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## **NATURAL FAMILY PLANNING**

### **End-expiratory CO<sub>2</sub> Pressure as a Measure for the Beginning of the Fertile Phase of the Menstrual Cycle**

There are few self-detected natural biological indicators for estimating the beginning of the fertile phase of the menstrual cycle for use in Natural Family Planning. The current measures include the first observation or sensation of cervical mucus, the self-measure of the estrogen rise in the urine with an electronic fertility monitor, and/or some type of calendar based formula. However, it has been known for many years that a woman’s respiration changes during the phases of the menstrual cycle. A research team from Austria and Germany used this knowledge to determine if a woman’s end-expiratory carbon dioxide (CO<sub>2</sub>) pressure levels could be used as a self-measure for the beginning of the fertile phase.<sup>1</sup> If the CO<sub>2</sub> end-pressure was effective in estimating the fertile phase, the researchers intended to develop a simple instrument for self-measuring end title carbon dioxide production.

The participants for this study were 160 women (18-48 years old) with a history of regular menstrual cycles between 24-32 days in length. They produced 195 menstrual cycles in which end-expiratory pressure levels were measured once daily. Serum levels of estrogen, progesterone, and luteinizing hormone (LH) were measured from day 10 of the menstrual cycle until the LH surge was observed.

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Partial pressure of CO<sub>2</sub> was measured by an infrared spectrometry device that was connected to a side stream end-expiratory air collection device (i.e., a capnometer). An ovulatory cycle for this study was defined as a rise in serum levels of estrogen followed by an LH surge or progesterone levels above 10 ng/ML. Of the 195 menstrual cycles, 150 were ovulatory.

The theory behind the carbon-dioxide levels as a measure of the beginning of the fertile phase is that the human respiratory center is sensitive to increases in estrogen or progesterone. The researchers found that there was a significant mean decrease in carbon dioxide levels (i.e., 5-9 mm Hg) about 1-5 days before the LH surge. They did not find a significant decrease in carbon dioxide pressure levels in the non-ovulatory cycles. They also discovered that administering estrogen or progesterone alone to women that had chemically suppressed ovaries also showed a decrease in carbon dioxide pressure. The authors concluded that the use of a capnometer might be used in Natural Family Planning as a means of estimating the beginning of the fertile phase along with another measure such as the urinary LH surge to estimate ovulation. They also indicated that a simple self-measure capnometer device has yet to be perfected.

### *Comments*

Obviously measures of end-expiratory carbon dioxide as a marker for the beginning of the fertile phase is exploratory at this time. However, the Austrian/German researcher team did find that there was no circadian rhythm aspects to that measure—i.e., the measure could be taken any time during the day—unlike urinary LH and basal body temperature. If a simple, accurate, and easy to use capnometer could be developed, this would be another tool to be used in NFP. The capnometer monitor—unlike measures of urinary estrogen and LH – would not require the use of expensive test strips. (RF)

1. Hadziomerovic D, Moeller K. T., Lict P., Hein A., Veitenhansel S., Kusmitsch M., Wildt L. **The biphasic pattern of end-expiratory carbon dioxide pressure: a method for identification of the fertile phase of the menstrual cycle.** *Fertility and Sterility*, 2007, (article in press).

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## **Method Discontinuation due to Dissatisfaction Found to be Low among Fertility Awareness Users Compared to Users of Hormonal Contraceptives**

**I**n the United States (US) approximately 50% of all pregnancies are unintended. Many of these pregnancies end in abortion. Most unintended pregnancies are due to discontinuation of contraceptive methods, and, in turn, discontinuation is often due to dissatisfaction with use of these methods.

Researchers from the Office of Population Research at Princeton University, therefore, sought to determine the reasons for (and percentage of) discontinuations among US women using reversible methods of contraception.<sup>1</sup>

The Princeton researchers utilized the Cycle 6 (2002) data set from the National Survey of Family Growth (NSFG). This data set involved 7,643 women participants between 15-44 years of age. The NSFG is a periodic national population-based survey of US women selected through probability statistical methods to obtain representative samples. The women are interviewed in person about their contraceptive and reproductive history with an average of 85 minutes per interview. The NSFG had an 80% response rate. Of the 7,643 women, 6,724 used a reversible method of contraception sometime during their reproductive life span. Of these women, 33% used fewer than 3 different reversible methods, and 50% used 3-4 different methods, and the remaining 17% used more than 4 methods.

The researchers found that users of the cervical cap and diaphragm had the highest (un-weighted) percentage (51.6%) of discontinuation due to dissatisfaction, with users of the sponge in second place at 47.6%. Users of the long acting contraceptives Depo-Provera and Norplant had a 42% discontinuation rate due to dissatisfaction, and users of oral contraceptives were associated with a 29% risk of discontinuation. However, users of fertility awareness methods had only a 14.6% discontinuation risk. The lowest rate of discontinuation (11%) was among users of the male condom. Among the users of the pill, Norplant, and Depo-Provera, the most frequent reasons for discontinuation were side effects, menstrual cycle disorders, and method failure.

The most frequent reasons that women provided for discontinuation of the male condom included partner dissatisfaction, decreased sexual pleasure, and aesthetics (e.g., perceived "messiness"). The authors suggested better contraceptive counseling might help improve dissatisfaction and discontinuation. However, the counseling should be based on a better understanding as to why women discontinue contraceptive methods.

### *Comments*

No matter how a contraceptive method is marketed, and no matter how women are counseled on why they should not discontinue a method if the method causes discomfort, menstrual cycle disorders, or interferes with sexual pleasure and has undesirable aesthetic effects, there will still be high rates of discontinuation. The "ever use" percentage of fertility awareness users listed in this study was 17.9%, compared with 84.5% ever users of the pill and 57.5% users of withdrawal. Fertility awareness was not defined, but probably included self devised calendar methods and the more modern cervical mucus and temperature based methods. It would be of benefit to study why users of fertility awareness methods discontinue their use. (RF)

## **Method Failure Most Frequent Reason for Discontinuing Periodic Abstinence Methods among Brazilian Women**

Researchers utilized a 1996 population-based data set of 12,612 Brazilian women between the ages of 15-49 (selected through a 2-stage random selection method) to analyze reasons for contraceptive dissatisfaction.<sup>1</sup> The data set contained variables on contraceptive use and discontinuation ascertained through retrospective survey methods. Researchers were interested in reasons for discontinuation of reversible methods of contraception and expressed a concern about the high rate of unintended pregnancy in that country. Furthermore, unintended pregnancy tended to occur during the time period of discontinuing and switching to another method of contraception. Greater than 50% of the women who use contraceptive methods in Brazil use sterilization (either female 49% or male 3%) as a method of family planning. Only 4% of Brazilian women list periodic abstinence as a method of family planning.

The researcher found that "method failure" was the most frequent reason (17%) why women discontinue periodic abstinence methods in Brazil. The most frequent reason given for abandoning use of the pill (11.8%) and injectable hormones (27.4%) was because of side effects and health. The most frequent reason for discontinuing the condom (5.1%) was method failure. The researchers calculated a 12 month cumulative failure rate for the various contraceptive methods and found a 22.7% failure rate for traditional methods (that included periodic abstinence and withdrawal), a 6.5% failure rate for the pill, and 9.1% for the condom. However, the abandonment rate for the pill was 13.4% and for injectable contraception 17%, whereas for the traditional methods only 3.7%. The highest continuation rate was found among pill users at 64%, followed by condom users at 46%, and then traditional methods at 44%. There was a greater rate of abandonment, switching, and failure rates among the less educated younger women. The researchers felt there was a need for increased access to a greater range of contraceptive methods.

