

Plasma levels of cortisol, oestradiol and progesterone in the cord of eutrophis infants born at term

by

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Numerous authors have studied the behaviour of plasma levels of the steroids in the maternal blood and the blood of the cord.

Tulchinsky (²⁸) and Shutt *et al.* (²⁰) have demonstrated the importance of the placental secretion in determining the high plasma levels of oestrogens in the maternal and cord blood; Salomon & Fuchs (¹⁷) and others have demonstrated that the most important source of the high levels of progesterone in the mother and foetus is the placenta.

Still more recently, following observations (¹³) relating to the close relationship said to exist between the structure of the suprarenal cortex of the premature foetus and the development of hyaline membrane disease, numerous investigations have been undertaken in order to compare the anatomo-pathological with the hormonal findings. For this purpose, in order to assess the activity of the suprarenal cortex in the pregnant woman, various investigations have been made into the plasma levels of the corticosteroids in the maternal blood (²²) in the cord blood (^{2,23,24}) and in the amniotic fluid (^{12,22}). Satisfactory functioning of the suprarenal seems in fact to play a fundamental role in encouraging maturation of the respiratory apparatus of the foetus, stimulating in particular the production of « surfactant » by the pulmonary alveoli (²⁴).

On the basis of these observations we felt it would be of value to examine the variations in the plasma levels of cortisol, oestradiol and progesterone that are found, in physiological conditions, in the maternal blood before and after birth, comparing them with those of the cord blood.

MATERIAL AND METHODS

Blood samples, each about 10 ml, were obtained from 19 pregnant women, at term both clinically and as regards the history, during labour and 30 minutes after the completion of spontaneous delivery.

Soon after birth, about 10 ml of blood was obtained from the cord of 19 foetuses without any signs of distress (Apgar score between 9 and 10).

All the samples were immediately centrifuged, the plasma was separated and kept at -20°C until analysed by the radio-immunological method.

The standard used for the radio-immunological determination of cortisol was Vister's chromatographically pure hydrocortisone; the substance used as antibody was anti-cortisol-21-hemisuccinate-BSA rabbit serum, absorbed on to a substrate of cellulose (SORIN); the tracer used was cortisol-2-4-6-7- H^3 (N.E.N.). Before analysis, the plasma was washed with petroleum ether (1:10) and extracted with

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dichloromethane (1:25). After incubation for 45 min. on a rotating stirrer and centrifugation at 2000 r.p.m. for 10 minutes, the count was made.

Progesterone and oestradiol, after extraction with ethyl ether (1:10), were determined, using as standard Vister's chromatographically pure substances and as tracer, progesterone 1-2-6-7 H^3 and oestradiol -2-4-6-7 H^3 (N.E.N.) respectively. As antisera, the antiprogesterone 11- α -BSA and antioestradiol-6-BSA rabbit sera (BIODATA) were used. After incubation for 30 min. at 37° C for 3 hours at 2°-4° C, the antigen-antibody complex was separated with charcoal-dextran (1 mg/tube) and subsequently centrifuged at 2000 r.p.m. for 10 minutes according to Abraham's method (¹).

Chromatographic purification on a celite column was done on 10 of the samples of blood obtained from the cord, according to the method of Facchinetti *et al.* (³). This chromatography was followed by radio-immunological determination of progesterone.

RESULTS

The plasma level of oestradiol in the maternal blood were found, at the moment of birth, to be 22.45 (± 13.34) ng/ml; 30 minutes later they had fallen to 6.69 ng/ml (± 3.80); while in the cord blood the mean value was 9.9 (± 3.85) ng/ml (Fig. 1).

