Radioimmunoassay was used to determine the levels of estrogens and progesterone in plasma of the following three groups: normal women in luteal phase, normal patients in early pregnancy, and patients whose pregnancy was threatened by abortion terminating both favourably and unfavourably. Cases with uterine pathology or maternal medical diseases were excluded. The data may be summarized as follows: the steroids examined (estrone, estradiol, estriol and progesterone) increase gradually in normal pregnancy. There is evidence of the beginning of placental steroidogenesis. In those pregnancies in which there was a risk of abortion that terminated favourably, the levels of estrogen (and notably estradiol-17β) remained normal, however this was not the case for those pregnancies resulting in abortion. It is therefore concluded that monitoring the levels of estrogens in plasma in early pregnancy has a prognostic value, whereas progesterone levels have less significance.

58. The early increase of plasma unconjugated estriol in pregnancy. Significance and clinical usefulness, R. DE HERTOGH, K. THOMAS and I. VANDERHEYDEN, Endocrinology and Nutrition Unit, University of Louvain, Hôpital Saint-Pierre, Leuven, Belgium

In early pregnancy, the production of estrogens results from the sequential activity of three endocrine tissues: corpus luteum, placenta and fetal adrenals. The latter produce dehydroepiandrosterone sulfate, which is hydroxylated in position 16 in the fetal liver and aromatized into estriol in the placenta.

The increase of estriol in mother's plasma could then mirror the start of this important fetal function. Plasma samples were obtained from pregnant women from the fifth week of pregnancy onwards and unconjugated estriol was extracted with diaethylether, separated from other estrogens on Sephadex LH_{20} column chromatography, and measured with a specific radioimmunoassay.

Plasma levels of unconjugated estriol remained below 100 pg/ml up to the ninth week of pregnancy in all cases. By the 10th week, a rapid increase took place which became steeper after the 12th week. The shape of the estriol increase and the mean levels were the same in normal and diabetic pregnancies. This steep increase was due to the activity of the fetal adrenals, as shown by the increase of the E_3/E_2 ratio in normal pregnancies, and by the low estriol levels in molar pregnancies.

By pooling the results of normal and diabetic pregnancies, the dispersion of the gestation ages in several ranges of plasma estriol levels were as follows:

Estriol ranges: (pg/ml)	100–150	150–200	200–300	300–400	400–550	550–800
Weeks of pregnancy: (mean ± s)	10·2±1·2	11·5±0·8	12·2±1·2	13·7±1·0	13·8±0·9	15±1·0
n	21	17	17	15	18	18

It is felt that repeated measurements of unconjugated plasma estriol in early pregnancy (between the 10th and 16th week) can contribute to determine the gestational age, particularly in diabetic pregnancies in which fetal maturity has to be carefully taken into account.

59. Pregnancies with low estriol production, PREBEN GAEDE and J. G. KLEBE, Departments of Obstetrics and Gynecology, Rigshospitalet and Oresundshospitalet, Copenhagen, Denmark

Estimations of estriol in blood and urine have for a long time been used as the best hormone parameter for foetal well-being. Nevertheless both placenta and foetus are involved in the production of the hormone. While a specific foetal hormone is still missing, both placenta lactogenic hormone (HPL) and chorionadotropin (HCG) are specific placenta hormones of great clinical value in cases of placental insufficiency.

Low estriol values in blood or urine are in most cases caused by abnormalities in the foeto-placental unit. Besides placental insufficiency several other reasons are possible such as enzyme defects in placenta (sulfatase defect), anencephali or foetal death, or medical treatment of the mother with drugs (fluorsubstituted corticosteroids or antibiotics).

In patients with low estriol values a placental functional test can make a differentiation between foetal and placental defects possible in a more detailed way than estimations of HPL. Infusion of dehydroepiandrosterone (DHA) and/or its sulfate ester (DHAS) to patients with low estriol production allow us to investigate both the aromatizing enzyme system in the placenta and the placental sulfatase activity by measuring the serum estradiol concentration. It is the same enzyme systems which are involved in the conversion of 16α-hydroxy-DHAS to estriol in the foeto-placental unit, and the paper deals with examples where the DHA/DHAS test has been of great clinical help.

