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PLASMA 17-KETOSTEROIDS OF FULL-TERM AND PREMATURE INFANTS [1, 2]

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The adrenal cortex of the newborn exhibits a relative lack of responsiveness to the administration of adrenocorticotrophic hormone which has been the subject of several investigations and is adequately reviewed elsewhere (1). These observations, together with the presence of the fetal reticular zone of the adrenal cortex and the recent report of very low concentrations of compound F-like substances in newborn plasma (2), are all reminiscent of the findings in infants and children with congenital adrenal hyperplasia (3, 4).

Since children with congenital adrenal hyperplasia have been shown to have markedly elevated concentrations of plasma neutral 17-ketosteroids (5), it was thought desirable to investigate the concentrations of these steroids in the plasma of newborn infants. The purpose of this paper is to describe analytic data obtained when plasma samples from a group of normal full-term infants and a group of premature infants were analyzed for neutral 17-ketosteroids.

METHODS

Normal full-term infants in the newborn nursery and premature infants in the premature unit of the Syracuse Memorial Hospital were utilized for the study. Seventeen analyses on plasma from 19 full-term newborns were done (plasma was pooled in two instances). Twenty analyses were done on as many premature infants. Venous blood was collected by femoral puncture and oxalated. Plasma was separated by centrifugation at about 2500 r.p.m. for 10 minutes and stored at 0° F. until analyzed. Neutral 17-ketosteroids were determined on 3 to 7 ml. samples of plasma as described elsewhere (6). The results were expressed as μg. per 100 ml. of plasma. This method utilizes chromatography on "Florisil" columns, the Zimmermann reaction being carried out on the residue of a chloroform eluate. The latter solvent is used, since crystalline 17-ketosteroids are eluted from the column by it, but not by ethanol-chloroform mixtures When plasma samples from premature infants 9, 10, and 12 were analyzed (Table I), the Zimmermann chromogen was eluted by pure chloroform, but not by 2 per cent ethanol in chloroform. This chromatographic distribution was consistent with that obtained using crystalline 17-ketosteroids.

Since hyperbilirubinemia is not infrequent in the newborn period, a 10 mg. sample of crystalline bilirubin was subjected to the entire analytical procedure. No measurable Zimmermann chromogen was found, indicating that elevated serum bilirubin concentrations should not cause falsely high values for plasma 17-ketosteroids.

RESULTS

Studies on full-term newborns

Measurement of plasma neutral 17-ketosteroids on samples from full-term infants during the first five days of life are shown in Figure 1. For purposes of comparison the transverse dotted line at 56 μg. per 100 ml. shows the mean value (± standard error of the mean) for plasma 17-ketosteroid concentration in non-pregnant women (6). The data indicate that the full-term newborn may have plasma neutral 17-ketosteroid values during the first 48 hours of life which are in excess of those found in the adult female. There is a rapid fall of plasma neutral 17-ketosteroid values during the first five days of life to very low concentrations by the fifth day. No measurable plasma values were obtained in normal full-term infants after the first week of life. Analyses done on samples from older infants and pre-adolescent children indicated that plasma 17-ketosteroids, if present, were in concentrations lower than this method could estimate.

Studies on premature infants

Table I provides data on 20 premature infants, age 1 to 42 days and with body weights of 793 to

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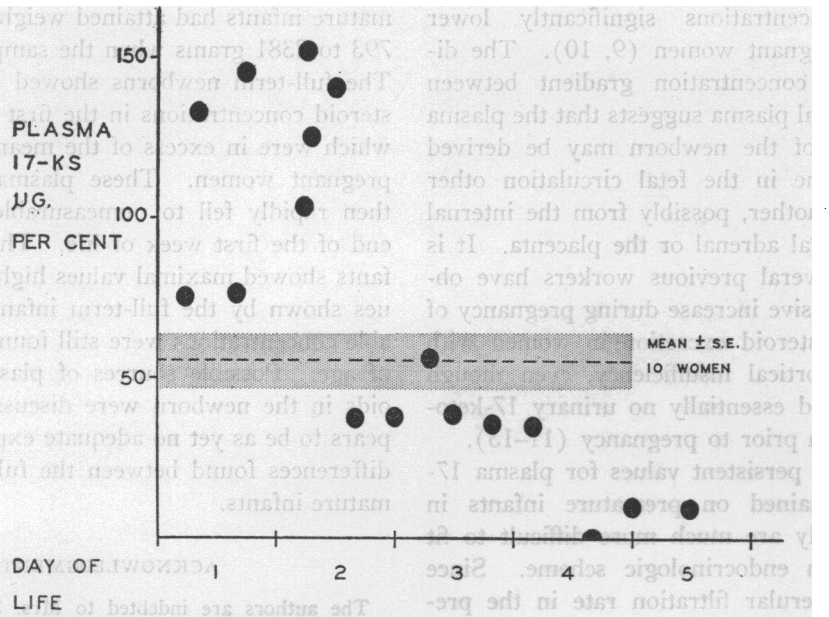

FIG. 1. PLASMA NEUTRAL 17-KETOSTEROIDS DURING THE FIRST FIVE DAYS OF LIFE IN NORMAL, FULL-TERM INFANTS

2381 gm. The value of 533 µg. 17-ketosteroids per 100 ml. of plasma in Patient 1 is the highest concentration thus far obtained on a human subject in this laboratory. Measurable concentrations of plasma 17-ketosteroids were found in all the premature infants examined.

