

PLASMA OESTRIOL IN NORMAL HUMAN PREGNANCY

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SUMMARY

Serial studies of the concentration of oestriol in plasma of pregnant women are reported. Plasma oestriol was measured by gas-liquid chromatography. Twenty-one women were investigated at weekly or fortnightly intervals throughout normal pregnancies from the 24th to the 42nd week. At the same time the excretion of oestriol in the urine was determined. The results demonstrate an extensive parallelism between the plasma concentration and the urinary excretion of oestriol. The mean values \pm the standard deviations are tabulated and the calculated curve of the mean values of the concentration of oestriol in plasma together with the area of 95% of the values are given.

INTRODUCTION

FEW REPORTS on the variation in plasma oestriol concentration during human pregnancy are available [1-3]. The oestriol concentration in plasma, like the urinary excretion appears to reflect pathological conditions in pregnancy. Low plasma oestriol concentrations have been found in toxæmia, diabetes mellitus, placental insufficiency, and foetal death [3-6].

Even though examination of a single function (oestriol production) cannot be expected to give an unambiguous evaluation of an organ so complex as the foeto-placental unit, experience has shown that estimation of urinary oestriol is of clinical value. The assay of the oestriol concentration in blood or plasma may have the same physiological significance as the measurement in the urine. To investigate this relationship and to determine the range of plasma oestriol concentrations in normal pregnancy, serial studies on blood and urine were performed throughout normal pregnancy.

EXPERIMENTAL

Material

The subjects studied were 21 women aged 17-40 years (average 26). They were all delivered vaginally with one normal, living child with a birth weight of more than 2500 g. Ten women were primiparas, the rest were secundiparas. Complications such as toxæmia, arterial hypertension, placental abruption, placenta prævia, diabetes mellitus, blood-group incompatibility etc. were not found in any of the pregnancies. All the women were seen frequently in the maternity clinic of the hospital, and all were delivered in the hospital. The duration of the pregnancy was calculated from the first day of the last menstrual period. All deliveries took place between the 38th and 42nd week.

Methods

Beginning between the 22nd and the 28th week of pregnancy, venous blood samples were withdrawn in the morning and at intervals of one or two weeks

thereafter. When attending the clinic for venipuncture the women brought with them the urine specimen collected in the preceding 24 hr. The urinary oestriol was estimated at the Hormone Department, Statens Seruminstitut, Copenhagen, according to the method of Frandsen [7].

Plasma oestriol was determined in duplicate by a method described by the author [8]. The plasma was either processed immediately or frozen at -21°C . until used.

RESULTS

The values can be seen in Table 1 where the mean values of the plasma oestriol concentration and the simultaneous oestriol excretion in urine are given together with the standard deviations. It is apparent from the table that the relationship between the plasma oestriol and period of gestation is non-linear. Therefore, the logarithms of the individual oestriol estimations are plotted in a semi-logarithmic graph in Fig. 1. The plot scatter indicates a linear relationship and therefore the equation type $\log Y = bX - a$ was used to construct a line through the mean values in the logarithmic scale and the area of 95% of the values.

There is an extensive parallelism when the mean plasma oestriol concentration and the urinary excretion for each week of pregnancy are compared (Fig. 2). It should be emphasized that the urinary values are within the normal range [7].

In Fig. 3, the curve connecting the mean values fortnightly from the present investigation is compared with similar curves from three reports in the literature,

Table 1. The mean values \pm the standard deviations of the concentration of oestriol in plasma, μg per 100 ml, and of the excretion in urine, mg per 24 hr, in 21 normal pregnant women

	Week of pregnancy						
	23	24	25	26	27	28	29
Plasma	3.9	4.7 \pm 1.9	6.7 \pm 2.7	5.8 \pm 2.8	5.7 \pm 3.3	6.4 \pm 3.2	5.3 \pm 2.1
N	4	7	9	11	18	18	18
Urine	7.1	10.4 \pm 3.0	10.0 \pm 1.2	10.5 \pm 3.1	11.2 \pm 4.1	10.8 \pm 4.1	12.0 \pm 4.1
N	2	6	7	10	15	19	17

	Week of pregnancy						
	30	31	32	33	34	35	36
Plasma	6.8 \pm 3.2	6.9 \pm 3.1	7.1 \pm 3.6	8.3 \pm 2.8	8.8 \pm 4.2	10.5 \pm 5.5	11.1 \pm 5.9
N	16	17	18	18	17	18	20
Urine	13.5 \pm 4.8	13.5 \pm 5.2	14.3 \pm 4.2	13.1 \pm 5.0	16.4 \pm 5.1	18.3 \pm 4.9	18.8 \pm 6.7
N	17	16	19	18	18	17	20

