The correlation coefficient between 15α-hydroxy-oestriol and its epimer was 0·88 and with total oestrogens determined by the Kober reaction, 0·69, while that with 18-hydroxy-oestriol was −0·03. The poor correlation between 18-hydroxy-oestriol and 15α-hydroxy-oestriol may signify an important difference in the pathways of their production. Measurement of 18-hydroxy-oestriol may prove to be of more clinical significance in pregnancy monitoring that 15α-hydroxy-oestriol has so far proved to be .

47. Plasma levels of estriol, estradiol-17β, progesterone, 17-hydroxy-progesterone and prostaglandins-$F_{1\alpha}$ and $F_{2\alpha}$ in pregnant women near term, S. DELL'ACQUA, A. MONTEMURRO, A. LUCISANO, C. PATRONO, D. GROSSI-BELLONI, E. PARLATI, B. CINQUE, E. ARNO and A. BOMPIANI, Instituto di Clinica Ostetrica e Ginecologica e Istituto di Farmacologia, Università Cattolica del S. Cuore, Roma, Italia

It is still not clear whether the levels of circulating progestins and estrogens in late pregnancy can influence the beginning of labour. The purpose of the present investigation was to determine the plasma levels of these steroids in normal pregnant women near term through a serial sampling and to correlate them with the plasma levels of prostaglandins-$F_{1\alpha}$ and -$F_{2\alpha}$. In a group of normal pregnant women plasma samples have been collected every 24 h at 38th week of gestation, every 12 h at 39th week of gestation and then every 6 h until labour began. Prostaglandins-$F_{1\alpha}$ and -$F_{2\alpha}$ and estriol, estradiol-17β, progesterone and 17-hydroxy-progesterone in free form have been measured in plasma samples by means of specific RIA.

From the analysis of the profiles obtained and the ratiòs between the different compounds studied we could not demonstrate any significant variation in the steroids and prostaglandins plasma levels before the beginning of labour.

48. Effect of ACTH administration into the fetus, on onset of labour and on maternal plasma steroid levels, O. GAMISSANS, E. DAVI, E. PEREZ-PICAÑOL, P. PUGOL-AMAT and G. R. WILSON, Department of Obstetrics and Gynaecology, School of Medecine, Universities of Barcelona (Spain) and Aberdeen (Scotland)

In a previous study (Gamissans *et al.*, Acta Endocrinologica Congress, Amsterdam, 1975) it was shown that the intraamniotic injection of β-metasone (20 mg) is ineffective in precipitating the onset of labour in humans. However, the following modifications in maternal serum steroid levels were found as a result of the corticosteroid administration: a decrease in total immunoreactive oestrogens and of unconjugated estriol. In an attempt to study further the role of the fetal adrenal gland on the mechanisms of onset of labour, synthetic ACTH (Synacthen depot 1 mg) has been injected into the fetal breech, in a group of nine pregnant women at 38–41 weeks. In a control group of eight pregnant patients, 1 ml of isotonic saline was also injected into the fetal breech. In all patients blood samples were taken daily, for two before injection into the fetus, until delivery. Injection-delivery interval and blood pH of umbilical vessels at delivery were recorded. Maternal serum progesterone, total immunoreactive oestrogens, unconjugated oestriol and oestradiol-17-β were measured by R.I.A. The results did not show any significant difference between treated and control groups recording injection-delivery interval, and umbilical artery and vein pH at delivery. Maternal serum total immunoreactive oestrogens and progesterone levels did not show, after ACTH injection, a different pattern than that observed in the control group. Results on unconjugated oestriol and oestradiol-17-β will also be presented. The ACTH injection into the fetus has no influence on the onset of labour in the conditions and dose level used in this study.

49. Monitoring of foetal well-being by the determination of estriol-16α-glucuronide in urine and plasma, HERMAN ADLERCREUTZ, TESSA LEHTINEN and KATARINA BIRATH, Department of Clinical Chemistry, University of Helsinki, Meilahti Hospital, SF-00290 Helsinki 29, Finland

