PLASMA PROGESTERONE LEVELS IN NORMAL HUMAN CYCLE

by

R. K. NARULA,* M.D., D.G.O.

and

V. L. CHANDRA**

Introduction

Plasma progesterone plays a key role in reproductive physiology. Estimation of plasma progesterone during menstrual cycle provides valuable information about the function and life span of the corpus luteum.

Like other steroids, measurement of plasma progesterone has passed through several phases from indirect study like vaginal cytology, cervical mucus, endometriuum, basal body temperature and measurement of urinary metabolites such as pregnanediol estimation. This has been used extensively, but has the disadvantage that it needs 24 hours, urine collection and represents variable fraction of the progesterone secreted. Most direct methods of progesterone estimation are time consuming and need large amounts of blood sample and are unsuitable for daily studies. Competitive protein binding method described by Murphy (1967) has been used for progesterone estimation. This method is rapid, accurate, needs very small amount of plasma and is suitable for daily studies.

*Medical Superintendent, Kamala Nehru Memorial Hospital and Hony. Professor of Obstetrics and Gynaecology, Motilal Nehru Medical College, Allahabad, U.P., India.

**Assistant Research Officer, Indian Council of Medical Research, New Delhi, India.

Material and Methods

Eight women with regular ovulatory menstrual cycles, in the age group between 20 years to 36 years, attending the gynaecological out-patient of All India Institute of Medical Sciences, New Delhi, were selected for study.

Plasma progesterone estimation, vaginal cytology and cervical mucus studies were carried out on day 3, 7, 10 and daily from day 12 onward, till the onset of next menstrual period. Endometrial biopsy was taken in the premenstrual phase.

Plasma Progesterone

Five ml. blood was collected in heparinised syringe, centrifuged at 3000 rpm for 20 minutes, and supernatant plasma was stored in duplicates at—15°C till the time of analysis. Analysis of all the samples from one cycle was carried out at the same time.

Plasma progesterone was estimated by Competitive Protein Binding method, originally described by Murphy (1967) and later modified by Johansson et al in 1968. This method utilises the properties of Petroleum ether for semiquantitative assay of progesterone. A properly selected Petroleum ether extracts 80 to 90% of Progesterone, 25% of Cortisol, corticosterone and 25% of 17 hydroxy-progesterone. It does not interfere with the Competitive Protein Binding system.

TABLE I

Progesterone Levels in Eight Cases with Normal Menstrual Cycle

Days of cycle	NUMBER OF CASES							
	I	II	III	IV	V	VI	VII	VIII
1st	—	—	—	—	—	—	—	—
2nd	—	0.6ng	—	0.6ng	—	—	—	—
3rd	—	—	0.4ng	—	0.1ng	0.1ng	0.1ng	—
4th	—	1.1ng	—	—	—	—	—	—
5th	0.2ng	—	—	—	—	—	—	—
6th	—	—	—	—	—	—	—	—
7th	—	—	0.7ng	—	0.1ng	0.1ng	0.3ng	—
8th	—	—	—	—	—	—	—	—
9th	0.5ng	1.1ng	1 ng	1.3ng	0.1ng	—	—	—
10th	—	—	1.1ng	—	0.1ng	0.3ng	0.3ng	0.4ng
11th	—	1.2ng	—	—	—	—	—	—
12th	1.0ng	1.3ng	1.6ng	5.7ng	0.5ng	0.7ng	0.5ng	0.4ng
13th	1.2ng	—	1.8ng	7.5ng	0.5ng	0.9ng	0.7ng	—
14th	3.8ng	2.8ng	2 ng	7.8ng	1 ng	1 ng	1.1ng	2.0ng
15th	3.9ng	2.8ng	3.2ng	8.4ng	2.7ng	1.1ng	4.8ng	4.6ng
16th	4 ng	7.6ng	6 ng	11 ng	3 ng	2.6ng	7.2ng	7.0ng
17th	—	10.8ng	8.6ng	10.8ng	3.4ng	3.3ng	10.5ng	—
18th	—	11.6ng	10.4ng	10.8ng	3.9ng	8 ng	10.7ng	7.2ng
19th	7.8ng	—	10.8ng	7.4ng	4.1ng	10.5ng	11.1ng	8.6ng
20th	11.6ng	11.9ng	11.8ng	6.6ng	9.4ng	11.2ng	11.5ng	10.8ng
21st	7.4ng	—	7.2ng	2 ng	10.4ng	11.2ng	11.3ng	11.6ng
22nd	6.4ng	7 ng	6.4ng	1.6ng	9.6ng	10.2ng	11.3ng	—
23rd	2 ng	2 ng	1 ng	1.4ng	5.6ng	7.4ng	8.4ng	9.8ng
24th	1.4ng	0.8ng	.8ng	1.4ng	—	3.9ng	7.6ng	6.8ng
25th	0.8ng	0.6ng	0.6ng	1.2ng	—	2.8ng	6.1ng	1.2ng
26th	0.2ng	—	—	1.2ng	0.5ng	0.8ng	2.4ng	0.6ng
27th	—	—	—	0.6ng	—	0.3ng	1.1ng	—
28th	—	—	—	—	—	0.1ng	0.3ng	0.4ng
29th	—	—	—	—	—	0.1ng	0.2ng	0.2ng
30th	—	—	—	—	—	—	—	0.2ng

