

skin, hypophysectomy appeared to increase the amount of testosterone metabolized from 40 to 60%, but of the major identified metabolites, namely 3 α -androstenediol, androstenedione, 5 α -dihydrotestosterone and androsterone, only the last was produced in significantly greater amounts.

68. Steroid metabolism by cultured Sertoli cells

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The ability of cultured Sertoli cells, from testes of 80d rats, to metabolize [7(*n*)-³H]-progesterone (P) (10 μ Ci/3.0 nmol) to testosterone (T), androstenedione (A), 5 α -dihydrotestosterone (DHT), 17 α -hydroxyprogesterone and 20 α -dihydroprogesterone was demonstrated. Calculations from crystallization data indicated C-19 steroids (T, A & DHT) increased linearly between 0.5 to 3 h and 19.4 ng of androgen per 1×10^6 cells was formed (3 h) with the largest amount being DHT. Although the amount of C-19 steroids formed (19.4 ng) was relatively small (1.8%, conversion) compared to T formation by isolated interstitial cells, it may be physiologically important for intratubular functions. Sertoli cells from adult and immature rat testes failed to aromatize T to estrogens even in the presence of FSH. Cultures of Sertoli cells from testes of 36d rats were incubated with 4-[¹⁴C]-T (1 Ci: 5×10^{-7} M) with and without FSH (5 μ g/ml NIH-FSH-S11). T (unconverted), A, 5 α -androstane-3 α ,17 β -diol and DHT were identified by crystallization, while ¹⁴C activity behaving like estrone or estradiol did not crystallize to constant specific activity.

69. Metabolism of [1,2-³H]-androstenedione in skin from hirsute women

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The metabolism of 4-[1,2-³H]-androstene-3,17-dione was studied in skin from the axillary region and from the inner side of the upper arm of ten healthy, normally menstruating nonhirsute and thirty oligomenorrhoeic amenorrhoeic hirsute women between 17 and 39 years of age. All skin specimens metabolized 4-androstene-3,17-dione into 5 α -androstane-3,17-dione, 3 α -hydroxy-5 α -androstane-17-one, 3 β -hydroxy-5 α -androstane-17-one and small amounts of 17 β -hydroxy-4-androstene-3-one. Hirsute women were found to have a 30%, lower ($P < 0.01$) 5 α -reductase activity in axillary skin than normal women. Hirsute women also tended to have a lower 5 α -reductase activity in skin from the inner side of the upper arm than healthy subjects. The hypothesis is suggested that the biologically active androgen in skin may be a 3-oxo-4-ene-steroid (testosterone or 4-androstene-3,17-dione) rather than a 5 α -reduced metabolite (e.g., 5 α -dihydrotestosterone) and that the androgen hyperactivity in skin from hirsute women may be related to a relatively slower deactivation of the active androgen than in skin from non-hirsute subjects.

70. Androgen levels in the homogenate, cytosolic and nuclear fractions of rat prostate (PR), skeletal muscle (SM), heart muscle (HM) and bulbocavernosus/levator ani muscle (BCLA)

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Besides typical androgen target organs such as the prostate, different muscle types have also been shown to pos-

sess a specific androgen receptor for testosterone (T)/5 α -dihydrotestosterone (DHT) in the cytosol. To see whether cytosolic androgens in muscles are also able to be translocated into the nuclei, we measured the distribution of endogenous T and DHT between cytosolic and nuclear fractions in prostate and three types of muscle of male rats. The excised tissues of three animals (approx. 350 g) were pooled for each experiment, washed with buffer (0 °C) and pulverized at -180 °C to yield the homogenate (HOM). To one weight part was added 3 vol. of buffer and the mixture was centrifuged at 800 g. The pellet was washed 3 \times with buffer containing 0.1% Triton X-100, 1 \times with buffer and was regarded as the nuclear fraction (NUC). The 800 g supernatant was recentrifuged at 100,000 g to yield the cytosol (CYT). Aliquots of HOM, CYT and NUC were extracted with ether. T and DHT were separated by celite chromatography and measured by RIA. The main results are: (1) DHT is mostly accumulated in prostate (HOM: 11.1 ± 2.6 ng/g wt. weight, CYT: 1.23 ± 0.64 ng/ml of dil. cytosol, NUC: 2.35 ± 0.33 ng/g wt. weight, $\bar{x} \pm S.D.$), considerably lower values were found for T (0.70 ± 0.40 , < 0.1 , 0.38 ± 0.10 , respectively). (2) In the three types of muscle, T is the predominant androgen present (SM: 1.3 ± 0.5 , 0.17 ± 0.06 , 0.30 ± 0.13 , HM: 2.8 ± 0.8 , 0.33 ± 0.08 , 0.99 ± 0.47 and BCLA: 1.4 ± 0.2 , 0.13 ± 0.04 , 0.51 ± 0.27). (3) T is distinctly more accumulated in all fractions of HM compared to BCLA and SM. (4) Considerable amounts of the androgens found in the homogenate are located in the nuclear fraction (ca. 20-40%) in all organs. In conclusion: As in prostate, the three types of muscle also possess a mechanism that enables them to concentrate T and/or DHT in the nuclei. This might be related to the above mentioned cytosolic receptor proteins. (Supported by the DFG, Sonderforschungsbereich 34 (Endokrinologie).)

71. Thyroxine (T₄) and triiodothyronine (T₃) kinetics during prolonged estrogen administration

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Circulating levels of total thyroxine (TT₄), total triiodothyronine (TT₃), T₄-binding globulin (TBG) and T₄ and T₃ kinetics were studied before, during and after estradiol monobenzoate (E₂B, 50 μ g/kg b.wt/day subcutaneously for 110 days) treatment. The mean \pm S.E. plasma levels of TT₄, TT₃ and TBG prior to E₂B therapy were 7.5 ± 0.24 μ g/dl, 117 ± 30 ng/dl and 1.52 ± 0.2 mg/dl respectively. A significant increase ($P < 0.01$) over the basal levels in plasma TT₄, TT₃ and TBG was recorded on day 6 of E₂B and continued to rise progressively up to day 19 and plateaued thereafter. Prolonged E₂B therapy significantly decreased ($P < 0.01$) distribution space (DS), metabolic clearance rate (MCR) and daily production rate of both T₄ and T₃. These data suggested that elevated hormone levels following E₂B were mainly due to decreased DS and MCR of the hormones, and not due to increased production by the thyroid.

72. Effect of aldosterone upon urinary kallikrein excretion in rats

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Aldosterone (ALD) would be one of the main factors which increase kallikrein (KAL) excretion in the urine (Margolius *et al.*, 1972-76). However, acute NaCl overloading, which inhibits aldosterone release, increases considerably KAL