INTERNATIONAL REVIEW

NATURAL FAMILY PLANNING HUMAN LIFE ISSUES

Volume XII, Number 4 Winter 1988 $6.00 a copy

Continuous Mucus: Correlation of Point of Change with Preovulatory Rise in Estradiol-17 Beta

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Introduction

THE OVULATION METHOD of natural family planning (OM) has as one of its advantages a wide applicability to women of all reproductive categories (breastfeeding, premenopause, anovulation, etc.) and therefore is not limited only to those women with regular, ovulatory cycles. This versatility is based on its reliance on the presence or absence of a developing ovarian follicle rather than on the presence of a corpus luteum. The cervical mucus symptom has also been shown to be more precise than other periovulatory and postovulatory signs.[6,7]

The ease with which any NFP methodology can be individually applied depends on the clarity and consistency of the sign or signs of fertility which the woman is monitoring. Within the Creighton Model of the Ovulation Method, only standardized, external vulvar observations of the cervical mucus are monitored.[8] For the majority of women, there is an absence of mucus during the times in the menstrual cycle when no follicle is developing, and so the

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mucus days accurately portray the fertile interval. There are, however, some women, who, upon charting their cervical mucus, note either a prolonged mucus cycle (>8 days) or continuous mucus throughout the cycle which initially obscures the true time of fertility.

In such situations, the method can still be utilized. The woman is taught to distinguish a mucus discharge that is essentially the same from day to day (the base infertile pattern or BIP) from a mucus discharge that, for her, indicates fertility and approaching ovulation.[5] The first day on which the client identifies mucus which is different from her BIP is defined as the point of change (POC). The BIP should correlate with preovulatory ovarian quiescence and the POC should correlate with the beginning of the preovulatory estrogen rise. While clinical experience with the use of this protocol has suggested that the days of the BIP are reliably infertile, no study has previously been done which correlates the actual hormone changes with the change in the mucus pattern.

It is the purpose of this study to correlate the woman's identification of the POC with the estrogen hormone profile in the same cycle. In this way, the accuracy of the protocol can be better defined.

Materials and Methods

The study group was chosen from clients attending one of four Creighten Model Centers.* All clients accepted into the study had regular cycles (25-38 days), mucus cycles >8 days in duration, and normal luteal phases as indicated by post-Peak phases of 9-16 days. None of the participants were using exogenous hormones, prescription drugs, antihistamines, or high dose B or C vitamins during the study cycle. There were 10 patients in this study, 6 of these were of proven normal fertility.

The participants ranged in age from 22-39 years. Four of 10 were nulliparous and the other six had had from 1-9 pregnancies with 1-9 live births. All were married, and 9 of the 10 were currently

* Lincoln NFP Education Center, Lincoln, Nebraska; Marian Health Center NFP, Sioux City, Iowa; Pope Paul VI Institute, Omaha, Nebraska; St. John's Mercy NFP Center, St. Louis, Missouri.

using the OM to avoid a pregnancy. Two of the 10 had a previous history of oral contraceptive use which was remote from the time of the study cycle.

All clients had previously been managed by a certified natural family planning practitioner (CNFPP) according to the protocol for long mucus cycles. The protocol required that each client be identified as a candidate for pre-Peak yellow stamps by virtue of having a mucus cycle of greater than 8 days in duration, 3 cycles of good charting and observations, and confident identification of the point of change (POC) and the Peak Day. When the long mucus cycle was initially identified, the client was instructed to ask the essential sameness question ("Is today essentially the same as yesterday?") and to chart her answer on a daily basis. From this basic protocol, the BIP and POC were identified. If after three months the client was consistently able to identify the point of change and the Peak Day, she was given yellow stamps to be used for those days prior to the point of change where only mucus consistent with her base infertile pattern was noted. The days of the BIP were considered infertile, and the days from the POC until three full days past the Peak Day were considered fertile.

