58. Altered *in vitro* metabolism of testosterone in human liver disease

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The formation of free and glucuronic metabolites after incubation of [^{3}H]-testosterone (T) with needle biopsy samples of normal tissue, fatty liver, hepatitis and cirrhosis was investigated. T and metabolites were separated by radiogaschromatography. Incubations with hydrogen donating cofactors revealed that T was transformed mainly to the unconjugated metabolites androst-4-enedione, 3α,5β-androsterone and 3α,5β-androstanediol. There was no correlation between the liver alteration and the extent of the transformation of T to unconjugated metabolites. Incubations with hydrogen- and glucuronic acid donating cofactors showed that T was transformed to glucuronic 3α,5β-hydrogenated metabolites in normal tissue to a high extent and in pathologic tissue to a lower degree. There was a high negative correlation ($P < 0.001$) between the extent of the formation of glucuronic metabolites of T and the elevation of SGPT or SGOT. Cirrhotic tissue formed only minor quantities of glucuronic metabolites from T. These *in vitro* data account for the low urinary excretion of glucuronic metabolites of T in patients with hepatitis or cirrhosis. (Supported by the DFG.)

59. Effects of prolactin, ACTH and cortisol on testicular function in man

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Prolactin (PRL) increase by means of metoclopramide (10 mg t.i.d.) administration was accompanied by a rise in plasma 17OH progesterone and testosterone (T). The peripheral conversion of T into 5α-dihydrotestosterone (DHT) and androstenedione observed after injection of long-acting T (100 mg Sustanon 100) was decreased during concomitant metoclopramide administration. PRL suppression by means of bromocriptine (2.5 mg b.i.d) treatment was followed by an increase in DHT plasma levels. Experimentally induced hyperprolactinemia might have therefore a stimulatory effect on testicular androgen secretion and a lowering effect on the 5α reduction and oxidative T metabolism in man. Testicular androgen plasma levels were clearly lowered after long-acting ACTH injection (Synacthen, 1 mg), as well as after cortisol (275 mg in 24 h) administration. A metoclopramide-induced PRL increase prevented the suppressive effects of ACTH on plasma T. The ACTH-induced androgen suppression appears to be mediated through high circulating levels of corticosteroids. PRL and corticosteroids might have some reciprocal modulating influences on their effects on the testicular function.

60. Transport of [6,7,^{3}H]-oestrone sulphate by rat intestine *in vitro*

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There is increasing interest at present in the use of 'natural' oestrogens (oestradiol, oestrone and oestrone sulphate) for hormone replacement therapy or for contraception in combination with gestagens. Oestradiol is known to undergo transformation to oestrone glucuronide during intestinal absorption in the rat as well as in man but there is no information available on the metabolic fate of oestrone sulphate in the intestine. We incubated [6,7,^{3}H]-oestrone sulphate with everted and uneverted sacs of rat duodenum, jejunum and ileum and observed net transport of radioactivity to the serosal medium in all segments of the small intestine. Transport of oestrone sulphate was higher with the uneverted sacs in all cases and was accompanied by hydrolytic cleavage of the conjugate. 30–43% Of the administered oestrone sulphate was recovered as unconjugated oestrone bound to the intestinal tissue.

61. The metabolism of androgens in human skeletal, stomach, and heart muscle

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A comparative study of *in vitro* metabolism of 4-[^{14}C]-testosterone (T), androst-4-ene-3,17-dione (Δ^4A) and 5α-dihydrotestosterone (5α-DHT) on skeletal, stomach, and heart muscle (M) in men and women was performed. 100 mg of thin tissue slices were incubated in duplicate for 2 h with substrate in 1.5 ml Krebs–Ringer-phosphate buffer containing a NADPH generating system. The homogenized tissue was extracted by florisil adsorption and paper chromatographed (Bush A2). The eluted radioactive metabolites localized by scanning were converted to trimethylsilyl ethers and separated by radio gas chromatography (1% XE 60). The radioactivity of the gas fractions was then measured corresponding to nonradioactive carrier steroids. T was metabolized in striated M to Δ^4A only in non significant traces ($6S_1$); in heart M to 2% 3α + β,5α androstandiol (Adiol), while in stomach M (with mucosa and connective tissue) we found 19.7% Δ^4A. In addition Δ^4A was converted only in stomach M in 40% to T. On the contrary when 5α-DHT was incubated it was converted in striated M to 3α,5α-Adiol in 47% ($n = 6$), to 3β,5α-Adiol in 9.4% to androsterone(A) in 1.6% and to 5α-androstane-3,17-dione in 1.2%; in heart M however only to 3α,5α-Adiol in 10% and 3β,5α-Adiol in 7% ($n = 2$); in stomach M to 3α,5α-Adiol in 26.5%, 3β,5α-Adiol in 6.3% and to A in 27.4%. Atrophic skeletal M (type II, $n = 2$) yielded a significantly lower metabolism (29%) from 5α-DHT to 3α,5α-Adiol.

62. Testosterone metabolism in chronically inflamed male gingival tissue

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The gingival tissue is influenced by physiological changes in the hormonal balance (e.g. gingivitises in puberty, pregnancy). 4-[^{14}C]-Testosterone was incubated with subcellular preparations of male gingiva with chronic inflammation or hydantoin hyperplasia. The metabolites were determined with column and thin-layer chromatography and radioautography. In the homogenate preparations, 4-androstene-3,17-dione, 5α-androstane-3,17-dione, 3α-hydroxy-5α-androstan-17-one, 17β-hydroxy-5α-androstan-3-one, 5α-androstane-3α,17β-diol, and 5α-androstane-3β,17β-diol were tentatively identified. The 100,000 *g* supernatant preparations produced 4-androstene-3,17-dione and 5β-androstane-3α,17β-diol. The mitochondrial and microsomal preparations were quite inactive. No great qualitative differences between samples of different stages of inflammation were found. Quantitative differences will possibly be demonstrated with kinetic studies of the reactions.