ficant ($p < 0.01$). Release by Group 3 animals was not different from Group 2 rats. If however, release is expressed per gram of tissue nitrogen, the statistical significance of the differences disappear.

Table I indicates that the presence of epinephrine did not change the release significantly in Groups 1 and 2, and it increased release in Group 3. Occosional increases were noted in all groups but they failed to occur consistently enough in Groups 1 and 2, reach statistical significance.

The triglyceride content per weight of adipose tissue of Group 1 rats was lower than that of Group 2 and 3 animals. No significant differences existed between the latter two groups (Figure 2). Differences in triglyceride content among the groups became more marked when expressed per gram of tissue nitrogen.

Tab. I. Release of FFA by epidymal adipose tissue of nephrotic rats in the absence and presence of epinephrine (μEq/g/h)

	Group 1	Group 2	Group 3
Weight in g	<100	200–300	350–475
Age, days	30	90–120	120–180
Release without epinephrine	19.78 ± 3.56[a] N = 22	7.67 ± 1.53[a] N = 14	7.92 ± 1.25[a] N = 27
Release with epinephrine	30.4 ± 4.82[a] N = 22	12.26 ± 2.35[a] N = 14	12.42 ± 1.13[a] N = 27

[a] S.E.

Tab. II Release of FFA by different adipose tissues of nephrotic rats (μEq/g/h)

	Group 1	Group 2	Group 3
Weight in g	<100	200–300	350–475
Age, days	30	90–120	120–180
Epididymal adipose tissue	24.05 ± 2.96[a] N = 22	7.67 ± 1.53[a] N = 14	7.92 ± 1.25[a] N = 27
Mesenteric adipose tissue	17.69 ± 2.24[a] N = 21	7.21 ± 1.44[a] N = 12	8.59 ± 0.85[a] N = 25
Perirenal adipose tissue	–	10.99 ± 1.89[a] N = 13	9.27 ± 1.02[a] N = 25

[a] S.E.

The FFA content of epididymal adipose tissue was higher in the Group 1 animals than in Group 2 or 3 rats (Figure 3). No consistant difference was found in adipose tissues FFA level after incubation in any of the three groups.

In Table II the release of FFA by epididymal, mesenteric and perirenal adipose tissue is compared in nephrotic rats of different ages (not enough perirenal adipose tissue was found in Group 1 rats to perform the analyses). Group 1 rats released the most FFA both from epididymal and mesenteric adipose tissues. No difference was noted between Groups 2 and 3 in any tissue.

Discussion. The findings that the release of FFA by the epididymal adipose tissue of nephrotic rats is different in young and old rats is similar to results reported previously in normal rats[4]. No significant differences were found between normal and nephrotic rats in this respect. The presence of epinephrine caused a more consistant increase in release by all Groups of rats using normal animals than using nephrotic ones.

Adipose tissue triglyceride content of nephrotic rats was significantly higher in Group 1 and lower in Group 3 than in normal animals. The cause of this difference is presently not known. The diminished triglyceride content in the adipose tissue of Group 3 rats is in agreement with MALMENDIER's finding[5] that grown nephrotic rats have less total body fat than have normals of the same weight.

The lack of difference in release of FFA by the adipose tissue between normal and nephrotic rats seems to be in accord with the current view[5,6], that the primary change in causing nephrotic hyperlipemia is an increased lipid output by the liver and not by the adipose tissue.

Zusammenfassung. Bei nephrotischen Ratten verschiedenen Alters wurde *in vitro* die Abgabe freier Fettsäuren aus dem Fettgewebe untersucht. Bei jungen Tieren war letztere am grössten, der Fettgehalt des Gewebes am niedrigsten. Diese Resultate stimmen mit an normalen Tieren gewonnenen überein und stützen die Ansicht, dass die nephrotische Lipämie nicht durch Mobilisation des Depotfettes entsteht.

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Altered Vascular Reactivity of Rats with Adrenal-Regeneration Hypertension[1]

Since the description of hypertension developing in rats subjected to adrenal enucleation following contralateral nephrectomy and adrenalectomy (AR–HT)[2] efforts have been made to determine the possible hormonal influence at work[3] and to define the state of adrenal steroid secretion[4]. The nature of the vascular lesions in AR–HT have been studied[5] and their prevention[6], to-

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gether with the changes in tissue electrolytes which are associated with the development of AR–HT[7] and its treatment[8]. Few observations have been described on the response of the cardiovascular system in AR–HT to vaso-active drugs. The experiments briefly reported in this paper were made for this purpose. The results suggest that a qualitative difference in vascular reactivity appears early in the course of AR–HT.

