testosterone itself may be the predominant active androgen principle *in vivo* in most androgen target organs and that conversion to 5α-dihydrotestosterone is generally not a prerequisite for androgen activity.

Using an ultrasensitive micromodification of isoelectric focusing it was possible to show that cytosol from kidney, submaxillary gland, thigh muscle and levator ani muscle and nuclei from kidney and submaxillary gland contained androgen-binding proteins with pI:s in the region 4·6–5·1 ("4·6–5·1 Complex")' This complex also formed *in vitro* after incubation of [1,2,6,7-^{3}H]-testosterone with cytosol from kidney and submaxillary gland. [1,2,6,7-^{3}H]-Testosterone was bound with high-affinity to receptor proteins in cytosol from both kidney, submaxillary gland and thigh muscle.

On the basis of these results the hypothesis is presented that a common class of testosterone receptors is present in most organs and that these receptors can be detected both *in vivo* and *in vitro* provided methods sensitive enough are utilized.

40. Glucocorticoid-protein interactions in rat liver cytosol, ÖRJAN WRANGE, JAN CARLSTEDT-DUKE, JAN-ÅKE GUSTAFSSON and SVEN A. GUSTAFSSON, Department of Chemistry and Department of Germfree Research, Karolinska Institutet, S-104 01 Stockholm 60, Sweden

The intracellular binding of [^{3}H]-corticosterone and [^{3}H]-dexamethasone and their metabolities to macromolecules in rat liver cytosol were studied both *in vivo* and *in vitro*. After intraperitoneal injection of [^{3}H]-corticosterone to adrenalectomized rats, the radioactivity was recovered in three major steroid-macromolecular complexes in both sexes. A marked sexual difference in radioactivity bound to protein was noted with approximately ten times more in male liver cytosol. The steroid-macromolecular complexes were characterized by gel-filtration, ion-exchange chromatography, density gradient centrifugation and isoelectric focusing. The macromolecules were characterized as: (1) a steroid disulphate-binder (Stokes radius 25 Å and sedimentation coefficient 4·1S in high ionic strength; pI 8·9); (2) transcortin and (3) a corticosterone "receptor" (Stokes radius 77 Å in high ionic strength; sedimentation coefficient >10S in low ionic strength). The corticosterone "receptor" was found to be very unstable. Approximately four times as much radioactivity was bound to the "receptor" in male than in female liver cytosol after administration of [^{3}H]-corticosterone *in vivo*. The radioactivity bound to the receptor was identified as [^{3}H]-corticosterone and [^{3}H]-5-α-dihydrocorticosterone. When studied *in vitro*, [^{3}H]-corticosterone bound only to transcortin and the "receptor".

After intraperitoneal injection of [^{3}H]-dexamethasone into adrenalectomized rats, the radioactivity was recovered in two (male) or one (female) steroid-macromolecular complex(es). The steroid-"receptor" complex was found in liver cytosol from both sexes, both *in vivo* and *in vitro*. It sedimented both at 8·5S and >10S in low ionic strength and had a sedimentation coefficient of 3·8S and a Stokes radius of 66 Å in high ionic strength.

It is speculated that both corticosterone and dexamethasone may bind to the same site of a single receptor molecule but that each steroid induces different conformational changes (Stokes radii 77 Å and 66 Å, respectively) which results in different aggregation states of the binding protein. It is suggested that use of natural corticosteroids may be preferable in studies on mechanism of action of glucocorticoids in rat liver.

I. Steroids in early pregnancy, E. MENINI*, D. MANGO† and P. SCIRPA†, *Department of Biological Chemistry and Department of Obstetrics and Gynaecology, Università Cattolica, Rome, Italy

Steroid hormones play a major role in the maintenance of pregnancy and many of the maternal adjustments and physiological adaptations which occur during this period are the result of the increases in steroids produced, first by the ovary and subsequently by the placenta.

The present review will deal, mainly, with the biosynthesis, the blood levels, the metabolism, the excretion and the significance of the steroid hormones in the initial stages of normal pregnancy, complicated pregnancies, and pharmacologically induced pregnancies.

Immediately after conception, the most dramatic changes in steroid hormones production are observed in the oestradiol-17β, progesterone and 17-hydroxyprogesterone. The site of this steroidogenesis is the corpus luteum gravidarum and there is evidence that by the 7–8th week of gestation a luteoplacental shift occurs. By this time both the corpus luteum and the placenta contribute to the production of oestradiol-17β and progesterone while 17-hydroxyprogesterone is probably being synthesized mainly by the corpus luteum.

As far as we know, the enzymic reactions involved in the formation of steroid hormones in the early stages of pregnancy and in the non-pregnant female are the same, nevertheless there are differences in the utilization of precursors by the corpus luteum and the trophoblast, specially with regard to the biosynthesis of the oestrogens.

As the placenta is relatively deficient in the enzyme 17α-hydroxylase, this organ forms oestrogens to a great extent from C_{19} steroidal compounds. On the other hand the main precursors of the oestrogens in the corpus luteum are the 17-hydroxylated steroids with 21 carbon atoms. In recent years, with the advent of accurate, sensitive and practical methodology for the measurement of steroid hormones in blood and urine, many studies have been conducted with the purpose of establishing reference values for the blood levels and the urinary excretion of the main steroids implicated in pregnancy.

Hormone assays in early pregnancy are valuable, at least from two points of view. First, they contribute to the understanding of the complex interactions among the different types of hormones during this period of life and, second, they allow, in some cases, to distinguish between values which are presumptive of normal pregnancy and those which are suggestive of associated complications.

It is now well established that during the first 5–6 weeks which follow the last menstrual period, the blood and urinary concentration of oestrogens is only slightly increased or it is not increased at all with respect to the levels that are usually found in the luteal phase of a normal menstrual cycle. Oestrogens begin to increase rapidly in coincidence with the first signs of the luteoplacental shift. 17-Hydroxyprogesterone appears to be the best biochemical marker of this event. In fact the blood concentration of this compound, prevalently of ovarian origin, increases rapidly after conception and begins to decline 5–6 weeks after the last menstrual period. The 17-hydroxyprogesterone peak probably indicates the impending luteoplacental shift.

The blood levels of progesterone in the initial stages of pregnancy do also support the concept that the luteoplacental shift takes place around the 7–8th week of gestation. In fact after an initial period of 8–10 weeks in which the levels of this hormone show a plateau or in some cases a broad peak, with values of the order of those usually found in luteal phase of a normal menstrual cycle, the blood concentration of progesterone steadily