### *Comments*

Since the fertility rate (2.1) among the more wealthy and educated Brazilian women is much lower than among the poor and less educated, and since the failure rates are also lower among the more educated, perhaps the Brazilian government would do better to concentrate its efforts on better education and economic opportunities for the poor. More efforts should be made

to increase access to a greater variety of choices of modern fertility awareness based methods, especially for the poor that cannot afford oral contraceptives or injectables. (RF)

1. Leite I.C., Gupta N. **Assessing regional differences in contraceptive discontinuation, failure and switching in Brazil.** *Reproductive Health*, 2007;4:6. (BioMed Central)

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## **Study Finds 7.7% Failure Rate among French Fertility Awareness Users**

**F**rench researchers recently conducted a retrospective population-based study to determine method-specific contraceptive failure rates among women participants in a French national database.<sup>1</sup> A stimulus for the study was the concern that 1 of 3 pregnancies among French women is unintended, and, of these, 65% occur while on some form of contraception. The data base was from the population-based cohort 2000 Cocon Study. This study involved a representative sample of 1,689 women aged 18-44 years who were randomly selected to answer a series of questions on their contraceptive and reproductive history, i.e., the time from first intercourse to the date of the interview. The sample was over represented by women who had had an abortion or an unintended pregnancy. Life table survival analysis (Kaplan-Meier) was used for data analysis.

The researchers discovered that the lowest first year failure rate of 1.1% was among IUD users, followed by a 2.4% failure rate among oral hormonal contraceptive pill users, then the male condom at 3.3%, 7.7% among fertility-awareness users, 10.1% among withdrawal users, and 21.7% among those using spermicides. They also found a 24 month failure rate of 4.3% among IUD users, 3.6% among pill users, 7.8% with condom users, and 18.8% among fertility awareness users. The researchers mentioned that the contraceptive failure rates among French women are in the same order of effectiveness but significantly lower than those among US women. They speculated on possible reasons for this difference, including underreporting of abortion and the fact that the US data analysis includes all pregnancies regardless of intention. Furthermore, the French data set could be limited by recall bias and lack of data on sexual activity. The researchers concluded that comparative contraceptive failure rates between French and US women suggest differences in contraceptive practices. They recommended further study of contraceptive failure rates and practices among different populations.

The “unintended” label given by the researchers to pregnancies was rather liberal since it included: a) “not being planned at all”; b) “being planned later”; and c) “did not remember if she had planned to become pregnant at that time.” The types of fertility awareness methods listed in the study included 31.6% using “periodic abstinence” and 68.4% “safe period by temperature or Ogino.” This is ambiguous in that it is not clear what they mean by “periodic abstinence” other than maybe this was a self determined guess by the woman when she was fertile or not. Furthermore, it is surprising that there was not an inclusion of more modern fertility awareness methods, such as the ovulation method and/or the Sympto-Thermal methods. I wonder whether this retrospective cohort population of women contraceptive users was representative of the entire female reproductive population, i.e., the authors did not attempt to provide evidence for representation of their sample of women. (RF)

1. Moreau C., Trussell J, Rodriquez G., Bajos N., Bouyer J.  
**Contraceptive failure in France: results from a population-based survey.** *Human Reproduction*, 2007;22:2422-2427.

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## Use of Passive Lactation Amenorrhea Method related to Low Empowerment among Egyptian Women

**E**mpowering women to make decisions about family planning and other health behaviors is important for the health of the woman and her family. An Egyptian researcher was interested in the association of the lactation amenorrhea method (LAM) and passive LAM on the empowerment of household decisions among Egyptian women with children below 6 months of age.<sup>1</sup> Passive LAM was defined as women who: a) satisfied all elements of LAM, b) did not report the use of another method of family planning, and c) did not report relying on prolonged breastfeeding as a method of family planning.

The author obtained data from the 2000 Egypt Demographic Health Survey which included 15,773 ever married women. From that data set she selected women whose last born was less than three years of age, were currently married, were not sterilized, and were currently breastfeeding their children. There were 3,447 women who met those criteria, and, of these, 1,141 had children less than six months of age.

The researcher found that nearly 58% of the sample had children under six months of age and were exclusive breastfeeders, and, of these women, 70% had amenorrhea, i.e., they met the LAM criteria of: a) full or near full breast-

feeding, b) post-partum amenorrhea, and c) an infant under 6 months of age. Most of the women (82%) who met the LAM criteria were passive LAM users. Almost 12% of the LAM users also used another method of contraception. The most frequent method among the entire sample was the IUD (33%). The researchers also found that empowerment in household decision making inversely predicted passive LAM along with increase in child age, i.e., the less empowered, the greater use of passive LAM. They concluded that women who had a low empowerment index in household decisions were more likely to use passive LAM. The passive use of LAM, however, might lead to discontinuation and unnecessary use of contraceptives. They felt that if women were provided knowledge of LAM, they would more likely continue to use LAM and progress to use modern methods of contraception.

### *Comments*

I would add that increasing the knowledge of Natural Family Planning and fertility awareness methods might empower the woman and her spouse. This type of empowerment may result in less use of hormonal or IUD methods of contraception. A recent study of LAM among 1,490 Mexican women found that the main reasons for accepting the use of LAM were "conviction following postpartum counseling" and "use of LAM initially before switching to another method of contraception."<sup>2</sup> (RF)

1. Afifi M. **Lactational amenorrhea method for family planning and women empowerment in Egypt.** *Singapore Medical Journal*, 2007;48:758-762.

2. Lopez-Martinez M.G., Romero-Gutierrez G., De Leon A.L. **Acceptance of lactational amenorrhea for family planning after postpartum counseling.** *European Journal of Contraception and Reproductive Health Care*, 2006;11:297-301.

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## **FERTILITY**

### **Consuming Multivitamins (at least three per week) associated with Reduced Risk of Ovulatory Infertility**

**I**nfertility occurs among 1 of 6 couples over a reproductive lifetime, especially among couples in developed countries that are delaying childbearing to later in life. Use of IVF for treating infertility, besides unethical, is extremely expensive and time consuming. Therefore, less expensive and less invasive methods of treatment or prevention are important. There is some evidence that the use of folate supplements aids in the ovarian response to

FSH. Harvard University researchers sought to determine the association of multivitamin supplementation on the incidence of ovulatory infertility.<sup>1</sup>

The participants for this study were a subset of The Nurses' Health Study (NHS) that began in 1989 with 116,671 female United States registered nurses between the ages of 24 to 42 years who were followed with a mailed questionnaire every 2 years. The questionnaire included information on dietary patterns, vitamin use, whether the respondents were unsuccessful in achieving pregnancy, and what caused the inability to conceive. The researchers identified 18,555 women without a history of infertility who tried to become pregnant or who became pregnant during the 8 year follow-up period of the study. In the 8 year follow-up period women who reported infertility caused by an ovulatory disorder were considered cases, and the remaining women were considered non-cases.

The researchers discovered that during the 8 year follow-up period of the NHS, there were 26,971 pregnancies and pregnancy attempts among 18,555 women. Of these pregnancy attempts, 3,430 reported infertility from any cause, and, of these, 438 reported ovulatory infertility. When adjusted for age and calendar time, multivitamin users had approximately a 1/3 lower risk of developing ovulatory infertility than nonusers ( $p < 0.001$ ). The association of multi-vitamin use was dose dependent in that there was no difference in risk of infertility with those that consumed 2 or less multivitamins per week. The researchers estimated that 20% of ovulatory infertility could be avoided if women consumed 3 or more multivitamins per week. Specifically, the intake of folic acid, iron, vitamins B<sub>1</sub>, B<sub>2</sub>, and D attenuated the inverse association between multivitamins and ovulatory infertility. Furthermore, there was a strong inverse association between folic acid intake and ovulatory infertility. There was no interaction between use of multivitamins and age or presence of long menstrual cycles. However, multivitamin users were more likely to consume less alcohol and coffee, to smoke less, and to be physically active compared with nonusers of multivitamins. The authors concluded that the consumption of multivitamins at least 3 times per week was associated with a reduced risk of ovulatory infertility and that this association appeared to be partially mediated by folic acid.