Material and Methods. One hundred and twenty Wistar rats weighing 150 to 250 g were subjected to right nephrectomy and adrenalectomy and to left adrenal enucleation[2]. They were subsequently maintained on 1% sodium chloride solution. The behaviour of the blood pressures as measured by tail plethysmography and of the regenerating adrenal did not differ significantly from previous descriptions[2,6]. Forty-nine animals died following operation or during anaesthesia, or were unsuitable as preparations for study.

The remaining rats were divided into 4 groups and studied at intervals of 7–10 days (group I–24 rats), 14–17 days (group II–15 rats), 25–30 (group III–17 rats) and 56–60 days (group IV–20 rats) after the operation. The rats were anaesthetized with intraperitoneal pentobarbitone sodium (Nembutal), 5–7 mg 100 g. The blood pressure was recorded on a kymograph from the cannulated right carotid artery and injections were made into the cannulated left femoral vein. It was not always possible to inject each animal with all the drugs selected for study. The drugs used were vasopressin (Pitressin-Parke, Davis), oxytocin (Syntocinon-Sandoz), val 5-hypertensin II-asp-β-amide (Hypertensin-Ciba), acetylcholine (Roche), adrenaline (Parke, Davis), noradrenaline (Levophed-Bayer), dihydroergotamine (Sandoz) and atropine sulphate.

Results. Adrenaline: No sensitization to adrenaline (0.1 µg) in AR–HT was observed and the carotid blood pressure response of both males and females at each of the 4 periods of observation tended to fall to or below the normal minimum range of response (Table I). A striking qualitative difference in reaction was established. Instead of the usual monophasic pressor response to adrenaline, there developed a triphasic response in which a sharp rise in pressure was followed by a fall back to or beyond the baseline and by a smaller secondary rise. This triphasic response was observed in all groups of males but was less frequent among the rats of groups II and III. Females reacted triphasically less frequently than males. In group III, however, the female response was never triphasic (Table II).

Noradrenaline: No evidence of increased responsiveness to noradrenaline (0.08 µg) was obtained. In both male and female rats, there was no significant quantitative difference in reaction. However, an important qualitative difference was present. In group I, each of the 12 males and 6 of the 12 females gave a diphasic response, a preliminary fall in blood pressure being followed by a rise. In group IV, by contrast, only 2 of 12 males and 2 of 8 females responded diphasically. The initial depressor phase was never influenced by bilateral vagotomy but was always suppressed by atropine. It was concluded that the initial noradrenaline-induced depression was not vagally mediated but depended upon a peripheral cholinergic mechanism, presumably the sympathetic cholinergic vasodilators to skeletal muscle blood vessels.

Hypertensin: No qualitative or quantitative differences in response to 0.05 µg hypertensin from normal were found in any group in both sexes. As in normal rats, there was no relationship between the height or duration of the response and the initial blood pressure level. After dihydroergotamine (DHE) and atropine the responses to hypertensin were increased but were not greater than those of normal rats after these blocking agents.

Acetylcholine: No quantitative difference in response to acetylcholine (0.001 µg) was found in either male or female rats. An occasional increase in the size of the depressor response was seen in each group and in both sexes.

Vasopressin: The sensitivity of the vasculature to vasopressin has been shown to depend in both sexes upon

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Tab. I. The size of the pressor response to intravenous adrenaline (0.1 µg) in the adrenal-regeneration hypertensive female rat

Group	Postoperative interval (in weeks)	Males No. of rats used	Males Range of response in mm Hg	Females No. of rats used	Females Range of response in mm Hg
	Normal	10	10–28	15	10–35
I	1	10	4–18	9	3–20
II	2	7	6–12	7	3–23
III	4	7	5–26	9	5–21
IV	8	10	6–32	8	8–23

Tab. II. The response of adrenal-regeneration hypertensive rats to intravenous adrenaline (0.1 µg)

Group	Postoperative interval (in weeks)	Males No. of rats showing triphasic response	Males No. of rats showing monophasic response	Females No. of rats showing triphasic response	Females No. of rats showing monophasic response
I	1	7/10	3/10	1/9	8/9
II	2	3/7	4/7	2/7	5/7
III	4	3/7	4/7	–	9/9
IV	8	8/10	2/10	5/8	3/8

the hormonal background[9–11]. In the present study the vascular sensitivity to the drug was determined in terms of the dose per 200 g body weight required to raise the blood pressure by 10 mm Hg. In normal males 0.8–1.2 mU/200 g proved adequate. In the hypertensive animals of group I 1.4–3 mU/200 g was required to produce the standard response. In the remaining groups a smaller dose than normal (0.01–0.8 mU/200 g) was adequate. These changes in sensitivity were rarely associated with prolongation of the pressor response.