	Week of pregnancy					
	37	38	39	40	41	42
Plasma	11.1 \pm 4.5	14.5 \pm 6.9	14.5 \pm 5.0	13.1 \pm 6.8	14.7	17.5
N	19	17	17	9	5	2
Urine	21.6 \pm 6.7	22.4 \pm 7.1	24.2 \pm 6.6	23.0 \pm 7.6	19.8	26.2
N	19	17	16	8	5	2

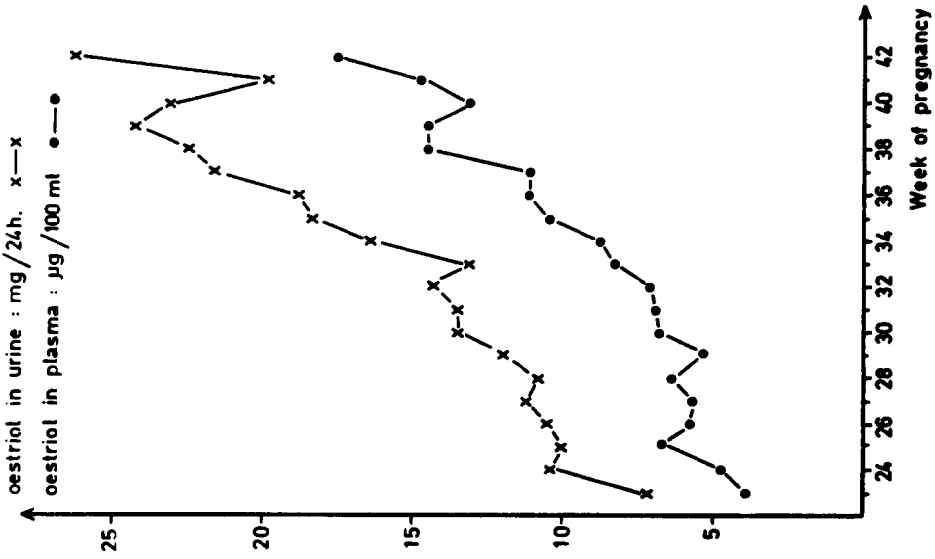


Fig. 2. Mean values of oestriol in plasma and in urine and weeks of pregnancy, showing the parallelism between the concentration in the plasma and the excretion in the urine. The curves are simply connecting the mean values in each week of pregnancy. Data of Table 1.

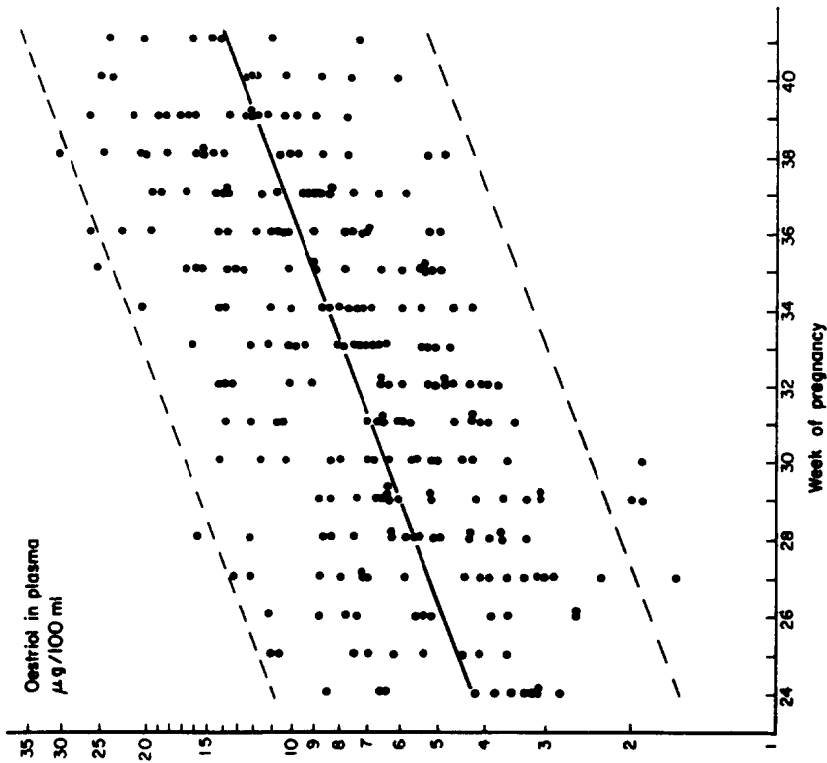


Fig. 1. Oestriol in plasma and weeks of pregnancy, including the line of the mean values and the zone of $\pm s. l. 66$. Logarithmic vertical scale. The equation of the mean values (solid line) is $\log Y = 0.0302, X - 0.0976$.