60. Plasma progesterone and estriol determinations in normal and high-risk pregnancies, E. R. JAEGER-WHITEGIVER, E. FRIEDRICH, B. FAUSER, P. NOTTEBAUM and A. E. SCHINDLER, Universitätsfrauenklinik, Tübingen, Germany

The measurement of estriol (E_3) in plasma or urine is used to monitor fetal-placental function in high-risk pregnancies. Data in the literature indicate that in pregnancies complicated by Rh-incompatibility, the quantitation of this steroid does not directly reflect the severity of fetal jeopardy caused by Rh-incompatibility. Therefore, specific radioimmunoassays for plasma E_3 and progesterone (P) were used to reevaluate the effects on the hormone patterns found in Rh-incompatibility and other pathological conditions. Plasma P and E_3 were measured following other extraction and a Sephadex LH-20 chromatographic step by using specific antisera. P and E_3 ranges for uncomplicated pregnancies were calculated from 300 samples taken at various weeks of gestation from a total of 275 women. Values were measured from 3 normal twin pregnancies. Single determinations were made from 54 plasma samples taken randomly throughout gestation from 49 women with complicated pregnancies (e.g., diabetes, pre-eclampsia, anencephaly, pre- and postmaturity) and serial determinations were made from 9 women with pregnancies complicated by Rh-incompatibility. the mean E_3 values for normal pregnancies range from 0·38 ng/ml plasma ±0·38 S.D. (n = 5) in the eighth week to 13·77 ng/ml ± 3·16 S.D. (n = 8) in the 40th week. The normal P values range from 20·86 ng/ml ± 10·49 S.D. (n = 5) in the eighth week to 136·97 ng/ml ±33·4 S.D. (n = 8) in the 40th week. Even in severe cases of Rh-incompatibility, normal to high E_3 and P values were found, confirming previous results. Only shortly prior to intrauterine death, a rapid fall of plasma E_3 and P concentrations occurred.

61. Hormonal pattern of threatened abortion, J. GERGELY, J. VAN PEBORGH, M. L'HERMITE-BALERIAUX and R. HECHTERMANS, Department of Obstetrics and Gynaecology (Pr. R. Vokaer), Brugmann University Hospital, Free University of Brussels, Belgium

Sixty cases of threatened abortions were studied, from

which 34 aborted and 26 had a favourable evolution. Serial determinations of urinary total oestrogens (fluorimetry according to Brown), pregnandiol (gas chromatography), HCG (inhibition of hemagglutination) and plasma progesterone (protein binding competition), oestradiol, HCG and HPL (radioimmunoassay) were performed. 1124 samples were assayed and related to normal values previously established in the laboratory. Correlation of results with clinical outcome was established for each of these hormones. For each hormone assayed, the percentage of infraliminary values corresponding to abortions was quoted and, similarly the percentage of values within the normal range corresponding to abortions was also established. Concerning the incidence of abortion when abnormal levels were noticed, we were able to conclude that 90% of these levels belonged to pre-abortion group as far as plasma HCG was concerned. The results are 87% for urinary HCG and plasma oestradiol 86% for plasma progesterone, 84% for urinary pregnandiol, 74% for plasma HPL (after the 12th week) and 68% for urinary oestrogens. When levels are within the normal range the probability that they belong to the abortion group is 22% for plasma progesterone, 28% for plasma HPL after 12th week, 30% for plasma HCG and 39% for plasma oestradiol and 41% for urinary and oestrogens. The conclusion of this study is that when abnormal levels of urinary or plasma HCG, plasma progesterone or oestradiol, and urinary pregnandiol are observed the probability of abortion is high. But when plasma progesterone levels are within the normal range probability of abortions is very low; correlation between normal values of other hormones and evolution of pregnancy is far less clear. This work emphasizes the value of plasma progesterone assay in monitoring threatened abortion as a factor of prediction of clinical outcome.

62. Changes in plasma dehydroepiandrosterone before and during pregnancy and in labour, A. E. SCHINDLER*, T. WALK* and E. NIESCHLAG†. *Universitätsfrauenklinik, Tübingen and †II. Med.-Univ. Klinik, Düsseldorf, Germany

Dehydroepiandrosterone sulfate (DS) is secreted by the maternal and fetal adrenal and represents the direct precursor of placental estradiol production and the indirect precursor of placental estriol biosynthesis. Since the measurement of this steroid has been used in recent years for placental function tests, the purpose of this investigation was to measure the changes of free dehydroepiandrosterone (D) and DS before and during pregnancy and in labour. D was measured by radioimmunoassay (Nieschlag *et al.: Steroids* 19 (1972) 669) and DS was measured by gas-liquid chromatography (Walk *et al.:* Archs. Gynäk. **214** (1973) 318). D determinations were made in 26 non-pregnant women, in 96 women during pregnancy and in 37 women at the beginning and at the end of labour. DS measurements were carried out in 42 non pregnant volunteers, 157 women at various stages of pregnancy and in 30 women at the start and at the end of labour.

