these effects may be considered. The impairing effects of narcotic and sedative substances on the thermoregulatory efficiency result in the conclusion that a high arousal state is necessary for effective thermoregulation especially in small mammals. Although measurable sedative influences were difficult to find out in the present experiments, such effects have been produced in adult rats and mice by 5-HT, A and by large doses of NA[14–16]. It can be suggested that the intraventricularly injected monoamines impair the thermoregulation in infant rats by an inhibition of the brain stem reticular formation which is responsible for the maintenance of the activation level and which is, on the other hand, in interaction with the hypothalamus[17].

Zusammenfassung. Injektionen von 5-Hydroxytryptamin und Noradrenalin in die Gehirnventrikel junger Ratten verursachen einen verminderten Sauerstoffverbrauch und eine Hypothermie bereits am ersten Tag nach der Geburt Effekte, die mit dem Alter verstärkt, auftreten.

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The Effects of Δ-Amino-Laevulinic Acid on Sodium and Water Movement Across Frog Skin

A high frequency of electrolyte disturbances has been noted in acute Variegate Porphyria, and in acute Intermittent Porphyria[1–3]. In addition, urinary hyperosmolality in the presence of serum hypoosmolality, marked sodium depletion, with or without excessive total body water may be present[4,5]. While a number of mechanisms may be invoked to explain these phenomena, notably the inappropriate secretion of antidiuretic hormone, one possibility is that excessive concentrations of porphyrins, or their precursors, may directly induce a renal tubular sodium-losing state[5,6]. We have endeavoured to explore this hypothesis by investigating the effect of Δ-amino-laevulinic acid (ALA) on Na transport and water movement across the skin of *Xenopus laevis*.

Frogs were prepared by injection of 0.6 mg deoxycorticosterone acetate in olive oil into the dorsal lymph sac 18 to 72 h prior to each experiment. Each frog was then pithed, and the ventral abdominal skin removed; this was divided by a midline incision, one piece of skin serving as the control for the other. Two different experimental protocols were followed; in one, the skin was mounted between Lucite chambers, bathed in normal frog Ringer's solution on either side, and the potential difference (PD) and short circuit current (SCC) measured as a function of time. In some of these experiments ^{22}Na kinetics were also studied. In the other procedure, the outer bathing solution was replaced by frog Ringer's diluted tenfold with distilled water; water movement in response to the osmotic gradient across the skin was followed by observation of movement of a meniscus in a capillary tube[7]. In both procedures the effects of ALA, with and without antidiuretic hormone (ADH)[8], were observed once equilibrium had been established.

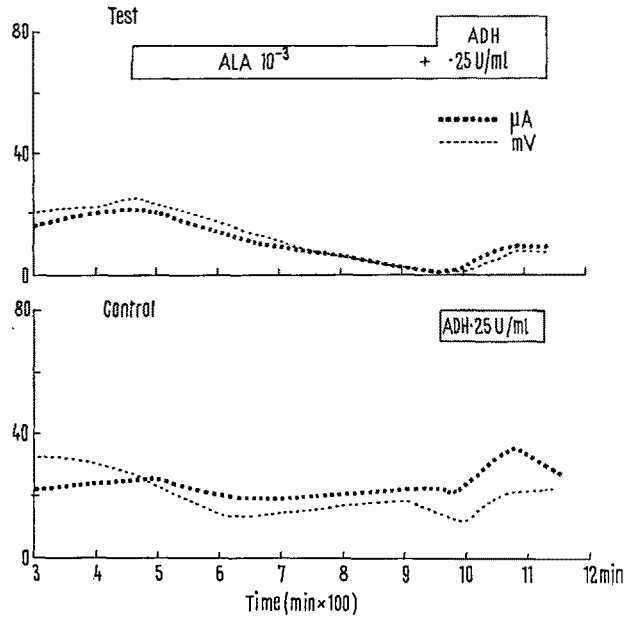

Fig. 1. The effects of ALA and ADH on short-circuit current (μA) and potential difference (mV) across paired skins. The abscissa is in hundreds of minutes.

ALA caused prolonged falls in SCC and PD, sometimes down to zero (Figure 1). These were occasionally preceded by slight and shortlived (30 min) rises. The minimal dose of ALA found to produce these effects consistently was $10^{-3}M$; this was most effective if added to the solution bathing the inside of the skin. Tracer studies (^{22}Na) have revealed a simultaneous gross reduction in the movement of Na from the outer to the inner bathing solutions; the permeability of the outer-facing barrier to Na is much reduced by ALA.

