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DHAS HALF-LIFE IN PREGNANCY, ITS PROGNOSTIC VALUE IN HIGH RISK PREGNANCIES

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SUMMARY

The half-life of DHAS (Dehydroepiandrosterone sulfate) was measured after the infusion of non tritiated DHAS during the third trimester of human pregnancy to assess the feto-placental unit risks in pathological pregnancies.

In normal pregnancies, the mean value of the half-life of DHAS at 30 weeks was 3.64 h ± 0.7 ($n = 7$) and at 38 weeks it was 3.67 h ± 0.38 ($n = 7$). In non pregnant women, it was 8 h 20. Among 14 pathological pregnancies that we studied, 13 cases exhibited a DHAS half-life significantly longer than the average value obtained in normal pregnancies. In pathological pregnancies, the half-life of DHAS is closer to the value observed in non-pregnant women.

INTRODUCTION

During pregnancy, DHAS is the main precursor of estrogens in the mother's blood-stream. This conversion takes place predominantly in the placenta. A loading test has been described in which a large maternal intravenous dose of DHAS is injected and the rise of urinary or plasma estrogens is considered as an indicator of placental function. Some authors [1–4] have shown a subnormal rise of oestrogens after the loading test in pathological pregnancies such as toxemia but the response was normal in diabetes [2]. Other authors have not seen any correlation between the estrogen response after the loading test and fetal distress or placental disfunction [5]. Our purpose was to study the disappearance of DHAS in the plasma after DHAS injection and to determine its half-life.

MATERIAL AND METHODS

Subjects. A group of 14 normal pregnancies has been studied. The injection was done at 30 weeks for 7 women and at 38 weeks of gestation for the other 7 women. All showed normal clinical (weight gain, blood pressure) and biological data (albuminuria, glycemia, HPL levels) and spontaneously delivered healthy infants without any complication. Infants had normal weight for their gestational ages.

The second group contained 14 patients with pathological pregnancies including two with diabetes, six with toxemia, four with intrauterine-retarded fetal growth, one with Rh isoimmunization and one with anencephaly. Gestational ages in this group were estimated by means of ultrasound measurements of the biparietal diameter of the fetal head.

Infants were considered small for gestational ages if their birth weights were below the 10th percentile of the corresponding normal birth weight [6]. Clinical data are summarized in Table 2.

Protocol. Fifty mg of DHAS (obtained from Mann Chemical Company) were dissolved in 0.9% NaCl solution and passed through a millipore filter for sterilization before each intravenous injection. The injection was administered between 8 and 9 a.m. and the patients remained in bed during the test. Blood samples were taken once before the injection and at 30 min., 45 min., 1, 2, 4, 6 and 8 h afterwards.

Measurement of DHAS half-life. DHAS was measured by a rapid radioimmunoassay directly on diluted plasma [7] with an antiserum anti-3-hemisuccinate (HSA) (furnished by Dr. G. E. Abraham). The

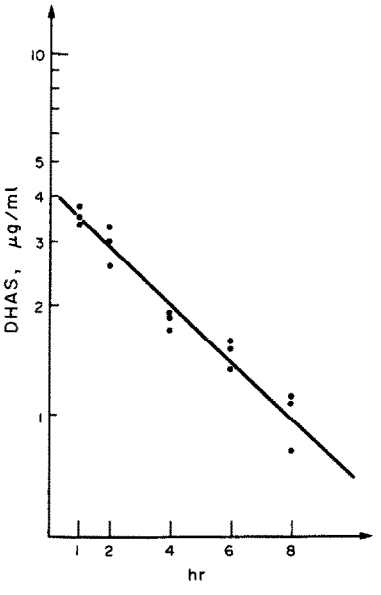

Fig. 1. Measurement of the half-life of DHAS.

Table 1. DHAS half-life (h ± 1 S.D.) in normal pregnancy

Gestational age			
30 weeks		38 weeks	
Per	3.47	Ben	3.26
Bu	4.93	Ney	4.11
Ben	2.94	Bal	3.10
Nug	3.68	Vas	3.85
Cle	3.29	Nug	3.71
Pek	4.31	Bis	3.89
Hab	2.91	Agu	3.78
Mean	3.64 ± 0.74	Mean	3.67 ± 0.38

values for each sample represent the mean of triplicate replications of three different assays. The logarithms of the mean values obtained from 1–8 h were analyzed by calculation of the least square regression line (Fig. 1). Half-life ($t_{1/2}$) was calculated from the slope of the regression line. The correlation coefficient ('r') of the regression line was statistically significant ($P > 0.05$) for all subjects.

RESULTS

The mean DHAS value before infusion was 574 ng/ml with a range of 272–1233 ng/ml. No difference was observed in pre-infusion DHAS values at 30 and 38 weeks of gestation.