### *Comments*

NFP and FAM teachers should recommend multivitamins that contain folic acid for those women who wish to attempt a pregnancy, particularly for those women who have long and irregular cycle patterns. Folic acid supplementation is already recommended for women wishing to become pregnant to prevent tubal defects. Therefore, the added effect of decreasing ovulatory infertility is a plus. (RF)

1. Chavarro J.E., Rich-Edwards J.W., Rosner B.A., Willett W.C. **Use of multivitamins, intake of B vitamins, and risk of ovulatory infertility.** *Fertility and Sterility*, 2007, article in press.

## Supplementary Feeding related to Resumption of Menstruation and Ovulation

The time after delivery of a child and before the onset of menstrual cycles is a difficult time for women (who wish to avoid pregnancy) because of the variability of return of menstruation and ovulation. The return of menstruation does not mean the return of ovulation. Furthermore, breastfeeding and supplementary feeding patterns confound this variability. Chinese researchers studied the relationship of supplementary feeding after child birth to the return of menstruation and ovulation.<sup>1</sup>

The participants for this study were 101 primiparous lactating women from one province in China. Each participant monitored her basal body temperature (BBT) every morning along with cervical mucus observations and completed a lactation history questionnaire. The participants were also monitored by ultrasonography, beginning at 6 weeks postpartum, to determine follicular development and to document ovulation.

Of these 101 women, 53 had ovarian follicles larger than 1.8 cm in diameter at the first measurement. The Chinese researchers found that those women with larger follicles (i.e., over 1.8 cm) began supplementary feeding earlier (a mean of 4 months;  $\pm 1.1$  months). The first ovulation occurred at 110 days past delivery (mean 155;  $\pm 45$  days), and the BBT was elevated 6-13 days afterwards. Of the 53 women, 23 (43.4%) had their first ovulation before their first menses. The other 30 had their first ovulation 8-172 days after the first documented menses— 14 of which had their first ovulation after their second recorded menses and 3 after the third menses. They also found that the start of supplementary feeding positively correlated with the resumption of ovulation ( $r=0.476$ ,  $p<0.01$ ) and menstruation ( $r=0.555$ ,  $p<0.01$ ). The rate of ovulation within the first 6 months post delivery was 1-5% among total breastfeeding mothers. The authors concluded that the starting time of supplementary feeding significantly affected the resumption of menstruation and ovulation. However, many other factors affect the resumption of menstrual cycles. They recommended that women prolong breastfeeding and postpone supplementary feeding to lengthen the time of amenorrhea.

### *Comments*

I found it remarkable that the BBT shift (that confirmed ovulation) was 6-13 days after the ultrasound documented ovulation. Furthermore, ovulation occurred before the first menses in a considerable number of cases. This would negate the use of the BBT shift and menses as a viable marker for the return of ovulation and the resumption of intercourse. (RF)

1. Li W., Qiu Y. **Relation of supplementary feeding to resumption of menstruation and ovulation in lactating postpartum women.** *Chinese Medical Journal*, 2007;120:868-870.

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## **Men with Excess Body Weight are at Increased Risk for Infertility**

**R**esearchers from the National Institute of Environmental Health Sciences (NIEHS) recently investigated the influence of male obesity on infertility.<sup>1</sup> Obesity in the United States (and worldwide) is increasing and is a risk related to many health problems. There have been few population based studies to determine the influence of body mass and infertility among males, and there are no studies that examined coital frequency as a confounding factor. Therefore, NIEHS scientists conducted a study to determine the influence of being overweight, i.e., having a body mass index (BMI) of 25 or over, in association with infertility that included frequency of intercourse around the time of conception as a confounding variable.

This study was retrospective and population-based, utilizing data from the ongoing Norwegian Mother and Child Cohort Study (MoBa). The MoBa study aims to enroll 100,000 pregnant women from 52 hospitals and birthing centers throughout Norway. Available to the NIEHS researchers were 45,132 women participants, of whom 26,303 met the study criteria and included the women's report of the man's height and weight. Of these women, 12 percent (3113) were infertile. A BMI of > 25, calculated from the man's height and weight, was considered overweight, and a BMI > 30 was defined as obese.

The researchers found that infertility was significantly related to the man's BMI, with overweight men having a 19% increase in infertility (OR = 1.19: 95% CI = 1.03–1.37) and obese men having a 36% increase incidence of infertility (OR = 1.36: 95% CI = 1.12–1.62). When the Odds Ratios were adjusted for coital frequency, there was not much of a change in results with an OR of 1.20 for overweight men and an OR of 1.36 for obese men. The results did not change as well when adjusted for age and parity of the woman. The researchers speculated that the increase in infertility among obese men was due to a decrease in reproductive hormone levels and a decrease in sperm production. They also speculated that weight loss would improve their chances of conception.

Fertility awareness and NFP teachers working with couples who wish to achieve a pregnancy should assess the BMI levels of both the woman and the man. If either has a BMI over 25, weight loss might be recommended. An important question to ask is whether intercourse during peak fertility as determined by fertility monitoring methods, would obtain the same results as found in this study? (RF)

1. Nguyen R.H.N., Wilcox A.J., Skjaervben R., Baird D.D. **Men's body mass index and infertility.** *Human Reproduction*, 2007;22:2488-2493.

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## Variability in LH Surge Found Among Young Ovulatory Women

In order to better understand physiological pathology of the menstrual cycle, one must first know the physiological norms of the menstrual cycle. Monitoring the menstrual cycle for potential health concerns, such as heart disease, has been recommended by a number of authors and the American Pediatric Association. There is a need to learn more about the physiological norms of the menstrual cycle and their relationship to the health of the woman. Researchers from the New Jersey Medical School recently conducted a study to determine the patterns of the luteinizing hormone (LH) surge among normal ovulating young women as expressed in urinary outputs.<sup>1</sup>

The participants for this study were 46 volunteer women between the ages of 20-35 with menstrual cycles between 21-35 days in length. The participants collected a daily first void urine sample for one menstrual cycle (i.e., from the first day of menses through the entire menstrual cycle). The urine samples were assayed in a laboratory for LH, follicle stimulating hormone (FSH), estrone conjugate (E1C), and prenanediol-3-glucuronide (PDG). The E1C/PDG ratio was used to estimate the day of ovulation.

The results showed that of the 46 women 43 (93.5%) had an ovulatory cycle. The mean length of the menstrual cycles was 29 days (SD=4.0; Range 22-43 days), the mean follicular phase was 17.0 days (SD=3.6; Range 10-29), and the mean luteal phase length was 12.1 days (SD = 1.57; range 9-16 days). The researchers found that LH surge varied in configuration with the onset being either rapid or gradual and the configuration being spiked, biphasic, or plateau in shape. They also discovered that the presence of an LH surge does not always result in an ovulation. In addition, they found that the FSH rise or surge did not always coincide with an ovulatory event. However, when there was an E1C rise before the LH surge, there was always an ovulatory event.

The researchers concluded that the patterns of LH surges are variable and that the FSH rise is not essential for ovulation. However, they also confirmed that the E1C rise was critical for the initiation of the LH surge.

