eye was subjected to histological examination. The results of this examination will be given in a separate report.

There were four groups of animals: I—15 controls, II—12 hypophysectomized animals, III—10 hypophysectomized animals with autografts, to which (in the anterior chamber of the eye) 0.02 ml physiological saline was administered daily from the first to the seventh day after transplantation, IV—15 animals with autografts, to which (in the anterior chamber of the eye) 0.02 ml aqueous solution of the non-protein fraction of rabbit hypothalamus, prepared by the method described in a previous communication<sup>1</sup>, was administered daily. 1 ml solution contained the equivalent of two rabbit hypothalami. One day after the seventh injection, all the animals were killed by exsanguination and the thyroids, adrenals, testes, and seminal vesicles were weighed.

The results are shown in the Table. Hypophysectomy was followed by plainly evident involution of all the organs in question, while autotransplantation of the adenohypophysis partially inhibited this involution. Administration of hypothalamic fraction to the autografts discernibly limited the involution of the thyroid (thyroids of the group IV were significantly—*p* < 0.01—heavier than those of group III). Involution of the other organs (adrenals, testes, seminal vesicles) was the same or greater in group IV than in group III, however. The 'weight of the adrenals: weight of the thyroid' quotient was 2.34 ± 0.16 in group III and 1.65 ± 0.14 in group IV; *p* < 0.01.

It appears that the local application of the hypothalamic fraction stimulated TSH-secretion by the adenohypophysial autografts and did not change, or possibly inhibited, secretion of ACTH and gonadotrophins. This is in agreement with findings mentioned on relationships between the hypothalamic factor, activating pituitary acid phosphatases *in vitro* (which is present in the non-protein fraction of the hypothalamic extract) and secretion of TSH by the adenohypophysis. The possibility that its action is non-specific cannot yet be excluded.

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Group	I Controls	II Hypophysectomized	III Hypophysectomized + autograft	IV Hypophysectomized + autograft + hypothalamic fraction
No. of animals	15	12	10	15
Initial weight g	235	248	232	244
Final weight g ± σ	247 ± 5	207 ± 8	204 ± 5	205 ± 7
Thyroids mg% ± σ <sub>M</sub>	7.00 ± 0.37	4.50 ± 0.37	4.92 ± 0.38	6.42 ± 0.39 <sup>a</sup>
Adrenals mg% ± σ <sub>M</sub>	14.90 ± 0.64	9.50 ± 0.36	11.1 ± 0.68	9.60 ± 0.42 <sup>b</sup>
Testes g% ± σ <sub>M</sub>	1.05 ± 0.04	0.88 ± 0.03	1.04 ± 0.05	0.95 ± 0.04 <sup>c</sup>
Seminal vesicles mg% ± σ	195 ± 15	107 ± 5	118 ± 14	96 ± 7 <sup>d</sup>
Quotient 'weight of adrenals: of thyroids' weight	2.19 ± 0.12	2.26 ± 0.22	2.33 ± 0.16	1.56 ± 0.14 <sup>e</sup>

Comparison of group III and IV by Fisher's *t*-test: *p* = <sup>a</sup> < 0.01; <sup>b</sup> 0.05; <sup>c</sup> 0.2; <sup>d</sup> 0.1; <sup>e</sup> < 0.01.

anterior chamber of the eye (only partial disintegration of the aspirated one-third of the adenohypophysis took place during the procedure). Only completely hypophysectomized animals were taken into account, and in animals

<sup>1</sup> V. SCHREIBER, M. RYBÁK, V. KMENTOVÁ, *Nature* 183, 473 (1959).  
<sup>2</sup> V. SCHREIBER and V. KMENTOVÁ, *Endokrinologie*, Leipzig 38, 69 (1959).  
<sup>3</sup> V. SCHREIBER and L. KRULICH, not published.

*Zusammenfassung*

Tglich lokal verabreichte eiweissfreie Fraktionen des hypothalamischen Extraktes zu adeno-hypophysren Auto-transplantaten in die vordere Augenkammer hypophysektomierter Ratten hemmte die Schilddrseninvolution und stimulierte mglicherweise den Vorgang bei Nebenniere, Hoden und Samenblschen.

**The Urinary Excretion of Noradrenaline and Adrenaline during Acute Alcohol Intoxication in Alcoholic Addicts**

High urinary excretion of noradrenaline and adrenaline has been reported<sup>1</sup> in the course of delirium tremens and allied conditions. There was no correlation between the catecholamine output and the intensity of single clinical symptoms, with the presence or absence of ethyl alcohol or drugs in the blood, or with the laboratory findings other than blood pressure and pulse rate. In patients with syndrome B<sup>2</sup>, however, the excretion of urinary catecholamines had a definite tendency to fall immediately after the disappearance of the blood alcohol. Therefore it was of interest to investigate, whether or not the presence of alcohol in the blood of alcohol addicts is accompanied by increased excretion of urinary noradrenaline and adrenaline independent of the above-mentioned syndromes.

