db mice, from 5.8 to 3 g. The effect of propylene glycol alone on db/db mice on the first day after the injection was approximately as great as that of the steroid in propylene glycol. However, the return to hyperphagia in glycol injected mice occurred rapidly over the next 2 days whereas food consumption in db/db mice injected with androstanolone remained at the depressed level (about 3 g per day) for 3 more days.

Enlargement of seminal vesicles was evident in mice fed 1% androstanolone, whereas their livers appeared essentially normal in contrast to the enlarged fatty livers of ob/ob, db/db, or goldthioglucose-treated controls. Rates of fatty acid synthesis from acetate-1-^{14}C determined as described previously[2] in liver slices from young, moderately obese ob/ob, or db/db mice fed 1% androstanolone for 1 to 2 weeks were 30 to 80% lower than values for ob/ob and db/db controls. However, in untreated ob/ob and db/db mice rates of lipid synthesis from acetate per g liver declined with increasing obesity. This decline was counteracted by dietary androstanolone to such a degree that rates of lipid synthesis in older treated ob/ob or db/db mice were often equal to or higher than values for untreated controls. Rates at which ^{14}C from either glucose-U-^{14}C or acetate-1-^{14}C appeared in the respiratory CO_2 of ob/ob and db/db mice were not significantly affected by the administration of a diet containing 1% androstanolone over a period up to 6 weeks. Blood sugar concentrations were stabilized at normal levels (140 to 150 mg/100 ml) in db/db mice fed 1% androstanolone whereas concentrations in untreated db/db controls rose to above 450 mg/100 ml as shown previously[3]. Blood sugar concentrations in untreated ob/ob controls were moderately elevated (200 to 300 mg/100 ml) and were normal or hypoglycemic (110 to 160 mg/100 ml) in ob/ob mice fed adrostanolone.

Although dietary androgens may affect body weight by altering metabolism-including protein and lipid metabolism – it seems likely that the marked weight losses as well as most of the metabolic alterations detected in mice fed androstanolone in the present studies were secondary to the dramatic and rapid reduction in food consumption. However, any attempt to account for the effect of androstanolone on the level of food intake must be speculative since we are not aware of any information bearing upon this question other than a finding that progesterone and estrogen influence food consumption in female rats[4,5]. It is possible that each of the three types of obesity involves some deficiency of the hypothalamic system as has been proposed for db/db mice[6]. Androstanolone may affect food consumption in these mice by raising the concentrations of circulating factors high enough to stimulate a relatively insensitive satiety center. Alternatively, it is conceivable that androstanolone acts directly upon neurons in the lateral or ventromedial hypothalamus to lower their threshold to satiety factors already present in the circulation[7].

Zusammenfassung. Es konnte gezeigt werden, dass die Gewichtszunahme bei genetisch oder durch Goldthioglukose induzierter Fettsucht von Mäusen durch Androstanolol oder Testosteron verhindert werden kann.

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The Effect of Calciferol, Parathormone and Calcitonin on the Biochemical Composition of Kidney

The influence of vitamin D and parathormone on the metabolic processes in kidneys, especially on calcium, phosphorus and citric acid, is a well known fact. The third factor which plays a role in the homeostasis of calcium is calcitonin. There is no agreement concerning its effect on the kidney and on the excretion of calcium, its main direct influence being that on the bone [1–5]. In our present paper we tried to compare the effects of all three calcium-influencing factors on the amount of calcium, phosphorus and citric acid in the different parts of the kidneys.

Material and method. 134 intact male rats of the Wistar strain (150–160 gg) were on a low calcium diet (wheat grain Ca 0.07%) 4 days previous to the experiment. 70 rats served as controls, of which 25 animals received, in case of the experiment with vitamin D, the corresponding dose of sunflower oil, 25 as controls for parathormone, 0.5 ml of