### *Comments*

It is interesting that the LH surge has many different patterns. This is not surprising, since there is a lot of variability in follicular development and resultant hormonal production. Of interest is that the LH surge or rise (as de-fined in this study) actually occurred on average over 7.6 days, (i.e., from the first rise from baseline readings until the LH surge returned to baseline). Furthermore, not all LH surges resulted in ovulation. As the author stated, this has clinical implications for women who use LH ovulation detection kits to time intercourse for achieving a pregnancy. Based on this information, those women who use a hormonal monitor to detect the rise of estrogen before the LH surge would have a better chance at achieving pregnancy by using menstrual cycles that indicate both the estrogen rise and LH surge. I also wonder if some of the LH test kits miss the LH surge in the biphasic LH cycles, where the LH peak is only around 28 mIU/mg.

1. Park S.J., Goldsmith L.T., Skurnick J.H., Wojtczuk A., Weiss G.  
**Characteristics of the urinary luteinizing hormone surge in young ovulatory women.** *Fertility and Sterility*, 2007;88: 684-690.

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## **Sialidase Activity of Female Cervical Mucus Highest in Ovulatory Phase**

**I**t is well known by Natural Family Planning and fertility awareness teachers that the rheological properties of cervical mucus change during the menstrual cycle in response to estrogen and progesterone. Human cervical mucus is primarily composed of mucins and glycosylated proteins secreted by the epithelial cells in the endocervical canal and vaginal mucosa. However, it has been speculated that the changing rheological properties of cervical mucus are not due to the protein structures of the mucins but, rather, to their carbohydrate components and, in particular, the oligosaccharide moieties of mucins, i.e., sialic acid (a nine carbon sugar). It is also thought that sialic acid-modifying enzymes, such as sialidases, are important for proper development of physiological functions of sperm, e.g., sperm capacitation and sperm progression in the female genital tract. Most studies on the presence of sialic acid and sialidase activity do not take into account the timing of the women's menstrual cycle. Researchers from the University of Siena, Italy, conducted a study to describe the endogenous sialidase activity in cervical mucus during the phases of the menstrual cycle and during pregnancy.<sup>1</sup>

The researchers obtained 158 women volunteers between the ages of 17 and 45 and collected cervical mucus samples (with sterile cotton swabs) during a gynecological exam. The samples were classified as to when during the menstrual cycle the samples were collected, i.e., days 5-11 were considered the pre-ovulatory phase, days 12–16 the ovulatory phase, and days 17–29 the post-ovulatory phase. They also collected samples from 150 women during weeks 27–39 of pregnancy. The cervical mucus samples were assayed for sialidase activity, centrifuged, and observed under an electron microscope.

The researchers found that sialidase activity reached a maximum during the ovulatory phase of the menstrual cycle. They also found significant sialidase activity in the cervical mucus of pregnant women. When the sialidase was observed under electron microscope, they saw membrane vesicle structures that they speculated might facilitate intercellular communication before and after fertilization. The researchers concluded that female cervical mucus contains endogenous sialidase that increases during the fertile phase of the menstrual cycle—which helps to change the rheological properties of cervical mucus which serves to facilitate sperm progression.

### *Comments*

This study provided some good basic biological science of the nature and function of cervical mucus during the menstrual cycle. I would like to see a more precise indication for the timing of the samples during the menstrual cycle either through LH testing or other natural biological indicators of ovulation like BBT and/or self-observed peak in cervical mucus. (RF)

1. Flori F., Secciani F., Capone A., Paccagnini E., Caruso S., Ricci M.G., Focarelli R. **Menstrual cycle-related sialidase activity of the female cervical mucus is associated with exosome-like vesicles.** *Fertility and Sterility*, 2007, (e-edition).

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## **Two New Antimicrobial Factors found in Human Cervical Mucus**

**I**nfections in the female genital track are known to be deleterious for fertility, for the fetus, and for maintaining a pregnancy. The vagina is a microb-rich environment, but the uterine environment is sterile. Cervical mucus serves as a filtering and anti-microbial host defense system between the vagina and uterus. Although the anti-microbial activity of cervical mucus has been established, few anti-microbial factors have been identified and purified. Chinese scientists sought to identify new anti-bacterial molecules in human cervical mucus.<sup>1</sup>

The participants for this study were 8 healthy volunteer women between the ages of 24-35 (mean age 26) with a parity of 1 and at least one year after the delivery of their child. A specimen of cervical mucus was obtained by a 1 ml syringe from the cervix of each volunteer 3-4 days after menstruation. The samples were chemically analyzed for anti-microbial proteins.

The researchers found that the cervical mucus was a viscous hydrogel weighing between 0.15 and 0.30 g, with a median pH of 7.2, range 6.4-8.0. The researchers were able to discover two anti-microbial effectors (i.e., antibacterial peptides): 1) a high-mobility group nucleosomal binding domain (HMG N2) and 2) a secretory leukocyte peptidase inhibitor (SLPI). They concluded that these two anti-microbials serve as and constitute part of the cervix immune surveillance and defense system against pathogens in the human reproductive system.

### *Comments*

NFP and FA teachers need to be aware of and understand the female reproductive system, especially those components that involve biological markers of fertility such as cervical mucus. It would be good to have further studies to examine the makeup of anti-microbials in cervical mucus during the different states of the menstrual cycle and, in particular, during the fertile phase. (RF)

1. Ming L., Xiaoling P., Yan L., Wang L., Qi W., Xiyong Y., Boyao W., Ning H. **Purification of antimicrobial factors from human cervical mucus.** *Human Reproduction*, 2007;22(7):1810-1815.

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## **Women Unaware of Risks and Complications in Delaying Childbearing**

**W**omen in Western developed countries are increasingly delaying childbearing to a later age due to career development. Many of these women may be unaware of the potential maternal and fetal complications among older women. Researchers from Aberdeen University sought to determine women's awareness related to issues (social and medical) to delayed childbearing.<sup>1</sup> The researchers were also interested in whether there was awareness of the limitations of artificial reproductive therapies among two groups of women: 1) women who were unsuccessful in achieving a pregnancy and were currently seeking infertility treatments, and 2) women who were currently pregnant.

The participants for the study were 772 women who were approached at the Aberdeen University Maternity Hospital, 8 of which refused to participate. There were 382 in each group, i.e., the infertility and the pregnant group of women. They were all administered a 32 item questionnaire that ascertained their awareness of the limitations of infertility treatments, age limits for access to fertility treatment, and tests for the prediction of fertility.

The researchers found a higher portion of women in the sub-fertile group who sought pregnancy after the age 30 compared to the pregnant group. There was a higher portion of women in the sub-fertile group that used contraception in the past compared to the pregnant group. Most of the women in both the sub-fertile group (85%) and the pregnant group (77%) thought that IVF treatments could overcome the effects of age even though they knew that fertility decreased with age. Most women in both groups (86% and 85%) were aware that delaying childbearing increased the risk for a child with trisomy 21. The authors concluded that most women they surveyed were aware of the risks of delaying childbirth to a later age, but were misinformed erroneously that IVF would reverse the effects of age.

### *Comments*

Of interest, among the sub-fertile women in this study, over 80% felt that fertility decreases considerably among women between the ages of 30-39; however, about 40% felt that IVF would be able to reverse the effects of aging. Most of the women in both groups (>75%) felt that first-time motherhood after the age of 55 was unacceptable. One of the implications that this study has for NFP/FA teachers is that they probably will be seeing more older women seeking pregnancy for the first time. The NFP teachers need to be honest about the chances for achieving a pregnancy with normal intercourse. (RF)

1. Maheshwari, A., Porter M., Shetty A., Bhattacharya, S. **Women's awareness and perceptions of delay in childbearing.** *Fertility and Sterility*, 2007, (article in press).

