fonctionnement de la monoamineoxydase. Il est indiscutable, en outre, que le cuivre est lié à l'enzyme par des liaisons suffisamment fortes, puisque le métal n'est pas exclus de la lipoprotéine par passage sur Séphadex.

Nos résultats semblent en contradiction avec ceux de NARA[4] qui indiquait que la dialyse n'inactive pas la monoamineoxydase mitochondriale. Il est vraisemblable que cette contradiction s'explique par le fait que ces auteurs ont utilisé des temps de dialyse trop courts pour permettre une élimination de l'ion métallique.

Summary. The solutions of monoamineoxidase from rat liver mitochondria can be inactivated by a longlasting dialysis. The addition of cupric ions to these inactive preparations allows a complete reactivation.

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The Effect of Uremic Serum on Carbohydrate Metabolism in Rat Diaphragm

There are essential differences of opinions as to whether abnormal carbohydrate metabolism in patients with renal insufficiency is caused by a primary defect of carbohydrate metabolism in the liver or in the peripheral glucose utilization[1–4]. It is evident that liver takes a part[1], but only 1 direct proof of participation of muscle has been presented as yet: the forearm of patients with renal insufficiency takes up glucose to a smaller extent than is the case in healthy persons, if the glucose uptake was stimulated by insulin[5]. Additional data on muscle glucose metabolism and a more convenient model for these studies are presented in this paper.

Methods. Fasting venous blood was obtained from patients with renal insufficiency or from volunteers. After the 30 min standing at room temperature, samples were centrifuged and the sera were immediately used as media for incubation. Under the basal conditions it was not necessary to adjust pH of the serum. In cases, where lactate or α-ketoglutarate were added to the sera, pH was adjusted to 7.4.

Diaphragms: male Wistar rats weighing 150–180 g, last fed 20 h before the experiment, were decapitated, the diaphragm was withdrawn, cut into 4 pieces and randomized with diaphragms of other rats. The samples were immediately put into the cooled serum and incubated in Warburg vessels for 1 h at 37 °C in oxygen atmosphere. The diaphragms were weighed after the incubation.

Serum glucose concentrations before and after incubation were determined by the glucose oxidase method, α-ketoglutarate enzymatically both by standard commercial kits (Boehringer). Serum as well as tissue lactate concentrations were determined by the BARKER, SUMMERSON method[6], glycogen concentration in the diaphragm by the anthrone method[7] after double precipitation of glycogen by ethanol.

Results. Rat diaphragm incubated in the serum of patients with renal insufficiency utilized in the course of 1 h less glucose than diaphragm incubated in the serum of volunteers (Table). The difference was not conditioned by differences in glycemia which was approximately the same. Oxygen consumption did not change (Table), thus instead of glucose, other metabolic substrates must have been metabolized. Glycogenolysis was therefore measured; while synthesis of glycogen was found in diaphragms incubated in control sera, the diaphragms incubated in uremic sera utilized glycogen (Table). That means that glycogen served in these conditions as a substrate for energetic metabolism. It should be mentioned that, from the quantitative point of view, glycogen value is low.

Under the conditions mentioned, lactate was released from the diaphragm into the serum. However, the diaphragm released lactate into the uremic serum in a significantly lower amount (Table). If lactate concentration was increased by 20 mE/l, diaphragms incubated in control sera still released lactate, diaphragms incubated in uremic sera took up lactate (Table).

Substrate utilization by diaphragms incubated in serum. Negative values mean synthesis and eventual release of substrate into the serum

Substrate	Added concentration mM/l	Control sera	Uremic sera	Difference
Glucose mg/g/h	–	16.7 ± 6.32 ($n = 13$)	7.82 ± 4.25 ($n = 13$)	$P < 0.001$
Glycogen mg/g/h	–	-0.310 ± 0.069 ($n = 9$)	0.326 ± 0.035 ($n = 8$)	$P < 0.01$
Lactate mg/g/h	–	-2.75 ± 1.47 ($n = 13$)	-0.789 ± 1.45 ($n = 17$)	$P < 0.001$
	20	-0.287 ± 1.60 ($n = 10$)	1.80 ± 0.79 ($n = 6$)	$P < 0.05$
α-ketoglutarate mg/g/h	10	-0.237 ± 0.138 ($n = 6$)	0.181 ± 0.230 ($n = 5$)	$P < 0.01$
Oxygen $\mu l/g$ d.w./h	–	6.44 ± 0.54 ($n = 15$)	6.90 ± 1.41 ($n = 17$)	–

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On adding to the sera 10 m*M* α-ketoglutarate, a similar difference was found between the groups studied as in the case of lactate.