The definitions used in charting were those standardized within the Creighton Model[8] as follows: The *mucus cycle* is the number of days from the first day of mucus counted continuously through to and including the Peak Day. The *Peak Day* is the last day of any mucus discharge that is clear, stretchy, or lubricative. The *base infertile pattern* is the preovulatory pattern of mucus which the client identifies as essentially the same from day to day. The *point of change* is the day on which the client with a long mucus cycle (greater than 8 days in length) notices a change in the mucus from the base infertile pattern.

Each client kept a duplicate Ovulation Method chart with the POC and Peak Day clearly marked. The chart was then sent in at the end of the study cycle for review and correlation with the hormone levels.

Each participant contributed one cycle. During the study cycle, the client came for phlebotomy between 6:00 and 10:00 a.m. or 4:00 and 8:00 p.m. daily starting on day 5 or 6 of her cycle. From

day 5 through 2 days past the Peak (P+2), 7cc of blood were drawn for estradiol-17 Beta and progesterone. From 3 days past Peak (P+3), 10cc of blood were drawn on alternate days until the end of the cycle and analyzed for estradiol-17 Beta, progesterone, and follicle stimulating hormone (FSH). For those with longer cycles or late Peak days, initiation of daily hormone evaluation was individualized. The blood was refrigerated and then sent by mail to the Pope Paul VI Institute within six days. If the blood could not be sent so that it would arrive within six days, it was centrifuged and the serum decanted prior to refrigeration. Serum estradiol-17 Beta and progesterone levels were obtained by Double Antibody I-125 Radioimmunoassay (Diagnostic Products Corporation) and I-125 Extraction Radioimmunoassay (Pantex) respectively.

Eleven women participated although one client discontinued due to an auto accident at mid-cycle. Of the ten remaining cycles, three had a mucus cycle of only eight days during the study cycle despite having met the criteria of a mucus cycle >8 days in the preceding cycles. Because these women had been managed appropriately with yellow stamps prior to the study cycle, their cycles were included in the data. One cycle demonstrated some spotting in the pre-Peak phase, one cycle demonstrated a split Peak, and an ectopic pregnancy was achieved in one cycle.

The estimated time of ovulation (ETO) was determined by a previously described method.[4]

Results

A typical cycle is seen in figure 1. There is a total mucus cycle of 12 days (day 4 through day 15) with the discharge noted as the client's BIP indicated by yellow stamps on days 5 through 8 (hatched area). The length of the true mucus cycle was 7 days with the POC on day 9, the ETO on day 12, and the Peak Day on day 15.

Table 1 lists the statistical characteristics of the 10 individual cycles. The average length of the mucus cycle in the seven cycles with a mucus cycle >8 days was 11.7 days (range 10-13 days). The true mucus cycles (defined as the number of days from the POC to the Peak Day) averaged 6.8 days for the group with >8 day mucus cycles, 6.3 for the group with mucus cycles =8 days, and