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## **CONTRACEPTION**

### **Flip Chart Contraceptive Counseling Fails to Decrease Contraceptive Discontinuation**

**C**ontraceptive discontinuation is considered a major reproductive problem since there is a relatively high rate of unintended pregnancies during this period. Furthermore, there is a very high rate (> 50%) of discontinuation of hormonal contraception within the first year of use. Studies have recommended decreasing contraceptive discontinuation with improved contraceptive counseling that includes help in contraceptive decision making and honesty in regards to side effects—and how to manage the side effects. In order to standardize a mechanism for better contraceptive counseling, a contraceptive counseling tool (flip chart) was developed through Johns Hopkins University. The flipchart counseling tool has simplified information about contraceptive methods, contraceptive decision-making, contraceptive side effects, and contraceptive benefits and risks. Researchers recently tested the effects of using the contraceptive flipchart on

contraceptive continuation among clients that seek contraception through Nicaraguan health department clinics.<sup>1</sup>

The researchers used a quasi-experimental design in which they determined prospectively which Nicaraguan clinics would provide the flip chart counseling intervention and which clinics would be considered control clinics. In the 41 experimental clinics the contraceptive flip chart counseling system was used by all trained counselors on first time family planning clients for 3-5 months. The first-time family planning clients in the 24 control clinics received standard care. There were a total of 1,633 users at the clinical sites.

After 3-5 months of intervention, the researchers found that there was no difference in contraceptive use rate, with the experimental group at 80% and the control group 86%. In fact the control group had a higher injectable contraceptive use rate than the experimental group. However, those exposed to the flip chart expressed that they had a better counseling experience. The authors concluded that there is sufficient evidence that contraceptive counseling (with or without flip charts) does not increase contraceptive use rates. They felt that newer strategies need to be developed.

### *Comments*

The authors admitted that, although they had control clinics, there might have been some crossover in use of the charts system and/or that there was some good contraceptive counseling in the control clinics. Furthermore, the flip chart was not always used in the experimental clinics. The researchers speculated that there are other factors that influence discontinuation of contraceptive methods, including side effects and lack of support from the husband. I would point out that no matter how much counseling there is, if women experience negative side effects, like unusual bleeding, they are not going to continue—nor should the health professional expect them to. A similar flip chart counseling system could be developed and tested on NFP methods to help with NFP decision making. (RF)

1. Chin-Quee D.S., Janowitz B., Otterness C. **Counseling tools alone do not improve method continuation: further evidence from the decision-making tool for family planning clients and providers in Nicaragua.** *Contraception*, 2007, (article in press).

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## Post-fertilization Effects Influence Women's Choice of Family Planning Methods

Providing information about the mechanisms of action of family planning methods by health providers is important for the decision-making process of potential users. One of the concerns is whether family planning methods act post-fertilization and cause early embryo loss. Spanish researchers recently surveyed 755 potentially fertile women in order to determine their attitudes towards post-fertilization effects of family planning methods.<sup>1</sup>

The 775 female participants were between the ages of 18-49 and were approached by health providers at 10 primary health centers in Pamplona, Spain. They were asked to complete a 30 item questionnaire about family planning methods, mechanisms of action, and medical and surgical abortion. Of the 755, the researchers were able to obtain 581 (80%) usable questionnaires.

The researchers found that almost half of the respondents (46.3%) believed that life begins at fertilization, and most (58.7%) felt it was important to distinguish between natural embryo loss and those caused by family planning methods. A majority of respondents (57%) would not use a family planning method that sometimes works after implantation of the embryo, and a large minority (39.4%) would not use a family planning method that sometimes works after fertilization but before implantation. The researchers realized that the respondents (who were mostly well educated Catholic women) did not represent the entire population of Spanish women and recommended further studies with other populations. The authors concluded that the results emphasize that full information about the mechanisms of action for family planning methods is important for many women.

### *Comments*

Since some bioethicists claim that NFP methods are a cause of early embryo loss due to aging gametes, I wonder if those Spanish women would consider NFP a natural cause. The researchers also asked an open-ended question as to what are the most important characteristics in choosing a method of family planning? The three highest rated responses were: 1) efficacy (76%), 2) convenience and ease of use (53.4%), and 3) absence of side effects (28.6%). Although most of the respondents listed their religion as Catholic, there was a low level of religiosity among the participants based on church attendance and self-reported importance of religion. (RF)

1. De Irala J., Lopez del Burgo C., Lopez de Fez C., Arredondo J., Mikolajczyk R.T., Stanford J. **Women's attitudes towards mechanisms of action of family planning methods: survey in primary health centres in Pamplona, Spain.** *BMC Women's Health*, 2007;7:1-10.

## Oral Hormonal Contraceptive use Increases Estrogen Receptors in Vulvar Vestibular Mucosa

Swedish researchers sought to determine the effects of combined oral contraceptive (COC) use on the sex steroidal receptors in vulvar vestibular mucosa in healthy women.<sup>1</sup> The background reason for conducting this study was that this area of research has few studies, and these same researchers recently found morphological changes in vulvar vestibular mucosa during COC use. Furthermore, the Swedish researchers believe that there is some connection between COC use and vestibular pain during intercourse.

The researchers recruited 45 healthy sexually active subjects of which 20 (mean age 23.7) were on COCs for a minimum of one year (actual use ranged from 2-15 years) and 25 control women (mean age 25.6 years) who used non-hormonal means of contraception. A vestibular punch biopsy was obtained on the 7-11th day after the beginning of the menstrual cycle in all subjects. Serum samples for estradiol and progesterone levels were drawn to determine the phases of the menstrual cycle. Tissue from the punch biopsies were subjected to immunohistochemistry analysis for sex steroid receptors. Five of the control women were determined not to have ovulated during the test cycle and were not included in the analysis.

The researchers found that there were significantly more beta type estrogen receptors in the vulvar vestibular tissue of the COC users compared to the controls ( $p < 0.024$ ). They also found a greater abundance of progesterone receptors in the vulvar tissue during the follicular phase than in the luteal phase ( $p < 0.01$ ) among the non-COC users. They did not find any significant differences in the abundance of progesterone, androgen, or glucocorticoid receptors between the two groups. However, the researchers did point out a limitation in the small number of participants in each group. They concluded that the results indicated a hormonal influence on the steroid receptor expression by ethinyl estradiol as well as by progestins. They believed that the hormones in the COCs not only effect the expression of the estrogen receptors but the morphology of the vestibular mucosa as well.

### *Comments*

The Swedish researchers indicated that the clinical implication for the findings was unknown. However, they have proposed that COCs make the vestibular tissue more sensitive and that this is a possible reason why COC users report more sexual pain compared to non-users. I wonder if the increase in estrogen receptors also occurs in the cervical endometrial tissue

and is one reason why there is an increase of cervical mucus found in post COC users who switch to a mucus based method of fertility awareness? (RF)

1. Johannesson U., Sahlin L., Masironi B., Rylander E., Bohm-Starke N. **Steroid receptor expression in the vulvar vestibular mucosa – effects of oral contraceptives and menstrual cycle.** *Contraception*, 2007, (article in press).