Discussion. It is evident from the results of these experiments that either the transmembrane transfer of glucose, or glucose phosphorylation by hexokinase are the sites of inhibition of glucose utilization in the diaphragm incubated in the uremic serum. Though it was not examined, it seems more probable that the site of metabolic block is on the level of transmembrane transfer, as there are evidences that patients with renal insufficiency react poorly to the applied insulin[2-4]. Whatever the exact mechanism, there is no doubt that the carbohydrate metabolism of muscle incubated in uremic serum is abnormal.

Diaphragm compensates decrease in the utilization of glucose by an increased utilization of other substrates and so ensures an unaltered oxygen consumption. This finding corresponds also to the in vivo conditions, as it was shown that the basal metabolic rate of patients with renal insufficiency is not significantly altered[8].

THÖLEN et al.[9,10] found in patients with renal insufficiency also inhibition of pyruvate oxidation with the secondary increased formation of acetoin. The results with kidney cortex slices incubated in uremic sera[11] are in accordance with this view. An increased concentration of some acids of citric acid cycle in the blood of uremic patients testifies to the inhibition of oxidative processes[12].

On the basis of the experiments presented, the block on this level in the muscle is improbable. However, it is a question whether this block is not valid only in some organs, i.e. liver and kidney, which have a suitable cell structure as well as active transport processes for the uptake of these substrates.

Zusammenfassung. Das Serum von Uremikern inhibiert die Glukoseutilisation im Rattendiaphragma. Der Sauerstoffverbrauch ändert sich nicht trotz niedrigerer Glukoseutilisation, da dieselbe durch eine erhöhte Auswertung anderer Substrate im Diaphragma kompensiert wird. Ein erhöhter Glykogen-, Laktat- und α-ketoglutarat-Verbrauch konnte bewiesen werden.

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The Role of Renal Hyperaemia and Plasma Oncotic Pressure in Proximal Tubular Reabsorption in the Rat

In 1966 EARLEY and FRIEDLER[1] postulated an important role of renal vascular resistance in the regulation of sodium reabsorption. They expressed the idea, which was later worked out in more detail by RECTOR et al.[2], that there is an inverse relationship between the capillary blood volume and tubular volume: tubular volume decreases during vasodilatation and vice versa. Since RECTOR et al.[3] showed that proximal tubular reabsorption is a function of tubular volume – as had been presumed by GERTZ[4] – and since further experiments existed indicating that renal hyperaemia was followed by natriuresis[5,6,1], we measured the tubular flow rate and the intrinsic reabsorptive capacity in the proximal tubule of the rat after the administration of acetylcholine, bradykinin and Pyrogen and after total body heating; these maneuvres are known to produce renal hyperaemia. The transit time of the fluid in the proximal tubule was measured with Lissamine green according to STEINHAUSEN's method[7], modified by GERTZ et al.[8]. The intrinsic reabsorptive capacity was estimated by means of the shrinking-drop technique as described by GERTZ[9]; in this method the half-time of the intratubular shrinkage of an isotonic saline drop injected between two oil drops is measured. The original method of GERTZ based on photographic recording of drop-shrinkage was replaced by direct measurements with an ocular micrometer. Fractional reabsorption in the proximal tubule was calculated according to the equation of BRUNNER, RECTOR and SELDIN[10] originally introduced by GERTZ et al.[8]:

$$\% \text{ reabsorption} = \left(1 - \frac{1}{\text{antilog}\,(0.301\ T/t_{1/2})}\right) \cdot 100$$

where T is transit time of Lissamine green in the proximal tubule, and $t_1/_2$ is half-time of the drop shrinkage. As is obvious from the Table, no change was found in the in-

	IRC	TT	FR
Controls	9.10 ± 1.37	9.00 ± 1.10	49.6
Pyrogen	9.31 ± 0.95	6.89 ± 0.48	40.0
Acetylcholine	9.88 ± 1.45	6.50 ± 0.31	36.4
Bradykinin	9.81 ± 1.17	7.48 ± 0.25	40.9
Overheating	9.40 ± 1.11	6.24 ± 0.52	36.6
Saline infusion	14.60 ± 2.18	6.60 ± 0.55	26.7
Saline and albumin infusion	11.92 ± 1.84	8.11 ± 0.76	37.5

IRC, intrinsic reabsorptive capacity as measured by shrinking-drop technique ($t_1/_2$ in sec); TT, transit time of Lissamine green (sec); FR, calculated % reabsorption in proximal tubule. Values presented as mean ± residual standard error.

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