

## PREGNANEDIOL ESTIMATIONS IN THREATENED MISCARRIAGE

by

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Abortion is one of the most common and potentially serious complications of pregnancy. In the Irwin Hospital, Delhi during the year 1970 the total number of obstetric admissions was 4293 out of which 1210 were cases of abortions (spontaneous and induced) i.e. an incidence of 28.1% of all obstetric admissions. This is probably much higher than the general incidence as these cases are likely to be concentrated in big hospitals. Analysing further it was found that 522 aborted giving a foetal wastage of 43%. These figures give us some idea of the enormity of the problem. Deficiency of progesterone as a cause of spontaneous abortion on the basis of pregnanediol excretion was first studied by Brown *et al* (1937) and later supported by Klopper (1957), Cox *et al* (1964). - Vaginal cytology and cervical mucus reflect faithfully the level of sex hormones in the circulation. A review of the literature shows many conflicting reports (Goldzieher and Benigno, 1958; Morgan *et al*, 1960) between the levels of pregnanediol, cervical fern and vaginal cytology. The administration of progesterone in threatened abortions has

been the subject of much discussion and there is no uniformity of opinion regarding its administration. The present study was undertaken to correlate pregnanediol estimations with cervical mucus fern and vaginal cytology in threatened abortions and to find out the value of 17 hydroxyprogesterone caproate in the treatment of threatened abortions.

### *Material and Methods*

*Group I:* Twenty-five cases of normal pregnancy upto 20 weeks to serve as control.

*Group II:* Seventy-five cases of threatened abortion upto 20 weeks and those patients continuing pregnancy upto 28 weeks. Only those cases were included who showed no other obvious cause for the abortion. Pregnancy was termed successful if the patient carried beyond the 28th week. Besides routine clinical examination and investigations, cervical mucus fern, vaginal cytology and a 24 hours urinary pregnanediol estimation (by Klopper *et al* method) was carried out in all cases. These investigations were repeated every month till either the patient aborted or successfully completed 28 weeks of pregnancy.

### *Observations*

*Urinary pregnanediol excretion in normal pregnancy:* Total number of estimations performed were 108 (Table I). The

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TABLE I

*The Pregnanediol Excretion in Normal Pregnant Cases at Different Periods of Gestation*

No. of estimations	Weeks of gestation	Mean pregnanediol excretion mg./24 hours	Range of pregnanediol mg./24 hours	S.D. +
6	6-8	4.583	3.96-5.72	.217
9	9-11	5.88	2.31-12.76	3.070
20	12-15	6.809	3.96-14.08	2.183
25	16-20	8.22	4.62-15.84	2.358
24	21-24	10.394	7.26-16.28	2.083
24	25-28	12.704	8.14-16.78	1.823

mean pregnanediol excretion was 4.583 mgs./24 hours at 6-8 weeks, thereafter it rose to 5.88 mgs./24 hours at 9-11 weeks, 6.809 mgs./24 hours at 12-15 weeks. On the basis of the above data, 4.583 mgs./24 hours was taken as the minimum normal value. In 6 cases i.e. 24% pregnanediol excretion at the first estimation was found to be below 4.583 mgs./24 hours. Out of these 6 cases, 3 were first examined at 6-8 weeks pregnancy one at 9-11 weeks pregnancy and 2 at 12-15 weeks of pregnancy. All six cases continued pregnancy normally and the pregnanediol levels became normal as the pregnancy advanced. The cornification index was below 15% in all normal cases and it gradually decreased as pregnancy advanced (Table II). All cases except one showed absence of ferning of the cervical mucus smear. This case had a grade II positive fern but the pregnanediol excretion and vaginal smear did not indicate any progesterone deficiency. She, however, aborted at 16 weeks pregnancy. Out of 25 cases, one patient aborted giving the abortion rate of 4% in the normal pregnancy group.

#### Group II

Urinary pregnanediol excretion was

TABLE II

*The Percentage of Cornified Cells in the Vaginal Smears of Normal Cases*

No. of smears	Weeks of gestation	Mean percentage cornified cells
5	6-8 weeks	12.5%
7	9-11 "	8.33%
16	12-15 "	7.43%
24	16-20 "	5.90%
21	21-24 "	5.22%
18	25-28 "	5.12%
Total 91		

studied in 65 out of 75 cases of threatened abortion. Total number of estimations performed were 157 (Table III). The mean pregnanediol excretion was 5.916 mgs./24 hours, at 6-8 weeks, 5.572 mgs./24 hours at 9-11 weeks, 6.595 mgs./24 hours at 12-15 weeks and 8.174 mgs./24 hours at 16-20 weeks. Twenty-six out of the 65 cases of threatened abortion, aborted, giving a foetal wastage rate of 40% in this group. The abortion rate was maximum at 6-8 weeks (46.66%), at 9-12 weeks was 42.86% and then dropped to 18% at 12 weeks (Table IV). The mean