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## Return of Menses Occurs Rapidly after Use of Continuous Oral Contraception

**T**raditional oral hormonal contraception produces an artificial menses every 28 days due to the withdrawal of exogenous hormones with the use of hormone free placebo pills or by a pill free interval. Recently, continuous oral hormonal contraception has been introduced that reduces the frequency of artificially induced menses. There is some concern that use of continuous hormonal contraception might delay the return of menses and ovulation. Therefore, researchers conducted a study to determine the effect that prolonged use of continuous hormonal contraception has on the return to fertility—with spontaneous menses as the marker of fertility return.<sup>1</sup>

The participants for this study were 198 women who were a subset of the 2,134 subjects (with regular menstrual cycles of 21-35 days) who participated in a phase 3 efficacy and safety trial of daily continuous oral levonogestrel (LNG) 90 µg/ethinyl E<sub>2</sub> (EE) 20 µg (trade name Lybrel) and who completed at least 6 months of use. Most (81.8%) of the 198 subjects had completed 12 months of Lybrel with a mean duration before enrollment of 349 days. Of the 198 participants, 187 completed the study. Of these, 185 (98.9%) returned to spontaneous menses or became pregnant within 90 days of stopping LNG/EE. Of the two subjects that did not experience a return of menses within 90 days, one did so at 124 days and the other approximately 2 months after the completion of the study. The median time to return of menses was 32 days. Furthermore, the researchers found that the length of amenorrhea (i.e., length of use of LNG/EE) was unrelated to the time to return of menses. The authors concluded that the inhibition of menses with continuous use of LNG/EE was readily and quickly reversible.

### *Comments*

NFP teachers who have women coming off of continuous LNG/EE (Lybrel) to achieve a pregnancy or to use natural methods for avoiding pregnancy can assure them that menses (and presumably ovulation) will most likely return within 1-3 months. However, these results apply only to those women who previously had regular length menstrual cycles. (RF)

1. Davis R., Kroll R., Soltes B., Zhang N., Grubb G.S., Constantine G.D. **Occurrence of menses or pregnancy after cessation of a continuous oral contraceptive.** *Fertility and Sterility*, 2007, (article in press).

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## MENSTRUAL CYCLE

### **Slow Follicular Growth Rate Contributes to Longer Follicular Phases in Adolescents**

**A**lthough it is accepted knowledge that irregular menstrual cycle lengths are commonly experienced by adolescent females, little is known about the mechanisms that cause the irregularities. Of particular interest is the rate of follicular growth, follicular dynamics, and the length of the follicular phase in this population. Researchers from the Federal University of Mato Grosso, Brazil, recently conducted a study to verify the prevalence of long follicular phases among healthy adolescents and to correlate the phase lengths with endocrine patterns and follicular growth rates.<sup>1</sup>

The participants for this study were 55 healthy and sexually active female adolescents between the ages of 14 and 19 (mean age 16.9) who attended an Adolescent Clinic for the purpose of obtaining birth control. The participants re-ceived daily ovarian ultrasound measurements (of follicular growth) from day 2 to 5 of their menstrual cycle until ovulation was confirmed through visual col-lapse of the dominant follicle. In addition, blood was drawn from days 2 to 5 of the menstrual cycle to determine FSH, LH, and estradiol (E2) levels.

The researchers found that the menstrual cycle ranged from 25 to 35 days (with a mean of 29.5 days, SD = 1.6). The follicular phase length was a mean of 16 days, SD = 0.5 days. Twenty-five of the participants had follicular phase lengths greater than 16 days. There was a mild inverse correlation ( $r = -0.464$ ) between FSH levels and follicular phase length, but there was no significant correlation between follicular phase length and LH and basal E2 levels. The researchers did find a faster speed of follicular growth among the adolescents with follicular phases 16 days or less compared to those with follicular phases greater than 16 days, i.e., 1.33 mm/day vs. 0.88 mm/day. The researchers concluded that long follicular phase lengths were common among adolescents and are probably a result of slow follicular growth.

#### *Comments*

NFP teachers involved in adolescent chastity education can expect menstrual cycle length variability among their students. According to this study

the variability is most likely a result of the variation in rate of follicular growth. I would point out, however, that this was a rather small study with only 55 participants. A recent study by this author also found a mean of 16 days for follicular length among 141 healthy women with a mean age of 29.<sup>2</sup> This small cohort of adolescents did not display variability much different than a larger population of healthy women. (RF)

1. Cabral Z.A.F., de Medeiros S.F. **Follicular growth pattern in normal-cycling Brazilian adolescents.** *Fertility and Sterility*, 2007, (e-journal).

2. Fehring R, Schneider M, Raviele K. **Variability in the phases of the menstrual cycle.** *JOGNN*, 2006;35:376384.

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## Time to Pregnancy Shortened by Focused Intercourse (Theoretically)

Couples in the United States and other Western nations are delaying marriage and postponing starting a family (i.e., having children) for the purpose of developing careers and stabilizing relationships. Delaying childbirth to an older age brings with it the risk of a diminished fertility and the expense of infertility diagnosis and treatment. There is some evidence that focused intercourse during the six day fertile phase of the menstrual cycle will aid in a quicker time to pregnancy and avoidance of infertility care. However, what is not known are the optimal patterns of frequency and timing of intercourse to achieve pregnancy. Research statisticians from Italy and the United States sought to determine—based on an existing data set of menstrual cycles and utilizing Bayesian analysis—the optimal timing and frequency of intercourse to achieve a pregnancy.<sup>1</sup>

The data set included information from 193 women who were taught a mucus only (Billings) method of NFP. These women produced 2,755 menstrual cycles of data and 177 pregnancies. However, of these 193 women, 191 produced 2,536 complete data cycles, and, of these 191 women, 132 of them achieved 161 clinical pregnancies. The median length of the cycles in the data set was 28 days with a range of 18 to 76 days. The menstrual cycle data included acts of intercourse and cervical mucus secretions descriptions. The investigators rated the cervical mucus descriptions on a scale from 1 to 4, with 1 = no mucus, dry sensation to 4 = slippery, wet, stretchy, clear mucus. The mean age of the 2,536 women participants was 29.95 years and their male partners 32.64. Each woman produced a mean of 13.28 cycles of data.

The researchers developed multiple scenarios of intercourse patterns with or without mucus during the middle most fertile days of the menstrual cycle (i.e.,

days 6–25) and during the estimated highest probability of fertility (i.e., days 13-17). They discovered that when intercourse is focused only on those days and not outside of days 6-25, the highest probability of pregnancy was with intercourse on each day from days 6–25 (i.e., 20 acts of intercourse). This pattern of daily intercourse yielded a cycle probability of conception = 0.687. This pattern also resulted in only 3 cycles of trying to achieve a 90% pregnancy rate. For couples who focused intercourse on the high rated fertile mucus (i.e., a number 4 rating) days (13–17) of the menstrual cycle, the cycle probability of conception decreases to 0.347, with a mean intercourse rate of 2.42 days. With this scenario, the number of cycles to achieve a 90% pregnancy rate would take an average of 15 cycles.

Interestingly, if the couples have intercourse (on average) every other day (regardless of the mucus rating) and focus on days 10-18 of the menstrual cycle, the cycle probability of conception drops only slightly to 0.647 and increases one additional cycle to pregnancy (i.e., 4 cycles) to achieve a 90% pregnancy rate.

The researchers also analyzed intercourse scenarios not only with intercourse during the middle of the cycle (i.e., days 6–25) but also with 1/7<sup>th</sup> of the acts of intercourse outside of that range. According to the data set, this increases the probability of pregnancy. For example, if the couples have intercourse every other day (i.e., a mean of 9 days of intercourse between days 10-18), and have 1/7<sup>th</sup> of the acts of intercourse outside of that range, the cycle probability of pregnancy is 0.654 and a 90% pregnancy rate within 3 cycles of trying.

The authors concluded that focusing intercourse on days of high fertile mucus (i.e., 4-rated mucus) would be useful for couples to shorten their time to pregnancy and not require a high frequency of intercourse. They also admitted that just using a calendar method and having intercourse on average every other day (during the estimated fertile window) and occasionally outside of the fertile window are sufficient. With this scenario, mucus identification does not add to the efficiency of achieving pregnancy.

