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# **Natural Family Planning**

## **Efficacy of Electronic Hormonal Monitoring plus Cervical Mucus Monitoring as a Method to Avoid Pregnancy**

**R**esearchers and clinicians at Marquette University developed a method of Natural Family Planning (NFP) that utilizes self-monitoring of cervical mucus along with an electronic hormonal fertility monitor (EHFM) as a double check for the beginning and end of the fertile phase of the menstrual cycle. The EHFM is a hand held device that reads a threshold level of urinary metabolites of estrogen (estrone 3 glucuronide) and luteinizing hormone (LH; on test strips) and provides the user with a low, high, and peak reading of fertility. The monitor is sold in the United States as a method to help couples achieve pregnancy but can be used as an aid to track fertility.

A prospective efficacy study of this method was reported in an earlier issue of *CMR* and in the *Journal of Obstetrics, Gynecological, and Neonatal Nursing.*<sup>1</sup> Since then two new efficacy studies of this method has been published, one study was a retrospective analysis of the method developed at Marquette<sup>2</sup>, and the second was a retrospective cohort comparison of the Marquette method with a cervical mucus only method of NFP.<sup>3</sup>

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The retrospective study involved 204 couples (i.e., women with a mean age of 28.6 and their male partners, with a mean age of 30.3) who were taught NFP (by health professionals, physicians and nurses) at four sites in the United States (Saint Augustine, Florida, Atlanta, Saint Louis, and Milwaukee). Health professionals helped the couples decide which combination of fertility indicators, i.e., basal body temp (BBT), cervical mucus monitoring (CVM), or EHFM fit best with their lifestyle and reproductive needs. There were a total of twelve unintended pregnancies, only one with correct use. The twelve month correct use pregnancy rate was 0.6 (i.e., 99.4% survival) and the typical use (total pregnancy rate) was 10.6 (i.e., 89.4% survival) per 100 users. (See Table One for a breakdown of the combination of fertility indicators utilized in the study.) The researchers concluded that, when used correctly, the MM system of NFP is a very effective means of avoiding pregnancy.

Biological Marker*	Number	Number of pregnancies	<u>Rate</u>
BBT + CVM	76	5	12.9
EHFM + CVM	69	4	7.8
CVM only	29	1	NS**
BBT+EHFM+CVM	25	2	NS
EHFM only	5	0	NS
Total	204	12	10.4

Table 1. Twelve month total unintended pregnancy rate by combination of biological markers of fertility used for natural family planning.

\* BBT = basal body temperature; CVM = cervical mucus monitoring; EHFM = electronic hormonal fertility monitoring.

\*\* NS = not significant.

The second study was as retrospective cohort comparison of couples who were taught the Marquette method of NFP (but only those who used the EHFM along with CVM) in comparison to a CVM only method.<sup>3</sup> The participants for this study came from the same four clinic sites as the previous study and involved 313 couples who were taught how to avoid pregnancy with the EHFM plus CVM and another 315 who used CVM only. Both methods involved standardized group teaching and individual follow-up. All unintended pregnancies were reviewed by health professionals, pregnancy rates (over 12 months of use) were determined by survival analysis, and comparisons of unintended pregnancy rates were made by use of the Fisher exact test. The researchers found a total of 28 unintended pregnancies with the EFHM plus CVM group and 41 with the CVM only group. The 12 month correct use pregnancy rate of the EHFM group was 2.0%, and the total pregnancy rate was 12.0%, in comparison with a 3.0% correct use and 23.0%, total pregnancy rate with the CVM only group. There

was a significant difference in the total pregnancies between the two groups applying the Fisher Exact test (p < 0.05). The researchers concluded that the EHFM aided CVM method was more effective than the CVM only method.

## Comments

Although both studies involved retrospective chart audits of the NFP methods utilized, all of the couples were taught the methods prospectively with standardized formats and follow-up sessions. Even so, both studies have limitations in that they were not randomized clinical trials. The differences in results of the EHFM plus CVM with CVM could only be due to factors other than use of the methods to avoid pregnancy – including investigator bias. However, the results do confirm earlier studies that compared CVM only with CVM plus BBT, and with later highly effective cohort studies of CVM plus BBT and calendar formulas as double checks for the beginning and end of the fertile phase of the menstrual cycle.<sup>4-6</sup> (RJF)

1. R. Fehring, M. Schneider, and K. Raviele, K. "Efficacy of hormonal fertility monitoring as a method of natural family planning," *Journal of Obstetric, Gynecologic, & Neonatal Nursing* 36 (2007):152-160.