A rapid and specific radioimmunological method for the assay, in pregnancy, of estriol-16α-glucuronide in urine and plasma has been developed. No extraction or purification is necessary. Antisera to estriol-16α-glucuronide, raised in two sheep and coupled to Sepharose particles, showed good specificity. Both antisera cross-reacted less than 4% with unconjugated estradiol and estriol, and less than 1% with unconjugated estrone. When tested against a number of conjugated estrogens, the antisera cross-reacted less than 1% with all except one. The exception was 17-epiestriol-16-α-glucuronide with which one antiserum cross-reacted about 17% and the other not at all. The method calls for samples of plasma to be diluted, 1:100 (v/v), samples of urine, 1:5000–100,000. Antibody diluted to give a 20% binding in the absence of unlabelled steroid, is added, and the samples are incubated while gently rotated for 30 min at room temperature. [^{3}H]-estriol-16α-glucuronide in buffer is added and incubation is continued for 1·5 h at room temperature and, while the tubes are still rotated, for 1 h at +4°C. After centrifugation the particles are washed three times with saline. Radioactivity, released from the particles by shaking with 1 M HCl, is then counted. This step enhances the sensitivity of the method 40-fold as compared to a direct counting of the particles. The coefficient of variation calculated from 30 duplicate urine samples was 8·7%. The limit of detection is 10 pg. Some preliminary data indicate that the day-to-day variation in urinary output of estriol-16α-glucuronide is about 7 to 13% and is hence smaller than that reported for total estriol. Preliminary clinical results suggest that, because of this smaller variation, the determination of estriol-16α-glucuronide is more useful than the measurement of total estriol in monitoring of foetal well-being. The results obtained with this method correlated well with those obtained with a

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Structure	Mean mg/24h	Range mg/24h	No.
Oestratriene-3,15ξ,16ξ,17ξ-tetrol	0·74	0·3 –3·0	20
Oestratriene-3,15α,16α,17β-tetrol	1·69	0·75–4·1	20
Oestratriene-3,16ξ,17ξ,18-tetrol	0·39	0·2 –1·5	20
3, 15ξ,16ξ-trihydroxy oestratriene-17-one	0·08	0·05–0·10	3
3,16ξ, 18-trihydroxy oestratriene-17-one	0·07	0·05–0·10	3

specific gas chromatographic procedure. It is a specific and rapid procedure that allows for a great number of assays to be carried out in a short time. The method also seems amenable to further refinement, e.g., the introduction of radioactive iodine into the tracer might not only reduce counting time but also make possible the direct counting of the particles without excessive loss of either sensitivity or precision.

50. Control of aldosterone secretion in mother and newborn under delivery and in childbed, J. NUSSBERGER, H. BUCHER, J. SCHMID, U. SCHMIED, J. MICHELI, D. MIETH, G. DUC, W. SIEGENTHALER and W. VETTER, Departments of Medicine, Obstetrics and Neonatology, Kantonsspital, University of Zürich, Switzerland

Plasma aldosterone (PA), plasma cortisol (PC), angiotensin II (A II) and renin activity (PRA) were determined in 6 healthy women during and one week after delivery, in umbilical blood and in the 6 newborns one week after birth. PA, A II and PRA were measured by radioimmunoassays. PC was determined by the protein binding method. Diazepame and N_2O were the only therapeutic regimens used.

In the mothers, mean PA, PC, A II and PRA decreased significantly ($P < 0{\cdot}001$) within one week from elevated levels under delivery to normal or even subnormal values: PA from 873 ± 470 ($\pm$ S.D.) to 58 ± 8 pg/ml, PC from 53 ± 25 to 13 ± 2 μg/100 ml, A II from 46 ± 18 to < 6 pg/ml and PRA from $11{\cdot}5 \pm 7{\cdot}5$ to $0{\cdot}6 \pm 1{\cdot}2$ ng/ml3h. PA correlated significantly with A II ($P < 0{\cdot}001$), PRA ($P < 0{\cdot}01$) and PC ($P < 0{\cdot}01$).

In the umbilical vessels, PA, PC, A II and PRA showed no significant arteriovenous difference (artery: PA 589 ± 300 pg/ml, PC 11 ± 4 μg/100 ml, A II 73 ± 45 pg/ml and PRA $15{\cdot}5 \pm 22$ ng/ml·3h; vein: PA 632 ± 391 pg/ml, PC 11 ± 4 μg/100 ml, A II 87 ± 53 pg/ml and PRA $16 \pm 22{\cdot}6$ ng/ml·3h). Under these conditions no significant correlations were found between PA and PRA, PA and A II and between PA and PC.

In the newborns, one week after birth, lower PA, PC, A II and PRA values were observed than in umbilical blood (PA 437 ± 404 pg/ml, PC 4 ± 4 μg/100 ml, A II 30 ± 22 pg/ml and PRA $12 \pm 22{\cdot}3$ ng/ml·3h). Under these conditions significant correlations were found between PA and PRA ($P < 0{\cdot}001$) and between PA and A II ($P < 0{\cdot}05$), whereas PA did not correlate with PC.