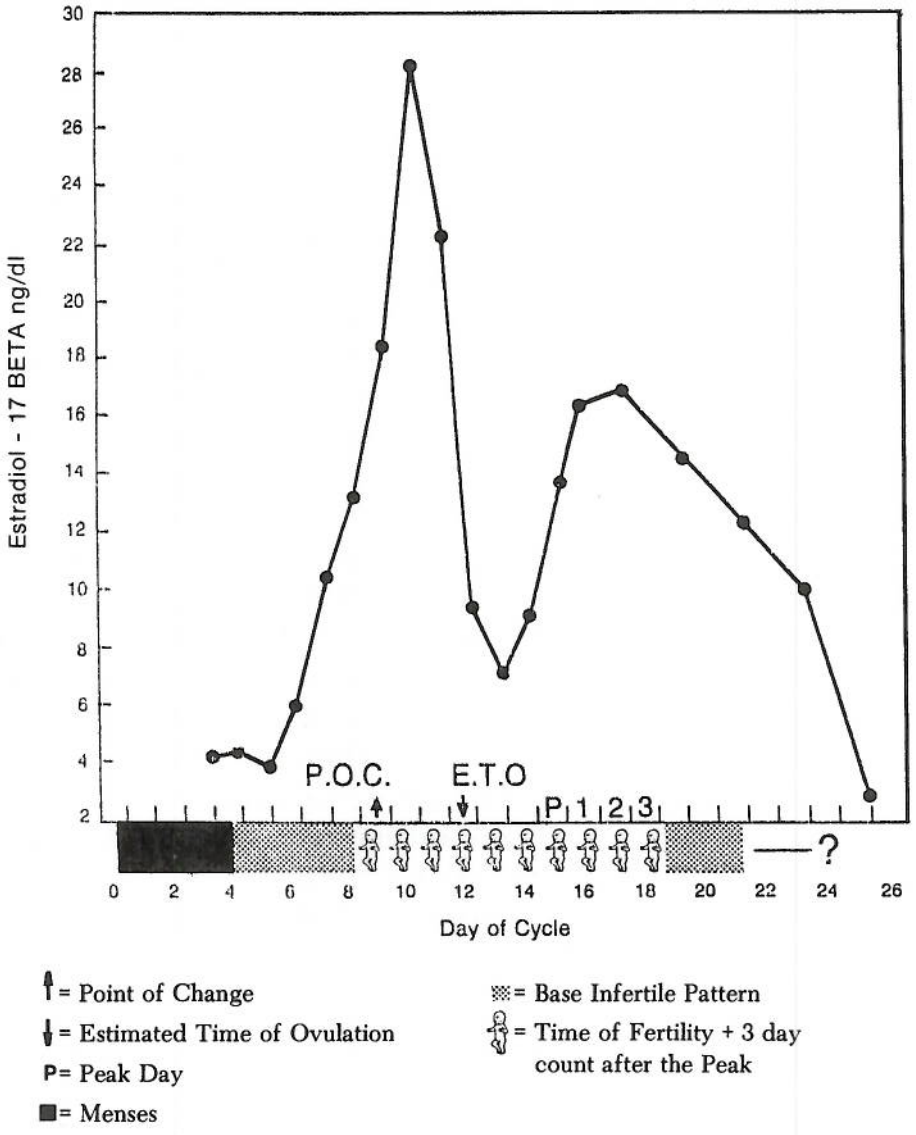

Fig. 1. Correlation of estradiol levels and OM charting in a woman with continuous Peak type mucus managed with pre-Peak yellow stamps.

6.7 overall. The average number of days from the POC to the ETO was 5.4 (range 2-10) for the group with mucus cycles >8 days and 5.3 overall. As shown, the post-Peak phases ranged from 7-13 days with an average of 10.2 for the group with cycles >8 days and 12.0 for the three with mucus cycles equal to 8 days. The average for

TABLE 1
STATISTICAL CHARACTERISTICS OF INDIVIDUAL CYCLES

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(N = 10)

SUBJECT		PEAK DAY[1]	ETO[1]	POINT OF CHANGE[1]	MUCUS CYCLE[2]	TRUE MUCUS CYCLE[3]	POINT OF CHANGE TO ETO[4]	POST-PEAK PHASE[5]	CYCLE LENGTH	ADDITIONAL INFERTILE DAYS
1.		19	20	11	12	9	10	11	30	3
2.		18	17	15	12	4	3	13	31	8
3.		16	13	9	13	8	5	10	26	5
4.		24	23	17	12	8	7	NA°	NA°	4
5.		15	12	9	12	7	4	10	25	5
6.		18	16	15	10	4	2	7	25	6
7.		14	13	7	11	8	7	10	24	3
SUBTOTAL N = 7	X				11.7	6.8	5.4	10.2[6]	26.8[6]	4.9
8.		14	13	9	8	6	5	13	27	2
9.		18	15	11	8	8	5	10	28	0
10.		12	12	8	8	5	5	13	25	3
SUBTOTAL N = 3	X				8.0	6.3	5.0	12.0	26.6	1.7
TOTALS N = 10	X				10.6	6.7	5.3	10.7[7]	26.7[7]	3.9

