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*In this issue*

# Fertility

**Fertility in Both Males and Females Decline with Age**

David Dunson, PhD, a bio-statistician from the National Institute of Environmental Health Sciences (NIEHS) has recently developed a mathematical model to determine the probability of pregnancy on given days of a woman's menstrual cycle. His statistical model takes into consideration a number of variables that affect day specific fecundability, including frequency of intercourse, accuracy of biomarkers of fertility and age. Dunson, Professor Bernardo Columbo from the Department of Statistical Science at the University of Padua, Italy and Donna Baird (a colleague from NIEHS) utilized Dunson's statistical model to estimate the effects of male and female age on natural fertility and the length of the fertile window.[1] They determined probabilities of pregnancy associated with intercourse on specific days relative to ovulation and compared them across the following age groups; 19-26, 27-29; 30-34 and 35-39 years. Data for the analysis was obtained from a large European multinational study that enrolled 782 women between the ages of 18 and 40 who kept records of their daily BBT, acts of intercourse and menstrual bleeding. Study results were based upon 2539 cycles of data from 647 participants that had at least 1 day of intercourse during a generous 10-day estimate of the fertile window (i.e., 7 days prior to and 2 days after the estimated day of ovulation). Ovulation was estimated as the first day of the temperature shift. There were 433 detected pregnancies that occurred in the 2539 cycles.

The data showed that there was a 6 day window of fertility in which there was a 5% chance or more that intercourse would result in pregnancy. This 6-day window of fertility that included the day of ovulation and the 5 days before, was the same for the youngest three age categories and one day shorter for the 35-39 age category. The shortened fertile window for the older age category was not statistically significant. Dunson, Columbo and Baird also found that the day specific probabilities of pregnancy in the 6-day fertile window decreased with age. There was a close to 50% decrease in fertility among women in their late 30s compared to women in their early 20s. The researchers also found a decreased fertility among men. When they adjusted for the woman's age, the men in the 40 plus age range had significantly reduced fertility. For example, the probability of pregnancy for a 35 year old woman with a partner of the same age was 0.29 as compared to 0.18 with a male partner that was 40 years old. Of interest was that the highest probability of pregnancy was two days before the estimated day of ovulation for all age categories.

The authors also pointed out that there was a great amount of variability of fertility among healthy couples. For example, the probability of pregnancy on the peak day of the fertile window extended from a low of 20% to a high of 60%. At present the reasons for this broad range of fertility probabilities is largely unknown. The authors concluded that fertility for women begins to decline in the late 20s and that the decrease accelerates by the late 30s. Men's fertility is less affected by age, but does show a significant decline by the late 30s.

**Comments**

Dunson et al., speculated that the potential fertile window would decline in each age range (for men) due to declining sperm survival. This did not happen except for men 40 years or older. The authors concluded that the reduction of fertility with older men is not buffered by the overproduction of sperm.

Although I agree with the results of this study, the data source used for analysis is not without error. As most NFP teachers realize, the self-reporting of intercourse is not always accurate. Likewise, the determination of the first day of the temperature shift is not always easy to do. The shift in basal body temperature has much variability around the day of ovulation. The authors say that the error in estimation based on BBT is not great since they found a 6 day window of fertility that was similar to a hormonally estimated fertile window reported by Wilcox et al. (1995).[2] I also wondered to what degree the analyzed cycles were representative of the whole. The authors were only able to use less than half of the 5,860 cycles generated by the women participants because the participants were trying to avoid pregnancy and abstain from intercourse during the estimated fertile phase. I would recommend a prospective study that enrolled a similar number of couples who were trying to achieve pregnancy.

Sandra Ann Carson, MD commented on this study in a recent issue of *Journal Watch: Women's Health*.[3] She stated that the decline in women's fertility indicated in this study caused "sensationalized" media reports and misrepresented the age-related fertility decline. She calculated the cyclic fecundity of the cycles in the Dunson study and stated that "one can see that for fertile couples trying to avoid pregnancy, the cyclic fecundity drops with age, but not in such a dramatic manner." She calculated a cyclic fecundity of 21.4% in the 19-26 age range, 16.7% in the 27-29 age range, 7.3% in the 30-34 age range and 11.0% in the 35-39 age range. She also indicated that the findings from the Dunson study show that NFP is more successful in older women. (RJF)


1. Dunson, D. B., Columbo, B. and Baird, D. D., **Changes with age in the level and duration of fertility in the menstrual cycle**, *Human Reproduction* 17 (2002): 1399-1403.

2. Wilcox, A. J., Weinberg, C. R. and Baird, D. D., **Timing of sexual intercourse in relation to ovulation; effects of the probability of conception, survival of the pregnancy, and sex of the baby**, *The New England Journal of Medicine* 333 (1995): 1517-1521.

3. Carson, S. A., **Mathematical model misrepresents age-related fertility decline**, *Journal Watch: Women's Health* 7 (2002): 64.


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**Vaginal Fluid Charting and Clearplan Easy Fertility Monitor Recommended for Achieving Pregnancy**

Researchers from the Health Research Center at the University of Utah recently published an article that reviewed and evaluated methods of identifying the fertile phase of the menstrual cycle in light of the new data on the probability of fecundity. The purpose of the review was for making clinical recommendations about timing intercourse to achieve pregnancy and methods that identify the fertile phase of the menstrual cycle. The new data referred to in the article was that the fertile window is about 6 days long, i.e., the 5 days before ovulation and the day of ovulation. Research also has indicated that the two most fertile days are the two days before ovulation and that fertility decreases precipitously on the day of ovulation, i.e., the newly released ovum is probably only fertilizable within the first 16 hours. Based on this information the Utah researchers point out that an act of intercourse on the day of ovulation may be sufficiently late in the 24 hour period to achieve pregnancy. They recommended that couples who wish to become pregnant have intercourse daily during the fertile window rather than less frequent. They believe the increased probability of pregnancy on each day leading to ovulation outweighs the benefit of increasing the sperm count by less frequent intercourse. Some of the other recommendations from the Utah researchers for identifying the fertile window are:

1. Calendar calculations are unreliable for use in timing intercourse to achieve pregnancy
2. Serial ovarian ultrasound is highly accurate but is limited by its high cost and availability
3. Basal body temperature is not recommended since the temperature rise often occurs after the day of ovulation and the rise is often hard to interpret
4. Urine Luteinizing Hormone (LH) kits are useful but since the urinary LH surge occurs from 16 to 48 hours before ovulation a significant number of women users might miss the days of highest fecundity
5. Ovarian Monitor – developed by Dr. James Brown from Australia is accurate but it requires timed urine collections; the system is not available in the United States
6. ClearPlan Easy Fertility Monitor – detects urinary metabolites of estrogen and LH with a monitor that reads wick type test strips and provides users with high and peak fertility readings. The device is not suitable for women with cycles longer than 42 or shorter than 21 days
7. Salivary Electrolytes and Ferning – fertility monitors that measure salivary and vaginal electrical resistance have some evidence of accuracy in identifying peak fertility but the vaginal probe is invasive. The microscope monitors that view dried saliva for ferning have not been found accurate in determining the beginning and end of the fertile phase
8. Fertility Charting of Vaginal Discharge – the self-assessed peak day of cervical mucus correlates well with the timing of ovulation and has reasonable inter-rater reliability. Learning how to observe and chart vaginal-cervical fluids is recommended.