2. R. J. Fehring, M. Schneider M, and M.L. Barron. "Efficacy of the Marquette method of natural family planning," *MCN, American Journal of Maternal Child Nursing* 33 (2008):348-54.

3. R. Fehring, M. Schneider, M.L. Barron, and K. Raviele. "Cohort comparison of two fertility awareness methods of family planning," *Journal of Reproductive Medicine*.

4. J. E. Medina, A. Cifuentes J.R. Abernathy J.M. Spieler, and M.E. Wade. "Comparative evaluation of two methods of natural family planning in Columbia," *American Journal of Obstetrics and Gynecology* 138 (1980):1142-1147.

5. M. E. Wade, P. McCarthy, and J. R. Abernathy, et al. "Randomized prospective study of the use-effectiveness of two methods of natural family planning: an interim report," *American Journal of Obstetrics and Gynecology* 134 (1979):628-31.

6. P. Frank-Herrmann, J. Heil, and C. Gnoth, et al. "The effectiveness of a fertility awareness based method to avoid pregnancy in relation to a couple's sexual behavior during the fertile time: a prospective longitudinal study," *Human Reproduction* 22 (2007):1310-1319.

# Natural Family Planning Content Included in 62% of U.S. and Canadian Medical Schools

In 1993 a group called Medical Students for Choice (MSFC) was formed due to the perceived lack of training content on contraception and abortion in medical schools throughout the United States and Canada.<sup>1</sup> MSFC has over 10,000 members and 134 chapters in medical schools in the US and Canada. Two members of MSFC (medical school faculty sympathetic to the group) and a member of a reproductive health advocacy group recently conducted a survey of medical students to determine the inclusion of contraception and elective abortion content in US and Canadian medical schools. A secondary purpose was to collect data to help reform medical school curricula in regards to reproductive health issues (i.e., abortion, contraception, homosexual health care).

A survey was developed that included questions about many aspects of reproductive health, including pregnancy, infertility, contraceptive techniques, abortion techniques, reproductive ethics, and other women's health topics (e.g., sexual violence and homosexual safe-sex issues) – topics that followed Association of Professors of Gynecology and Obstetrics guidelines. The question-naires were sent to 122 MSFC coordinators of which 77 were returned (a 63% return rate) and included 68 U.S. schools and 9 Canadian. This return represented 68 of the 149 U.S. schools (46%) and 9 of the 17 Canadian schools (53%).

Most schools (97-100%) reported content in pregnancy physiology and sexual transmitted diseases. Seventy-three schools (95%) reported content on hormonal contraception (mostly in pharmacology classes), and 61% had content on medical abortion. Surgical first trimester abortion and late term abortion techniques were covered in 43% and 28% of the medical schools respectively. Of interest is that 62% of medical schools had content on "rhythm/natural family planning." However, fewer schools in the South (20%) listed content in this area. The authors pointed out that the content on abortion and contraception varied widely among the medical schools contacted. They advocated that medical schools need to integrate content on comprehensive family planning into their standard curricula.

## Comments

The results of this study had many limitations, e.g., there was no control on how content was determined by the MSFC coordinators. The content on rhythm and Natural Family Planning was probably very limited. It is also scandalous that three of the five Catholic sponsored medical schools have MSFC chapters - that advocate for abortion, contraception, and assisted suicide. It is clear that NFP promoters need to find entry into the curriculum of health care professionals to ensure that NFP content is strong. Finally, it is important to consider how to help create strategies to combat groups like MSFC on Catholic campuses. (RJF)

1. J. Steinauer , F. La Rochelle, M. Rowh, L. Backus, Y. Sandahl, and A. Foster. "First impressions: What are pre-clinical medical students in the US and Canada learning about sexual and reproductive health?" *Contraception* 2009, E-published (In Press).

# Fertility/Infertility

## **Retrospective Cohort Efficacy Study of Natural Procreative Interventions to Treat Infertility**

In the recent papal document, *Dignitatis personae*, Pope Benedict XVI called on Catholic physicians and scientists to develop ethical treatments for infertility that do not violate human dignity, the sanctity of life, and the marital bond. Thomas Hilgers, M.D., (an obstetrician gynecologist) has developed, through many years of practice and study, what he calls natural procreative technology or NaProTech. NaProTech is a system of medical and surgical interventions that cooperates with the women's natural menstrual cycle to treat infertility and other women's health problems.<sup>1</sup>

A base practice of NaProTech is the reliance on menstrual cycle monitoring (through the use of the Creighton Model *FertilityCare* System) as a means for assessment, treatment, and evaluation of outcomes. Hilgers also offers an intensive educational program for physicians. This program trains physicians in the use of natural procreative technologies and the interpretation of the Creighton Model (CrM) system. Several primary care family medicine physicians recently reported on the efficacy of NaproTech methods in the treatment of infertility.<sup>2</sup> One of the reasons for this article was to demonstrate that NaProTech methods could be used effectively and safely in a primary care practice and to demonstrate that it is not necessary to refer women immediately to high-tech and expensive infertility specialist that often utilize unethical means to obtain good outcomes.