1. Day of Cycle.
2. Defined as the number of days from the beginning of mucus through the Peak Day.
3. Defined as the number of days from the point of change to the Peak Day.
4. Defined as the number of days from the point of change to the estimated time of ovulation.
5. Defined as the number of days from the day after the Peak Day through the last day of the cycle.
6. N = 6
7. N = 9

° Patient became pregnant in the study cycle.

all 10 cycles was 10.7 days. Cycle length ranged from 24-31 days with an average of 26.7. Finally, in the group with mucus cycles >8 days, 3-8 additional days of infertility (x=4.9 days) in the cycle of use were defined by management with pre-Peak yellow stamps.

The relationship of the ETO to the observation of the Peak Day is shown in table 2. For the 7 cycles with a mucus cycle >8 days, the ETO occurred from P-3 to P+1 with 85.7% occurring from P-3 to P-1.

TABLE 2
RELATIONSHIP OF THE ETO TO THE OBSERVATION OF THE PEAK DAY IN WOMEN USING PRE-PEAK YELLOW STAMPS
(N = 10)

		P-3	P-2	P-1	PEAK	P+1	P+2	P+3	TOTALS
MUCUS CYCLE >8d.	N	2	1	3	0	1	0	0	7
	%	28.5	14.3	42.8	0	14.3	0	0	100.0
MUCUS CYCLE = 8d.	N	1	0	1	1	0	0	0	3
	%	33.3	0	33.3	33.3	0	0	0	100.0
TOTAL STUDY CYCLE	N	3	1	4	1	1	0	0	10
	%	30.0	10.0	40.0	10.0	10.0	0	0	100.0

ETO on average = Peak - 1.6 days for N = 7
Peak - 1.4 days for N = 10

ETO = P-3 to Peak = 90% for N = 10
P-3 to P-1 = 85.7% for N = 7

For the three cycles with a mucus cycle equal to 8 days, the ETO occurred from P-3 to the Peak Day. The ETO on average occurred 1.6 days prior to the Peak Day for N=7 and 1.4 days prior to the Peak for all 10 cycles.

Table 3 presents the estradiol-17 Beta levels on the day before, the day of, and the day after the POC and the maximum estradiol-

TABLE 3

COMPARISON OF ESTRADIOL-17 BETA LEVELS WITH RELATIONSHIP TO THE POINT OF CHANGE (POC)
(N = 10)

		ESTRADIOL 17-BETA (ng/dl) POC-1	ESTRADIOL 17-BETA (ng/dl) POC	ESTRADIOL 17-BETA (ng/dl) POC+1	PEAK ESTRADIOL 17-BETA (ng/dl)
		4.7	6.9	8.6	28.5
		9.8	12.8	19.9	19.9
		6.1	8.5	11.1	23.7
		4.7	5.7	8.3	23.1
		11.6	14.3	19.4	29.3
		14.5	8.6	12.1	15.7
		16°	19.3	31.3	39.0
SUBTOTALS N = 7	X	9.6	10.9	15.8	25.6
		4.3	4.9	6.5	21.9
		5.8	8.2	13.5	18.9
		6.6	8.2	11.0	20.7
SUBTOTALS N = 3	X	5.4	7.1	10.3	20.5
TOTALS N = 10	X	8.4	9.7	14.2	24.1
	SE	1.4	1.4	2.4	2.1

° Estimated value calculated from estradiol-17 Beta levels before and after the day.

