hypoxia was tested by FHR recording. In maternal *peripheral blood,* HCG remained unchanged until evacuation. HPL, P, E_2 and E_3 showed a uniform fall during hypoxia with subsequent restitution. In the *uterine vein* (UV) HPL, P, E_2 and E_3 rose during the tourniquet period, demonstrating probably an accumulation by the reduced outflow from the site of hormonal production. Following the tourniquet release UV levels showed a fall to pretourniquet values at the time of peripheral restitution, demonstrating restituted synthesis. In the *amniotic fluid,* no significant concentration changes occurred during hypoxia. An increase of HPL, P, E_2 and especially E_3 was found at the end of the restitution period.

65. Saturated metabolites of progesterone in maternal and fetal plasma at delivery, H. MICKAN* and J. ZANDER, *(DFG Mi 109/5), I. Frauenklinik und Hebammenschule der Universität D-8000 München 2, Maistrasse 11, Germany.

The metabolic reduction of progesterone at positions C-3 and C-5 has been demonstrated *in vitro* by perfusion and incubation of different human tissues. In order to determine quantitatively the epimeric pregnanolones in small plasma samples a sensitive method was developed using gas-liquid chromatography (g.l.c.). In brief, plasma is extracted with ethanol–diethylether. Extracts are purified by thin-layer chromatography, "free" and "sulfate" fractions are separated, the hexadecafluoronanoyl derivative is formed and determined by g.l.c. and electron capture detection. The sensitivity of the method is 1 ng steroid per sample, accuracy 102 ± 21% (S.D.), precision 17–26% (CV). Fifteen sets of plasma samples (maternal vein, umbilical vein and arteries) were obtained at termination of pregnancy by cesarean section. Recovery of added radioactive labelled tracers was 48·2 ± 8% (S.D.). In fetal and maternal plasma the metabolites were present mainly as sulfoconjugates up to 1·8 μg/ml. The free steroids were sometimes undetectable especially in fetal plasma (range 0–170ng/ml). 3α-hydroxy-5α-pregnan-20-one and 3β-hydroxy-5α-pregnan-20-one were found in similar concentrations in fetal arteries, vein and maternal vein. Only for 3α-sulfoxy-5β-pregnan-20-one a definite arteriovenous difference was demonstrated with higher concentrations in arterial plasma of the fetus.

These results show that ring A saturated metabolities of progesterone are present in fetal plasma also at concentrations higher than the parent steroid. 3α-hydroxy-5β-pregnan-20-one seems to be eliminated more effectively from the fetal compartment than the 5α-epimers.

66. Effects of surfactant stimulating agents on plasma estriol and progesterone in third trimester pregnancy, E. FRIEDRICH, A. ETZRODT, H. CHANTRAINE and W. SCHWENZEL, Abteilung Gynäkologie und Geburtshilfe der RWTH Aachen, Germany

Medication with betamethasone (BM) in cases of premature labour results in a significant decrease of respiratory distress syndrome (RDS) in the newborn. BM exerts its effect by surfactant stimulation of the fetal lung. Only recently a new compound, "Bromhexine", metabolite VIII, (NA 872), has been shown to have a similar effect as BM. BM however causes a fall of total estrogens in 24 h urine and thus impairs monitoring of fetal well-being. It was the purpose of this study to investigate the effect of NA 872 on plasma estriol and progesterone in comparison to BM.NA 872 was applied by i.v. infusion to 15 patients with premature labour (30–38 weeks of gestation). The initial dose was 500 mg on the first day of medication and 200 mg daily on 4 following days. BM (6 mg BM-sodiumphosphate plus 4·5 mg BM-acetate) was given by intramuscular injection on two subsequent days to 15 patients with premature labour (30–38 weeks of gestation). Unconjugated plasma estriol (E_3) and progesterone (P) were measured by radioimmunoassay and the following results were obtained: BM caused a rapid fall of E_3 concentrations to 47% (mean) and 49% (mean) of pretreatment levels on days 2 and 3 after injection. This was followed by gradually rising E_3 levels on the following days. In contrast, a slight increase of E_3 was observed in patients treated with NA 872. P showed uncharacteristic day to day fluctuations in both treatment groups. These results suggest that NA 872 does not interfere with steroid biosynthesis of the feto-placental unit and thus offers a major advantage compared to BM treatment.

67. Urinary cortisol in normal and anencephalic pregnancy, SATI C. CHATTORAJ, ADRIAN K. TURNER and DAVID CHARLES, Departments of Obstetrics and Gynecology, Boston University School of Medicine, Boston, Mass. 02118 and Memorial University of Newfoundland, St. John's, Newfoundland, Canada

The urinary excretion of free cortisol was measured in 17 normal pregnant women, 9 pregnant women bearing anencephalic fetuses and 10 non-pregnant females in reproductive life. In normal pregnancy, during the last trimester, the urinary excretion of free cortisol (29·71 ± 19·10 μg/24 h) is close to three times than that noted in normal non-pregnant women (11·03 ± 6·42 μg/24 h). In pregnancies associated with an anencephalic fetus, the urinary free cortisol (8·07 ± 5·18 μg/24 h) is significantly lower ($P < 0{\cdot}005$) than that found in normal pregnancy but is within the non-pregnant range. However, the distinction of excretion values among the three groups becomes less apparent when measurements are carried out without purification of urinary extracts by chromatography.

The decreased urinary excretion values of cortisol in the presence of an anencephalic fetus indicates that during normal pregnancy the fetus substantially contributes to the maternal plasma cortisol pool. Furthermore, such a contribution is significant, enough to increase the non-protein bound fraction in the plasma which is reflected by the urinary excretion. Measurements of urinary free cortisol may be a useful index of fetal well-being (Supported by NICHD, Grant No. HD-06799.)

68. Plasma concentrations of aldosterone and progesterone during normal and hypertensive pregnancy, H. H. WEINBERGER, N. J. KRAMER, L. P. PETERSEN, R. CLEARY and P. YOUNG, Indiana University School of Medicine, Indianapolis, Indiana, U.S.A.

During normal pregnancy aldosterone production increases sequentially, similar increases are seen in plasma renin activity. The production of progesterone, a natriuretic agent with potent anti-aldosterone activity is also known to increase during pregnancy, but the relationship between the 2 steroids has not been examined. In pregnancy complicated by hypertension, aldosterone and progesterone excretion have been reported to be suppressed, as has plasma renin activity, in comparison to observations in normotensive pregnant subjects of the same gestational period. The present study was undertaken to examine whether plasma concentrations of these

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.