of reference 6β-hydroxy-4-androstene-3,17-dione. Percentage formation of steroids from 4-$C^{14}$-testosterone by placental tissue is summarized in Table II.

*Discussion.* From these results it is apparent that the only pathway for the metabolism of testosterone by the mouse placenta is via reduction to 5α-androstane derivatives, namely to: 3α-hydroxy-5α-androstan-3,17-dione, 3β-hydroxy-5α-androstan-3,17-dione and 5α-androstane-3,17-dione. The failure of mouse placental tissue to aromatize 4-$C^{14}$-testosterone suggests that the placenta of mouse is probably not a source of estrogens. These results are in agreement with our previous observations that 4-androstene-3,17-dione formed by mouse placentae from progesterone and pregnenolone was not converted to estrogens[1]. However, VINSON and JONES[4] reported that phenolic compounds appeared when fetal tissue was incubated with progesterone. These observations provide suggestive evidence that the fetus may convert placental androgens to estrogens. This problem is under study in our laboratory.

Table II. Distribution of radioactivity in metabolites isolated following incubation of mouse placental tissue with 4-$C^{14}$-testosterone

| Metabolite identified | Conversion (%) |
|---|---|
| Testosterone | 1.65[a] |
| I | 12.32[b] |
| 4-Androstene-3,17-dione | 2.27 |
| 3α-Hydroxy-5α-androstan-3,17-dione | 43.58 |
| 3β-Hydroxy-5α-androstan-3,17-dione | 8.78 |
| 5α-Androstane-3,17-dione | 12.41 |

The results are expressed as percentage conversion of incubated substrate following recrystallization of the isolated metabolite to constant specific activity. [a] Percentage of substrate remaining following incubation. [b] Percentage conversion was calculated by eluting radioactive peak present on chromatograms.

*Zusammenfassung.* 4-$C^{14}$-Testosteron wurde durch Mäuseplazenta in vitro zu Steroiden umgesetzt: 3β-Hydroxy-5α-androstan-3,17-dion, 3α-Hydroxy-5α-androstan-3,17-dion, 4-Androsten-3,17-dion und 5α-Androstan-3,17-dion. Eine Umsetzung von Testosteron zu Östrogenen wurde nicht nachgewiesen.

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## Varying Degrees of Ventromedial Hypothalamic Destruction in the Weanling Rat and its Effect on Plasma Triglyceride and Cholesterol Levels[1]

Recent studies[2] have shown that bilateral lesions in the area of the ventromedial hypothalamic nucleus (VMN) in weanling rats resulted in hypertriglyceridemia and hypercholesterolemia despite normophagia. The results of these studies suggested that the hypothalamic area involved in the regulation of plasma triglyceride levels is more circumscribed than that involved in the regulation of cholesterol. They also raised the question of whether or not a greater response to destruction required involvement of areas outside the VMN. To examine this question, two experiments were performed, each with three groups of animals. In one group, a small lesion, produced by a single electrolytic focus, was placed bilaterally in the VMN. In a second group, an anteroposterior series of closely-spaced lesions, each of a size comparable to that of the single foci in the previous group, were placed bilaterally in order to destroy a greater longitudinal extent of the VMN while avoiding destruction medial and lateral to these nuclei. A third group of animals served as sham-operated controls.

All methods (operational procedures, maintenance of animals, duration of experiment, and lipid determinations) have been described previously[2]. The lesions were produced in experiment 1 with a current of 1.0 mAmp flowing for 3 sec (3 m-Coulombs), and in experiment 2 with a current of 1.0 mAmp flowing for 4 sec (4 mC). The lesion analysis has been described previously[3] and visualizes the destroyed area common to all rats of each

Experimental data on rats with pairs of single electrolytic lesions ( (Group 2) and triple lesions (Group 3) in the ventromedial hypothalamic nuclei compared with their sham-operated controls (Group 1)

| Group (N) | Change in body wt. (g) | Change in body length (mm) | Food intake (g/day) | Lee index[b] | Plasma triglyceride (mg/100 ml) | Plasma cholesterol (mg/100 ml) |
|---|---|---|---|---|---|---|
| 1 (16)[d] Control | 74.0 ± 3.6[a] | 60.2 ± 2.7 | 19.7 ± 0.5 | 309.4 ± 1.6 | 49.4 ± 3.4 | 87.8 ± 2.7 |
| 2 (15) Single lesion | 57.8 ± 4.4 | 52.7 ± 3.0 | 14.0 ± 0.6 | 313.7 ± 1.2 | 60.3 ± 5.1 | 89.0 ± 2.8 |
| 3 (30) Triple lesion | 79.0 ± 4.5 | 53.5 ± 2.6 | 21.8 ± 0.7 | 318.9 ± 1.9 | 76.9 ± 5.6 | 98.1 ± 2.4 |
| | Statistical significance | | | | | |
| 1 vs 2 | 0.01[c] | | | 0.05 | | |
| 1 vs 3 | | | | 0.01 | 0.01 | 0.02 |
| 2 vs 3 | 0.01 | | 0.02 | | | 0.05 |