TABLE I

Plasma 17-ketosteroid data on premature infants of various body weights and ages

Patient No.	Sex	Age days	Body weight: At birth gm.	Body weight: Attained wt. gm.	Plasma 17-KS µg. per 100 ml.
1	M	1	1,134	1,134	533
2	F	1	793	793	181
3	F	2	1,871	1,757	183
4	F	2	1,843	—	106
5	M	2	1,871	—	105
6	F	2	2,154	—	67
7	M	3	1,615	—	310
8	M	4	2,097	1,984	36
9	M	8	1,049	964	76
10	M	8	1,615	1,361	8
11	F	13	1,984	1,928	32
12	F	15	1,899	1,984	22
13	F	16	2,041	2,381	7
14	M	17	1,729	1,729	105
15	F	17	1,672	1,928	49
16	M	18	1,956	1,871	62
17	M	27	1,331	1,729	19
18	F	32	1,361	1,956	42
19	F	34	1,700	2,268	34
20	F	42	1,446	2,069	40

DISCUSSION

The present finding in full-term infants of elevated plasma 17-ketosteroid concentrations in the first days of life with subsequent fall, fits in with the results obtained by Read, Venning, and Ripstein on urinary 17-ketosteroids in the newborn (7). These workers found a sharp diminution in the excretion of urinary 17-ketosteroids during the first nine days of life. Whereas the plasma 17-ketosteroid values in the full-term newborns of the present study are somewhat higher than the values found in adult females, the urinary excretion of 17-ketosteroids in the newborn was found by Read, Venning, and Ripstein (7) and also by Klein (8) to represent only a small fraction of the adult figure. This disparity between plasma and urine may be the result of an endogenous "load" of 17-ketosteroids presented to the kidneys of the newborn infant for urinary excretion.

The possible sources of the elevated plasma 17-ketosteroids in the newborn infant represent an interesting enigma. Recent findings which may throw light on this problem are the observations that the 17-ketosteroid concentration is consistently greater in umbilical cord plasma than in simultaneously collected maternal plasma and that women near the end of pregnancy have plasma 17-

ketosteroid concentrations significantly lower than do non-pregnant women (9, 10). The direction of the concentration gradient between cord and maternal plasma suggests that the plasma 17-ketosteroids of the newborn may be derived from some tissue in the fetal circulation other than from the mother, possibly from the internal cortex of the fetal adrenal or the placenta. It is relevant that several previous workers have observed a progressive increase during pregnancy of urinary 17-ketosteroid excretion in women with proven adrenocortical insufficiency, even though these women had essentially no urinary 17-ketosteroid excretion prior to pregnancy (11–13).

The high and persistent values for plasma 17-ketosteroids obtained on premature infants in the present study are much more difficult to fit into any known endocrinologic scheme. Since values for glomerular filtration rate in the premature infant are lower than in the full-term newborn, it is not too surprising that the highest plasma 17-ketosteroid values of the neonatal period were obtained in premature infants. On the other hand it is hard to see how this mechanism could be invoked to explain elevated plasma 17-ketosteroid values in premature infants four or five weeks old, unless there were a continuous endogenous source of plasma 17-ketosteroids. It would be tempting to suggest that delayed involution of the internal cortex of the fetal adrenal is responsible for this phenomenon in the premature infant. However, Lewis and Pappenheimer (14) and Potter (15) state generally that premature infants show no delay of involution of the internal adrenal cortex. In contradistinction Moeri presents specific protocols of premature infants showing retardation of internal zone involution (16). The latter observation would go along nicely with the finding of persistent elevation of plasma 17-ketosteroid concentration in the premature infant. Since the histological studies referred to are in disagreement, it would appear that judgment on this point should be reserved until our state of knowledge is more satisfactory.

SUMMARY

Plasma samples have been analyzed for neutral 17-ketosteroids from 19 full-term, newborn infants, and from 20 premature infants. The premature infants had attained weights ranging from 793 to 2381 grams when the samples were taken. The full-term newborns showed plasma 17-ketosteroid concentrations in the first 48 hours of life which were in excess of the mean value for non-pregnant women. These plasma concentrations then rapidly fell to unmeasurable values by the end of the first week of life. The premature infants showed maximal values higher than the values shown by the full-term infants, and measurable concentrations were still found up to 42 days of age. Possible sources of plasma 17-ketosteroids in the newborn were discussed. There appears to be as yet no adequate explanation for the differences found between the full-term and premature infants.

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