Our results indicate that in the mother both the renin angiotensin system and ACTH influence the secretion of aldosterone. In the newborn, adrenal aldosterone release seems to be predominantly controlled by renal renin secretion. The inability to correlate umbilical PA with PRA, A II or PC might be caused by the following reasons: (1) Aldosterone crosses the placenta and (2) The placenta seems to produce renin.

K. Sexual steroids in the neonatal period, MAGUELONE G. FOREST and JEAN BERTRAND, Unité de Recherches Endocriniennes et Métaboliques chez l'Enfant, INSERM U. 34, 29 Rue Soeur Bouvier, 69322 Lyon Cedex 1, France

It is now well established that the gonadal endocrine function is under the control of a complex neuroendocrine system and that in adults the regulatory mechanisms are different in male and female. From experimental studies in the last decade, it became clear that the cybernetical hypothalamic-pituitary-gonadal system was not fully mature at birth. Recent technical improvements led to precise measurement of sexual and pituitary hormones. It has been established that the pituitary gonadal system functions in childhood and also in infancy.

Although it is often difficult to extrapolate studies between species particularly since the maturation of the central nervous system at birth is quite different from one species to the next, experimental studies have considerably advanced our comprehension of the establishment, maturation and change with age, in the regulatory mechanisms controlling the gonadal function.

The purpose of this presentation is to report our ongoing studies of the ontogenesis of plasma concentration of gonadal steroid hormones in human and particularly the chronology of their secretion by the neonate and the infant as one aspect of development and maturation of the hypothalamo-pituitary-gonadal axis in the neonatal period.

We have developed sensitive and specific radioimmunoassay technics to quantify plasma levels of testosterone, [1] 4-androstenedione and [2] 17-hydroxyprogesterone (present). Blood was obtained from the cord at 105 normal full term babies at the time of spontaneous vaginal delivery and from a peripheral vein of 245 normal infants aged 0 to 361 days. Normal children and adults were also studied for comparison.

A. *Testicular function in the neonatal period*

Total unconjugated testosterone. In a previous study of 81 normal neonates we have shown that cord blood levels of testosterone were significantly higher in males ($33{\cdot}8 \pm 9{\cdot}5$ ng/100 ml; $n = 35$) than in female newborns ($26{\cdot}4 \pm 7{\cdot}4$ ng/100 ml; $n = 46$) [3]. The simultaneous measurement of testosterone (T), 4-androstenedione (Δ) and 17-hydroxy-progesterone (17-OH-P) was made in another smaller group of normal neonates and results are given in Table 1. Although mean values in T levels are slightly higher in this second group the same sex difference is observed. Our results strongly suggest that testicular activity is present at birth. However in none of the available studies in the literature was a sex difference in cord T levels demonstrated. We therefore studied androgens in the peripheral veinous blood of normal neonates. Results are given in Table 1. In male newborns on the first day of life, T plasma concentrations are considerably higher in experipheral blood than in cord blood and the sex difference is even more significant. These results further evidence the fetal and testicular origin of T at birth. In female newborns, circulating levels of T are slightly but significantly higher than in cord plasma. These mean T levels of $46{\cdot}3 \pm 13{\cdot}9$ ng/100 ml, comparable to those we observed in adult females ($37{\cdot}2 \pm 9{\cdot}6$ ng/100 ml), decrease rapidly within the first two weeks of life to low values and remain constant throughout the first year of life ($7{\cdot}1 \pm 3{\cdot}3$ ng/100 ml).

In contrast the pattern in T plasma concentration is quite different in male infants and follows a triphasic evolution. The high T levels present at birth (228 ng/100 ml, comparable to those of boys at stage P_3 of puberty), decrease very sharply within the first week of life to a nadir observed at 5–7 days of age when values average 31 ng/100 ml. T plasma concentrations increase thereafter rapidly to peak values of $265 \pm 31{\cdot}3$ ng/100 ml reached between 30 and 60 days of age. From the second to the seventh month of life T values decrease again, more slowly, and correlatively with time. From 7 months of age onwards T levels remain low in male infants ($7 \pm 4{\cdot}7$ ng/100 ml) and identical to those of female infants 1 to 12 months old and to those of prepubertal children of both sexes ($6{\cdot}7 \pm 2{\cdot}5$ ng/100 ml).

The binding capacity of plasma proteins for testosterone was measured by equilibrium dialysis. At birth this binding capacity is low in both sexes and similar in cord and peripheral bloods. It increases very rapidly after birth, reaching prepubertal values in 2–3 weeks. The unbound