This method was further modified by using depleted pregnancy plasma, as a source of C.B.G. (Costicosterone Binding Globulin) and labelled Progesterone 1-2-H³ (Specific activity-0.0093) milligram/millicuries), instead of corticosterone. The recovery rate was 85-90% and Plasma and water blanks were between 0-0.2/ng.ml.

Results

Cycle length of the 8 cycles studies varied between 25 to 30 days.

Plasma Progesterone Levels

Progesterone concentration in the peripheral plasma in 8 normal cycles studied is shown in Table I.

Plasma progesterone levels in the first 7 days of the cycle ranged between 0.1 ng. to 0.7 ng./ml. Maximum value in the follicular phase was 1.3 ng./ml. A slight rise of plasma progesterone levels was observed on 12th day in cases 1, 2 and 3 and on day 14 in cases 5, 6, 7 and 8 and a definite rise of plasma progesterone was seen on day 14 in first 3 and on day 15 in last 4 cases. Plasma progesterone concentration was highest on day 20 of the menstrual cycle in 3 cases i.e. 11.6 ng., 11.9 ng., and 11.8 mg./ml. in cases No. 1, 2 and 3. In cases No. 5, 6, 7 and 8 peak levels were observed on 21st day of the cycle. In case No. 4 the plasma progesterone levels showed a different pattern all through the later half of the cycle. Plasma progesterone levels at the time of onset of menstruation were same as in the follicular phase in all cases. Figs. 1 and 2 show plasma progesterone levels in cases with 25-26 day cycle and in those with 28-30 day cycles.

Cervical mucus and vaginal cytology showed changes consistent with ovula-

Fig. 1

Fig. 2
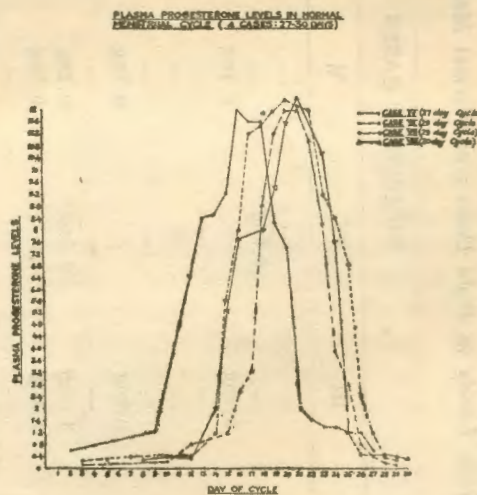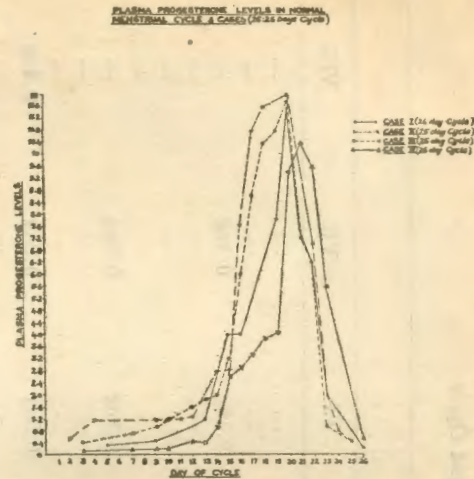
tory cycle in all cases. Endometrial biopsy was taken between day 24 to 30th day of the menstrual cycle, showed secretory endometrium consistent with the day of biopsy in all cases.