17 Beta levels in each cycle. For N=7, the average estradiol-17 Beta levels were 9.6 ng/dl, 10.9 ng/dl, and 15.8 ng/dl on POC-1, POC, POC+1, respectively, and, for N=10, the levels were 8.4 ng/dl, 9.7 ng/dl, and 14.2 ng/dl on POC-1, POC, and POC+1, respectively, with standard errors of the mean of 1.4, 1.4, and 2.4.

The average estradiol-17 Beta values around the POC are graphed in figure 2, and the composite estradiol-17 Beta curve with respect to the POC is seen in figure 3. Both graphs reveal a significant break in the estradiol-17 Beta curve on the day of POC where the slope of the composite estradiol-17 Beta curve rises from 1.34 before the POC to 4.46 after the POC.

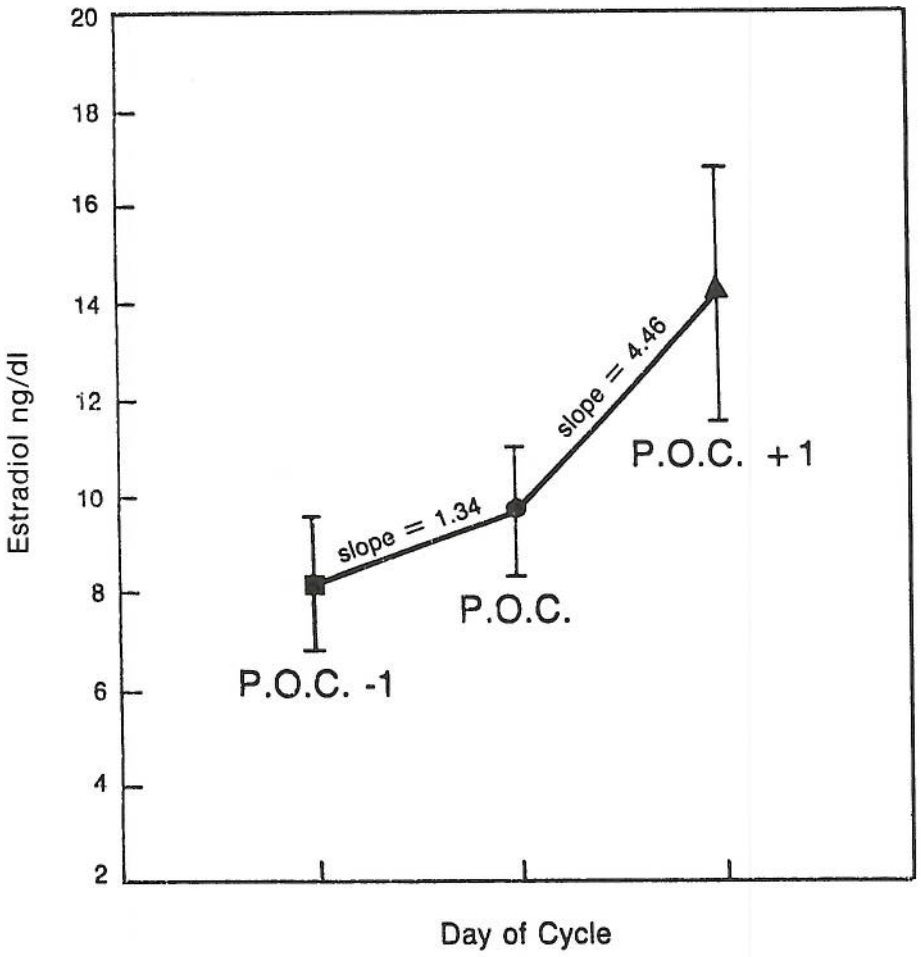

Fig. 2. Mean estradiol levels and standard error the day before, the day of, and the day after the P.O.C.