TABLE III  
*The Mean Pregnanediol Excretion in Threatened Abortion*

Weeks of gestation	No. of estimation	Mean pregnanediol excretion mg./24 hrs.	Range of pregnanediol excretion	S.D. ±
6-8	15	5.916	3.08-12.76	2.468
9-11	20	5.572	2.20-9.46	2.008
12-15	32	6.595	1.45-14.96	3.326
16-20	35	8.174	2.42-13.44	3.012
21-24	25	10.742	3.45-15.40	2.748
25-28	29	13.770	9.46-16.88	1.900

TABLE IV  
*The Abortion Rate at Different Duration or Pregnancy*

Weeks of gestation	No. of cases	No. of abortions	Abortion rate percentage
6-8	15	7	46.66
9-11	21	10	42.86
12-15	39	7	18.91
16-20	39	4	10.25
21-24	26	2	7.67
25-28	29	—	—

values of pregnanediol excretion for patients with normal pregnancy and threatened abortion did not show any significant difference. In cases of threatened abortion pregnanediol excretion was higher in patients who continued their pregnancy than in those who aborted (Table V). Out of 26 pati-

ents who aborted, 17 (65.38%) had pregnanediol excretion less than 4.583 mgs./24 hours and 9 cases (34.62%) had more than 4.583 mgs./24 hours. Among 65 cases of threatened abortion, 23 (35.38%) had urinary pregnanediol levels below 4.583 mgs./24 hours and 17 (73.91%) of these aborted while 6 (26.09%) continued their pregnancy successfully (Table VI) Forty-two patients had a normal urinary pregnanediol and of these 9 (21.43%) aborted. The abortion rate was 3 times higher in patients with a lowered pregnanediol level as compared to those with a normal urinary pregnanediol excretion.

Vaginal cytology was done in 48 cases of threatened abortion and could not be done in others because of excessive bleeding. Twenty-eight cases (58.33%) had a cornification index below 15% and none aborted, while 20 cases (41.67%) had a

TABLE V  
*The Mean Pregnanediol Excretion in Patients Who Continued Pregnancy*

Weeks of gestation when first	Total number of cases	Mean pregnanediol excretion in mg./24 hours	
		In aborting cases	In continuing cases
6-8	15	5.213 (7)	6.542 (8)
9-11	13	4.037 (8)	5.35 (5)
12-15	21	4.202 (6)	6.04 (15)
16-20	13	2.64 (2)	6.062 (11)
21-24	3	— —	12.83 (3)

TABLE VI

*The Pregnanediol Excretion in Patients with Threatened Abortion*

No. of cases	Less than 4.583 mg./24 hrs.	4.583 mg./24 hrs. or above	Clinical result	
			Retention	Abortion
65	23	—	6 (26.09%)	17 (73.91%)
	—	42	33 (78.53%)	9 (21.43%)

cornification index above 15% and 14 (70%) aborted. Ten cases with an oestrogenic smear had a normal pregnanediol excretion and yet 6 aborted. In 4 cases the smear later became normal. Thus the abortion rate in cases with an oestrogenic smear and a normal pregnanediol excretion was 60%. In the remaining 10 cases with an oestrogenic smear and a low urinary pregnanediol the abortion rate was 80%. Out of the 28 cases with a normal smear, 24 had normal urinary pregnanediol excretion, 4 had a lowered urinary pregnanediol excretion, but all continued pregnancy successfully.

*Cervical mucus smear for ferning was studied in 56 cases (Table VII)*

The abortion rate in patients with a positive fern was 1½ times compared to

nal cytology had been done in 10 of these cases and all showed an oestrogenic smear. Seventeen patients out of 75 were given 17 Hydroxy-progesterone caproate in addition to general treatment. Of these 7 aborted given an abortion rate of 41.18% which is the same as the abortion rate in the untreated group.