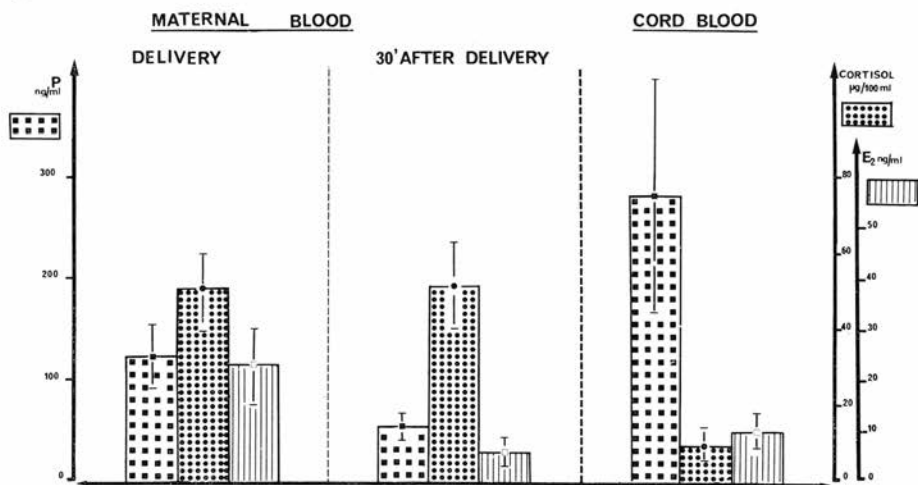


FIG. 1

Statistical analysis with the « paired t » test showed a significant difference between the concentration of the maternal blood before birth as compared to 30 minutes later ($p < 0.001$) and as compared to the cord blood ($p < 0.005$). No statistically significant difference was demonstrated between the levels of oestradiol in the maternal blood, obtained 30 min. after birth, and those in the cord blood.

The maternal plasma progesterone was found at the time of birth to be 119.9 ng/ml (± 31.4); 30 minutes later the values had fallen to 54.15 ng/ml (± 16.81). In the cord the concentrations of progesterone were 277.94 ng/ml (± 137.49) (Fig. 1). Comparison between the maternal and cord levels, done by the « paired t »

test, showed that the cord concentrations were significantly higher than the maternal concentrations ($p < 0.05$). Likewise, the maternal results were statistically higher at the time of birth as compared to 10 minutes later.

The plasma progesterone levels obtained prior to chromatographic purification were markedly less (258.32 ± 87.57 ng/ml) than those obtained by the direct extraction method.

In the mother, cortisol reached concentrations of $49.84 (\pm 14.25)$ $\mu\text{g/ml}$ at the time of birth, maintaining similar values even 30 minutes later (46.42 ± 15.05 $\mu\text{g/100 ml}$). In the cord, concentrations of 12.1 ± 3.24 $\mu\text{g/100 ml}$ were measured, significantly less than those encountered in the maternal blood both before and after birth ($p < 0.001$) (Fig. 1).

The concentrations of the three steroids measured separately in the vein and in the umbilical artery in 10 of the 19 cases examined, are shown in the following table:

Tab. 1. Plasma levels of cortisol (F), Oestradiol (E_2) and Progesterone (Pr) in the umbelical vein and artery (M+O.S.).

| | Vein | Artery | n | Paired « f » | p |
|----------------------------|----------------|----------------|----|--------------|-------|
| F ($\mu\text{g/100 ml}$) | 14.5 ± 5.8 | 14.8 ± 3.1 | 7 | 0.1596 | n.s. |
| E_2 (ng/ml) | 15.4 ± 4.7 | 10.9 ± 5 | 6 | 3.3990 | 0.01 |
| Pr (ng/ml) | 344.8 ± 99 | 213.4 ± 66 | 10 | 3.6500 | 0.005 |

DISCUSSION

The highest concentrations of oestradiol and progesterone were measured in the maternal blood before birth. This confirms the role of the placenta in determining the high levels of these steroids in pregnancy. In fact even at about the time of birth (as many authors have maintained), the placenta is able to ensure not only continuous production of steroids, but can also increase the production of some steroids such as oestradiol (²⁹).