### *Comments*

The intercourse scenarios presented in this study are theoretical and need to be tested in actual life and, in particular, with randomized control trials—for example comparing calendar based intercourse patterns versus high fertile mucus focused intercourse patterns. It seems, based on this theoretical data, that intercourse every other day during the estimated fertile phase of the cycle has very high probability of efficiently achieving a pregnancy. This article was very similar to a recent article by the same authors that focused on the statistical models used for this study.<sup>2</sup>

I wonder if an externally observed mucus data base is the best to determine efficient intercourse patterns to achieve pregnancy. One of the reasons for my skepticism of this type of data set is that cervical mucus is not very efficient or accurate in estimating the fertile window. Based on the data presented in this article, the mean number of days of 2-4 rated mucus was 18.92 days for women between the ages of 20–26 and ranged from 15–19 days for all women in the data set. Since the mean length of the cycles was 28 days, this means that on average more than half the days had mucus rated days, and, on average, cervical mucus overestimates the fertile window by a factor of 3.

1. Scarpa B., Dunson D.B., Giacchi E. **Baysian selection of optimal rules for timing intercourse to conceive by using calendar and mucus.** *Fertility and Sterility*, 2007, (e-edition).

2. Scarpa B., Dunson D.B. **Baysian methods for searching for optimal rules for timing intercourse to achieve pregnancy.** *Statistics In Medicine*, 2007;26:1920-1936.

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## Anti-Mullerian Hormone found to be best Predictor of Menopausal Transition

The years leading up to menopause can be a difficult time for women using natural methods of family planning due to the variability of the menstrual cycles, increased anovulatory cycles, and increased menopausal symptoms. Also difficult at this time, are the decisions to be made with regard to use of supplementary hormones. In 2001, experts on the physiological changes of the menstrual cycle developed what is called the “Stages of Reproductive Aging Workshop” and the STRAW model of menopausal transition. The STRAW has 5 stages leading up to the final menstrual period, i.e., phases -5 to -3 are the early, peak, and late reproductive phases, and stages -2 to -1 are the early and late menopausal transition phases. These stages are primarily based on the increased variability in the menstrual cycles and increased levels of FSH. Researchers from the University of Sidney, Australia, were interested in determining and clarifying the endocrine changes during the stages of menopause transition as identified by the STRAW model.

To do so, the researchers measured key hormones during the menstrual cycle of 77 women recruited through community advertisement. The women volunteers included 21 between the ages of 21 to 35 and 56 between the ages of 45 to 55. The older cohort of women were categorized based on the last 3 stages of the STRAW Model, i.e., stage -3, the late reproductive age but regular menstrual cycle lengths (LRA); stage -2, early menopausal transition with variability in menstrual cycle lengths greater than 7 days (EMT); and stage -1, the

late menopause transition with at least one menstrual cycle interval lasting 60 days or more (LMT). The women collected menstrual cycle diaries that included first morning basal body temperatures for 3-6 months. Researchers collected blood samples three times a week through the first 7 days of the next menstrual cycle. The blood samples were analyzed for FSH, LH, estradiol (E<sup>2</sup>), progesterone (P), inhibin A (INHS), inhibin B (INHB), and anti-Mullerian Hormone (AMH).

Of the 93 subjects, 77 women contributed data for the study, and 21 were classified as mid-reproductive age (MRA), 16 in the LRA stage, 17 in EMT, and 23 in LMT. They found that ovulatory cycle lengths were shorter in the LRA group compared to the MRA and EMT group, but luteal phases were similar in all four groups. They discovered that FSH, LH, and E<sub>2</sub> levels increased with the progression of the STRAW stages, and mean P levels decreased. Inhibin levels also decreased steadily across the STRAW stages but were undetectable in the anovulatory and long ovulatory cycles. The AMH decreased steadily and markedly across the stages of menopause transition. The researchers felt that the marked changes in AMH might be a good marker of indicating and predicting menstrual cycle stage changes. However, they indicated that large cohorts of women would be needed to verify these findings.

### *Comments*

From a natural methods perspective, researchers should have to provide evidence that the changes in AMH are more precise in predicting menopause transitions than normal menstrual cycle variability and natural biological markers of fertility. For example, are the AMH changes better predictors than the criterion of having menstrual cycle length variability greater than 7 days and having menstrual cycle lengths greater than or equal to 60 days? These changes could be found among women who use natural methods of fertility regulation or those women who just monitor the lengths of their menstrual cycles. Natural methods of fertility monitoring would be a less expensive means of monitoring menopausal transitions compared to undergoing blood tests to measure AMH levels.

1. Hale G.E., Zhao X., Hughes C.L., Burger H.G., Robertson D.M., Fraser I.S. **Endocrine features of menstrual cycles in middle and late reproductive age and the menopausal transition classified according to the Staging of Reproductive Aging Workshop (STRAW) staging system.** *Journal of Clinical Endocrine Metabolism*, 2007, (e-edition).

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## UNDER THE MICROSCOPE

### **Stress and Menstrual Cycle Variability**

Stress is a common experience in modern Western cultures. For women using fertility awareness based (FAB) methods of family planning, the effect of stress on the menstrual cycle is of concern. In particular the concern is whether stress causes menstrual cycle variability, suppression or delay in ovulation, and disruption in the biological signs of fertility. When women are under stress, the impression is that FAB methods are more difficult to use because of menstrual cycle variability and confusing biological indicators of fertility.

Stress can be defined as the response of the organism to demands placed upon it.<sup>1-3</sup> These demands can be thought of as stressors. Stressors can be physical, mental, or spiritual and can be of a chronic or acute nature. Extreme acute stressors elicit physically what is known as the "flight or fight" response within the individual or, as defined by Selye, the "adaptation response."<sup>2</sup> This response involves increased levels of adrenaline that elicit increased heart rates, increased blood pressure, quicker clotting time, and more blood to the major muscles during the immediate phase response. This immediate stress response is a good adaptive response if the person truly needs either to fight or flee a dangerous situation. The problem is that this response can also be elicited in situations of everyday modern life that do not necessitate flight or fight and will be maladaptive in the long run. This response when of a chronic nature causes damage to organs and individuals. Normal individuals when placed under stress will soon recover to a pre-stress physiological level. However, some individuals have physiological systems that do not recover as well from stressors, e.g., heart rate and elevated blood pressure do not come down to normal levels as readily as non-blood pressure responders. These individuals have systems that are susceptible to stress related disease processes. A women's reproductive system, as well, could be susceptible to chronic life stressors.

Social and medical scientists have accumulated many studies to show that as stress events accumulate during a calendar year (or longer), the more likely the person will experience a stress related illness.<sup>2</sup> Researchers have developed a list of events from death of a spouse at the top to a minor parking ticket at the bottom, while marriage is ranked as the number two stressor just below death of a spouse. The more life changes and the higher on the list are those life changes that an individual experiences, the more likely she will experience stress related health problems. Anecdotally, NFP teachers often comment that the menstrual cycle during the week of the marriage event is extremely variable as a result of the stress of the marriage and marriage preparations.

Stress is thought to be a common cause of amenorrhea. Physiologically, stress affects the hypothalamic-pituitary-ovarian-adrenal (HPOA) axis.<sup>1</sup> With stress there is an increased release of corticotrophin releasing hormone and vasopressin which are two flight or fight hormones. These hormones work centrally and peripherally. The central action affects the gonadotropin releasing hormones (GnRH) and, thus, follicular growth and the ovulation process. Peripherally, there is an increase in gonadotropin secretions. A related peripheral effect is the secretion of peak type mucus not related to ovulation. Recent evidence has conceptualized the effects of stress on the menstrual cycle and the HPOA axis as an energy deficit mechanism.<sup>3</sup> Stress (such as extreme exercise) will cause an energy deficit for the individual, and the ovulatory process will be affected, since it requires energy for ovulation, and the energy supplied during stress will go to more vital organs that modulate stress and prepare the individual for stressful life events. If the stressed woman can ameliorate the effects of stress by increasing the energy supply through nutrition and rest, there will be less of an effect on the menstrual cycle and the ovulatory processes.