*Discussion*

Biologically active progesterone is converted to pregnanediol by the liver and this is excreted in the urine as the pregnanediol complex. Urinary pregnanediol represents only 10-20% of endogenous progesterone (Goldzieher and Benigno, 1958). There is a wide variation in the level of pregnanediol excretion in normal pregnant cases, hence the mean excretion values at different stages of pregnancy

TABLE VII

*The Effect of Ferning on the Percentage of Abortion*

Cervical mucus	No. of cases	No. of abortions	%age of abortion
No ferning	38	16	42.1%
Positive ferning	18	12	66.66%
Grade I	11	7	63.63%
Grade II	5	3	60%
Grade III	2	2	100%

those with a negative fern. Out of 18 cases with a positive fern test, 17 (93.34%) showed a lowered urinary pregnanediol excretion, whereas one patient had a pregnanediol excretion of 6.6 mgs./24 hours and yet she aborted. Vagi-

have been taken to be the minimum normal value for that period of pregnancy in the present series. The mean urinary pregnanediol at 6-8 weeks, was 4.583 ± .217 mg./24 hours which is in agreement with the findings of Klopper (1957).

Goldzieher (1964) and others. However, Brown *et al* (1937) reported higher values of 10 mgs./24 hours. While Nilsson (1963) reported very low values of 3 mgm./24 hours. 24% of the normal pregnancy group had urinary pregnanediol excretion below the mean for that period of pregnancy and yet the pregnancy continued normally. This is in agreement with the observations of Guterman *et al* (1949) in whose series, 12.6% of normal cases had a lowered excretion.

In the present study, 15% cornified cells were taken as the upper limit of the normal which is in agreement with Hochstaedt (1960) and Abrahams *et al* (1964). In the normal pregnancy group 100% cases showed a normal vaginal cytology, whereas only 76% were normal by pregnanediol excretion. Cervical mucus smears in normal pregnancy showed absence of ferning in all but one case (96%). This one patient with a positive fern later aborted although pregnanediol excretion and vaginal cytology did not indicate an impending abortion. In Zondek's series (1955) 50% of cases with a positive fern aborted which he believed was due to the functional insufficiency of the chorionic villi. Ullery and Shabanah (1957) on the other hand reported that 30% of all normal pregnant women at some stage of pregnancy showed some degree of cervical ferning. In their series 93.4% of pregnant patients showing a fern reaction carried to term provided they reflected plentiful amount of turbid mucoid material and exfoliated cells symbolising progestational activity in their smears. In abortion cases the fern pattern was present with a clear matrix or very little mucoid material, low cell count with distinct pattern of stripped nuclear lysis. This could not be confirmed in the present study. The abortion rate in 65 cases of threatened abortion was 40% which

was much higher than that reported by Randall *et al* (1955), but is in agreement with that of Crowder (1958) 43% and Dass (1960) 46.5%. Cox *et al* (1964) on the other hand reported a figure of 52.27%.

Abortion rate in the low pregnanediol excretion group was 73.91% as compared to 21.43% in the normal pregnanediol excretion group. This is in agreement with the observations of Menon (1959), Goldzieher (1964). Guterman and Tulskey (1949) concluded that urinary pregnanediol excretion in cases of threatened abortion had a 90% accuracy in interpreting the outcome of threatened abortion.

The previous obstetric history did not appreciably affect the prognosis of the present pregnancy. This is contrary to the findings of Malpas (1938).

Vaginal cytology had a better correlation than the levels of pregnanediol excretion in cases of threatened abortion. Cervical mucus fern test and pregnanediol excretion have a positive correlation in 80% of the cases. Our results with Proluton were not much different from those obtained by bed rest and symptomatic treatment. However, Morgan *et al* (1960) had a foetal wastage of 80% in the low pregnanediol excretion group and by treatment with progesterone, the foetal wastage dropped to 20%.

#### *Summary and Conclusions*

Urinary pregnanediol, vaginal cytology and cervical fern have been studied in 25 cases of normal pregnancy and 75 cases of threatened abortion. 24% of the normal pregnant had urinary pregnandiols levels below the mean -4.583 mgs./24 hours. Correlating pregnanediol excretion, cervical mucus ferning and vaginal cytology, the minimum normal limits were obtained in 76%, 96% and 100% respectively. Mean pregnanediol excre-

tion in patients of threatened abortion who carried pregnancy was higher than in those who aborted. Foetal wastage in threatened abortion was 73.91% with low excretion and 21.43% with normal pregnanediol excretion, and serial estimations are a better guide to prognosis. The abortion rate in threatened abortion cases was 40%. 34.62% of the patients who aborted had a normal urinary pregnanediol excretion. With non-cornified vaginal smears abortion rate was 0% while with cornified smears, it was 70%. Abortion rate was 66.66% with positive ferning and 42.1% with negative ferning. Administration of progesterone did not improve the salvage rate.

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