

Plasma 17OH-progesterone concentrations in newborn infants

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SUMMARY Plasma concentrations of 17OH-progesterone were determined in 60 normal newborn infants aged between 3 and 36 hours. Mean levels decreased rapidly during this time after removal of the placental contribution of this steroid. A further 70 normal infants, studied between ages 2 and 7 days, showed a mean plasma 17OH-progesterone concentration of 3.5 nmol/l (1.2 ng/ml). By comparison, plasma concentrations in untreated infants with congenital adrenal hyperplasia were markedly raised. At 36 hours of age, there was an obvious difference between plasma levels of this steroid in normal and affected infants. Determination of plasma 17OH-progesterone concentrations are valuable in the evaluation of disorders of sexual differentiation and electrolyte balance in newborn infants, provided due care is given to the timing of sample collections.

It is now well established that plasma concentrations of 17OH-progesterone are markedly raised in untreated congenital adrenal hyperplasia (CAH) due to C-21 hydroxylase enzyme deficiency (Barnes and Atherden, 1972; Youssefnejadian and David, 1975; Hughes and Winter, 1976). Consequently, requests for measuring this steroid in plasma collected from newborn infants with ambiguous genitalia are increasing in frequency. The Supraregional Assay Service Laboratory at the Tenovus Institute receives numerous blood samples each week for determination of plasma 17OH-progesterone concentrations. Many of these samples have been collected within the first 48 hours of life at a time when, because of placental 17OH-progesterone production (Tulchinsky and Simmer, 1972), plasma concentrations are raised in normal newborn infants. There is a limited amount of information on plasma concentrations of 17OH-progesterone during early life and on the time taken for levels to decrease to values observed in later infancy and childhood. This report gives data on plasma 17OH-progesterone concentrations in mixed cord blood and in a group of normal newborn infants studied during early postnatal life. The results are compared with those found in untreated newborn infants with CAH.

Patients and methods

Mixed cord blood samples were obtained from 19 babies (10 boys and 9 girls) immediately after cord clamping. Their gestational ages ranged from 37 to 41 weeks. Capillary blood was collected by heel prick from 60 infants who were products of uneventful term pregnancies. There were 32 boys and 28 girls, whose postnatal ages ranged from 3 to 36 hours at the time of sample collection. Maternal consent for the study was obtained in each case. Plasma samples collected from 70 infants up to 7 days' postnatal age and sent to this laboratory were also available for analysis. Several infants with CAH due to C-21 hydroxylase deficiency were studied during the first week of life before starting steroid replacement therapy. Their plasma 17OH-progesterone concentrations were compared with those determined in normal infants.

Plasma 17OH-progesterone was measured by radioimmunoassay (RIA) using an antiserum kindly donated by Dr D. L. Loriaux, NIH, Bethesda. The sensitivity of the assay was 4 pg/tube using 200 μ l plasma. Apart from 11-deoxycortisol (3.3%) and 21-deoxycortisol (1.6%), the cross-reactivity of the 17OH-progesterone antiserum with numerous other steroids, including progesterone, was less than 0.1%. The intra-assay coefficient of variation was $\pm 6.3\%$; the inter-assay coefficient of variation was $\pm 7.5\%$ (high pool) and 11.9% (low pool). All RIA data processing was performed using the method of

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Rodbard and Hutt (1974) and quality controlled by the method of Kemp *et al.* (1978). The mathematical relationship between plasma concentration (Y) and the age of the newborn infant (t) was reasonably described by a power function of the form $Y = At^B$ within the time-span of sampling. The index of determination was 0.72 and values of A and B determined by least squares analysis of data contained in Fig. 1, using a linear transformation of this equation, were 151 and -0.906 respectively.

Results

Mean values for plasma 17OH-progesterone concentrations in mixed cord blood were 203 ± 37.8 SD nmol/l (69 ± 12.9 ng/ml) for boys and 184 ± 34.5 SD nmol/l (62.6 ± 11.7 ng/ml) for girls. There was no significant sex difference. The individual plasma

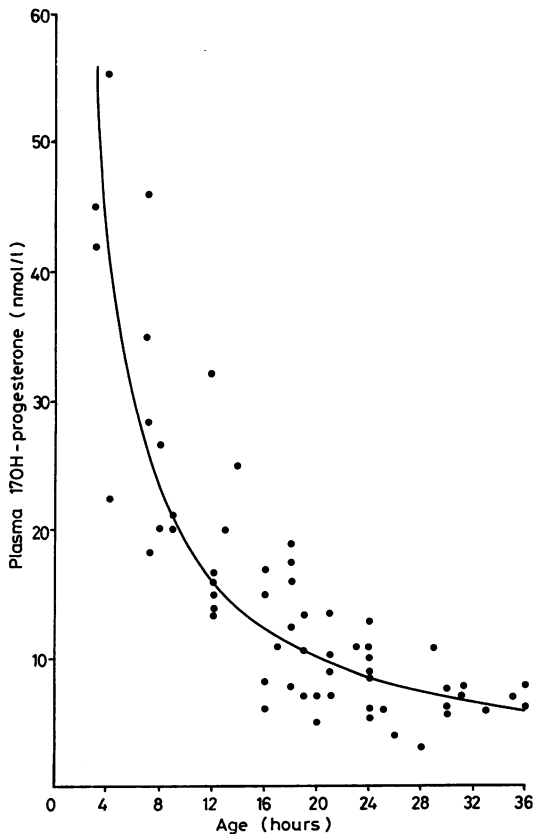


Fig. 1 Plasma 17OH-progesterone concentrations in normal infants during the first 36 hours of life. The line represents the mean plasma concentration of this steroid in baby boys and girls.