This retrospective cohort study involved 1,234 infertility patients from one family medical practice in Ireland during the years 1999-2006. Treatment involved having the woman patient track her fertility with the CrM system (which focuses primarily on the estrogenic changes in cervical mucus), assessing the

timing of intercourse, evaluating the quality of cervical mucus production, measuring luteal phase lengths, and determining levels of progesterone and estrogen on certain days of the menstrual cycle. When menstrual cycle deficits were detected, treatment included the use of clomiphene (to stimulate ovulation), medications to stimulate cervical mucus production, and progesterone supplementation. The study involved the analysis of live births as an outcome over 24 months of care.

The mean age of the couples in the study was 35.6 years, and the mean number of years of trying to conceive was 5.6. The gross live birth rate at twelve months of treatment was 27.6% and at twenty-four months 33.9%. When the couples who withdrew prematurely were taken out of the analysis, the rates were 45% at twelve months and 56% at twenty-four months of treatment. The authors made comparisons with published IVF pregnancy rates and concluded that the results compare well with IVF treatments even though this study included a relatively older population of women. The authors emphasized that the comparison is very tentative due to the limitations of a non-comparison retrospective design.

### Comments

The development and implementation of NaProTechnology, an ethical system of treating infertility, is commendable. So too, is the desire to gather evidence for its efficacy as presented in this article. Although this study provides some evidence for its efficacy, the level of evidence is somewhat low. The authors point this out clearly in the article and advocate the use of prospective cohort studies. However, a stronger study would be a comparison of the use of natural procreative technologies with other ethical treatments, such as expectant waiting, life style changes, or focused intercourse during the fertile phase.

A medical critique could include the question as to whether the use of clomephene, progesterone supplementation, mucus enhancers, the integration of menstrual cycle charting, and focused intercourse is new. Furthermore, there is the question of why other standard medical treatments were not mentioned, such as the use of metformin for polycystic ovaries, and medications for treating endometriosis. Over 25% of the participants had these medical problems. (RJF)

1. T. Hilgers, The Medical and Surgical Practice of NaProTECHNOLOGY. Omaha, Nebraska: Pope Paul VI Institute, 2004.

2. J. B. Stanford, T. A. Parnell, and P. C. Boyle, "Outcomes from treatment of infertility with natural procreative technology in an Irish general practice," *Journal of the American Board of Family Medicine* 2008;21:375-384.

## **Clomifene Citrate and Intrauterine Insemination Found** to be no More Effective than Expectant Waiting

Approximately one quarter of all infertile couples have unexplained infertility. These couples are good candidates for low cost methods of treatment, including the use of clomifene citrate, intrauterine insemination (Catholic Church teaching has "neither approved nor disapproved" this procedure when the semen is licitly obtained—after normal intercourse— but technologically prepared washed, etc. Catholic theologians are split on the morality of this procedure), and expectant waiting. Although single cohort studies have shown improvement with these methods, few studies have compared the relative efficacy of these methods in helping couples to achieve pregnancy. Furthermore, many of these studies have few participants, are not adequately designed, or do not have enough statistical power to show differences. Therefore, British scientists designed a study to compare the effectiveness of clomifene citrate and intrauterine insemination with expectant waiting.

The scientists used what they called a pragmatic randomized control trial design, in which they randomized 580 couples (who had at least two years of unexplained infertility and who exhibited bilateral tubal patency) from three hospitals in Scotland into one of three treatment arms, i.e., the administration of an oral dose of 50 mg of clomifene citrate (plus recommended intercourse on days 12–18 of the menstrual cycle), intrauterine insemination within thirty hours of a self identified luteinizing hormone surge, and expectant waiting. The couples were followed for six months to determine and confirm clinical pregnancies through ultrasound. The primary outcome was live birth rates. Secondary outcomes were clinical pregnancy rates, multiple birth pregnancy rate, adverse events, and anxiety and depression.