The overall recommendation was that the best means of self-identifying the entire 6 day fertile window (prospectively) was either daily observing and charting vaginal-cervical fluids or use of the ClearPlan Easy Fertility Monitor. The authors mentioned that most physicians still recommend BBT for the timing of intercourse.

**Comments**

I would recommend that NFP teachers and health professionals obtain a re-print of this article. The information in it is of relevance for teaching and using NFP. Of interest is that this article was referenced in the *New York Times* and the February (2003) issue of *Consumer's Report* (CR).[2] The CR article rated the ClearPlan Easy Ovulation Test Pack and the Clearplan Easy Fertility Monitor as number one and two products available commercially for determining the fertile window. Please see a further analysis of the self-assessment of cervical mucus as a biological marker to determine the fertile window in the "Under the Microscope" section of this publication. (RJF)

1. Stanford, J. B., White, G. L. and Hatasaka, H., **Timing intercourse to achieve pregnancy: current evidence**, *Obstetrics and Gynecology* 100 (December 2002): 1333-1341.

2. **The fertility window,** *Consumer Reports* 68 (February 2003): 48-50.

## Menstrual Cycle

**Monitoring Menstrual Cycle Hormones in At Risk Female Athletes**

The association between intense training among female athletes and the suppression of ovulation has been well established. Altered menstrual cycles in athletes can be a result of intense training, restricted dietary intake, the stress of competition, and higher testosterone levels. Although the suppression of the hypothalamic-pituitary-ovarian axis function in female athletes is an adaptive process, in the long run the reduced production of estrogen and progesterone can lead to an increased risk of stress fractures and reduced bone mineral density. Researchers at the University of Melbourne (Australia) recently evaluated an economical way of monitoring estrogen and progesterone levels in "at risk" female athletes during intense training and weight loss.[1] The female athletes were 14 adolescent rowers, 12 elite lightweight rowers, and two groups of 10 matched control subjects. The 26 female athletes were matched with the control subjects for age, height, weight, gynecological age, calcium intake and school. The age range of the adolescent rowers and matched controls was 14-15 years. The average age of the elite rowers and matched controls was 21.5 + 3.5 years and 22.0 + 3.5 years respectively. Each participant was provided with a collection kit and 15 collection tubes allowing them to collect urine samples every second day of the cycle beginning with day one. The urine samples were tested for urinary metabolites of estrogen (i.e., estrone glucuronide) and progesterone (i.e., pregnanediol glucuronide) by an assay technique that was developed by Professor James Brown at the Royal Women's Hospital in Melbourne.

The results showed that 5 (35%) of the adolescent rowers and 9 (75%) of the lightweight rowers had anovulatory cycles during competition season. The results also indicated that the levels of urinary estrogen and progesterone were significantly lower in the rowers compared to the controls during the competition season. The length of the menstrual cycles of the lightweight rowers during competition season was significantly longer than those during the off season and

compared to the non-rower controls. During the competition season the cycle length of the rowers was 47.9 + 3.0 days compared with 28.0 + 3.0 days during the off season. Although 25% of the elite rowers and 65% of the adolescent rowers had normal cycle lengths, on average the estrogen and progesterone levels were lower than the controls. The authors concluded that the urinary assay monitoring was an effective means of monitoring estrogen and progesterone levels in "at risk" female athletes. They recommended frequent monitoring of female athletes in order to detect low estrogen and progesterone levels and to prevent detrimental effects of bone loss.

**Comments**

This study demonstrates that a significant number of female athletes will have low estrogen and progesterone levels and may be at risk for bone density loss. It also demonstrated that there exists a simple means of monitoring urinary metabolites of estrogen and progesterone. This is essentially the technique that Dr. James Brown uses with the Brown Ovarian monitor. Monitoring female athletes with the Brown Ovarian monitor would be recommended for athletic programs and would not be too expensive. However, having female athletes monitor their cycles with traditional natural biological markers, i.e., basal body temperature and cervical mucus changes might be an economic alternative to determining menstrual cycle irregularities. (RJF)

1. Morris, F. L. and Wark, J. D., **An effective, economic way of monitoring menstrual cycle hormones in at risk female athletes**, *Medicine and Science in Sports and Exercise* 33 (2001): 9-14.

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**Lifestyle Factors and Menstrual Cycle Variability**

Researchers from the epidemiology branch of the National Institute of Environmental Health Sciences, the University of Michigan School of Public Health, and the National Cancer Institute recently completed one of the largest ever studies on menstrual function among adult women.(1) Three thousand nine hundred forty one women participants were selected from the (1994-96) Agriculture Health Study. They met the criteria of: being between the ages of 21-40; not currently taking oral contraceptives; and not currently breastfeeding or pregnant. The study sample was primarily white (98%) rural women (farm wives) from Iowa (78%) and North Carolina. The purpose of the study was to describe medical and lifestyle factors that might be associated with menstrual cycle characteristics. The rationale behind the study was that menstrual cycle patterns or characteristics might be indicative of certain health problems. Menstrual cycle characteristics, lifestyle and medical factors were measured by use of a self-recall questionnaire developed by the researchers.

The cross sectional data revealed that 9.7% of the sample experienced short cycles, 3.2% experienced long cycles, and 5% irregular cycles. Some of the key study results were as follows:

- Body fat, measured by body mass index (BMI) was strongly associated with long and irregular cycles. The odds of having a long cycle were 5 times higher among women with BMI's of 35 or more.
- Experiencing menarche before age 12 was moderately associated with an increased chance of short and irregular cycles.