After birth the concentration of both steroids will markedly diminish, since they are no longer produced by the placenta, which has now been expelled. Nevertheless, many authors have found low levels of oestradiol and progesterone after birth, with higher levels of the metabolites (^{14,17}), confirming the fact that catabolic transformation of both steroids is in progress, on the part of the liver and other maternal organs.

As regards the behaviour of cortisol in the maternal blood, the high levels measured before and after birth cannot be accounted for except by the presence of labour stress. In fact, even though plasma cortisol gradually increases throughout pregnancy (^{19,6}) it is only during labour that it reaches the highest concentrations (⁸). In our opinion, the stress can justify such high concentrations of corticosteroids even 30 minutes after birth.

In addition, notwithstanding that numerous authors have studied the possibility that the increase of cortisol during pregnancy might be linked to the development of pregnancy itself (¹¹), or to the onset of labour (^{14,15}), the existence of any direct connexion between the levels of cortisol and the development of pregnancy or labour is at present denied, as indeed has been demonstrated in various animal species, for example the sheep.

The levels of oestradiol in the cord, although significantly less than those found in the mother, show clearly how important is the placental source of these steroids for the foetus as well. The significantly higher values in the vein as

compared to the artery also show that there is « fixation » of this steroid in the foetal area. These data justify the special attitude of the pituitary in the neonate which, under the influence of the high values of oestradiol, has been shown to be clearly incapable of responding to stimulation by exogenous LHRH (?), as will on the contrary occur after 7 days when the oestradiol values have fallen to normal levels.

Contrary to what has been observed in the case of oestradiol, progesterone shows significantly higher values in the foetus as compared with the mother, thereby indicating the accumulation of this steroid in the foetal area. This phenomenon appears to be of great importance physiologically, in view of the considerable utilization of progesterone as a precursor in the suprarenal production of steroids (^{17, 25, 26, 27}). The increased gradient between values in the umbilical vein and artery explains the considerable foetal « consumption » of progesterone.

In conclusion, our data confirm the apparent non-importance of foetal cortisol in determining the values for the maternal circulation and as regards the phenomena capable of inducing or maintaining labour, and once more confirm the nature of the placental contribution of oestradiol and progesterone in the foetal circulation.

These data also indicate that there is quite considerable consumption of these steroids by the foetus, and this is found to be quantitatively of greater importance as regards progesterone, which is known to play the part of precursor in suprarenal foetal steroid production.

Further research will assess the importance of deficient synthesis of progesterone on the part of the placenta, which occurs in some pathological conditions in pregnancy, for example premature labour (?) also characterized by a high incidence of perinatal mortality, in the functioning of the foetal suprarenal gland and in its capacity to respond to situations of stress such as labour and neonatal adaptation.

SUMMARY

The plasma variations of oestradiol, progesterone and cortisol in the maternal blood were assessed before birth and 30 minutes after it. These variations were compared with their progress in the umbilical cord of the respective neonates.

In 10 cases evaluations were made of the steroid levels in the mixed blood of the cord as well as separately in the venous and arterial cord blood.

The importance of the placenta as a source of circulating steroids in the maternal blood was confirmed. Cortisol did not show any correlation with the progress of labour, but it did with the stress of labour. In the cord, the levels of oestradiol and cortisol were less than those in the mother, while progesterone was found to be equally high.

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Comments on some current trends in perinatal medicine and obstetric anaesthesia

by

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The following are personal opinions based on observations of everyday occurrences or on preliminary work still in progress. They are reported only with the purpose of stimulating further constructive discussions.

A. THE MONITOR SYNDROME

The growing tendency to indiscriminate use of monitoring devices for normal parturients has a number of disadvantages, the most relevant of which are:

A.1. Concerning the patient

A.1.1. Unless the parturient is properly instructed (and sometimes even following a lengthy discussion), to be connected with a monitoring machine represents for

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