The scientists found that the live birth rates for the clomefine group (N=194) was 26/192 (14%), for the intrauterine insemination group (N=193) it was 43/191 (23%), and for the expectant management group (N=93) 32/193 (17%). There were no statistical differences among the three pregnancy rates of these three treatment groups. Furthermore, there were no differences in anxiety levels, depression levels, rate of multiple pregnancies, clinical pregnancy rates, and ectopic and miscarriage rates. However, the women in the active treatment group found the treatments to be more satisfying than expectant waiting. The authors concluded that the use of clomefine citrate or intrauterine insemination were unlikely to offer superior live birth rates compared to expectant management among couples with unexplained infertility.

## Comments

Although the women in the clomefine group experienced more abdominal pain, bloating, hot flushes, and headaches compared to women in the other treatment groups, they still felt that this treatment was more acceptable than the expectant waiting group. Obviously women in these groups had high hopes that some type of intervention would be a help and that doing nothing might be a waste of time. It would be interesting to conduct a double blind study in which the investigators and the participants did not know whether they were in a clomiphene treatment group or a placebo pill group. Another study might have the expectant waiting group learn Natural Family Planning, engage in focused intercourse during the fertile phase, and adopt lifestyle changes. These would allow this group to feel they were active in some type of treatment. The fact that the clomefine group had intercourse during days 12-18 might have enhanced their chances of pregnancy. (RJF)

1. S. Bhattacharya, K harrild, J Mollison, et al., "Clomifene citrate or unstimulated intrauterine insemination compared with expectant management for unexplained infertility: pragmatic randomized controlled trial," *British Medical Journal* 2008;337:a716.

## **Timed Intercourse Considered Possible Deleterious Intervention for Sub-fertile Couples Attempting Pregnancy**

**H**.K. Snick a physician scientist from the Netherlands has contended in past articles that there is no good evidence that purposeful timing of intercourse (even with the use of self-observed fertility indicators) helps to increase the time to pregnancy.<sup>1</sup> He now maintains that timed intercourse might even impair fertility. In a recent study, he and other scientists sought to determine if timed intercourse (TI) was more effective than expectant management when TI was used as a control group in intrauterine insemination (IUI) efficacy studies.

The researchers were able to identify eleven studies from an extensive review of the existing literature that represented thirteen trials of IUI in comparison to either TI or expectant management. This review provided a comparison of IUI with TI among 1,329 sub-fertile couples. They found the differences in pregnancy rates with IUI in comparison with TI was 6.1% and with expectant management 3.9%. The adjusted difference in pregnancy rates be-

tween TI and expectant management was 2.8%. This difference in rates was not statistically significant. Even so, the researchers concluded that the use of TI as a control when comparing IUI was not significantly different than expectant management, and they felt there was sufficient evidence to consider the possibility that pregnancy was less likely with TI.

### Comments

The authors of this article speculated as to why TI might be detrimental to fertility. First of all, they suggested that couples who follow their natural sexual instincts will most likely have intercourse during the most fertile days of the menstrual cycle. Secondly, they felt that by timing intercourse, especially by use of urinary LH markers, they might miss the most fertile days of the menstrual cycle (which are the two days before ovulation), and the cervical mucus (that nourishes the sperm) might be diminished. A third reason is that the couples might be stressed with having to have intercourse on a schedule that follows fertility markers. The evidence for TI impairing rather than aiding fertility is rather thin. Randomized comparison studies of TI with expectant management would help to further understanding of the mechanisms of intercourse patterns and fertility. (RJF)

1. H. K. A. Snick, "Should spontaneous or timed intercourse guide couples trying to conceive?" *Human Reproduction* 20 (2005):2976-2969.

2. H. K. Snick, J. A. Collins, and J. L. H. Evers, "What is the most valid comparison treatment in trials of intrauterine insemination, timed or uninfluenced intercourse? A systematic review and meta-analysis of indirect evidence," *Human Reproduction* 23 (2008):239-2245.

## Microscopic Structure of Cervical Mucus Appears to be Different in Women with Polycystic Ovarian Syndrome

Polycystic ovarian syndrome is one of the most common endocrinemetabolic disorders for women of reproductive age, with an incidence of approximately 5-10%.<sup>1</sup> Cervical mucus is reflective of the endocrine hormonal patterns of the menstrual cycle and is an essential component of fertility for couples wishing to achieve pregnancy through normal intercourse. P. Vigil listed a number of important functions of "healthy" cervical mucus including: 1) allowing for sperm transport, 2) filtering out abnormal sperm, 3) preventing a premature acrosome reaction, 4) protecting the female genital track, and 5) acting as an antimicrobrial barrier.<sup>2</sup> The classification of the microscopic structures of cervical mucus has been described and developed principally by Odeblad and others, and includes the classic ferning structure of estrogenic type mucus and the dense structure of progestogenic mucus. Vigil and others carried out a descriptive comparative study to determine if there are microscopic structural differences in cervical mucus among women with normal menstrual cycles in comparison with women who have irregular cycle patterns due to polycystic ovarian syndrome (PCOS).