- Experiencing menarche after 15 was associated with almost 3 times the chance of having long and irregular cycles.
- Smoking a pack or more of cigarettes per day increased the risk (odds ratio) of short and irregular cycles by more than 3 fold.
- Long, irregular, and cycles with inter-menstrual bleeding were associated with increased odds of infertility.
- Long and irregular cycles were associated with increased odds for fetal loss.

Although the sample size for this study was large, the authors admit that the sample was primarily white women living on farms and that the sample might differ from women in the general population. They also speculated that they might have underestimated the prevalence of long and irregular cycles, because women often take oral contraceptives for that purpose and these women were eliminated from the study. Furthermore, they did not identify women who recently stopped breastfeeding, discontinued oral contraceptives, and ended a pregnancy. All of these women would have more irregularity in their cycles. The authors concluded that menstrual cycle patterns are often influenced by lifestyle and environmental factors and that menstrual cycles that are disturbed by these factors might precipitate other reproductive disorders.

**Comments**

Studies on how characteristics of menstrual cycles can provide important information on women's health and potential medical problems are needed. As the authors of this study indicated, most of the previous studies done in this area were based on college or graduate students. I found the study remarkable in that they were able to find such a large group of women who were not on oral contraceptives. Maybe rural women from Iowa would rather not use artificial chemicals to control their fertility.

The problem I have with the study is that they used cross sectional data that was based on recall. As NFP teachers know, how women first describe their cycle and what they look like after some months of charting are often different. A study of women who chart their cycles prospectively across time would be more powerful and believable. Furthermore, many of the characteristics from the menstrual cycle that might provide even more information, like cervical mucus characteristics, when inter-menstrual bleeding actually took place, the length of the pre- and post-peak phases, were not indicated. Women and couples who practice NFP and chart their cycles are a rich source for this information. (RJF)

1. Rowland, A. S., Baird, D. D. and Long, S. et al, **Influence of medical conditions and lifestyle factors on the menstrual cycle**, *Epidemiology* 13 (2002): 668-674.

# Contraceptives

**Prolonged Use of Oral Contraceptives Found to Increase Fecundity**

Common knowledge among NFP teachers is that the use of oral hormonal contraceptives will decrease fertility due to its aging affect of the cervix and the disruption of the menstrual cycle. That the use of oral hormonal contraceptives might impair fertility is also of concern among health professionals and the general public. Previous research on the effects of oral contraception on fertility has been mixed. The mixed results are due largely to small samples and not controlling for other confounding factors like age, cigarette smoking and body weight. Researchers at the University of Bristol and Brunel University (England) recently studied the impact of oral contraceptive use on "time to conception" among a large group of women participants in South-West England.[1] The subjects for the study were couples intending to become pregnant and were a part of the Avon Longitudinal Study of Parents and Children. There were 12,106 couples initially eligible for the study and of these, 8,497 (70.6%) conceived intentionally.

The researchers collected data on total duration of usage of oral contraceptives, body mass index, level of cigarette smoking, alcohol consumption, age of both parents at time of conception, employment status and other factors that might affect fertility. The measure of fertility was "time to conception" to achieve a pregnancy that reached 24 weeks of gestation. The "time to conception" was determined retrospectively by a questionnaire given to couples at 18 weeks of gestation.

The results indicated that 74.2% of the couples achieved a pregnancy within the first 6 months, 13.9% within the second 6 months, 8.5% in the years 2 and 3, and 3.4% after 3 years. The researchers also found that increasing duration of oral contraceptive use was significantly associated with an increased proportion of pregnancies within the first 12 months of trying. The factors that were found to significantly delay conception were older age of the man and woman, the woman's greater exposure to cigarette smoke, lower levels of education and the extremes of body mass index (i.e., either being too thin or too heavy). The researchers also found a statistically significant association between odds of conception within 12 months and the use of oral contraception for 5 years or more. The authors concluded that women who have prolonged use of oral contraceptives might be reassured that they will not be disadvantaged in terms of time to achieve a pregnancy.

**Comments**

Some of the factors that the authors speculated might contribute to an increased fecundity with prolonged use of oral contraception was the minimization of endometrial proliferation and shedding, preventing the damaging effects of endometriosis, and improved stores of iron. They also speculated that the use of oral contraceptives by suppression of ovulation might preserve the number of follicles.

A limitation of the study was that the women participants were asked to recall the length of time to conception, i.e., they used retrospective recall rather than a prospective measure.

Recall might have been in error and overly optimistic. There also might have been selection bias since they did not compare oral contraceptive use with other means of family planning. However, given the limitations, this study provides strong evidence that oral contraceptives do not cause infertility or damage to the reproductive system that would result in infertility. (RJF)

1. Farrow, A., Hull, M. G. R. and Northstone, K. et al., **Prolonged use of oral contraception before a planned pregnancy with a decreased risk of delayed conception**, *Human Reproduction* 17 (2002): 2754-2761.

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**Ovarian Function after Use of a Contraceptive Vaginal Ring**

NuvaRing® is a combined contraceptive vaginal ring that provides a continuous release of etonogestrel and ethinyl estradiol over a 3 week period. This new type of contraceptive requires using the ring for a 3 week period followed by a 1 week free period. Previous studies have shown that the vaginal ring is an effective contraceptive method and completely inhibits ovulation when used correctly. However, as with all methods of contraception there will be compliance issues that will decrease contraceptive effectiveness. Researchers from The Netherlands and Belgium conducted a study to determine the contraceptive effectiveness (i.e., suppression of ovulation) among women subjects who deviate from the recommend use of the product.[1]

Fifty-one healthy women between the ages of 18-35 years were provided with one (pre-treatment) cycle of a combined oral contraceptive and then were randomly distributed to three treatment groups. All of the subjects were provided the contraceptive vaginal ring and then were asked to use it as prescribed – i.e., 3 weeks of continuous use and then one free week without use. The 15 women who remained in Group A used the contraceptive ring according to the recommended regimen after which they were assessed for ovulation by daily transvaginal ultrasound and serum hormone levels. The 15 women in Group B only used the ring for 3 days and then were followed by ultrasound and serum hormones until ovulation was determined. The remaining 15 women in Group C did not start the use of the vaginal ring until a follicle size of 13 mm was observed through ultrasound.

After removal of the contraceptive vaginal ring, the LH surge was detected on average on day 17 in Group A and day 16 in Group B. In Group A, follicle growth started 3 days after removal of the ring and in Group B follicle growth started 7 days after removal. The median time to ovulation (as confirmed by serum progesterone levels and ultrasound) in Group A was 19 days and in Group B 17 days. Women in Group C did not begin to use the vaginal ring for the second cycle until follicle growth reached a diameter of 13 mm. This happened on average on day 11 (range 8-21 days). None of the women in Group C ovulated during the second treatment cycle.

