steroids are suppressed in hypertensive pregnancy and, whether suppression of progesterone production may play a permissive role in the hypertensive state. Prospective studies were performed serially in 112 ambulatory pregnant subjects between the 12th week of gestation and term. Plasma renin substrate (PRS), activity (PRA), aldosterone (PA) and progesterone (PP) concentrations were measured by radioimmunoassay techniques. On the basis of blood pressure observations during and after pregnancy, patients were classified as normotensive (45), chronic hypertensive (26) or pre-eclampsia/eclampsia (41). There was a progressive increase in PRS in all pregnant subjects during pregnancy with a plateau during the last trimester, but there were no significiant differences among the pregnant groups. PRA rose during the first trimester and remained elevated throughout normal pregnancy but became significantly suppressed during the last trimester in both hypertensive groups. PA rose steadily in normal pregnancy with the greatest increment appearing during the last trimester in normal pregnancy when the hypertensive groups demonstrated a significant suppression. PP followed a pattern parallel to PA in normal pregnancy, but in contrast to PA, no suppression of PP was observed during the last trimester in the hypertensive groups. These observations confirm that PRA and PA rise sequentially during the course of normal pregnancy and are suppressed during the last trimester of hypertensive pregnancy. The results suggest that the terminal rise in PA observed in normal pregnancy is related to PP and demonstrate no abnormality of PP in hypertensive pregnancy, indicating that an abornality in progesterone production is not involved in the pathophysiology of hypertensive pregnancy.

69. Biological effects of a new long-acting progestational steroid: Org 2793, J. DE VISSER, J. VAN DER VIES, G. H. DECKERS and A. COERT, Organon International, Endocrinological R & D Laboratories, Oss, The Netherlands

The steroid 21-hydroxy-16α-ethyl-19-nor-4-pregnene-3,20-dione has approx. 50 times the progestational activity of progesterone after sc administration in the Clauberg–McPhail test. A number of 21-esters of this steroid was investigated for prolonged progestational activity after a single sc dose. The duration of activity of these esters increased from 1 week up to 3 months with increasing chain length of the mono- or dicarboxylic organic acid. The endocrine profile of one of these esters, Org 2793 (16α-ethyl-21-heptanoyloxy-19-nor-4-pregnene-3,20-dione), is presented. Single sc doses of Org 2793 in oily solution were used in all experiments. Org 2793 was active in the Clauberg–Junkmann test, and maintained pregnancy in ovariectomized rats, hamsters, guinea-pigs and rabbits. Parturition was delayed in intact pregnant rats. Org 2793 induced deciduoma formation in ovariectomized mice and was active in the McGinty test. The duration of activity is dose-dependent, as shown by suppression of oestrus in mature rats. Org 2793 showed anti-oestrogenic activity in spayed rats treated with 17β-oestradiol. In oestrous rabbits migration of spermatozoids through the cervix was inhibited by Org 2793; unfertilized ova were present in the oviducts after HCG-induced ovulation and vaginal insemination. High doses of Org 2793 had no androgenic or anti-androgenic effects. Masculinization or feminization (assessed on the basis of ano-genital distances) was not observed in offspring of rats resulting from pregnancies maintained by Org 2793. Fertility of the F_1 generation, reared by foster-mothers, of New Zealand White rabbits treated with high doses of Org 2793 during pregnancy, was normal. No teratogenic effects were observed in offspring examined after caesarian section. High doses of Org 2793: did not induce anti-inflammatory effects in the rat paw kaolin oedema test; had no diuretic activity in intact rats; slightly prolonged the survival time in adrenalectomized rats and did not affect liver glycogen, adrenal weight or function in intact rats. Org 2793 was found to be a potent progestational compound with prolonged activity.

70. A rapid method to distinguish total cortisol binding globulin (CBG) bound cortisol from biologically active free cortisol in pregnancy by plasma tetrahydrocortisol (THF) estimation, W. VIELHAUER, H. WILL and P. VECSEI, Department of Pharmacology, University of Heidelberg, Heidelberg, Im Neuenheimer Feld 366, West Germany