Table I. Values of citric acid, calcium and phosphorus in the serum

		Citric acid (mg/100 ml)	Calcium (mg/100 ml)	Phosphorus (mg/100 m
Controls		5.50 ± 0.54	10.8 ± 0.41	7.5 ± 0.55
Calciferol	300,000 U	6.67 ± 1.15[a]	12.4 ± 0.31[a]	9.2 ± 0.77[a]
	600,000 U	9.75 ± 1.2[a]	12.8 ± 0.33[a]	7.6 ± 0.56
	900,000 U	9.12 ± 0.82[a]	12.8 ± 0.53[a]	7.7 ± 0.12
Parathormone (20 U)	1 h	7.70 ± 0.21[a]	10.3 ± 0.68	5.7 ± 0.59[a]
	3 h	6.90 ± 0.33[a]	10.2 ± 0.26	6.2 ± 0.36[a]
Calcitonin	30 min	4.38 ± 0.49[a]	9.4 ± 0.50[a]	7.0 ± 0.29
12 HIRSCH U. = 1,2 MRC U.	60 min	4.77 ± 0.34[a]	8.1 ± 0.44[a]	5.7 ± 0.33[a]
2 × 12 HIRSCH U.	60 min	5.23 ± 0.11	7.2 ± 0.61[a]	6.4 ± 0.25[a]

[a] Statistical significance $P < 1\%$.

Table II. Values of citric acid, calcium and phosphorus in kidneys

	Time	Dose	No. of animals	Citric acid (μg/g wet. wt.) Cortical zone	Intermed. zone	Papillary zone	Calcium (mg/g wet wt.) Cortical zone	Intermed. zone	Papillary zone	Phosphorus (mg/g wet wt.) Cortical zone	Intermed. zone	Papillary zone
Controls			70	40.3 ± 5	63.3 ± 8	137 ± 20	0.132 ± 0.015	0.414 ± 0.054	1.32 ± 0.22	0.451 ± 0.033	0.492 ± 0.043	0.494 ± 0.072
Calciferol	2 days	300,000 U	8	43.9 ± 2	47.4 ± 2[a]	109 ± 7[a]	0.124 ± 0.007	0.456 ± 0.058	1.97 ± 0.23[a]	0.486 ± 0.002[b]	0.527 ± 0.033[a]	0.537 ± 0.061
Calciferol	4 days	600,000 U	6	78.9 ± 5[a]	273.0 ± 98[a]	239 ± 6[a]	0.174 ± 0.0[a]	0.831 ± 0.032[a]	2.13 ± 0.44[a]	0.531 ± 0.06[a]	0.785 ± 0.017[a]	0.733 ± 0.044[a]
Calciferol	6 days	900,000 U	7	93.1 ± 9[a]	175.0 ± 85[a]	483 ± 3[a]	0.197 ± 0.031[a]	0.669 ± 0.10[a]	1.66 ± 0.10[a]	0.711 ± 0.01	0.809 ± 0.12[a]	0.627 ± 0.097[a]
Calciferol	4–6 days	600,000–900,000 U	2	172.0	492.0	475.0	1.120	4.36	1.71	0.943	2.54	0.738
			1	341.0	1010.0	357.0	3.820	11.40	2.70	1.012	6.35	1.480
			Nephro-calcinosis	386.0	870.0	720.0	1.640	5.90	2.80	1.785	2.50	1.060
Parathyroid extract	1 h	20 U	8	55.6 ± 5[a]	90.7 ± 10[a]	261 ± 31[a]	0.183 ± 0.025[a]	0.794 ± 0.076[a]	2.07 ± 0.65[a]	0.457 ± 0.011	0.491 ± 0.01	0.581 ± 0.035[b]
Parathyroid extract	3 h	20 U	8	49.7 ± 4	110.0 ± 13[a]	484 ± 28[a]	0.160 ± 0.006[a]	0.403 ± 0.047	1.51 ± 0.11	0.416 ± 0.022[b]	0.524 ± 0.009	0.398 ± 0.053[a]
Calcitonin	30 min	12 Hirsch U 1.2 MRC U	8	33.1 ± 1[a]	65.7 ± 6	139 ± 25	0.103 ± 0.005[a]	0.339 ± 0.057[a]	1.20 ± 0.12	0.438 ± 0.010	0.488 ± 0.049	0.375 ± 0.027[a]
Calcitonin	1 h	12 Hirsch U 1.2 MRC U	8	40.8 ± 6	63.6 ± 8	119 ± 7[b]	0.105 ± 0.009[a]	0.341 ± 0.042[a]	1.18 ± 0.14	0.433 ± 0.012	0.434 ± 0.010[a]	0.418 ± 0.011[a]
Calcitonin	1 h	2×12 Hirsch U 2× 1,2 MRC U	8	31.0 ± 3[a]	61.3 ± 5	116 ± 16[b]	0.121 ± 0.013	0.316 ± 0.033[a]	0.92 ± 0.05[a]	0.425 ± 0.022	0.474 ± 0.076	0.287 ± 0.014[a]

