

In our previous paper, we have described an increase in the citric acid level in the whole kidney<sup>13</sup>. Now we have proved that this increase comprises all parts of the kidneys and that in the same parts the calcium content increases as well. This rise is in good agreement with the conception of the kidney as one target organ of the parathormone action. This effect is a rapid one, because, 3 h after the application, the levels tend to normalize.

In the 3rd group treated with calcitonin, a rapid drop of calcium content showed within 30 min after the application. The citric acid level in this case does not follow that of calcium, except in the cortex. Somewhat surprising was the decrease of phosphorus in the papilla. The very rapid action of calcitonin in the homeostasis of calcium represents a great problem. There is no doubt that calcitonin has a definite effect on the metabolism of bone, but the influence of this hormone on the kidney has not yet been fully elucidated<sup>14-16</sup>. As far as is known, all calcium-influencing factors have several so-called target organs. There is a possibility that calcitonin does not make any exception. Our findings indicate that calcitonin has a definite influence on calcium and phosphorus in the kidneys, but its effect on the amount of these compounds varies in the different parts of the organ. It is also probable that the time, dose and mode of application play an important role.

It has been demonstrated that there is a gradient in calcium concentration between the renal papilla and medulla<sup>17</sup>. We have shown that a similar gradient exists also for citric acid. Our present experiments do not permit any conclusions concerning these findings. Citric acid is on one hand a compound with great affinity for the calcium ion, and on the other hand a metabolite of a rapid turnover.

Perhaps the investigation of this relationship would be of some interest in the case of formation of calcium deposits and renal stones.

**Zusammenfassung.** Es wurde festgestellt, dass Calciferol die Stauung von Calcium, Phosphor und Zitronensäure in allen Teilen der Niere verursacht. Parathormon erhöht den Gehalt von Calcium und Zitronensäure in der Niere während einer Stunde. Nach Verabreichung von Calcitonin wurde Verminderung von Calcium in der Cortical- und Medullarzone beobachtet.

A. KOMÁRKOVÁ, I. BILYK, Z. ZÁHOŘ and V. CZABANOVA

Department of Clinical Chemistry of the Charles University, Institute of Pathology of the Charles University, Praha 2 (Czechoslovakia), 1 June 1971.

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## The Influence of the Hypophysis upon the Calorigenic Action of Catecholamines

The calorigenic effects of epinephrine were detected in dogs by BELAWENEZ in 1903<sup>1</sup>. In the following decades it could be demonstrated by many investigators that the calorigenic action is a general property of other catecholamines, too, being present in laboratory animals as well as in man (reviews<sup>2-4</sup>).

The mechanism of the calorigenic action of the catecholamines could not be clarified exactly until now; nevertheless there are important investigations showing that calorigenic effects of catecholamines are not influenced by  $\alpha$ -sympathicolitics<sup>5</sup> but completely abolished by  $\beta$ -sympathicolitics<sup>6</sup>. Moreover, it is of great interest that the calorigenic action of catecholamines strongly depends on age<sup>7-10</sup>. Norepinephrine increases oxygen con-

sumption in 20-day-old rats maximally by about 300% compared with the control level, while showing less effects in 60-day-old rats (increase of 50% only).

In regard to the age dependence of the calorigenic action of catecholamines, a role of growth hormone in calorigenic responses to sympathicomimetics is supposed. Therefore

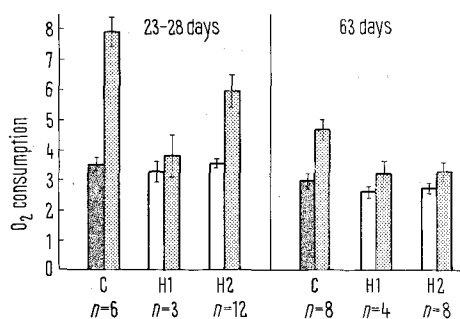


Fig. 1. Influence of norepinephrine (0.6 mg/kg body wt.) upon oxygen consumption (ml/min/100 g body wt.  $\pm$  S.E.M.) in 23-28- and 63-day-old control and hypophysectomized rats. C, control rats; H1, rats with complete hypophysectomy (checked by craniotomy after experiment); H2, all hypophysectomized rats included rats with pituitary residues.  $\blacksquare$  oxygen consumption before administration of norepinephrine in control resp. hypophysectomized rats;  $\square$  oxygen consumption after administration of norepinephrine.

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<sup>8</sup> D. MÜLLER and H. ANKERMANN, *Acta biol. med. germ.* **23**, 819 (1969).

<sup>9</sup> D. MÜLLER and H. ANKERMANN, *Acta biol. med. germ.* **24**, 673 (1970).