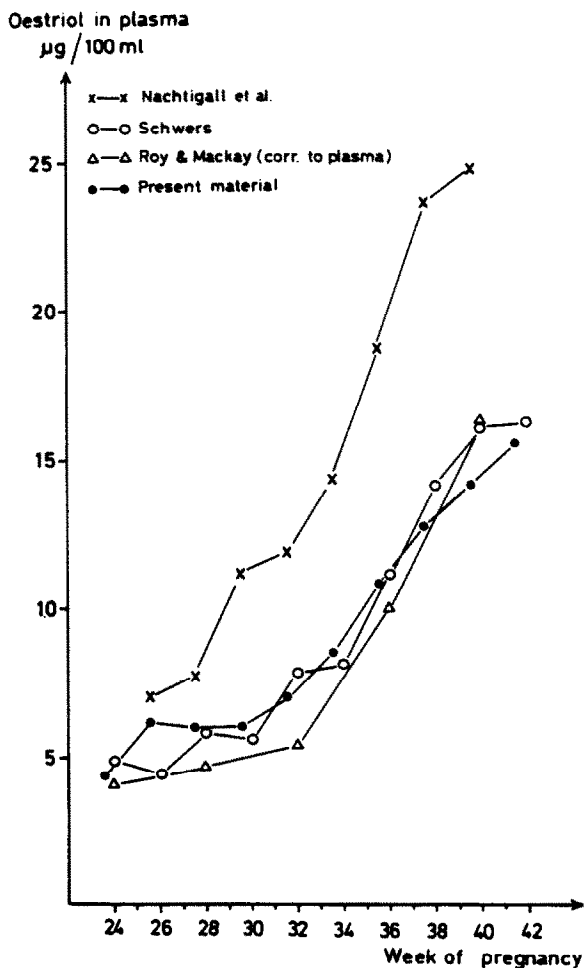


Fig. 3. The mean values of oestriol in plasma and weeks of pregnancy, as found by various investigators. The curves are simply connecting the mean fortnightly values. Data from tables in the respective publications.

dealing with serial investigations of total-oestriol in plasma during the 24th–42nd week of pregnancy: Nachtigall *et al.*, 22 women, 230 analyses[4], Roy and Mackay, 10 women, 50 analyses[2], and Schwerts, 38 women, 210 analyses[3]. In the two last mentioned studies, investigations earlier than the 24th week have also been made. The present material is represented by 278 analyses from 21 women. It must be pointed out that Roy and Mackay gave results for whole blood. These have been converted to plasma levels, using an average haematocrit value of 40[9].

DISCUSSION

Judging by the clinical course and the oestriol excretion, the pregnancies in the subjects studied were normal. The results show that this method of estimating plasma oestriol gives values which rise exponentially during the progress of pregnancy. The rise was similar to that observed when oestriol excretion was

determined. In plasma as well as in urine the problem is the determination of total-oestriol, i. e. the oestriol which is extractable after acid hydrolysis.

Other authors have shown that in the blood, oestriol is mainly (95–100%) found in the plasma-fraction[2, 3]. The same authors have further shown that there is no significant 24 hr variation in the oestriol-concentration of the blood.

From Fig. 3 it can be seen that there is a similarity between the results of the present investigation and those in two of the other reports[2, 3], which both use the same method[10]. The third report used for comparison[4], gives considerably higher values. This method is characterised by being a very quick fluorimetric estimation without extensive purification. The results are corrected for the methodological loss on the basis of the radioactive recovery of internal standards of a mixture of tritium-labelled oestriol-conjugates. This is later altered to the mere adding of ^3H -oestriol-16-glucosiduronate[11]. As far as can be seen from the two other reports, their values are not corrected for the methodological loss. If these values were corrected, the levels of their curves in Fig. 3 may be higher than that of the present investigation. Here the values are corrected on the basis of tritium-labelled, free oestriol[8].

In Table 2, the mean values and ranges for the plasma oestriol for the 39–40th week of pregnancy in the three reports and in the present investigation are

Table 2. Plasma and blood oestriol values found by various investigators in 39–40th week of pregnancy. Mean oestriol value and range of oestriol values in μg per 100 ml

Investigator	Number of women	Mean	Range	Biological fluid
Nachtigall <i>et al.</i> [4]	28	24.7	7.7–43	Plasma
Roy and Mackay[2]	29	9.1 (15.2)	2.6–19.6 (4.3–32.7)	Blood (Plasma) *
Schwens[3]	30	16.0	6–55.7	Plasma
Present investigation	26	14.1	6.2–26.6	Plasma

*Converted from the blood values on the basis of an average haematocrit value of 40[9].

compared. While the lower limits of the ranges are comparable, the upper limits are considerably higher for methods involving fluorimetry or colorimetry than for that using gas-liquid chromatography. All four methods apply in principle the same form of hydrochloric acid hydrolysis.

A clinical application of plasma oestriol determination will presumably have the same limitations as the urine oestriol determination. Because of the great variation in the normal values it will be of no help in the assessment of the duration of the pregnancy. On condition that this is known from the date of the last menstrual period, perhaps from the first time foetal movements are recognised, repeated determinations of plasma oestriol will most likely be of the same value as determinations of oestriol in the urine.

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