Normal female rats required 0.25–0.5 mU/200 g for the 10 mm Hg rise in pressure. In group I larger doses were needed (0.75–2 mU/200 g) whereas in group II smaller amounts were adequate (0.025–0.2 mU/200 g). After 4 weeks, however, the female rats again required larger doses of vasopressin, the amounts being 0.6–1.5 mU/200 g in group III and 0.7–1.4 mU/200 g in group IV.

In all groups of both sexes a preliminary fall in pressure after the injection of vasopressin preceded the pressor effect. This diphasic pattern was most common in group I, in which it was observed in each of the 12 males and in 8 of the 12 females. In every instance DHE failed to delete the depressor phase and occasionally enhanced it. Atropine given before or after DHE regularly abolished the depressor phase but bilateral vagotomy did not interfere with it. It was concluded that the depressor component was not mediated by sympathetic vasoconstrictor fibres and was similar to that induced by noradrenaline, being dependent upon some peripheral cholinergic mechanism. The pressor component was always enhanced by DHE but was enhanced, unaffected or even depressed by atropine.

Oxytocin: Like vasopressin, oxytocin exhibits vascular effects in the rat depending upon its hormonal status[9–11]. In the normal male and normal dioestrous female 100 mU oxytocin has no effect on the blood pressure trace although mesenteric vascular dilatation can be observed under direct vision. In the oestrous female the same dose of oxytocin produces a transient rise in blood pressure, while any interference with the sympathetic system converts oxytocin into a pressor substance[10].

In the present experiments the responses to 100 mU oxytocin were observed. Three patterns were obtained: (1) monophasic depressor; (2) monophasic pressor and (3) diphasic (depressor-pressor). In males, there was a predominance of the depressor response in groupe I (8 of 12 rats), of the pressor response in group III (7 of 8 rats) and again of the depressor response in group IV (7 of 9 rats). In females, the reaction was more variable. In groups III (8 of 9 rats) and IV (5 of 8 rats) oxytocin was predominantly pressor.

The monophasic depression and the preliminary depression in the diphasic pattern were not abolished by DHE or by bilateral vagotomy but were always suppressed by atropine. The depressor response to oxytocin, like those induced by vasopressin and by noradrenaline, was dependent upon a peripheral cholinergic mechanism. As in normal males and females, DHE enhanced the pressor component if already present or led to its appearance. Atropine caused further enhancement. The phase of the sexual cycle at the time of the experiment did not alter the response of the female hypertensive rat to oxytocin. No potentiation of the pressor response to oxytocin in the oestrous rat was seen.

Conclusions. During the development of adrenal-regeneration hypertension the pattern of vascular response to noradrenaline, adrenaline, vasopressin and oxytocin is changed but the response to hypertensin and to acetylcholine is unaltered. The change in pattern differs at different phases of the hypertensive state. With the exception of vasopressin, there is no increase in pressor reaction. The altered responses are presumably mediated by the endocrine disorder accompanying this form of experimental hypertension.

Résumé. La forme d'hypertension qui accompagne la régénération de la glande surrénale énucléée à été étudiée chez les rats. Au cours de l'évolution de l'hypertension, la réaction vasculaire à la noradrénaline, l'adrénaline, la vasopressine et l'ocitocine est modifiée de manière qualitative, mais les effets vasculaires de l'hypertensine et de l'acétylcholine restent inchangés. Ces modifications diffèrent selon la phase de développement de l'hypertension. Hormis la vasopressine, les agents hypertenseurs ne sont pas plus actifs. Ces changements reflètent en toute probabilité le déséquilibre hormonal lié à ce type d'hypertension.

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The Effect of Nandrolone Decanoate upon the Alkaline Phosphatase of the Adrenal Cortex of the Mouse

The sexual dimorphism in the distribution of alkaline phosphatase in the adrenal cortex of the adult mouse has been previously reported[1]. This enzyme occurs in a marked concentration in the cells of the fascicular and reticular zones of the adrenal cortex of the male mouse. It is absent, or present only in traces, in the female. Castration abolishes activity of alkaline phosphatase in the male; and the treatment with testosterone results in the reappearance of the activity after castration.

It has been considered that testosterone has two main effects on the living body: the virilising and the anabolic. Many other steroids possess both of these effects too, though they are proportionally very different in various compounds. Thus, the virilising effect of nandrolone decanoate is very weak, but it is, on the other hand, regarded as an extraordinarily powerful anabolic agent.

The purpose of this study was to analyse the mode of action of testosterone on the mouse adrenal cortex: whether the effect produced by it is due to the virilising or to the anabolic 'factor'. It was performed by comparing the effect of testosterone propionate and nandrolone decanoate on adrenocortical alkaline phosphatase of the mouse.

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