The total plasma cortisol concentration is influenced by the concentration of binding proteins, particularly CBG, while free cortisol is directly controlled by pituitary adrenocorticotropin (ACTH) secretion. It has been suggested that the plasma concentration of the cortisol metaboilite (THF) depends primarily on the concentration of free cortisol. Pregnancy and oral contraceptives alter CBG concentrations in plasma. In this condition it is therefore preferable to measure free cortisol or THF. THF was measured in plasma after CH_2Cl_2 extraction with a radioimmunoassay developed in our laboratory. The plasma concentrations (mean ± S.D.) of total cortisol and THF in control persons were 9·63 ± 3·24 and 1·39 ± 0·345 μg/100 ml (n = 25) respectively. In 32 healthy pregnant women, total cortisol and THF plasma concentrations were 25·9 ± 7·96 and 1·33 ± 0·437 μg/100 ml respectively. In 10 women receiving oral contraceptive steroids the cortisol and THF concentrations were 22·4 ± 9·32 and 1·53 ± 0·36 μg/100 ml. Sixty minutes after the i.v. administration of 25 IE ACTH in 8 volunteers, a significant increase of total cortisol and THF from 10·48 ± 3·89 and 1·44 ± 0·46 and 25·27 ± 6·47 and 3·05 ± 0·674 μg/100 ml respectively was found. In 3 patients with Cushing disease elevated concentrations of THF (3·3 ± 0·1 μg/100 ml) were measured. The results indicate that plasma THF-concentration parallels free cortisol independent of CBG. Conclusion: Elevated total cortisol values resulting from increased CBG binding capacity as opposed to those resulting from adrenal stimulation by ACTH or hyperadrenocorticism can clearly be distinguished by THF estimation in plasma.

71. 16-substituted steroids in fetal and neonatal life, B. SALVADORI, A. MERIALDI, L. BENASSI, L. PINI, R. SPALLANZANI, Clinica Ostetrica e Ginecologica dell'Università, 43100 Parma, Italy

The C-16 substituted steroids constitute an important hormonal group, constantly present during fetal and neonatal life. These compounds are present in appreciable amounts in amniotic fluid and in maternal and newborn urine.

The following compounds are studied: 16α-hydroxy-pregnenolone; 16α-hydroxy-dehydroepiandrosterone; 16β-hydroxy-dehydroepiandrosterone; 16-oxo-androstenediol; oestriol. Some of the above compounds are oestriol precursors, far or near, and are elaborated by the adrenals and the liver of the fetus. Therefore their trend can be helpful in discovering the place and the degree of the enzymatic defects.

An ethyl-acetate extract of urine or amniotic fluid, performed after enzymatic hydrolysis and β-glucuronidase and sulfatase, was subjected to t.l.c. and g.l.c. Final identification of the isolated steroids was accomplished by g.l.c.–mass spectrometry.

At birth, in cases of premature delivery, EPH gestosis, feto-placental insufficiency, retarded fetal growth and so on, lower values of excretion of these steroids are present. In the first few days of neonatal life we have observed an increasing trend of almost all these compounds. Generally, when low oestriol levels are present during fetal life, low levels of all 16-substituted steroids appear in newborn urine too. This fact confirms the opinion that, as hormonal activity, the newborn in the first few days of life would be a kind of fetus model.

72. Cortisol metabolism in the neo-natal period, C. H. L. SHACKLETON, J. W. HONOUR and N. F. TAYLOR, Division of Clinical Chemistry, Clinical Research Centre, Harrow, Middlesex, England

1β-Hydroxycortolone was recently shown to be an important urinary metabolite of cortisol in an infant with renal-tubule insensitivity towards aldosterone (Shackleton C. H. L. and Snodgrass G. H. A. I.: *Ann. clin. Biochem.* 11 (1974) 91) and this compound may well be identical to an unidentified metabolite isolated from infant urine by Danilescu-Goldenberg and Giroud (*J. clin. Endocr. Metab.* 38 (1974) 64) following administration of labeled cortisol. The present investigation was undertaken to ascertain the quantitative excretion of urinary 1β-hydroxycortolone relative to other cortisol metabolites in the normal and pre-term newborn. Total steroid extracts of urine were obtained following enzymic hydrolysis, Amberlite XAD-2 extraction and purification on Sephadex LH-20 columns (Shackleton C. H. L., Gustafsson J.-Å. and Mitchell F. L.: *Acta endocr., Copenh.* 74 (1974) 157). Methyloxime-trimethylsilyl ethers of the steroids were prepared and analysed by combined gas chromatography-mass spectrometry (GC–MS). Complete spectra in the mass range 100–800 nm were acquired at 10 s intervals throughout the GC–MS analysis. The mass spectra were stored in mass converted format on magnetic tape. The data were processed (DPLOT module Varian SpectroSystem 100 MS) and intensities of up to eight selected ions from the series of mass spectra were plotted in graphic form on an oscilloscope and photographed. The intensities of selected ions specific for cortisol and its metabolites (e.g. cortisone, 6β-hydroxycortisol, 6β-hydroxycortisone, 20-dihydrocortisol, 20-dihydrocortisone, tetrahydrocortisol, tetrahydrocortisone, cortolones, cortols, and 1β-hydroxycortolone) were determined and related to intensities of ions given by standard mixture of cortisol metabolites. The major metabolites of cortisol present in infancy urine were found to be tetrahydrocortisone, 6β-hydroxycortisol, cortolone and 1β-hydroxycortolone. The excretion of tetrahydrocortisol and *allo*-tetrahydrocortisol was found to be extremely low. A significant amount of cortisol was excreted unmetabolised.