*Material and Method.* 16 male alcoholic patients showing no acute signs of alcoholic syndromes were used as test subjects at least one week after recovery. Eight patients consumed brandy or wine, and eight other patients received intravenous infusions of ethyl alcohol 25 vol.% in Ringer solution, on an average 2.3 g/kg within ca. 5 h. The blood alcohol concentrations were determined with the method of WIDMARK<sup>4</sup> in all cases. The peak level varied between 1.5<sup>0</sup>/<sub>00</sub> and 3.3<sup>0</sup>/<sub>00</sub>. The urinary catecholamines were determined in 24 h collections before, during and after alcohol uptake by the method of EULER and LISHAJKO<sup>5</sup>.

*Results.* There was no statistical difference between the excretion of urinary noradrenaline and adrenaline in convalescent alcoholic addicts before, during, and after ethyl alcohol administration, and that of 12 healthy persons<sup>1</sup> (Table). In no case following induced alcohol intoxication could the neurological symptoms of syndrome B be detected.

*Discussion.* The 24-h excretion of urinary catecholamines in alcohol convalescents showed no alteration when compared with the values of healthy subjects<sup>1</sup>. Ethyl alcohol administered during a short period neither increased the urinary excretion of noradrenaline and adrenaline nor did it induce the picture of syndrome B in these subjects, even if the doses were as high as 2,3 g/kg intravenously. The increase of urinary catecholamines occurring in acute alcohol intoxications together with SB in alcohol addicts<sup>1</sup>, seems therefore to be connected with a longer lasting abuse of ethyl alcohol than was the case in our experiments. It is evidently not dependent on the immediate effect of alcohol on the organism but on some factors developing in the course of SB and alcohol hallucinosis. In this connection, it is of interest that alcohol given intravenously in two patients during delirium tremens and SB respectively, did not influence the patterns of the urinary excretion of catecholamines.

The excretion rate of urinary noradrenaline and adrenaline during the 5-h infusion period was found to be in the range of normal diurnal variations reported by EULER

	Healthy persons	Convalescent alcoholic addicts		
		day before experiment	day of experiment	day after experiment
Noradrenaline $\mu\text{g}/24\text{ h}$	$18.0 \pm 6.9$	$16.9 \pm 7.8$	$17.3 \pm 6.9$	$17.0 \pm 5.7$
Adrenaline $\mu\text{g}/24\text{ h}$	$6.4 \pm 3.1$	$8.2 \pm 4.4$	$7.6 \pm 2.7$	$8.1 \pm 2.8$
Urinary excretion of catecholamines in convalescent alcoholic addicts before and after acute alcohol administration.				

and LISHAJKO<sup>5</sup>. Since, in our experiments, the catecholamines were not measured in shorter periods, a slight transient increase such as that shown by other authors<sup>6-8</sup> may have escaped notice.

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*Zusammenfassung*

Die Katecholaminausscheidung im 24-h-Urin rekonvaleszenter Alkoholpatienten wird durch einzelne thylalkoholdosen (2,3 g/kg) nicht beeinflusst.

<sup>1</sup> E. GIACOBINI, S. IZIKOWITZ, and A. WEGMANN, A. M. A. J. gen. Psych., in press (1960).

<sup>2</sup> Syndrome B (SB) is the most frequent acute state following an intense or long lasting alcohol or drug abuse. It is characterized by anxiety, tremor, vasomotoric reactions, hyperhidrosis, sleep disturbances, and anorexia, but without disorientation or hallucinations (for nomenclature see IZIKOWITZ<sup>3</sup>).

<sup>3</sup> S. IZIKOWITZ, Nord. Med. 60, 1009 (1958).

<sup>4</sup> E. M. P. WIDMARK, Biochem. Z. 131, 473 (1922).

<sup>5</sup> U. S. v. EULER and F. LISHAJKO, Acta physiol. scand. 45, 122 (1958).

<sup>6</sup> E. S. PERMAN, Acta physiol. scand. 44, 241 (1958).

<sup>7</sup> I. ABELIN, Ch. HERREN, and W. BERLI, Helv. med. Acta 25, 591 (1958).

<sup>8</sup> G. I. KLINGMAN and M. GOODALL, J. Pharmacol. 121, 313 (1957).

PRO EXPERIMENTIS

**An Ultra-High Vacuum System  
Using an Oil-Diffusion Pump  
with a Non-Refrigerated Isolation Trap<sup>1</sup>**

We found that an oil-diffusion pump with a modified Biondi trap<sup>2</sup> charged with activated alumina was very satisfactory in continuously maintaining ultra-high vacuum for periods of several months. The trap did not require refrigeration and the activated alumina beads could be reconditioned by bakeout. Because of the high conduct-

<sup>1</sup> This work was done for the Lawrence Radiation Laboratory at Livermore, California, under the auspices of the Atomic Energy Commission.

<sup>2</sup> M. A. BIONDI, Rev. Sci. instr. 30, 831 (1959).