We thank Professor I. MacGillivray and Professor S. C. Frazer for interest and encouragement, Professor W. Klyne and Dr D. N. Kirk for reference steroids, C. F. Boehringer und Soehne G.m.b.H. (Mannheim, Germany) for enzyme and the Medical Research Council for a personal grant to W. G.

Oestrogen Synthesis by the Pregnant Baboon: the Contribution of Maternal Circulating Precursors to Urinary Oestrogens

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A subhuman primate model is required for studies on the endocrinology of human pregnancy. Elevated urinary oestrogen concentrations during human pregnancy reflect increasing placental utilization of foeto-maternal precursors (Siiteri & MacDonald, 1966). We have studied the conversion of circulating precursors into urinary oestrogens by pregnant baboons (*Papio anubis*).

After intra-antecubital vein administration of 25 μ Ci of tracer 3 β -hydroxy[7-³H]androst-5-en-17-one or [7-³H]androst-5-en-17-on-3 β -yl sulphate 73% of the radioactivity appeared in the urine within 72h and negligible amounts thereafter. [4-¹⁴C]-Oestrogens added to urine permitted correction for losses and proof of radiochemical purity of [³H]-oestrogens after their isolation from urine (Brown, 1955). Less than 0.5% of ³H from either precursor was associated with urinary oestrone, oestradiol-17 β and oestriol from non-pregnant animals. The following percentages of the radioactivity of [7-³H]androst-5-en-17-on-3 β -yl sulphate administered to pregnant animals were incorporated into urinary oestrogens: oestrone, 0.84, oestradiol-17 β , 0.14, and oestriol, 0.02, at 93 days of gestation; oestrone, 0.89, oestradiol-17 β , 0.25, and oestriol, 0.07, at 142 days of gestation. Corresponding percentages of the radioactivity of 3 β -hydroxy[7-³H]-androst-5-en-17-one incorporated were: oestrone, 2.82, oestradiol-17 β , 1.08, and oestriol, 0.26, at 113 days of gestation; oestrone, 6.58, oestradiol-17 β , 0.98, and oestriol, 0.39, at 156 days of gestation.

In subsequent experiments tracer [7-³H]androst-5-en-17-on-3 β -yl sulphate plus [¹⁴C]oestradiol-17 β (³H/¹⁴C ratio 5.34) were administered. Within 72h 60% of the ¹⁴C was excreted; 92% of this was associated with oestrone, 7% with oestradiol-17 β and 2% with oestriol. ³H/¹⁴C ratios of urinary oestrone, oestradiol-17 β and oestriol increased from 0.01, 0.08 and 0.06 respectively in a non-pregnant animal to 0.14, 0.13 and 0.16 respectively at 132 days of gestation and 0.23, 0.22 and 0.27 respectively at 168 days of gestation.

Maternal precursors are increasingly utilized for oestrogen synthesis in the pregnant baboon, but oestrone, rather than oestriol, is quantitatively most important. The higher ³H/¹⁴C ratio of oestriol suggests that, as in the human, some oestriol is formed via pathways excluding oestradiol-17 β . The more extensive conversion of 3 β -hydroxy-androst-5-en-17-one than of androst-5-en-17-on-3 β -yl sulphate into oestrogens recalls similar findings with perfused human placentae. Townsley, Scheel & Rubin (1970) have proposed that human placental oestrogen synthesis may be limited by the rate of hydrolysis of conjugated precursors. Baboons appear to be suitable models for exploration of this and other aspects of the endocrinology of human pregnancy.

This work was supported by the John A. Hartford Foundation Inc.

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Properties of Renal Aldosterone-Binding Proteins

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Previous investigators have established that aldosterone binds to protein(s) of both the nuclear and cytosol fractions of kidneys of adrenalectomized rats *in vivo* and *in vitro* (Fanestil & Edelman, 1966; Herman, Fimognari & Edelman, 1968). The present communication describes attempts to characterize these binding protein(s) further and, in particular, investigations of the relationship between nuclear and cytosol binding protein(s).

The ratio of nuclear to cytosol binding was found to be greater in experiments where aldosterone had been injected (*in vivo*) than in experiments where the proteins were assayed by binding of aldosterone *in vitro* as described by Herman *et al.* (1968). This indicates either that the binding protein moves into the nucleus after the injection of aldosterone or that the nuclear and cytosol binding proteins decay at different rates after isolation. It was then found that, if the protein concentration of the binding assay *in vitro* were increased by the addition of bovine serum albumin, the amount of binding by nuclear extract increased but that by cytosol did not. Under these conditions the ratio of nuclear to cytosol binding was the