The findings of the study revealed that the median time to ovulation was similar, 17 and 19 days respectively, regardless if the vaginal ring was used for 3 days or for 3 weeks. The first woman to ovulate in each group was also similar, day 12 and 13 days respectively. The results also showed that it took a median time of 11 days for follicles to reach 13 mm after removal of the ring, meaning that it would need to extend the standard free-ring period by 4 or more days. The authors concluded that as little as 3 days of the vaginal contraceptive ring is sufficient to

suppress ovarian function and ovulation. They also concluded that the vaginal ring is robust enough if deliberate deviations from the standard usage regimen occurred provided that the recommended regimen was used in the previous or subsequent cycles.

**Comment**

Of interest is that 20 of the 45 women participants had adverse events due to the use of the vaginal ring. "Leukorrhoea" and "dysmenorrhoea" were the most frequent side effects documented. There was also a concern that many experienced increased vaginal discharge. Given the high frequency of adverse events, with only 1-2 cycles of use, you would wonder about continuation or correct use over a long period of time. You would also wonder that if the ring is causing vaginal and cervical irritation that it might be a health risk, i.e., might it result in pre-cancerous cells or other health problems? The readers should also be aware that the first author is an employee of Organon – the makers of the vaginal ring contraceptive. (RJF)

1. Mulders, T., Dieben, T. and Bennink, H., **Ovarian function with a novel combined contraceptive vaginal ring**, *Human Reproduction* 17 (2002): 2594-2599.

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**Male Hormonal Contraception with Oral Desogestrel and Depot Testosterone**

Two studies were recently reported on the effectiveness of suppressing spermatogenesis among male subjects in 4 countries through the use of a combination of sub-cutaneous (s.c.) administered pellets of testosterone and oral desogestrel (a form of progesterone).(1,2) The first study recruited 30 men from Scotland and 36 men from Shanghei, China. The second study recruited 31 male subjects from South Africa and 21 from Nigeria. Previous studies have shown that the administration of progesterone is effective in suppressing spermatogenesis but that the resultant decrease in testosterone levels was not tolerated. Testosterone alone was not consistently effective in suppression of sperm production. Furthermore there seems to be variability in sperm suppression among various ethnic groups. The men in the first (Scotland/China) study received either 150 or 300 micro grams mg of oral desogestrel daily for 24 weeks with 400 mg testosterone pellets s.c. on day one and at 12 weeks. The men in the second (African) study were randomized to receive either 150 or 300 mg of desogestrel with 400 mg of testosterone administered s.c. every 12 weeks.

The researchers in the first study were able to produce complete suppression of sperm production (azoospermia) in 28 out of 28 men who were on the 400 mg dose of desogestrel, versus 22 out of the 31 men in the lower dose of desogestrel. In the African study, after 20 weeks of treatment, 8 of 10 in the 150 mg group and 8 of 12 in the 300 mg group achieved azoospermia (in South African males) and in all 17 men in the Nigerian group. Therefore, the researchers were able to demonstrate azoospermia in 83 out of 98 men (85%) in the two studies. Both groups of researchers indicated that the combination of oral progesterone and s.c. testosterone pellets could be an effective male contraceptive regimen.

**Comments**

Approximately 18 percent of the male subjects (21men) withdrew from the study protocols before the end of the study. Some of the men withdrew due to non-compliance, impotence, raised blood pressure, extruded testosterone pellets and other study related problems. Of interest is that most men in both studies gained significant weight from 6 to 10 pounds. One reason for the development of a male form of hormonal contraception is to have a more fair gender balance in contraceptive responsibility. However, I would doubt that a type of contraceptive that required subcutaneous administration plus an oral dose and that resulted in weight gain and other side effects would be tolerated by males in the United States – i.e., unless there was some major paradigmatic shift in the male constitution. (RJF)

1. Kinniburgh, D., Zhu, H. and Cheng, L. et al, **Oral desogestrel with testosterone pellets induces consistent suppression of spermatogenesis to azoospermia in both Caucasian and Chinese men**, *Human Reproduction* 17 (2002): 1490-1501.

2. Anderson, R. A., van der Spuy, Z. M. and Dada, O. A. et al., **Investigation of hormonal male contraception by oral desogestrel with depot testosterone**, *Human Reproduction* 17 (2002): 2869-2877.

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# Menopause

**Post-Menopausal Hormones and Alcohol Increase Risk for Breast Cancer**

In 1976, 121,700 female registered nurses between the ages of 30 to 55 were enrolled in what is called the Nurses' Health Study. Every two years these nurses are sent extensive questionnaires on risk factors for cancer and heart disease and in 1980, they were also questioned about nutritional factors and alcohol consumption. Researchers from the Brigham and Young Hospital and Harvard Medical School and the Dana Farber Cancer Institute (Boston) recently reported on the relationship between concurrent use of hormonal replacement therapy, alcohol use, and invasive breast cancer among 44,187 of the original cohort of nurses that entered menopause by 1994.[1] Previous epidemiological evidence has suggested that alcohol consumption can increase breast cancer through a hormonal mechanism. By 1996, 1,722 of the original 44,187 nurses had documented invasive breast cancer.

Based on these results, the researcher calculated that the relative risk for breast cancer increased by 32% among the nurses who concurrently used hormonal replacement for 5 years or more and increased 28% when they drank 1.5-2 or more alcoholic drinks per day. However, the risk increased to 99% among nurses who concurrently used hormonal replacement for 5 or more years and drank 1.5-2 alcoholic drinks per day. The researchers determined that the lifetime cancer risk increases from 4% to 8% among menopausal women who use hormonal replacement and have daily alcohol consumption. They concluded that women should consider the increased risk for breast cancer when deciding about drinking alcohol, taking post menopausal hormone replacement, and especially taking both together.

**Comment**

A previous study has shown that alcohol can increase both plasma and urinary levels of estradiol and estrone by 15% to 30% and that levels can increase up to 300% among postmenopausal women.[2,3] This is one reason that the Boston/Harvard researchers speculate why there is an increased risk for breast cancer among postmenopausal women. This again brings to mind the question why women who use hormones for contraceptive purposes would not be susceptible to the same mechanisms? (RJF)


1. Chen, W. Y., Colditz, G. A., Rosner, B. and Hankinson, S.E. et al., **Use of postmenopausal hormones, alcohol, and risk for invasive breast cancer**, *Annals of Internal Medicine* 137 (2002): 798-804.