Ten women were recruited as participants from a fertility clinic, of which four were controls with normal ovulatory menstrual cycles, four were women with PCOS and anovulatory menstrual cycles, and two women with PCOS who demonstrated normal ovulatory menstrual cycles. Cervical mucus secretions were obtained from the women by aspiration from the cervical canal with a cannula. Urinary assays of metabolites of estrogen and progesterone were obtained on the day of the mucus aspiration and every five days until the end of the menstrual cycle. Cervical mucus was observed both with the use of a scanning electron microscope and, at low power, with a light microscope. The researchers found that the cervical mucus structure and hormonal levels of the regularly ovulating control were similar. However, the cervical mucus structure of the PCOS non-ovulating women did not show the characteristic ferning patterns that one would expect with ovulatory estrogenic type mucus. Furthermore, the mucus had dense looking mesh structures that appeared impenetrable, and the urinary estrogen hormone levels were lower than those found with the ovulating women. The author suggested further studies to compare the difference in the glycoprotein structure of the cervical mucus from normal cycling women and from women who have PCOS.

### Comments

Limitations of this study included the low number of participants and the sporadic nature of cervical mucus and hormonal obtainment—especially having only two anovulatory women with PCOS. Women with PCOS often have multiple LH surges and multiple peaks (i.e., fertile type mucus patterns) throughout the menstrual cycle due to the multiple follicles at various levels of maturation. (RJF)

1. P. Vigil, P. Contreres, J.L. Alvarado, A. Godoy, A. Salgado, and M.E. Cortez. "Evidence of subpopulations with different levels of insulin resistance in women with polycystic ovary syndrome," *Human Reproduction*, Advance Access published September 25, 2007.

2. P. Vigil, M.E. Cortes, A. Zuniga, J. Riquelme, and F. Ceric. "Scanning electron and light microscopy study of the cervical mucus in women with polycystic ovary syndrome," *Journal of Electron Microscopy* 58 (2009):21-27.

# **Contraception**

## Early Ovulation Considered Cause of Unintended Pregnancy among Women using Hormonal Contraception and Rhythm

Researchers hypothesized that there is a subset of women who ovulate early and for whom the usual pattern of hormonal contraception and the Calendar Rhythm method may not work as well, i.e., they will experience a high unintended preg-nancy rate.<sup>1</sup> The researchers speculated that women who use the 21 day on and 7 days off type of hormonal contraception might be more susceptible for an unintended pregnancy. They were able to test this hypothesis because some abortion clinics (including at the site of one of the researchers) routinely conduct endovaginal ultrasound prior to an abortion in order to estimate the day of conception. The objective of this study was to determine the menstrual cycle day of conception by using the history of the last menstrual period and endovaginal ultrasound dating of the pregnancy.

This was a retrospective chart audit study, in which all of the patients who obtained an abortion at two clinics between January and May of 2007 were included in the study. Data were taken from 913 charts, and the date of conception was estimated as the date of the ultrasound minus the estimated gestational age determined by ultrasound. The cycle day of conception was the estimated day of conception minus the woman's reported date of the last bleeding episode.

Results showed that there were 99 women who were on hormonal contraception and had an unintended pregnancy, and, of these 26 (26.3%) conceived between cycle day 1-9, and 73 (73.7%) conceived between cycle day 10-40. This was in comparison to a total of 679 women who were using other forms of contraception, of which 100 (14.7%) conceived between cycle days 1-9, and 579 (83.3%) conceived between cycle days 10-40. These results were considered statistically different by Firsher's exact test (p < 0.005). The researchers concluded that the data suggest that there is a sizable subset of women who ovulate earlier after onset of withdrawal bleeding when using the 21/7 hormonal contraceptives.

### Comments

Of interest is that women who had the most unintended pregnancies were those who used the condom (306 = 33.5%) followed by "other including none" (244 = 31.3%), oral hormonal contraception (90 = 9.9%), withdrawal (71 = 7.8%), and then rhythm (53 = 5.8%). The women who listed "rhythm" most likely used a self-devised method, i.e., counting from the day of menses to when they thought the fertile time started (these women would be susceptible to an unintended pregnancy due to an early ovulation). However, these women most likely were not using a modern method of NFP nor were taught a true method of Calendar Rhythm. (RJF)

1. E. R. Wiebe, and J. Trussell. "Contraceptive failure related to estimated cycle day of conception related to the start of the last bleeding episode," *Contraception* 79 (2009):178-181.