1. *DHAS half-life in normal pregnancy*

Table 1 shows the half-life values in normal pregnancies when the injection was administered at 30 and 38 weeks of gestation. At 30 weeks the mean value was 3.64 h ± 0.74 (S.D.) and at 38 weeks, it was 3.67 h ± 0.38 (S.D.) The difference between the mean values is not statistically significant (Student's t test).

2. *DHAS half-life in pathological pregnancies*

In Table 2 are indicated clinical data concerning the patients, the infants and DHAS half-life. The half-life was normal in the patient with Rh isoimmunization. It was significantly longer compared to normal values in all other pathological conditions. Values above the 2 S.D. confidence limit of the mean were found in 12 cases and above 1 S.D. in one case (Fig. 2).

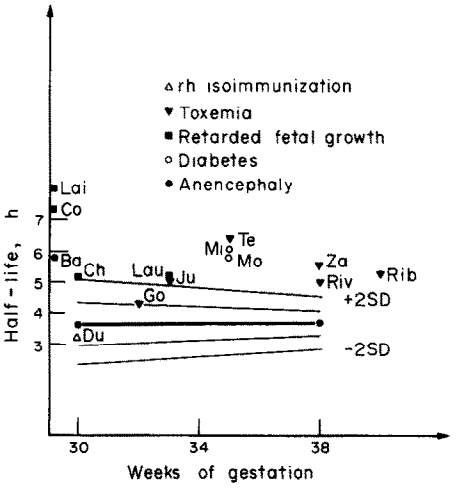

Fig. 2. DHAS half-life in pathological pregnancies.

In toxemia, the half-life of DHAS was always prolonged whether there were complications with intrauterine retarded fetal growth (patients Riv, Go, Te, Ju) or not (patients Za, Rib). The half-life of DHAS was significantly longer in all cases of severe intrauterine retarded fetal growth. It was closer to normal values in mild cases.

DISCUSSION

Pregnant women exhibit a reduced DHAS half-life compared to non pregnant women. Eight days after delivery, the values are back to those seen in non-pregnant women and normal men. This value is approximately 8.20 h [9]. In normal pregnancy, the half-life of DHAS appears to be constant after 30 weeks of gestation. Values obtained at 30 or 38 weeks of gestation are not significantly different and are close to the values obtained at 18–20 weeks by others [8]. An increase in the clearance rate during the gestational period has been described by Gant [10] but variations among individuals seem to be greater than

Table 2. Clinical data

	Complication	Gestational age at the time of infusion	Gestational age at delivery	half-life (h)	Apgar	Weight (g) fetal	Weight (g) placental	Delivery
Du.	Rh isiommunization	30	40	3.14	10	3500	600	spontaneous
Ba.	Anencephaly	29	29	5.76	mort	880	200	spontaneous
Lau.	Retarded fetal growth	33	34	5.12	9	1130	200	cesarean section
Ch.	Retarded fetal growth	30	36	5.13	9	1480	320	cesarean section
Co.	Retarded fetal growth	29	29	7.42	mort	850	200	spontaneous
Lai.	Retarded fetal growth	26	30	8.11	mort	650	150	spontaneous
Riv.	Toxemia	38	38	4.97	9	2050	350	cesarean section
Go.	Toxemia	32	36	4.27	5	2040	500	cesarean section
Ju.	Toxemia	33	37	4.97	5	2310	480	spontaneous
Te	Toxemia	35	37	6.43	7	1180	220	cesarean section
Za.	Toxemia	38	41	5.63	9	2900	580	spontaneous
Rib.	Toxemia	40	42	5.28	6	4300	850	spontaneous
Mi.	Diabetes D	35	36	5.92	6	3020	650	spontaneous
Mo.	Diabetes D	35	38	5.88	8	4440	960	spontaneous

variations with gestational age. Among 14 pathological pregnancies, 13 exhibited an abnormally long DHAS half-life. Values were scattered between pregnant and non pregnant women.

Our results confirm Gant's and similarly indicate a lower DHAS clearance rate in toxemia. The explanation for this increase of half-life of DHAS may differ with the maternal pathological condition. In toxemia, one may suggest a reduced feto-placental blood flow [10] or an enzyme deficiency. A decrease of 'aromatase' and 3β-hydroxysteroid-dehydrogenase activity in the placental microsomal fraction has been demonstrated by Lehmann *et al.* in pregnancies complicated by diabetes and toxemia [11]. These observations were not confirmed by Townsley who found normal values for 'aromatase' and 'sulfatase' activity in the same complications of pregnancy [12]. It may also be that modifications in estrogen production after DHAS injection and DHAS half-life variations could be related to a deficiency of plasma transport protein of DHAS or its metabolites.

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