ADH, given in supramaximal doses (0.25 U/ml) always reversed the ALA effects, even in those cases where the SCC and PD had fallen to zero (Figure 1). The converse

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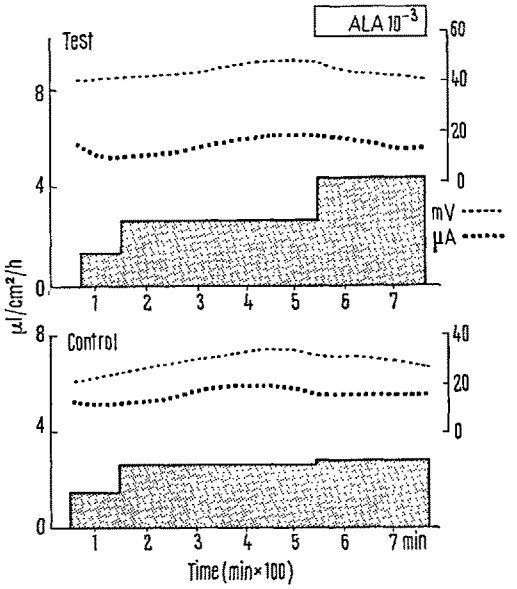

Fig. 2. The effects of ALA and ADH on short-circuit current ($\Psi\,\mu A$), potential difference (mV), and water movement ($\mu l/cm^2/h$) across a skin exposed to an osmotic gradient. The abscissa is in hundreds of minutes.

was also seen, although more rarely: ALA occasionally reversed ADH-induced increases in SCC, PD, and skin conductance.

ALA also increased the osmotic permeability of the skin to water. This was observed whether or not simultaneous changes in SCC or PD had occurred (Figure 2).

These studies thus support the hypothesis of a renal tubular locus of action of ALA, and suggest that the accumulation of this substance in advanced cases of acute porphyria may well be responsible, in part, for the water and electrolyte disturbances seen in these patients.

Zusammenfassung. Δ-Aminolävulinsäure (ALA) beeinflusst die Passage von Natrium und Wasser durch ein in vitro Präparat der Froschhaut. Dies bestätigt teilweise die Hypothese, dass ALA eine Rolle in gewissen Abnormalitäten der Nierenkanälchen bei akuter klinischer Porphyrie spielt.

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Urinary Renin and Norepinephrine Excretion in Dogs after Unilateral Renal Artery Constriction

There are only a few reports on renin excretion in urine[1–7]. Renin activity in urine of dogs was measured during variations in sodium balance[8] with the micromethod of Boucher et al.[9] with minor modifications[10]. In the present study we investigated renin activity and norepinephrine content in the urine collected separately from each kidney of dogs after constriction of one renal artery.

Material and methods. 14 femal mongrel dogs were anesthetized with pentobarbital and 1 renal artery was constricted according to the Goldblatt technique; the other kidney remained untouched. After 4 days (group A: 6 dogs) and after 4–6 weeks (group B: 8 dogs) the animals were anesthetized and catheters were placed in both ureters. The urine was collected in glass containers immersed in an ice-bath.

The following parameters were measured: Group A: Renin activity in renal venous blood (RVRA), in urine (URA), and renal cortex (RRA) was measured as recently described[9,10]. Group B: RVRA, URA, and RRA as in group A. In addition, granularity of the juxtaglomerular cells was determined by the juxtaglomerular index (JGI) of Hartroft and Hartroft[11]. Norepinephrine (NE) was measured by the method of Anton and Sayre[12]. Sodium was determined by flamephotometer. Results are expressed as mean value ± standard error (SE). Whenever possible, statistical analysis was made on paired measurements using Student's *t*-test; when the

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Table I. Renin activity[a] in renal venous plasma (RVRA), urine (URA), and renal cortex (RRA) of dogs 4 days after unilateral constriction of the renal artery ($n = 6$)

	Untouched kidney	*p*-value	Clipped kidney
RVRA/ml	6.73 ± 2.20	< 0.05	12.67 ± 3.35
URA/ml	10.34 ± 3.71	< 0.05	14.72 ± 3.66
URA/urine vol/h	82.02 ± 42.32	N.S.[b]	89.80 ± 39.27
RRA/g	28,400 ± 6,400	N.S.[b]	25,800 ± 3,000

[a] Expressed in ng angiotensin/h incubation, mean ± S.E. [b] Not significant.