The research evidence on the effects of stress on the menstrual cycle is mixed.<sup>4-9</sup> A study conducted with women from India showed that women who worked in physical type jobs, such as farm or craft work, had significantly longer cycles than women who worked in sedentary jobs, such as clerical work.<sup>4</sup> This would coincide with the energy depletion theory of the effect of stress on the menstrual cycle. Another study among US and Italian nurses found that there was a significant relationship between the perceived stress of their jobs and longer and monophasic cycles.<sup>5</sup> However, the Italian nurses that worked with rotating shifts compared to fixed shifts had significantly shorter menstrual cycles and shorter luteal phases determined by the basal body shift as the proxy indicator for ovulation.

Two recent studies indicated that the experience of stress was related to shorter menstrual cycles.<sup>6,7</sup> One study was conducted with 276 healthy premenstrual US women.<sup>6</sup> The researchers found that those women in "stressful jobs" had more than twice the risk of having shorter menstrual cycles than those women in non-stressful jobs. However, there was no relationship between the participants' perceived stress and menstrual cycle variability. Another study showed that there was no relationship between menstrual cycle length and accumulation of stressful life events over a calendar year among 206 healthy US women.<sup>7</sup> However, women with increased stress levels over a 2 year period had significantly shorter menstrual cycles compared to women with less stress.

Two other studies found no relationship between measures of stress and variability of the parameters of the menstrual cycle.<sup>8,9</sup> One study measured urin-

ary stress hormones (adrenaline, noradrenaline, and cortisol levels) and a psychological measure of mood states among 34 healthy menstruating women.<sup>8</sup> Neither the psychological measure of stress nor the urinary stress hormones did not correlate with menstrual cycle variability. Of interest was that the psychological measure of stress through perceived mood states did not correlate with the urinary measures of the stress hormones. Finally, a recent two-part study measured both ovarian hormones and stress hormones daily among 95 women and found no relationship between the levels of stress and cortisol stress hormones.<sup>9</sup> The researchers also found no differences in stress hormone levels or ovarian hormonal levels between 95 female students taking the medical school entrance exam (the stressor) and 27 female controls. The researchers also found no differences in pre- and post- entrance exam test stress hormone levels within the medical school entrance exam group.

Therefore, the evidence of stress on the menstrual cycle is not conclusive. Part of the reason for the mixed results is the mixed means of measuring stress (mentally and physically) and measuring menstrual cycle changes. Furthermore, there is no consistent meaning of "stress" whether the stress is chronic or acute, and how much stress is being experienced—and whether the stress was physical or psychological. In order to have a better idea of how stress affects the menstrual cycle, there needs to be a more standardized means of measuring stress and menstrual cycle parameters.

Researchers at Marquette University recently analyzed the effects of stress on the menstrual cycle by analyzing the effect marriage has on the menstrual cycle. As mentioned previously, marriage is considered a very high level life experience stressor. They measured the length of the menstrual cycle and the length of the luteal and follicular phases among 13 women during the pre-wedding menstrual cycle, the wedding menstrual cycle, and the next two post-menstrual cycles. The 13 women were between the ages of 20 and 37 (mean age 26.5, SD=5.28), and all 13 had regular cycle lengths. Repeated measure analysis indicated that there was a significant change in the length of the menstrual cycle from the pre- to the two menstrual cycles post the wedding cycle. Post hoc statistical testing indicated that the pre-wedding menstrual cycle length and the last menstrual cycle length (from the wedding cycle) were significantly shorter than the menstrual cycle experienced during the wedding month (*see Table One below*).

Table One: Menstrual cycle parameters pre and post wedding day (N=13)

Parameter	Pre-Wedding	Wedding Cycle	Post-Wedding	Last Cycle
Length	30.1 (SD=4.2)	27.8 (SD=3.6)	28.5 (SD=3.3)	30.0 (SD=4.4)
Follicular	16.7 (SD=3.7)	15.1 (SD=3.4)	16.1 (SD=3.3)	17.2 (SD=4.5)
Luteal	13.4 (SD=2.4)	12.8 (SD=1.9)	12.4 (SD=3.4)	12.7 (SD=1.8)

Although there was no significant change in the length of the follicular phase (as indicated by the day of the peak day of cervical mucus) and the length of the luteal phase, Table One results show that the peak day was almost (on average) two days earlier during the wedding cycle than the pre- and last cycle. The power to detect changes was low since there were only 13 participants in this analysis. Therefore, the data suggest that stress has the effect of shortening the menstrual cycle mostly due to a short follicular phase. This would indicate that rather than suppressing ovulation, stress actually stimulates ovulation to occur earlier. The stress hormones might be stimulating the reproductive hormones. These results coincide with the two studies mentioned above that provided evidence that stress shortens the menstrual cycle.

Fertility awareness methods and NFP method textbooks generally report that stress will lengthen the menstrual cycle and/or delay or suppress ovulation.<sup>10-14</sup> According to Weschler, stress will lengthen the menstrual cycle and either delay or suppress ovulation.<sup>10</sup> Weschler and others also indicated that the cervical mucus sign will be diminished or that there will be a build up, tapering off, and then another build up of cervical mucus during a stress cycle.<sup>12,13</sup> Some methods call this a double peak.<sup>12</sup> The double peak in the mucus build up supposedly indicates a suppression and delay in ovulation. Clubb and Knight also wrote that if stress is severe enough, ovulation will be completely suppressed.<sup>13</sup> Several of the texts mentioned that, besides the double peak phenomenon the basal body temperature shift will be delayed for up to one week.<sup>10,11,14</sup> Several of the texts provided example charts with delayed ovulation, double build up of mucus, and longer menstrual cycle lengths. One even mentioned the wedding cycle and provided an example of the menstrual cycle recorded during the wedding month.<sup>14</sup> None of the textbooks provided evidence of the effects of stress other than anecdotal cases.

A number of reproductive physiological texts concur with the NFP and fertility awareness textbooks that stress will cause a hypothalamic response possibly leading to anovulation and amenorrhea.<sup>15-17</sup> This happens with high intensity runners or women who participate in a high intensity type sport activity. However, the amenorrhea (and anovulation) is usually not due to the running or

high intensity of the sport but to having insufficient nutritional energy to make up for the deficit.<sup>15</sup> Authors also indicate that stress and the stress released hormones interfere with gonadotropic releasing hormone, the GnRH pulsatile mechanism, the LH surge, and, thus, ovulation. However, this is usually related to severe stress and starvation level dieting.

In summary, the effects of chronic and acute stress on the menstrual cycle are mixed. Generally, they will include a decrease in the length of the cycle and the follicular phase. However, if the stress is acute enough, ovulation will be suppressed. One of the big indicators of how the menstrual cycle will react is the energy factor—does the body have enough energy to sustain ovulation? Most women's bodies do, especially if they maintain an adequate diet, moderate exercise, and appropriate amounts of sleep and rest. If however, a young woman who is an avid runner or who is dieting severely in order to fit into a size smaller wedding dress, ovulation might be delayed and even suppressed. As always, a balanced life style of moderate exercise, appropriate diet that meets the energy requirements of the body, rest and sleep, and good mental outlook will help to moderate stress and the effects it will have on the menstrual cycle. Monitoring the normal parameters of the menstrual cycle through NFP can also be a way of monitoring a healthy lifestyle.

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