2. Reichman, M. E., Judd, J. T. and Longcope, C. et al., **Effects of alcohol consumption on plasma and urinary hormone concentrations in premenopausal women**, *Journal of the National Cancer Institute* 85 (1993): 733-27.

3. Ginsburg, E. S., Mello, N. K. and Mendelson, J. H. et al., **Effects of alcohol ingestion on estrogen in postmenopausal women**, *Journal of the American Medical Association* 276 (1996): 1747-51.


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**Hormone Replacement Therapy and Antioxidant Vitamins Found to be Ineffective in Reducing Risk of Heart Disease**

A randomized double blind control study was recently conducted to determine whether hormone replacement therapy (HRT) and/or antioxidant vitamins were effective in decreasing heart disease in post-menopausal women.(1) Four hundred twenty three postmenopausal women with significant coronary artery stenosis (i.e., with at least one coronary artery with 15%-75% blockage documented by angiography) were randomized into four groups: 1) a group that received 0.625 mg per day of conjugated equine estrogen, 2) a matching group of participants that received a placebo HRT pill, 3) a group that received 400 IU of vitamin E and 500 mg of vitamin C twice daily, or 4) a group that received vitamin placebos twice daily. This clinical trial took place from July 1997 until January 2002 in 7 clinical centers from the United States and Canada. The main outcome measure for the study was the change in coronary artery lumen size (measured in mm by angiography) from the time of enrollment until completion. At completion the mean interval between the first and final angiogram was 2.8 years (SD = 0.9).

The mean decrease in coronary artery lumen size was 0.047 (0.15) mm/y in the HRT group, by 0.024 (0.15) mm/y in the HRT placebo group ($p = 0.17$) by 0.044 (0.15) mm/y among women in the vitamin antioxidant group and by 0.028 (0.15) mm/y in the vitamin placebo group ($p = 0.32$). In other words there was no difference in the mean decrease in lumen size among the 4 groups of postmenopausal women participants. However, “death,” a “nonfatal myocardial infarction” (MI) or “stroke” occurred among 26 of the HRT participants and only among 15 in the HRT control group. There were 26 deaths, nonfatal MIs or strokes among the participants receiving vitamin therapy as compared to 18 of the vitamin control participants. The authors

concluded from the data of this study and previous studies that: 1) the evidence clearly indicates that HRT does not reduce coronary heart disease and that it is probably harmful in the short term, and 2) that therapy with high doses of vitamin C and E is not beneficial and may be harmful.

**Comment**

The findings of this study on the use of replacement HRT for post menopausal women concurs with the latest data from the Women's Health Initiative that was reported in the previous issue of CMR (Summer/Fall, 2002). The most surprising finding of this study was that high doses of vitamin C and E also showed an increased risk for cardiovascular mortality. The authors indicate that this could be a chance finding, however, a previous study (the Heart Protection Study) also showed an increased trend in mortality with vitamin therapy.(2) This study demonstrates that even what some might consider a "safe" therapy (i.e., vitamin use) might not be effective and, in fact, might cause harm. (RJF)

1. Waters, D. D., Alderman, E. L. and Hsia, J. et al., **Effects of hormone replacement therapy and antioxidant vitamin supplements on coronary atherosclerosis in postmenopausal women: A randomized controlled trial**, *Journal of the American Medical Association* 19 (2002): 2432-2440.

2. BHF, **Heart protection study of antioxidant vitamin supplementation in 20,536 high-risk individuals: a randomized controlled trial**, *Lancet* 360 (2002): 23-33.

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**Beans Are a Safe and Promising Treatment for Menopausal Symptoms**

Researchers from Columbia University (New York) and George Washington University (Washington, D.C.) recently conducted an extensive review of the research literature to determine the effectiveness of complementary and alternative medicine (CAM) for the treatment of menopausal symptoms.[1] The purpose of the review was to help inform practice and to guide future research in this area. The authors searched the medical literature from 1966 through March of 2002 for studies that reported randomized control trials of CAM as treatments for menopausal symptoms and in particular "hot flashes." They were able to identify 29 published studies with randomized control trials, 12 on the effects of soy products, 10 with herbs and 7 with other types of CAM treatments (e.g., relaxation techniques). The key findings are as follows

- For herbal treatments only black cohosh demonstrated some effects in reducing hot flashes. No herbal medicines, including black cohosh, has been determined to be safe for long term use. Some herbals such as dong quai contains coumarins and may cause bleeding,
- Soy and other foods that contain phytoestrogens (i.e., beans, clover and alfalfa) seem to have a modest effect in reducing hot flashes but studies are inconclusive. Since soy foods have long been a stable of Asian diets they are assumed to be safe for long term use,
- Single randomized trials of vitamin E, primrose oil, dong quai, and acupuncture have found these treatments not to be effective in reducing perimenopausal symptoms,
- Two studies have not found red clover to be effective in reducing symptoms.

The authors concluded that phytoestrogen containing foods (i.e., soy products and other beans) and black cohosh have promise as treatments for menopausal symptoms. However, long term safety for these treatments have not been determined.

**Comments**

This review report on the effectiveness of CAM points out that "non-traditional medicines" (e.g., over the counter herbs, acupuncture, etc) also need to be tested for safety and effectiveness. Even if some CAMs are safe they might not be effective, and might also be expensive. (RJF)

1. Kronenberg, F. and Fugh-Berman, A., **Complementary and alternative medicine for menopausal symptoms: a review of randomized, controlled trials**, *Annals of Internal Medicine* 137 (2002): 805-813.

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**Federal Report on Carcinogens Includes Estrogen Therapy**

The federal government recently published its biennial Report on Carcinogens, and for the first time included steroidal estrogens used in estrogen replacement therapy and oral contraceptives.[1] The Report on Carcinogens is the official list of "known" human carcinogens that is reported to Congress by the Department of Health and Human Services (HHS). The National Toxicology Program, an arm of the HHS located at the National Institute of Environmental Health Sciences, prepared this report. The reports are published every two years after lengthy study and scientific reviews by three successive expert panels of government and non-government scientists.

The report is mandated by Congress as a way for the government to help keep the public informed about substances or exposure circumstances that are "known" or are "reasonably anticipated" to cause human cancers. The report makes a distinction between "known" human carcinogens, where there is sufficient evidence from human studies and "reasonably anticipated" human carcinogens, where there is either limited evidence of carcinogenicity from human studies and/or sufficient evidence of carcinogenicity from experimental animal studies.