D was significantly higher in pregnant than in non-pregnant women (0·73 vs 0·57 μg/100 ml, $P < 0{\cdot}002$), but there was no correlation between the stage of pregnancy and the D concentration. In labour the D concentration increased from 0·97 to 1·42 μg/100 ml ($P < 0{\cdot}001$). 69 μg/100 ml DS was found in plasma from non-pregnant women and a decrease to 37 μg/100 ml during pregnancy was measured ($P < 0{\cdot}05$). However, during labour, a significant increase was determined (from 40 to 75 μg/100 ml, $P < 0{\cdot}001$). These findings indicate a rapid and increased utilization of maternal DS by the placenta which does not affect the free D levels. In labour, however, the increase of D and DS in the maternal circulation seems to be related to increased ACTH secretion. Influences of an altered utero-placental blood flow, changes in placental enzyme activity and transfer of D and DS from the fetal circulation could be additional factors.

63. Modification of urinary steroid levels after administration of DHEA-sulphate to pregnant women presenting different kinds of intrauterine growth retardation, G. AGOSTONI, E. KOVARICH, A. GARAGIOLA, D. COLOMBO and F. POLVANI, Università di Milano, II Clinica Ostetrica Ginecologica, Italy

Twenty cases of retarded fetal growth, diagnosed during pregnancy by ultrasonic technique and confirmed by birth weight (which was more than 2 standard deviations below the mean for gestational age), had one administration of 30 mg DHEA-sulphate intravenously in order to verify if the variation in urinary steroids excretion of small-for-date foetuses would be similar, independently from their different etiological origin. Urine was collected every 2 h, from 8 a.m. to 8 p.m., DHEA-sulphate was administered at noon. Urinary steroid levels determination was made by gas-chromatographic method on high resolution glass capillary column (modified from Roa, 1971). Using this technique a single analysis was sufficient to measure all steroids normally involved in placental metabolic pathways of DHEA-sulphate. Results showed that, though selected foetuses made up a homogeneous group from a quantitative point of view, the steroid response to DHEA-sulfate was not uniform. If the trial was interpreted as placental function test (Lauritzen, 1967), two groups with different metabolic behaviour could be pointed out, the first with normal, the second with unsettled replying ability. Metabolic behaviour resulting from the test could be related to etiological and pathogenetic characteristics of each case. Lauritzen Ch.: *Acta endocr. Copenh.* Suppl. **119** (1967) 188. Roa A. and Sommerville I. F.: *J. Obstet. Gynaec. Br. Commwlth.* 78 (1971) 1096.

64. Hormonal dynamics during different model conditions of foetoplacental distress in midpregnancy, J. STASTNY, H. de WATTEVILLE, V. WEISS, P. VASSILAKOS and R. WYSS, Clinique universitaire de Gynécologie et d'Obstétrique, Genève, Switzerland

The aim of the study was to demonstrate the predictive value of plasma hormone assays used as foetoplacental function tests, in terms of the earliest possible detection of a significant concentration decrease following an experimental foetoplacental compromise. Normal volunteers undergoing legal pregnancy interruption between the 14th and 24th week were investigated. Hormonal dynamics of HPL, unconjugated progesterone (P) oestradiol-17β (E_2) and oestriol (E_3) was studied in the following model situations: In *saline induced abortions* (n = 10) foetal death occurred between the 35th and 105th min following the exchange of amniotic fluid by the hypertonic NaCl solution (10%). The time from instillation to a significant decrease of maternal plasma level was 1 h for HPL and 4 h for P. In *mid-pregnancy interruptions by hysterotomy* with subsequent sterilization (n = 10 + 3) an elastic tourniquet, routinely fastened around the isthmus to avoid bleeding, was used to reduce the uterine blood flow during 25 min (hypoxia), thereafter released for 25 min (restitution), after which uterotomy with subsequent evacuation of the conceptus was performed (disappearance). The degree of