obtained after intravenous injection of C^{14}-cortisol.

^{14}C-Paramethasone (2.7 μc, 5 mg) was administered orally to two normal males. Per cent ^{14}C in free and glucuronide fractions in the 24 hour urine were 8.2, 7.1 and 19.9, 25.6, respectively. The former values were higher and the latter values were lower than those obtained after intravenous injection of ^{14}C-cortisol. When ^{14}C-paramethasone was administered orally to a male patient with liver cirrhosis with portacaval shunt, per cent ^{14}C in free and glucuronide fractions were much higher (16.43) and much lower (16.4), respectively.

These results indicate that the metabolism of synthetic glucocorticoids is slower than that of cortisol probably because they do not have such a specific metabolizing enzyme system in the liver as cortisol has, but that their metabolism becomes much more slower when the efficiency of hepatic metabolism is suppressed probably because some non-specific metabolizing enzyme systems in the liver are involved.

Volume of distribution per kilogram body weight and metabolic clearance rate (MCR) of androstenedione and dehydroepiandrosterone (D) were calculated after intravenous injection of H^3-androstenedione and H^3-D, respectively into each one normal male. The results were 0.656 L and 2250 L/day for androstenedione and 0.583 L and 1326 L/day for D. On the other hand, after intravenous injection of ^{3}H-dehydroepiandrosterone sulfate (DS) into three normal males, calculated volume of distribution per kilogram body weight and MCR were very low (0.062—0.093 L and 1.72—2.96 L/day, respectively). The former values were similar to and the latter values were lower than those for normal females reported by Wang et al.(2).

After intravenous injection of a mixture of ^{3}H-DS and DS-^{35}S into a normal subject, a patient with hyperthyroidism and a patient with liver cirrhosis, ^{3}H/^{35}S ratio in plasma DS increased gradually, and this indicated a presence of spacious non-radioactive sulfate pool. However this increase was not marked in liver cirrhosis, indicating a possible inferiority of sulfokinase activity (D→DS) relative to sulfatase activity (DS→D) in this disease.

Radioactive androsterone/etiocholanolone ratio in 48 hour urine was studied after intravenous injection of ^{14}C-testosterone. Compared to normal controls (6 cases), this ratio showed significant increase ($P<0.01$) in hyperthyroidism (3 cases), showed low values in a case of hypothyroidism and in two patients with Cushing's syndrome due to adrenocortical adenoma, but showed no significant change in liver cirrhosis (3 cases) and in chronic hepatitis (3 cases). These results indicate that 5α-hydrogenation of androstenedione formed from testosterone is predominant relative to 5β-hydrogenation of that in thyroid hormone excess and that the situation is reverse in thyroid hormone deficiency or glucocorticoid excess but that both 5-hydrogenations are probably suppressed to an equal extent in liver damage.

(References)

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Metabolism of Steroids in Feto-Placental Unit and Mother at Late Gestation

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The mechanism of estriol biosynthesis in late pregnancy was studied as follows: (1) Women in the third trimester of normal and pathological pregnancies received ACTH intramuscularlly, methopirone orally, and dexamethasone orally. Urinary excretion of estriol and 17-OHCS were measured before and after administrations. In normal pregnant women the urinary excretion of these estriol increased after ACTH administration. No increase of

estriol after ACTH administration was found in 5 women in whom intrauterine fetal death. Five women, each with a live anencephalic fetus, showed a low level of estriol in the urine after ACTH administration. In 3 women with pregnancies of twins the urinary estriol and 17-OHCS increased after metopirone administration. However, a remarkable decrease of estriol and 17-OHCS occurred after dexamethasone adrenal suppression. (2) Labeled pregnenolone was injected into the umbilical vein of 2 anencephalic monsters after delivery. As radioactive metabolites the following compounds were isolated and identified: 17α-hydroxypregnenolone, 16α-hydroxypregnenolone, dehydroepiandrosterone, and 16α-hydroxydehydroepiandrosterone. Homogenates of the adrenal and liver of a monster were incubated with labeled pregnenolone. As metabolites of pregnenolone the following compounds were isolated and identified: 16α-hydroxypregenolone, 17α-hydroxypregnenolone and dehydroepiandrosterone, androstenedione and testosterone from the adrenal, and 16α-hydroxypregnenolone, 17α-hydroxypregnenolone, and dehydroepiandrosterone from the liver. (3) Labeled dehydroepiandrosterone was incubated with homogenates of placentae obtained from normal double ovum twins and anencephalic monster. As metabolites of dehydroepiandrosterone estrone and estradiol were isolated and identified. These results indicate that estriol synthesis in late pregnancy is performed by feto-placental unit and the human fetal adrenal plays an important role in synthesis of the precursors under regulation of the fetal pituitary-adrenal system.