The tenth report newly lists the group of hormones known as steroidal estrogens as "known human carcinogens." The report does not assess the magnitude of the carcinogenic risk, nor does it address any potential benefits of listed substances such as certain pharmaceuticals. Listing in the report does not establish that such substance presents a risk to persons in their daily lives. Such formal risk assessments are the responsibility of federal, state, and local health regulatory agencies.

1. See **www.niehs.nih.gov/oc/news/10thrc.htm** (December 11, 2002).

# Under the Microscope

## Accuracy of Cervical Mucus as a Biological Marker for the Beginning of the Fertile Phase of the Menstrual Cycle

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A review study on the accuracy of the peak day of cervical mucus (PD) was recently published in the journal *Contraception*.[1] The purpose of the study was to provide evidence for the accuracy of the peak day of cervical mucus as a biological marker of peak fertility and the estimated day of ovulation. The study included an analysis of data from published peer reviewed research studies and data from108 menstrual cycle charts from 53 women participants that compared the self-determination of the peak day of cervical mucus with the urinary luteinizing hormone (LH) surge. The conclusion of the study was that self-determination of the peak day of cervical mucus is a very accurate means of determining peak fertility and a fairly accurate means of determining the day of ovulation and the beginning of the end of the fertile time. However, what is apparent in this and previous studies on the accuracy of the PD, is that there is little evidence to show how accurate the self-assessment of cervical mucus is as a biological marker for the beginning of the fertile phase. Furthermore there is no agreement among NFP models/methods as to what characteristics of cervical mucus indicate the beginning of the fertile phase. This purpose of this analysis is to review evidence from the literature to determine how accurate the self-assessment of cervical mucus is in predicting the beginning of the fertile phase.

### *Review of Literature*

Only a few published studies provide evidence for the accuracy of cervical mucus as a (self-assessed) natural biological marker of the beginning of fertility. Most of these studies were conducted to correlate the self-detected peak symptom of cervical mucus with a hormonally estimated day of ovulation. Some of these studies also included data on the beginning of the fertile phase as determined by the self-assessed presence of cervical mucus. Since we now know that the actual fertile phase of a woman's menstrual cycle is approximately 6 days, i.e., the day of ovulation and the 5 days preceding the estimated day of ovulation, we can judge how well various markers of fertility cover the 6 day fertile window in these past studies.[2]

One of the first published studies on the accuracy of self-assessed cervical mucus was by Billings et al. in 1972.[3] The Billings research group taught 22 woman volunteers how to "recognize a pattern of vaginal mucous discharge" and to record their observations in a daily record. The day of ovulation was estimated through serial measurement of plasma LH. They found the first mucus symptom occured a mean of 6 days before the day of ovulation. The correlation between the beginning of cervical mucus symptom day and the estimated beginning of the fertile period (i.e., estimated day of ovulation minus 5 days) was 0.73, $p < 0.001$. In this study the first day of self-observed cervical mucus symptoms did not cover the beginning of the estimated 6-day fertile window in 6 (or 27%) out of the 22 data cycles reported.

Flynn and Lynch[4] correlated cervical mucus ratings with plasma LH, estradial and progesterone with nine healthy woman subjects who generated 29 menstrual cycles. The peak

day was defined as the day of maximum mucus grading (MMG) based on a system that ranged from "-1" (dry sensation) to "9" (wet, slippery, variable amount). The first day of observed mucus in the 29 cycles occurred on average 5.2 days before the LH peak or 6.2 days before the estimated day of ovulation, i.e., the day after the LH peak. Flynn and Lynch found that 8 out of the 29 cycles (27.5%) had 2 or less days of pre-ovulatory mucus and did not cover the 6-day fertile window.

Hilgers et al.[5] used serum progesterone levels to determine the estimated day of ovulation among 24 healthy woman subjects. They found, in 65 hormonally confirmed cycles, the mean numbers of days of mucus before the estimated day of ovulation was 5.9, the median was 6 days, and the range was 0 – 15 days. Therefore, if the median was 6 days, 50% of the 65 cycles had mucus cycles of 6 days or less before the estimated day of ovulation. Hilgers stated in this article that intercourse on a dry day pre-peak could "represent an occasional mechanism for biological failure of the ovulation method", and that more work needs to be done in this area. In another publication he and Prebil[6] mentioned the observation of a pregnancy that resulted from intercourse on a dry day pre- peak.

Cortisi et al.[7] conducted a similar study to determine the correlation of the plasma LH surge with cervical mucus in 27 healthy young Italian women. They defined the beginning of the fertile phase as either seeing or feeling cervical mucus. In 31 of 32 ovulatory cycles, they found that cervical mucus began on average 6.0 days before the estimated day of ovulation, with a range of 3-10 days. Nine (28%) of the 32 cycles had 5 or less days of mucus before the estimated day of ovulation. They reported that the first day of recorded cervical mucus symptoms correlated closely ($r = 0.825$, $p < 0.001$) with the first day of a significant rise in plasma estradiol.

The World Health Organization (WHO) study of cervical mucus characteristics and fertility reported a mean of 5.6 days of mucus signs before the peak day (PD) of cervical mucus among 725 women participants who generated 7514 cycles of data.[8] However, in 18 (0.3 %) of the cycles there was no mucus observed before the PD, in 149 (2%) of the cycles only 1 day of mucus observed, in 479 cycles (7%) there was 2 days of mucus observed, and in 649 cycles (10%) there was 3 days of mucus observed before the PD. Therefore, there was on average only 3 days of observable mucus or less before the PD in about 20% of the cycles. Based on the data from the WHO study the self-assessed cervical mucus indicator will cover the beginning of the 6-day fertile phase in about 80% of cycles. There was no hormonal criterion marker of the estimated day of ovulation in the WHO study.

Another WHO sponsored study found that among 13 experienced users of the Sympto-Thermal Method of NFP (who generated 58 menstrual cycles of data) the first day of self-observed cervical mucus occurred a mean of 6.6 days before the day of the urinary LH surge.[9] They also found that the cervical mucus sign alone did not cover the estimated fertile period in 9% of the cycles. The fertile window of this study, however, was estimated from the day of the LH peak minus 3 days to the day of peak LH levels plus 2 days (i.e., a 6 day window of fertility that is shifted to the left by one day).

A more recent study compared the peak in cervical mucus with an estimated day of ovulation determined by the peak of urinary estrone glucuronide through use of the ovarian monitor developed by Brown et al.[10] The day of peak mucus varied plus or minus three days of the estimated day of ovulation in 100% of the 127 cycles generated by 37 women participants. However, although the first day of mucus correlated well (graph wise) with the rise of estrogen, the majority fell less than 4 days of the estimated day of ovulation.