Comments

Estimation of plasma progesterone affords a satisfactory method of measuring the corpus luteum function. The values obtained in this study compare

Fig. 3

Fig. 4

well with those of Yohimi and Lipsett (1968) Neil *et al* (1967). Peak plasma progesterone levels in this study were ●bserved 7 days after Ovulation whereas
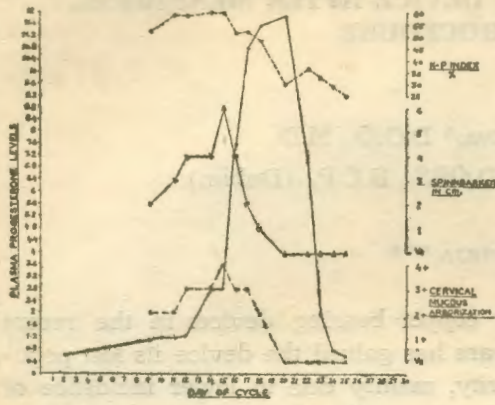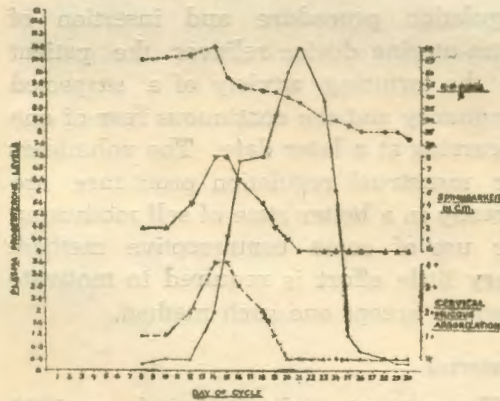
Yoshimi and Lipsett (1968) observed maximum level between 6-10 days after ovulation. They found that in some cases the plasma progesterone was still elevated at the time of onset of menstruation showing thereby that the disintegration of corpus luteum was not complete. Cook *et al* in 1972 in a study on correlation of endometrial biopsy and plasma progesterone levels found that plasma progesterone levels were fairly tightly grouped for each day of the cycle and it would be possible to define the limits of normality in relation to endometrium in normal population. A slight rise of plasma progesterone was observed on the day of ovulation and a definite rise on the next day. Rise of plasma progesterone preceded the change in cervical mucus and vaginal cytology by 48 hours in 7 out of 8 cases (Figs. 3 and 4). Rise in plasma progesterone is thus the earliest indication of occurrance of ovulation.

References

1. Cooke, I. D., Morgan, C. A. and Parry, T. E.: J. Obstet. Gynec. Brit. C'wealth. 79: 647, 1972.

2. Johansson, E. D. B.: Endocr. Khh. Sppl. 147: 188, 1070.

3. Murphy, B. E. P.: J. Clin. Endocrinol. 27: 973, 1967.

4. Noyes, R. W., Hertig, A. and Rock: J. Fertil. Steril. 1: 3, 1965.

5. Neill, J. G., Johansson, E. D. B., Datta, J. K. and Knohil, E.: J. Clin. Endocrinol. 27: 1167, 1967.

6. Yoshimi, T. and Lipsett, N. B.: Steroids. 527: 11, 1968.