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experiments in hypophysectomized rats<sup>11</sup> have been carried out. 5 days after hypophysectomy, norepinephrine was administered s.c. in doses markedly effective in control rats. In these animals norepinephrine failed to increase oxygen consumption (Figure 1), whereas the enhancement of cardiac frequency remained unchanged. The calorogenic effects of 2,4-dinitrophenol showing no age-dependent

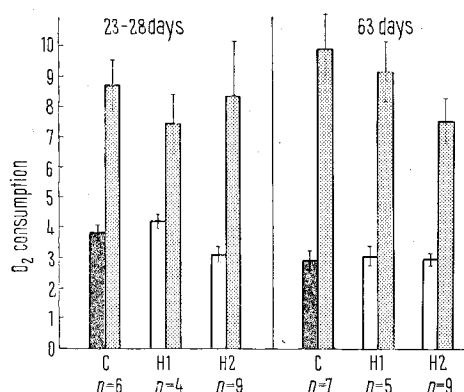


Fig. 2. Influence of 2,4-dinitrophenol (30 mg/kg body wt.) upon oxygen consumption (ml/min/100 g body wt.  $\pm$  S.E.M.) in 23-28- and 63-day-old control and hypophysectomized rats. oxygen consumption before administration of 2,4-dinitrophenol in control resp. hypophysectomized rats; oxygen consumption after administration of 2,4-dinitrophenol. Further explanations as in Fig. 1.

changes after the 20th day of life and not being annulled by  $\beta$ -sympathicolitics<sup>10</sup>, was hardly impaired by hypophysectomy (Figure 2).

Apparently the hypophysis is essential for the calorogenic action of sympathicomimetics, whereas other  $\beta$ -sympathicomimetic effects, as well as the calorogenic effects of substances acting otherwise, are not influenced by hypophysectomy.

Considering the age dependence of the calorogenic action of catecholamines, it may be suggested that among pituitary hormones the participation of growth hormone in metabolic responses to catecholamines is of especial importance. Further investigations will be undertaken concerning these problems.

**Zusammenfassung.** Durch Hypophysektomie wird die kalorogene Wirkung von Noradrenalin bei 23-28 sowie 63 Tage alten Ratten fast vollständig aufgehoben, während die Wirkung von 2,4-Dinitrophenol kaum beeinflusst wird.

H. ANKERMAN, F. W. TILLER, L. KERSTEN and D. MÜLLER

*Institut für Pharmakologie und Toxikologie der Friedrich-Schiller-Universität Jena, Zentraler Platz, 69 Jena (DDR), 18 October 1971.*

<sup>11</sup> F. E. D'AMOUR and R. R. BLOOD, *Manual for Laboratory Work in Mammalian Physiology* (University of Chicago Press, Chicago 1956).

## Effects of Testosterone-Stimulated Glycogen Synthesis in the Mouse Salivary Glands and 5-Fluorouracyl Inhibition

Since LACASSAGNE's<sup>1</sup> discovery of sex dimorphism in the mouse salivary gland, it appears to be well established that hormones have some effects on salivary gland morphology and metabolism<sup>2,3</sup>. Several investigators have found stimulatory effects of androgenic drugs on salivary glands of rats and mice<sup>4</sup>. On the other hand, the inhibitory effect of actinomycin, puromycin and 5-fluorouracyl on hormone stimulated growth of specific target tissues suggested the possibility of a more interesting study of testosterone-stimulated effect on organs other than the target organs<sup>5,6</sup>.

**Material and methods.** 3-week-old male A2G mice weighing 20 to 30 g were used. Mice were castrated bilaterally under ether anaesthesia. The influence of testosterone-stimulated glycogen synthesis and 5-fluorouracyl inhibition was investigated in 3 groups of castrated mice: 1. control mice; 2. testosterone-treated mice; 3. Testosterone-injected mice given 5-fluorouracyl. Animals from each group were sacrificed at 12, 24 and 48 h after administration of the last drug. Testosterone propionate (Lab. Gador, Buenos Aires) was injected in a single dose of 10 or 5 mg each 100 g body weight. 5-Fluorouracyl (15 mg/100 g b.w.) was injected 30 min prior to the hormone. The salivary glands were excised immediately and cleaned. The tissues were weighed and immersed in 30% boiling KOH.

Glycogen was determined by the method of ROE and DAILY<sup>7</sup>. The glycogen pellet was washed with 80% methyl alcohol with 0.1% LiCl and dissolved in water with an adequate internal standard.

**Results and discussion.** There are changes produced in the glycogen concentration in the submaxillary and parotid gland after a single injection of testosterone propionate. Testosterone increased salivary glycogen at 24 h to 200% as compared with the control mice. The effect of 5-FU administration on salivary glands under testosterone treatment is indicated by the data in the Table. In these experiments, both doses of testosterone caused an increase in glycogen in submaxillary and parotid gland. Similar inhibitory effect as on seminal vesicles was observed when 5-FU was given before to testosterone. After the classic investigations by LACASSAGNE<sup>1</sup> and his co-workers, other laboratories succeeded in establishing that endocrine glands are influential in the structural and biochemical configuration of the salivary glands of mice. JUNQUEIRA and TOLEDO<sup>4</sup> observed a significant increase in the protease activity in rat salivary glands by androgens. In addition,

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