In the recent review study (by this author) on the accuracy of cervical mucus as a biological marker of fertility, the estimated day of ovulation (ETO) was the day after the day of the urinary LH surge.[1] The beginning of the mucus sign was on average 5.7 days (SD = 4.8) before the estimated day of ovulation. Based on the assumption of a 6-day window of fertility – beginning 5 days before the ETO, there were 38 of 94 cycles (40%) that the self-assessed cervical mucus marker did not cover the estimated fertile phase. There was a 0.83 correlation ($p < 0.001$) with the beginning of the estimated beginning of the fertile phase and the first day of observable mucus.

**Table 1: Studies of Cervical Mucus as a Biological Marker of Fertility**

| Study | Cycles(a) | Mucus(b) | Not Covered(c) | Correlation(d) |
|---|---|---|---|---|
| Billings et al. 1972 | 22/22 | 6.0 | 6 (27%) | 0.73 |
| Flynn/Lynch, 1976 | 9/29 | 6.2 | 8 (27.5%) | NA |
| Hilgers et al. 1978 | 24/65 | 5.9 | 32 (50%)(e) | NA |
| Cortisi et al. 1981 | 27/32 | 6.0 | 9 (28%) | 0.82 |
| WHO, 1983(a) | 725/7514 | 5.6 | 1503 (20%) | NA |
| WHO, 1983(b) | 13/58 | 6.6 | > 5 (9%) | NA |
| Fehring, 2002 | 66/94 | 5.7 | 38 (40%) | 0.83 |

a = number of subjects and cycles
b = mean number of mucus days before the estimated day of ovulation
c = number and percent of cycles that do not cover the estimated 6 day fertile window
d = correlation of the beginning of cervical mucus with the estimated beginning of the fertile phase $p < 0.001$
e = number of cycles that had 6 or less days of mucus before the estimated day of ovulation
NA = Data not available

The 7 studies reviewed (See Table 1) are consistent in that the average number of self-assessed cervical mucus days before the estimated day of ovulation was about 6 days. However, in 10-30% of the cycles the mucus sign will not provide an adequate warning (i.e., at least 5 days) before the estimated day of ovulation. In other words, about 20-30% of the cycles, the 6-day fertile window is not covered. The question that needs to be answered is how fertile are couples on dry days in the 6-day fertile window. Does the fact that cervical mucus was not observed externally make that a day of low or no fertility? Do internal checks increase the

accuracy of self-assessing the beginning of the fertile phase?

### *Analysis of Data*

Three of the above published studies on the accuracy of cervical mucus provided the reader with raw data that can be added together for a larger data set and for further analysis.(1,3,7) The small data sets not only provided data on the length of the cycles, but also the estimated day of ovulation (based on hormonal markers) and the beginning of the fertile phase (based on the appearance of cervical mucus). The raw data also allows one to correlate the day of the beginning of the self-assessed cervical mucus with the first day of the estimated fertile window. There were 164 cycles of data from the combined studies with a mean length of 29.2 days (SD = 5.58). One hundred and two women participants generated these cycles.

On average, the first day of fertility based on the first appearance of self-assessed cervical mucus was day 11.02 (SD = 4.8) and the average first day of the fertile phase based on the estimated day of ovulation minus 5 days was 11.94 (SD = 5.34). In 48 or 29.3% of the 164 cycles, the appearance of cervical mucus failed to cover the first 5 days of the estimated fertile phase. The correlation of the beginning of the fertile phase based on the estimated day of ovulation minus 5 days and the beginning of the fertile phase based on the first appearance of self-assessed cervical mucus was $r = 0.826$ $p < 0.001$.

### *Differences in Interpreting the First Appearance of Mucus*

There are differences among the various systems of NFP in the interpretation of what is the beginning of the fertile phase (or phase II in some systems) based on the self-assessment of cervical mucus. The means of observing or self-assessing cervical mucus is also different. Several examples are provided below:

1. The Billings Ovulation method is primarily based on the first sensation of cervical mucus at the lips of the vagina or vulva. However, women users are told to observe for both appearance and sensation. This sensation is one of change from a sensation of dryness to non-dry, i.e., sticky, tacky, moist or wet. The sensation is determined throughout the day by mental checks during normal daily activity and/or when voiding. The woman observer might also observe actual mucus. There is no set frequency of observation other than to do so frequently during the day and at night before bedtime. The women observers are encouraged to watch for patterns of their own mucus. The beginning of the fertile phase could be based on a change from a dry pattern to non dry, or a continuous pattern of a mucus sensation or observation (e.g., sticky, tacky, flaky-type mucus) to a more thread like mucus.[11, 12]

2. With the Creighton Model Fertility*Care*$^{TM}$ System, - the assessment of cervical mucus is based on the sensation while wiping from front to back over the perineal area before and after each voiding during the day and before going to bed. Women users are taught to "bear down" before the last check. The appearance of mucus is included only if the women observer is able to lift the mucus off of the tissue and observe at eye level between the thumb and index finger. The woman observer could sense wetness or dampness and or observe damp, wet or shiny on the tissue but unless she also has an

obvious sensation of lubrication, the observation is considered a special category of a "dry day" observation. Any mucus that is observed on the undergarments is ignored and not considered in the determination of fertility or infertility. Women are instructed to observe for mucus on light and very light days of bleeding during menses. Determination of mucus and the interpretation of whether it is fertile or not is on a day-to-day basis. Women observers could also have a continuous mucus pattern and are taught to distinguish that pattern from the actual mucus pattern (fertile phase) based on an essential sameness pattern of mucus observations.[13]

3. In the Couple to Couple League – Sympto-Thermal system – the assessment of cervical mucus includes internal and external observations. The external observations are based on both the sensation at the vulva and when wiping after voiding. The woman observer is encouraged to check for mucus during the day before and after each voiding. When mucus is observed on the tissue, they are told to do a finger test of the consistency. If only dampness or shininess is observed and no mucus they are encouraged to do internal exams. The reader is informed that they might notice mucus at the cervical Os before they experience it externally. They are informed to begin observing both internal and externally when their menses stops or by the 6th day after menses begins.[14]

4. Weschler in her book *Taking Charge of Your Fertility* has a list of 16 items to guide a woman in self-observing cervical mucus.[15] She instructs women to begin checking for mucus after menses has stopped. She advocates focusing on vaginal sensations throughout the day and checking for cervical mucus at least three times a day, including morning and night, and when going to the bathroom. She encourages women to do "Kegel" exercises on the way to the bathroom to void. Cervical mucus is checked with fingers or tissue at the vaginal lips and then the quality of the mucus is judged by how it feels and looks between the fingers. Mucus on the undergarments and the use of internal checks is also recommended.