## **Evidence Shows Hormonal Oral Contraception Continues to be Risk for Inflammatory Bowel Disease**

Environmental factors such as smoking and hormonal contraception have been implicated as risk factors for developing inflammatory bowel disease, i.e., Crohn's Disease (CD) and ulcerative colitis (UC). The theory is that hormonal contraception contributes to multifocal small vascular infarctions in the bowel system. However, this association was originally established when the formulations of the early hormonal contraceptives had higher levels of estrogen and progestins. It is known that the risk for stroke has decreased due to lower levels of these dual hormones (in particular estrogen). What is not well known is the effect of lower hormonal dosages with the current formulations of oral hormonal contraceptives on the association with the development of inflammatory bowel disease (IBD).

Researchers from England conducted a meta-analysis of case controlled studies that investigated the risk of CD and UC with exposure to hormonal contraception controlling for smoking.<sup>1</sup> They utilized only studies that had a high quality scientific rating and were published since 1980. They were able to obtain 14 high quality studies that represented 36,797 women who were exposed to hormonal contraception and 39,018 who were not exposed to oral contraceptives. They found a 51% increase in relative risk for CD and a 46% increased risk when adjusted for smoking. The relative risk for UC for women taking oral contraceptives was 53% and 28% when adjusted for smoking. They also found an increased risk with length of use of oral contraceptives, i.e., a relative risk of 41% at 6 months of use, 83% at 12 months, and 248% at 3 years. The authors of the study concluded that the reduction of estrogen and progesterone content in the newer formulation of oral hormonal contraception has not reduced the relative risk of developing IBD. However, they did caution that the studies with negative results tend not to get published.

## Comments

Although the authors played down the risk for IBD and stated that overall oral contraceptives are safe and healthy, it would be prudent to advise women with a family history of IBD and taking oral contraceptives to be advised of the risk. (RJF)

1. J. A. Cornish, E. Tan, C. Simillis, S. K. Clark, J. Teare, and P. P. Tekkis. "The risk of oral contraceptives in the etiology of inflammatory bowel disease: a meta-analysis," *American Journal of Gastroenterology* 103 (2008):2394-2400.

# **Under the Microscope**

## **Optimizing Natural Fertility: Frequency of Intercourse, Focused Intercourse, and Lifestyle Factors**

Couples in the United States and other Western nations are delaying marriage and postponing children for the purpose of developing careers and stabilizing relationships.<sup>1-2</sup> Delaying childbirth to an older age involves risks. Among the risks are diminished fertility and the potential expense of infertility diagnosis and treatment.<sup>3-4</sup> Demographic studies have shown that there is a consistent decline in female fecundity with advancing age after 30-35 years.<sup>5</sup> Studies based on the Natural Survey of Family Growth have shown that the prevalence of infertility after 12 months of attempting to achieve a pregnancy is only 6.7% among those 20-24 years of age, but increases to 16.1% among women 30-34 years and 22.9% among women 35-39 years.<sup>6</sup>

In the reproductive literature women are considered "older" at 30 years and beyond. There is evidence that male fertility also declines (although much slower than women) after the age of 40. Recent studies have suggested that older women (i.e., 35 years or older), especially with an older spouse, should be referred for infertility workup after only 6 months of trying.<sup>7-8</sup> However, before engaging in expensive diagnosis and treatment for infertility, these couples should be encouraged to try the less expensive self-directed methods that have been shown to increase fertility.<sup>7,9</sup> Furthermore, couples with sub-fertility, with unknown reasons for infertility, or with mild male factor might benefit from these methods as well.<sup>9</sup>

The following report reviews some of the recent literature on self-help measures to optimize fertility and aid in the time to pregnancy (TTP) as found in past issues of *CMR*. These measures include the timing and frequency of intercourse, tracking natural fertility indicators to determine the best time for intercourse, and lifestyle modification. This report is based on a recent opinion piece by the Practice Committee of the American Society for Reproductive Medicine (ASRM).<sup>9</sup> This report contains suggestions for optimizing the chances for achieving pregnancy for couples who have no evidence of infertility.

### Theoretical Reason for Focused Intercourse during the Six Day Fertile Window

A man and woman together are fertile for approximately six days during the menstrual cycle. These six days are known as the fertile window. This fertile time frame was confirmed by Wilcox and others in a classic study reported in a 1995 article in *The New England Journal of Medicine*.<sup>10</sup> The six days are based on the physiological knowledge that a human female egg is viable and capable of being fertilized only 12-24 hours after ovulation and that sperm will survive 3-5 days in a cervical mucus-enriched environment.