73. Integrated serum gonatrophins and gonadal steroids during first weeks of life in premature male infants, A. ATTANASIO, E. STEIL, M. EICHNER, K. RAGER, H. MENTZEL and D. GUPTA, Departments of Diagnostic Endocrinology and Neonatology, University Children's Hospital, 74 Tübingen, Germany

Pituitary-gonadal relations in newborns and in infants have been investigated by several authors in the last years. Evidence for testicular activity in early infancy has been accumulated. While many authors evaluated hormonal data in infants in relation to later pubertal events, the significance of hormonal activity in the newborn period for the normal genital development has not been discussed so far. In this study, blood specimens from prematurely born male infants (27th to 39th week of gestational age) were obtained longitudinally. The specimens were assayed for plasma testosterone, serum LH and FSH by RIA. Most of the subjects were found to have undescended testes at the beginning of the observation period, and had them down in the scrotal position by the end of this period. During the longitudinal follow up, peak values of plasma testosterone, sometime reaching 2000 ng/100 ml, were observed, although the timing of the peak was individually variable. No such pattern was found for serum gonadotrophins, although, on the average, they were significantly elevated when compared to later developmental stages. The results of this longitudinal study show that the hypothalamo-pituitary-gonadal axis is highly active during this developmental period. The high gonadotropin values clearly demonstrate that the enhanced testicular activity found in these premature infants do not depend upon placental factors. Since descent of testis is known to occur between the 32nd and the 40th week of normal gestation, the pattern of plasma testosterone so far revealed in this longitudinal study suggests a relationship between high levels of circulating testosterone and descent of testis in the scrotal position.

74. Plasma dehydroepiandrosterone (DHEA) and pregnenolone (Δ_5P) in newborns after HCG stimulation, A. LUCISANO, G. TORTOROLO, E. ARNO and S. DELL'ACQUA, Instituto di Clinica Pediatrica e Istituto di Clinica Ostetrica e Ginecologica Università Cattolica del Sacro Cuore, Rome, Italy

The foeto-placental unit utilizes as estriol precursor mainly the DHEA, synthesized by foetal adrenals. The purpose of the present investigation was to elucidate the role of HCG in the regulatory mechanism of foetal DHEA synthesis.

In a group of 8 newborns, during the first days of the life, when the *paleocortex* is still present, total DHEA and total Δ_5P have been measured daily in plasma by means of a gas-chromatographic assay. The plasma levels of DHEA and Δ_5P decrease until the third day from birth, from 0·9 to 0·3 μg/ml for DHEA and from 0·8 to 0·4 μg/ml for Δ_5P. In a group of 6 newborn at third day after birth we injected 5000 IU of HCG and in the following 24 h we obtained a significant increase of plasma levels of DHEA and Δ_5P. These results suggest that as well as foetal ACTH, HCG can also be involved in the control of DHEA synthesis by foetal adrenals.

75. Perinatal adrenal anomaly associated with total absence of 3β-hydroxy-5-ene-steroids in the infants urine, K. CARLSTRÖM*, G. BJÖRK†, P. ENEROTH‡ and J.-A. GUSTAFSSON§, Hormone Laboratory* and Department of Obstetrics and Gynaecology†, Sabbatsbergs Sjukhus; Hormone Laboratory, Karolinska Sjukhuset‡ and Department of Chemistry §,Karolinska Institutet, Stockholm, Sweden

3β-Hydroxy-5-ene-steroids are the major steroids in the human foetus and in early infancy, and are excreted in large amounts in the infants urine. They are mainly synthesized by the foetal zone of the adrenal cortex and act as precursors for the foetoplacental oestrogens, notably oestriol. Foetal adrenal anomalies might therefore be accompanied by low maternal urinary oestriol excretion. As far as we know from the literature such