***Observations of Pregnancies from Intercourse on a "Dry" Day***

Over the past years, one of the reasons for method related pregnancies at the Marquette University NFP center has been intercourse on a dry day in the estimated 6-day fertile window. The following are three example cases of dry day pregnancies. These examples are of interest in that they have a hormonal estimate of the 6-day fertile window through use of the Clearplan Easy Fertility Monitor. Having a hormonal estimate of the fertile window helps to give the observer and NFP teacher a more confident picture of the cycle and that it was an actual method related pregnancy.

1. The first example is from a 24 year old (Gravida 0 Para 0) married woman (husband 27 years old) who was in her 5th cycle of charting. Her previous cycles were 26-28 days in length. She was observing for cervical mucus, basal body temperature and using the Clearplan Easy Fertility Monitor. The Peak in cervical mucus, the beginning of the temperature shift and her urinary LH surge were on day 11, i.e., they all correlated. The beginning of mucus was recorded on day 10 and the first day of a "high" reading on the fertility monitor was day 10 as well. The couple had intercourse on day 9 which would be within the 6 day fertile window if the day after the LH surge (i.e., day 12) was considered

the day of ovulation. They did not have intercourse any other day in the estimated 6 day window (i.e., days 8-13). Her mucus cycle had one day of mucus before the peak and one day after.

2. The second example is from a 43 year old married woman (Gravida 6 Para 5) who has been charting with an ST system for over 4 years. She switched to a mucus only system and had been using the Clearplan Easy Fertilty monitor for 3 cycles along with cervical mucus observations. The third cycle shows the peak day of cervical mucus and the urinary LH surge on day 14. However, she only had 2 days of mucus before the peak day and only two days of high readings on the monitor before the Clearplan peak. She had intercourse on day 10, which was recorded as a dry day. The estimated fertile window for this cycle is from day 10 through 15.

3. The third example is from a 32 year old married woman with one child. She has been charting (mucus and the Clearplan monitor) for three cycles and had established a basic infertile pattern of a "moist" sensation. The third cycle showed a peak day of cervical mucus on day 12 and an LH surge on day 10. She had intercourse on day 8. The day of change from the basic infertile pattern of moist to a day of minimal mucus was day 9. The estimated fertile window for this cycle was from day 6 through day 15.

***Discussion***

Research studies that correlated self-assessed cervical mucus with hormonal markers of fertility seem to indicate that on average there are 6 days of observable cervical mucus before the estimated day of ovulation. Research also shows that there is a strong correlation between the beginning of the fertile phase by observation of cervical mucus and the beginning of the fertile phase through the estimated day of ovulation minus 5 days. However, research also shows that approximately 20-30% of cycles will have less than 5 days of observable cervical mucus before the estimated day of ovulation. In other words, cervical mucus observations will cover the 6-day fertile window in about 70-80% of cycles. The question is how fertile are dry days in the fertile window?

Besides the three example cycles illustrated above, there is some evidence in the literature of fertility on a dry day in the estimated fertile window. A recent study by Dunson, Sinai, and Columbo seemed to indicate that the fecundity of a dry day in the estimated fertile window was about half of a day with observable cervical mucus.[16] A recent European study showed that a double check method for determining the beginning of the fertile phase (i.e., the presence of cervical mucus and a calendar formula) was more effective than a single indicator of cervical mucus to determine the beginning of the fertile phase.[17] The WHO multi-center trial of the Ovulation Method gave some evidence that the probability of pregnancy from having intercourse on a sticky mucus day was about the same as a slippery day within 3 days before the PD[8] The WHO study did not provide probabilities of intercourse on dry days within the same time period. The evidence of dry day pregnancies from the literature is minimal. There needs to be further study and evidence.

Why more method related pregnancies (due to dry day intercourse in the fertile window) are not reported in the literature might be because of the limited days for intercourse in the pre-

peak phase (i.e., phase one of relative infertility). In the WHO study on the characteristics of the menstrual cycle, the number of dry days in which intercourse was available with the Ovulation Method was (on average) 3.5.[8] Following the every other day rule for dry days pre-peak and the "wait and see 1, 2, 3 rule" after intercourse you would on average only have one day (and sometimes two) for intercourse in the pre-peak phase. In the effectiveness report of the Ovulation Method by the WHO, an average of 15.4 days of abstinence was required by the rules of the method. This allowed for an average of 13 days for intercourse per cycle. On average the rule of the Ovulation Method more than doubles the actual days of fertility. There is some evidence that the Sympto-Thermal methods of NFP overestimate the fertile phase a day longer (on average) than the Ovulation Method.

Brown et al. have indicated that their research shows that that the self-observation of cervical mucus observations is as accurate as hormonal markers.(10) Moghissi on the other hand believes that the self-assessment of cervical mucus is impractical and frequently inaccurate.(18) He stated this because of the subjective nature of self-assessment of cervical mucus and because endocervicitis and cervical surgery can effect cervical mucus interpretations. He stated that more objective measures of assessing the cyclical changes in cervical mucus could be developed and that this was a promising area of further research.

***Implications***

Based on the evidence for the probability of fertility on an external self-assessed dry day in the fertile window, an implication could be that if a couple has serious reasons to not become pregnant, use of another indicator for the beginning of fertility might be appropriate. Another course of action would be to avoid intercourse until after the peak day or other marker of ovulation has indicated the beginning of the end of the fertile phase. Other markers for the beginning of the fertile phase could include a calendar formula, measurement of the rise in estradiol in the urine through the use of a fertility monitor and internal observation of the cervix.

In conclusion, cervical mucus is a fairly good indicator of the beginning of the estimated 6-day fertile window. On average it provides 6 days of warning before the actual day of ovulation and correlates well with the first day of fertility. However, in about 20-30% of cycles, cervical mucus will not provide enough of a warning of pending fertility to cover the fertile window. In addition, cervical mucus alone methods and the Sympto-Thermal methods overestimate the actual fertile phase up to 150%.

"How fertile" a dry day is in the estimated fertile window is unknown. There is some evidence that there is a degree of fertility. Those who wish to avoid pregnancy might want to consider another indicator for the beginning of fertility. The most readily available is a calendar formula. NFP teachers might want to offer couples the decision of including another marker of fertility to determine the beginning of the fertile phase.

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