

63. Progesterone metabolism in healthy and inflamed female gingiva

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It is known that the inflamed gingiva metabolizes progesterone more actively than the healthy one. When incubating subcellular preparations of normal and inflamed female gingiva, several metabolites of 4-[¹⁴C]-progesterone could be identified with column and thin-layer chromatography and radioautography. The homogenate preparations yielded 5 α -pregnane-3,20-dione, 3 β -hydroxy-5 α -pregnan-20-one, 20 α -hydroxy-5 α -pregnan-3-one, 20 β -hydroxy-4-pregnen-3-one, and 5 α -pregnane-3 α ,20 β -diol. The mitochondria were inactive, but the microsomes produced 5 α -pregnane-3,20-dione. In the 100,000 g supernatant incubations, 5 α -pregnane-3,20-dione, 5 β -pregnane-3,20-dione, 3 α -hydroxy-5 β -pregnan-20-one, 20 β -hydroxy-4-pregnen-3-one, and 5 β -pregnane-3 α ,20 α -diol were found. As elsewhere in the alimentary canal, the β forms of metabolites can be shown in the supernatant but not in the homogenate incubations. The metabolic activity of the gingiva correlated with the degree of inflammation.

64. Steroid sulphates in ovarian tissues: determination of sulphohydrolase activity and influence of gonadotrophins

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Estrogen sulphation in ovarian tissues has been shown by us to be stimulated by gonadotrophins. To investigate whether sulphohydrolase activities are also influenced by gonadotrophins, these enzymes have been partially characterized and measured in bovine and rat ovaries. In both tissues similar K_M values have been observed, being 1.7 and 10×10^{-5} M for estrone sulphate (ES), pregnenolone sulphate (PS) and dehydroepiandrosterone sulphate (DS) respectively, thus demonstrating a high enzyme affinity towards ES. In immature rats treated with HCG and HMG for 3 days the gonadotrophins had no influence on the ovarian sulphohydrolase activity for DS and PS as compared with controls. However, the enzyme activity for ES was significantly decreased in treated groups, being 3.1 ± 0.9 ; 2.2 ± 0.8 and 1.5 ± 0.5 pmol/mg protein/min in the control, HCG and HMG:HCG groups, respectively. Thus, an inverse relationship between arylsulphotransferase and aryl sulphohydrolase activity following gonadotrophin treatment was observed, suggesting that changes in both enzymes favour an increased ES formation, presumably for the regulation of hormone production.

65. Androgen metabolism in human endometrium and endometrial carcinoma

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Former investigations indicated alterations of androgen metabolism in women with endometrial carcinoma (EC). We investigated the metabolism of testosterone (T) and 5 α -androstane-17 β -ol-3-one (DHT) to study the enzymes in endometrium (E) and alterations of their activities in EC. The tissue was obtained by curettage or operation and incubated with 4×10^{-12} mol 1,2-[³H]-T or 1,2-[³H]-DHT (Krebs-Henseleit phosphate buffer, NADPH generating system, 2 h, 37°C). The steroids were separated by gas chromatography (I^o, XE60) after adsorption with Flor-

isil, extraction with ethanol and conversion to TMSi ethers. In E and EC, T was metabolized to 4ene-androstene-3,17-dione (Δ^4 -A), 5 α -androstane-17 β -ol-3-one (DHT), 5 α -androstane-3 α -ol-17-one (A) and 5 α -androstane-3 α ,17 β -diol (A-diol). Degradation of T and formation of Δ^4 -A were diminished in EC compared with E. In contrast more DHT, A-diol and A, indicating the activity of 5 α -reductase, were formed in EC. In E and EC, DHT was metabolised to 5 α -androstane-3,17-dione (A-dione), A-diol, A and 5 α -androstane-3 β -17 β -diol (3 β -A-diol). The degradation of DHT and the formation of A-dione were significantly lower in EC than in E. In contrast, the formation of A-diol and of 3 β -A-diol was significantly higher in EC compared with E.

66. Inhibition of total corticosteroid secretion by metyrapone in man

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The purpose of the present study was to demonstrate an *in vivo* effect of metyrapone (M) on adrenal enzymes in the early steps of the biosynthetic pathway of corticosteroids. In four male subjects, serum concentrations of progesterone (P), 17-OH-progesterone (17-OH-P), 11-deoxycorticosterone (DOC), 11-deoxycortisol (S), corticosterone (B), 18-OH-11-deoxycorticosterone (18-OH-DOC), aldosterone (A) and cortisol (F) as well as plasma concentration of ACTH were measured before and after oral administration of 40 mg of M/kg at 8.15 h in short time intervals. **Results:** About one hour after drug administration plasma ACTH exhibited marked peaks. After a decrease, plasma ACTH started to increase, reaching maximum levels between 14.00 h and 16.00 h. Increase of serum DOC and S started 30-90 min after administration of M and peaked at about 10.00 h to 11.00 h. A second rise of DOC and S reached plateau values at 12.00 h to 14.00 h. Serum B, F, A and 18-OH-DOC fell during the first hour after administration of M. They increased from 14.00 h to 16.00 h. Serum P and 17-OH-P slightly increased or remained almost unaltered up to 12.00 h. They increased markedly from about 14.00 h. **Conclusions:** M inhibits adrenal 18-hydroxylase in addition to 11-hydroxylase. The relatively low serum levels of P and 17-OH-P during the first period after drug administration—although plasma ACTH is highly elevated at this time—indicate an inhibitory effect of M on an enzymatic step before corticosteroid biosynthesis.

67. The effect of hypophysectomy on the *in vivo* metabolism of testosterone in the skin and other tissues of the rat

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The responses to testosterone of the rat sebaceous glands, in contrast to those of the ventral prostate and seminal vesicles, are greatly diminished by hypophysectomy. On the other hand, the effects of 5 α -dihydrotestosterone and 5 α -androstane-3 β ,17 β -diol have been shown to be less dependent on the presence of the pituitary. The role of the pituitary was therefore further investigated by studying the metabolism *in vivo* of 4-[¹⁴C]-testosterone injected into castrated and hypophysectomized-castrated rats which were killed 1 h later. All the rats had been implanted with testosterone which had been removed 24 h previously. In the ventral prostate and seminal vesicles the testosterone was almost completely metabolized, with 5 α -dihydrotestosterone and 5 α -androstane-3 α ,17 β -diol as the major products, irrespective of the presence of the pituitary. In