[a] Mean ± S.E.M. [b] Lee index, cube root of body weight (g)/naso-anal length (mm) × 10,000. [c] $p <$; no notation when value is not significant. [d] (), refers to the number of animals per group.

respective group. Since the size and the extent of the lesions were indistinguishable for the two experiments, the findings in both experiments were pooled, as presented in the Table.

The data show that small bilateral, single-focus lesions (Group 2) produced no elevation in the plasma level of either triglyceride or cholesterol. Triple-focus lesions (Group 3) produced elevations of both triglycerides (36% increase, $p < 0.01$) and cholesterol (13% increase, $p < 0.02$). It is noteworthy that the lipid elevations in the two groups of rats with hypothalamic lesions were not associated with increased food intake. In fact, the plasma cholesterol levels in Group 3 showed a negative correlation with food intake ($r = -0.44$, $p < 0.05$). Body weight, length and obesity index have been included for comparison with previous findings[4-6].

The data indicate that lesions, entirely within the VMN, produced elevations in triglyceride and cholesterol levels and extension outside the VMN was not necessary to obtain an effect. However, as shown in our original study[2], the 'cholesterol area' appears to extend beyond the VMN into the dorsal and lateral areas.

*Zusammenfassung.* Es wurden ein- und dreipaarige elektrolytische Läsionen in den ventromedialen Kernen von Ratten gesetzt, wobei es zu einer Erhöhung von Triglyceriden und Cholesterin kam. Dieses Hypothalamus-Gebiet enthält Regulationszentren des Serumlipidspiegels.

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## The Threshold Osmotic Reactivity of the Hypothalamo-Hypophyseal Antidiuretic System and of the Thirst Mechanism

There is evidence that the hypothalamo-hypophyseal antidiuretic system and the thirst mechanism are both activated by an increase of extracellular fluid osmolality[1-4]. In our previous study[5], we found that a moderate increase of blood ADH level decreases the thirst threshold for osmotic stimuli and thus facilitates water intake. The question arose which of these two systems regulating water balance in the body is first activated due to increasing cellular dehydration. This problem has not yet been examined thoroughly. Wolf[4,6] suggested that osmotic reactivity of the thirst mechanism and of the antidiuretic system is much the same. The purpose of the present study was to find out whether the hypothalamo-hypophyseal antidiuretic system and the thirst mechanism are activated by the same degree of cellular dehydration.

*Material and methods.* Experiments were carried out on 56 unanaesthetized mongrel dogs. As osmotic reactivity of the thirst mechanism was different in individual dogs, 2 sets of experiments were performed. In the 1st set (10 dogs), the osmotic reactivity of the thirst mechanism and that of the antidiuretic system were compared in the same experiments carried out on the same animals. In the 2nd set, the osmotic reactivity of the thirst mechanism was studied in 25 dogs and the osmotic reactivity of the hypothalamo-hypophyseal antidiuretic system in another group of 21 dogs. The dogs were fasted for 18 h but they had free access to water also during the experiment. The control blood sample was taken and a 5% solution of saline was infused at a rate of 7.5 ml/min into the saphenous vein of a dog. Blood samples were taken every 4 min in the course of the infusion. In the 1st group of experiments, the blood samples were drawn from an external jugular and in the 2nd one from a saphenous vein. When the dog began to drink, the infusion was stopped and a sample of blood was taken instantaneously. If the osmotic reactivity of the antidiuretic system was examined alone, the infusion was stopped after 20 min. The osmotic reactivity was expressed as a threshold value of osmotic stimulus[4]. For the antidiuretic system it was a minimal cellular dehydration causing pronounced increase of plasma ADH concentration; and for the thirst mechanism, it was a minimal cellular dehydration necessary to induce the drinking response. In each dog the extracellular water was measured by using sodium thiocyanate. Total body water was measured by using tritium water in the 1st set of experiments and calculated as the percent of body weight in the 2nd one. The plasma Na concentration was also measured and the total amount of extracellular sodium calculated. As the amount of Na and water in the infusion and in the urine produced during the infusion was measured, hence the shift of water caused by hypertonic infusion and cellular dehydration could be calculated on the basis of the measurements mentioned above. Degree of cellular dehydration was expressed as a percent of initial (control) value of the intracellular water. Plasma antidiuretic activity was measured using a modified method of Czaczkes et al.[7]. ADH was iden-

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