The probabilities of achieving a pregnancy with an act of intercourse during those six days also have been determined to be approximately 10%, 15%, 20%, 39%, 40%, respectively on the five days before ovulation with the day of ovulation dropping off to 12%. The two most fertile days of the menstrual cycle are the two days before ovulation. Therefore, one would expect that having intercourse on the two days before ovulation, i.e., the high probability days, would increase the chances for pregnancy.<sup>11</sup> Researchers also have determined that the fertile window is often shorter than six days and that the average is only three days in length.<sup>12-13</sup>

Besides knowledge of the probability of pregnancy during the fertile window, there is knowledge of the probability of pregnancy on each day of the menstrual cycle based on population studies. Studies on women with fairly regular menstrual cycles, i.e., between 21-35 days in length, have shown that the highest probability of pregnancy is from days 8 (9.4%) to a peak around day 14 but drops to only 2% by day 21. <sup>14</sup> Based on these probabilities, the Practice Committee of the ASRM recommended that the likelihood of conception will increase by having frequent intercourse beginning soon after the cessation of menses.<sup>9</sup> To assure having intercourse during the six day fertile window, couples should have intercourse frequently during days 8-19 of the menstrual cycle. However, other factors come into play, such as frequency of intercourse, presence of cervical mucus, and the accuracy of methods to estimate the fertile phase.

## Frequency of Intercourse

Recommendations for frequency of intercourse for couples with infertility problems are often a topic of discussion and a source of disagreement. Of particular concern is the decrease in sperm and semen quality with frequent intercourse patterns. However, the thinking now is that prolonged abstinence is deleterious to fertility (i.e., in particular semen quality) and that frequent intercourse is preferred. Researchers from Israel conducted a retrospective study with 9,489 semen analysis samples to evaluate the relationship between sexual abstinence and characteristics of semen. They found the peak in sperm motility to be after only one day of abstinence, while other semen values peaked from 0-2 days of abstinence.<sup>15</sup> The researchers recommended that the best semen samples come after one day of abstinence. In fact waiting longer, especially over 10 days, results in semen parameters with a decrease in quality.<sup>16</sup>

A team of research statisticians from Italy and the United States have also investigated optimal intercourse patterns for the best chance of achieving pregnancy. They developed a statistical approach (based on Baysian modeling) to determine optimal rules for intercourse and found that the maximum probability of conception was 0.687 with intercourse everyday between days 6 and 25 of the menstrual cycle (i.e., 20 acts of intercourse).<sup>17</sup> However, having intercourse that often can be stressful for some couples. They also determined that the probability was still at 0.615 with 7 acts of intercourse during the same time period. It seems that the best timing of intercourse (so as not to be exhausting for couples) is to have intercourse every 2-3 days. The Practice Committee of the American Society of Reproductive Medicine recommended frequent intercourse (i.e., every 1-2 days), but that the optimal frequency should be left up to the couple to decide.<sup>9</sup>

### Focused Intercourse with Cervical Mucus

There have been a number of studies that have shown the importance of the presence and quality of cervical mucus as a factor in optimal fertility. An existing data set was used by a multi-national group of researchers to determine the influence of cervical mucus observations on day specific probabilities of pregnancy within the 6-day fertile window.<sup>18</sup> The data set was obtained from the 1992-1997 European Study of Daily Fecundability in which 782 women between the ages of 18-40 recorded their daily observations of cervical mucus and basal body temperature (BBT). The researchers were able to use 1,473 cycles of data with 353 pregnancies and determined that there was clear evidence for an increase in the probability of pregnancy with an increase in the mucus rating within the 6-day fertile window. Furthermore, there was a steady increase in pregnancy probability with each increase of the mucus rating. The researchers concluded that (within the fertile window) the type of mucus observed on the day of intercourse was more predictive of conception than the timing of intercourse. In addition, the highest rated mucus occurred most often on the 2 days before the estimated day of ovulation. They also observed that self-monitoring of cervical mucus provides additional information about fertility that is not provided by other methods or indicators of fertility, such as ultrasound and urinary LH testing. The application of these findings for women trying to achieve pregnancy using cervical mucus observations need to be confirmed in actual prospective studies.

As men age their reproductive capacity decreases. However, scientists were able to use the dame data set described in the above report to determine day specific probabilities of pregnancy in relation to cervical mucus quality on the suspected day of intercourse that resulted in a pregnancy with male reproductive age.<sup>19</sup> Controlling for the female partners age, researchers found that as the quality of cervical mucus increased, the effect of male age on fertility decreased. Specifically, among men in their late 30s and early 40s, when no mucus was observed, there was a 50% less likelihood of pregnancy from an act of intercourse; on days when a damp sensation was recorded, the less likelihood of a pregnancy decreased to 21%; on days of thick mucus, the less likelihood decreased to 11%; and on days with the most fertile-type mucus, the less likelihood decreased to only 4%. The researchers concluded that the age related decline in male fertility can be offset with intercourse on optimal mucus (i.e., clear, stretchy, and slippery type mucus) days of the menstrual cycle.