Conversion: SI to traditional units—17OH-progesterone: 1 nmol/l \approx 0.31 ng/ml.

17OH-progesterone concentrations for 60 newborn infants in relation to postnatal age are shown in Fig. 1. The line represents the mean plasma 17OH-progesterone concentration for the whole group of infants, there being no significant difference between mean concentrations in boys and girls. The mean plasma 17OH-progesterone concentration fell rapidly after birth, from 45 nmol/l (16 ng/ml) at 12 hours, to 8.5 nmol/l (2.9 ng/ml) at 24 hours, and 6 nmol/l (2 ng/ml) by 36 hours of age. This represents a 32-fold decrease from the mean cord plasma 17OH-progesterone concentration. The pattern of plasma 17OH-progesterone concentrations in normal infants during the first week of life is shown in Fig. 2. Mean levels reached a nadir of about 3.5 nmol/l (1.2 ng/ml) by 7 days of age. This contrasts with plasma 17OH-progesterone concentrations in untreated CAH infants during the first 7 days of life. At 12 hours' postnatal age, there was a wide difference between plasma 17OH-progesterone concentrations in normal and CAH infants. By the 2nd day there was a 40-fold

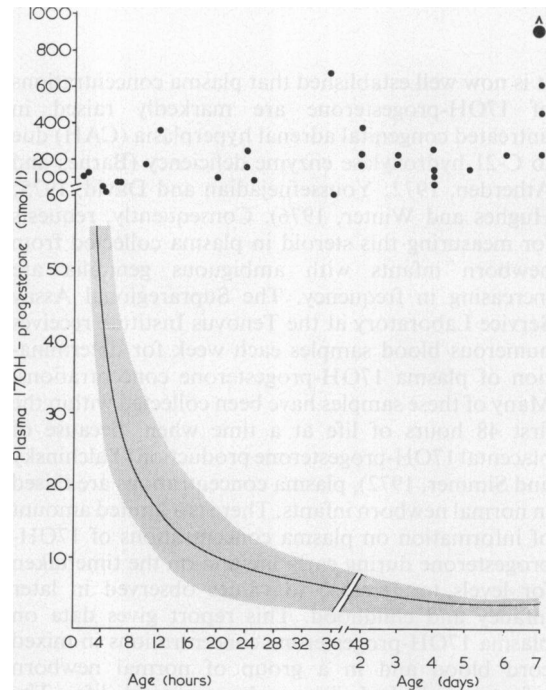


Fig. 2 Plasma 17OH-progesterone concentrations in normal and CAH infants during the first 7 days of life. The line represents the mean and the shaded area encompasses the range of plasma concentrations in normal babies. Also shown are individual plasma 17OH-progesterone concentrations determined in untreated CAH infants. \blacktriangle represents a value of 2430 nmol/l (826 ng/ml).

difference in mean plasma 17OH-progesterone concentrations.

Discussion

This study confirms previous reports of a raised cord plasma 17OH-progesterone concentration reflecting placental production of this steroid (Jenner *et al.*, 1970; Lippe *et al.*, 1974; Winter *et al.*, 1976). There are two recent studies which give data on plasma 17OH-progesterone concentrations during the first 24 hours of life of newborn infants (Forest and Cathiard, 1978; Sippell *et al.*, 1978). Both report the rapid fall in plasma levels within hours of birth, reaching a nadir by about 5 to 7 days of age. The results now reported confirm and extend this observation in a larger group of infants also studied during the first week of life. As measurement of plasma 17OH-progesterone is so valuable in the early diagnosis of CAH, a comparison was made between results of plasma 17OH-progesterone determinations in normal and CAH infants. The data clearly show that, by 36 hours' postnatal age, there is a pronounced difference between the two groups.

Congenital adrenal hyperplasia is the most common cause of ambiguous genitalia of the newborn (Hughes, 1977). In many instances, plasma 17OH-progesterone measurements will also aid in the assessment of other conditions. In addition, some infants who are stressed—for example, due to infection—have concentrations of plasma 17OH-progesterone up to 30 nmol/l (10 ng/ml) at 5 to 7 days of age. However, plasma 17OH-progesterone concentrations exceed 200 nmol/l (68 ng/ml) in untreated CAH infants of this age.

Therefore, determination of plasma 17OH-progesterone concentrations in the neonatal period can be extremely useful for the differential diagnosis of ambiguous genitalia, electrolyte disturbances, or for the investigation of baby boys with a positive family history for CAH (Hughes and Winter, 1977). It is recommended that plasma samples should be collected after 24 hours' postnatal age in order to eliminate the placental influence on plasma 17OH-progesterone levels. The exact age of the infants, in hours, at the time samples are collected should be known.

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