Discussion

While the etiology (or etiologies) of continuous mucus in women charting the Ovulation Method has remained obscure, the current practical management has proven effective. This is the first study attempting to place the present management on a scientific foundation and gain some insight into the problem of continuous mucus. Despite the small size of the group studied, the data suggests that the POC correlates well with the onset of the preovula-

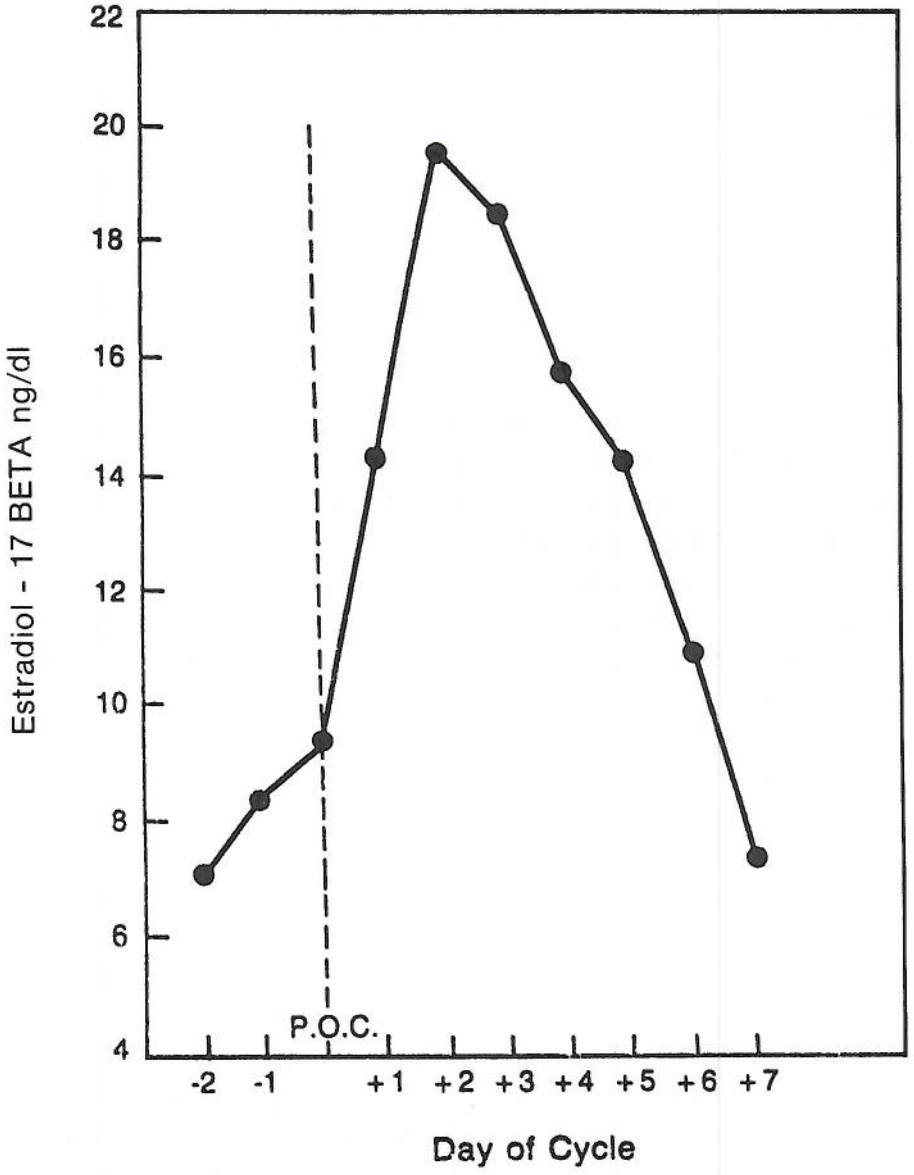

Fig. 3. Composite estradiol curve with respect to point of change (P.O.C.) in 10 menstrual cycles.

tory rise in estradiol-17 Beta and thus the onset of follicular growth.

