olized to 5β,3α-A(29–41%) and 5β-androstan-3α,17β-diol (8–16%). Skin slices from the pubic area metabolized T to androsterone (4–15%), 5α-androstanedione(5–9%), 5α-dihydrotestosterone(3–17%), 5α-androstane-3α,17β-diol(2–3%) and to Δ^4-A(2–7%), but not to 5β-hydrogenated metabolites. Slices from lung and gastric mucosa as well as fat tissue transformed T only to Δ^4-A(27–70%), but to neither 5α- nor 5β-hydrogenated metabolites. Under the conditions employed, tissue slices from kidney, striated muscle and myometrium did not metabolize T to an appreciable extent. (Supported by SFB 51 of the Deutsche Forschungsgemeinschaft.)

4A 2. Steroid catabolism: Androgens—II

97. Induction of androgen-metabolizing enzymes by testosterone in female rat liver

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There is a sex difference in androgen metabolism in the liver of rats. In the cytoplasmic fraction prepared from the liver, testosterone (T) is predominantly converted to 5β-reduced metabolites in males, whereas the formation of these metabolites is low in females. The induction of the enzymes involved in androgen metabolism in the female rat liver by T was investigated. The injection of T-propionate into female rats resulted in an increase of the production of labelled 5β-reduced metabolites when 4-^{14}C-T or 4-^{14}C-androstenedione (A) was incubated with the hepatic cytoplasmic fraction. This increase was prevented by the administration of actinomycin D or puromycin. The conversion of A to T was markedly higher in males than in females when A was used as a substrate. The injection of T-propionate into female rats increased the production of T from A, whereas actinomycin D or puromycin prevented the increased production of T induced by T-propionate. These findings suggest that the induction of Δ^4-5β-steroid reductase and 17β-hydroxysteroid dehydrogenase catalyzing the interconversion T $\rightleftarrows$ A occurred by the injection of T-propionate.

98. Testosterone and progesterone metabolism in the human prostate

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Preparations of minced or homogenized human prostatic tissue with benign hyperplasia obtained surgically were incubated with several concentrations of different steroid substrates in the presence of, or without various nucleotide phosphate cofactors.

Initially [17α-^{3}H,4-^{14}C]-testosterone incubations were carried out. Major 5α-reduction was shown in all cases with minor differences between 17β-hydroxy and 17-keto metabolites as expressed by the ^{3}H/^{14}C ratios.

Comparison of [4-^{14}C]-testosterone with [4-^{14}C]-progesterone metabolism in minced preparations of a single gland was made in several cases. Major progesterone radiometabolites were 5α-reduced and identified by crystallization to constant specific activity as 5α-pregnane-3,20-dione and 3β-hydroxy-5α-prègnan-20-one.

No significant differences in the amount of testosterone 5α-reduction or metabolism was found when samples from different parts of the human prostate gland (according to J. McNeal) were used. Since testosterone 5α-reduction and accumulation of 5α-dihydrotestosterone are intimately related with benign hyperplasia in human and canine prostate, these results suggest that progesterone may be used as a competitive inhibitor of the prostatic 5α-reductase. (Supported by a Grant from C.N.A.M.T.S. and funds from Lab. Besins-Iscovesco, Paris).

99. Structural and kinetic properties of microsomal 17β-hydroxysteroid dehydrogenase

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Because of the high 17β-hydroxysteroid dehydrogenase (17β-SDH) activity associated with microsomes from guinea-pig liver kinetic and structural studies of the enzyme from this source were undertaken. Livers were homogenized in 0·25 M sucrose. The microsomal fraction (105,000 **g**, 60 min pellet) was washed successively with 0·14 M NaCl, 1·0 M NaCl and 0·1 M Na_2CO_3–0·1 M Na HCO_3 and suspended finally in sucrose. Relative activities with testosterone (T) and estradiol (E_2) did not change during the washing steps. After fractionation by centrifugation in 1·23 M sucrose over 90 per cent of the activity was in the "smooth" microsome fraction. Activity was inhibited by 6·3 mM o-phenanthroline (67%) and 0·16 mM 1,8-ANS (59%) but not by 2,2″-bipyridine, isobutyramide or pyrazole suggesting inhibition by hydrophobic interaction at the active site rather than binding to Zn. With 1·6 nM NAD V_{max} was the same for T and E_2 and equimolar mixtures of the two substrates confirming the interaction of both steroids at the same active center. Activity with NADP was less than 10% of that with NAD. The identity of V_{max} values with T and E_2 is consistent with a reaction mechanism for the two substrates involving a common rate-limiting step. (Supported by the St. Paul-Ramsey Med. Educ. and Res. Foundation).

100. Metabolism of testosterone and androstenedione in human leucocytes

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No information is available on metabolism of androgens in human leucocytes and nothing is known about the significance of steroid degradation in normal and leucaemic blood cells. We therefore studied the *in vitro* metabolism of labelled testosterone and androstenedione in granulocytes and lymphocytes of 6 healthy subjects and of 4 patients with leucaemia. The cells ($1·85–7·5 \times 10^7$) obtained by separation with the NCI-IBM cell separator were incubated for 2 h with 500 nCi ^{14}C-testosterone or ^{14}C-androstenedione in Krebs–Ringer bicarbonate buffer (3 ml) containing an NADPH regenerating system. After incubation at 37 °C the steroids were extracted and paper chromatography performed. The radioactive metabolites were then separated as trimethylsilylethers by gas chromatography. The conversion rates (in % of the substrate) were calculated from the radioactivity of the gas fractions. In all experiments