[a] Statistical significance on the 1% level; [b] Statistical significance on the 5% level

phenol (0.2%); in the experiment with calcitonin 20 rats received the corresponding dose of acetate buffer pH 3.8. The amounts of calcium, phosphorus and citric acid did not differ considerably in any group and therefore all the control animals were looked upon as one control group. The experimental animals were divided in 3 main groups. First group (24 rats) received calciferol (Spofa) 150,000 U pro dosi in an i.m. injection. The total amount administered was 300,000 U during 2 days, 600,000 U in 4 days and 900,000 U in 6 days. Second group (16 animals) received 20 U of parathyroid extract (Lilly). 8 of these rats were sacrificed 1 h after the injection, 8 after 3 h. The third group was trated with calcitonin prepared in our laboratory according to HIRSCH[6]. 8 rats were killed 30 min after the application, 8 after 1 h and the last group received the repeated dose in the course of 120 min and was sacrificed 1 h after the last injection.

Blood from the control and experimental animals was collected by heart puncture and both kidneys were immediately removed and washed in cold saline solution. No perfusion was made prior to the extraction because in some of our previous experiments we found that the amounts of estimated compounds were within the errors of the methods with or without perfusion used. The kidneys were then dissected into 3 parts: a) the 'cortical' zone, containing the outer cortical zone and a variable part of inner cortical zone according to MCFARLAN[7], b) the 'intermedial' zone, containing the rest of inner cortical zone and the whole outer medullary zone, c) the 'papillary' zone, containing the whole inner medullary zone. After weighing, the tissue was extracted in 10% (v/v) trichloroacetic acid. Calcium[8], phosphorus[9] and citric acid[10] contents were determined in the sera and in the different parts of the kidneys.

Results and discussion. In Table I and II the data in the serum and kidneys are summarized. The values found in the serum are in accordance with previous findings. In the kidneys, the effect of vitamin D on the accumulation of calcium[11], phosphorus and citric acid[12] was expected and described in several papers. We have only contributed to this problem by the finding that all parts of the kidneys are attacked. Of some interest may be the initial decrease of citric acid after the smallest dose of vitamin D, which means a disproportion between the amount of this acid and calcium. In later days, the biochemical findings of even apparently intact animals indicate that the full development of nephrocalcinosis – which we found in 3 rats – depends on the time, dose and the individual sensitivity of the single animals.

In rats which were given parathormone, a considerable enhancement of citric acid and calcium occurred in all parts of the kidneys after 1 h, whereas after 3 h only changes of the citric acid level in deeper parts were more pronounced.

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In our previous paper, we have described an increase in the citric acid level in the whole kidney[13]. 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 surprizing 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[14–16]. 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[17]. 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.

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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[1]. 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[2–4]).

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 α-sympathicolytics[5] but completely abolished by β-sympathicolytics[6]. Moreover, it is of great interest that the calorigenic action of catecholamines strongly depends on age[7–10]. Norepinephrine increases oxygen consumption 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

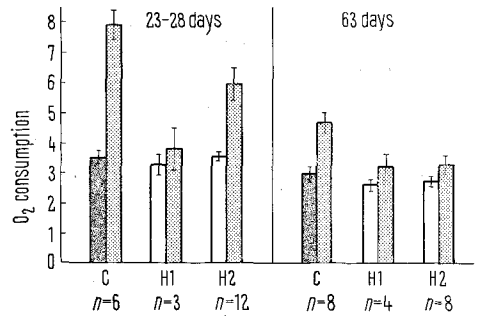

Fig. 1. Influence of norepinephrine (0,6 mg/kg body wt.) upon oxygen consumption (ml/min/100 g body wt. ± S.E.M.) in 23–28- and 63-day-old control and hypophysectomized rats. C, control rats; H1, rats with complete hypophysectomy (checked by craniotomy after experiment); H2, all hypophysectomized rats included rats with pituitary residues. ▩□ oxygen consumption before administration of norepinephrine in control resp. hypophysectomized rats; ⁞⁞ oxygen consumption after administration of norepinephrine.

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