Hilgers et al.,[4] reported on 65 hormonally normal cycles in which the ETO occurred from P-3 to P+3 with 95.4% occurring

from P-2 to P+2. In the present study, the ETO occurred somewhat earlier, from P-3 to P+1 with 90% occurring from P-3 to P+1. This apparent "early shift" of the ETO with respect to the Peak Day is also reflected in the mean ETO of P-1.4 days compared to P-0.3 days found by Hilgers[4] and P+0.9 days found by the Billings et al.[3] One could theorize that whatever process is producing the BIP could be interfering with the normal response of the cervical crypts to rising levels of postovulatory progesterone. In this way, the Peak Day could be delayed for 1 or 2 days in cycles with continuous mucus.

The obvious difference between the cycles studied and normal cycles is that the total length of the mucus cycles are much longer. The average mucus cycle for the 10 cycles studied was 10.6 days compared to 5.6 days found in 65 normal cycles.[4] When one looks at the true mucus cycle in women using pre-Peak yellow stamps, however, the average for the 10 cycles was 6.7 days, only 1 day longer than the previously reported 5.6 days.[4] This clearly substantiates the client's ability to accurately distinguish the BIP from the POC and the beginning of the time of fertility.

The post-Peak phases were shorter in the study group (mean = 10.7 days) when compared with the 65 normal cycles (mean = 12.4 days). The slight extension of the Peak Day past the ETO, seen in the continuous mucus cycles, may explain the shorter post-Peak phase noted here.

Although the POC could not be correlated with a given absolute estradiol-17 Beta level or a particular slope of the estradiol-17 Beta curve, it was, however, predictive of the rapidly increasing estradiol-17 Beta levels seen the last 5 or 6 days prior to ovulation. This is best demonstrated by the obvious break in the average estradiol-17 Beta curve seen in figures 2 and 3 and the individual cycle shown in figure 1.

The maximum estradiol-17 Beta levels seen in this study were from 18.9 ng/dl to 39.0 ng/dl (mean 24 ng/dl) and fell within the range for maximum estradiol-17 Beta levels of 15-40 ng/dl reported by Abraham.[1] However, when compared with peak estradiol-17 Beta levels of 31.8 ng/dl and 38 ng/dl reported by Baird and Guevara[2] and Korenman,[9] respectively, they are somewhat low. Given

the small number of cycles and the fact that estradiol-17 Beta levels have been shown to fluctuate widely in the periovulatory period[8] the significance of this finding is uncertain. It is of interest to note that in two cycles where the maximum estradiol-17 Beta levels were especially low (subjects 2 and 6), the true mucus cycles were short (4 days).

Most important to the management of clients using pre-Peak yellow stamps was the finding that the POC did define the onset of the time of fertility in these cycles. The POC was identified by the clients an average of 5.3 days prior to the ETO giving adequate prospective identification of approaching ovulation to allow for a sperm survival of 3-5 days. In the cycles where the POC was identified less than 4 days prior to the ETO, maximum estradiol-17 Beta levels were suboptimal, and one might wonder if these cases are analogous to limited mucus cycles where the interval of fertility is relatively shorter than normal.

Finally, it is important to note that in four cycles the pre-Peak days defined as infertile by the client were used for intercourse with no resultant pregnancies thus testing the infertility of the pre-Peak yellow stamp days.

In summary, in women with long mucus cycles greater than 8 days, managed with pre-Peak yellow stamps by well-trained teachers, the POC accurately marks the onset of rapidly increasing estradiol-17 Beta levels and thus the onset of the fertile phase of the cycle. These women were found to have true mucus cycles of normal length, but the ETO was seen to occur earlier with respect to the Peak Day than has been noted in normal cycles. This resulted in shorter post-Peak phases. These findings may impact the management of such cases in the future.

Thus this study, though limited, does support the accuracy of the Ovulation Method in identifying the times of fertility and infertility in cycles with continuous mucus. It also lends further credibility to the present protocol for the management of those cases with pre-Peak yellow stamps.

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