Italian researchers used the same data set of menstrual cycles and applied a statistical fecundity model to the data to determine day specific probabilities of intercourse based on the mucus ratings as graded by NFP teachers.<sup>20</sup> The results showed there was a range of probability of pregnancy from an act of intercourse with the lowest (0.003) on days with no noticeable cervical mucus secretions to (0.290) on days with high rated cervical mucus. However, the probability of a pregnancy from high rated mucus was less than 20% outside of days 10-17 to a peak of 59% on day 13 of the menstrual cycle. The researchers concluded that, regardless of the timing of intercourse during the menstrual cycle, the probability of pregnancy with an act of intercourse on days with no cervical secretion is near 0. They also stated that the probability increased dramatically to near 30% with the most fertile mucus. They concluded that cervical mucus secretions accurately predict both the timing of the fertile phase of the menstrual cycle and the day specific probabilities of conception.

Italian researchers also utilized a new data set of 2,755 menstrual cycles produced by 193 women users of the Billings Ovulation Method (BOM).<sup>21</sup> The purpose was to determine characteristics of the menstrual cycle, mucus cycle

patterns, intercourse patterns, and day specific probabilities of fecundity. The 193 women users were taught the BOM at 4 Natural Family Planning (NFP) centers in Italy. The peak day of cervical mucus was set as day 0 and was used as the estimate of the day of ovulation. There were 142 conception cycles produced from this data set. Day specific probabilities of pregnancy were based on a 12 day period, from 8 days before day 0 to 3 days after, and determined by the Schwartz Statistical Model. They found that there was some probability of pregnancy from an act of intercourse during 11 days of the 12 day study period, with the lowest probability (0.012) 7 days before day 0 and the highest (0.429) on day 0. The highest level of probability was from 4 days before day 0 until one day after, i.e., a 5-6 day period.

Utilizing the same data set as described above, (i.e., data produced by 193 women who were taught a mucus only—Billings—method of Natural Family Planning) 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).<sup>22</sup> 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 during 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 authors concluded that focusing intercourse on days of high fertile 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 to shorten the time to pregnancy (TTP). With this scenario, mucus identification does not add to the efficiency of achieving pregnancy.

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.

Members of the practice committee of the ASRM do not provide much of a recommendation about cervical mucus and fecundity other than to say the 6 day fertile window correlates well with the volume and quality of cervical mucus.<sup>9</sup> Part of the reason for not recommending cervical mucus monitoring and having intercourse on the high rated fertile mucus might be due to the time that it might take to teach and learn mucus patterns during the menstrual cycle.

#### Monitoring Ovulation to Achieve Pregnancy with Focused Intercourse

Stanford and Dunson recently published a paper illustrating models of the relationship between the frequency and timing of intercourse and the TTP.<sup>23</sup> They point out that merely including frequency of intercourse is not adequate because of the variability of the day specific probabilities of pregnancy within the six day fertile window. For example, if a couple has intercourse outside of this window of fertility (no matter how frequently), there will be a very small probability of pregnancy. They also point out that there might be intercourse patterns found in different cultures and that intercourse could be stimulated by libido patterns that peak during the fertile window.

The authors recommend that prospective TTP studies include the frequency and timing of intercourse relative to the six day fertile window, and to do this by having the participants chart their daily intercourse patterns. They recommended that the fertile window could be estimated by use of basal body temperature, home urinary hormonal tests, or the observations of cervicalvaginal mucus.

Stanford, Smith, and Dunson also conducted a study to determine the day specific probabilities of pregnancy in relation to the timing of intercourse and the quality of self-observed vulvar mucus among a group of normal and sub-fertile couples.<sup>24</sup> The couples were obtained from six different Creighton Model Fertility *Care* System centers in four different cities (Missouri, Nebraska, Kansas, and California). The Creighton Model (CrM) is a cervical mucus system of Natural Family Planning that utilizes a standardized vulvar discharge recording system. The researchers retrospectively obtained two groups of CrM system users, one group entailed couples with normal fertility that had the initial intention of avoiding pregnancy, and the other group consisted of couples that were defined as sub-fertile based on having previous difficulty in achieving pregnancy. There were 309 couples in the normal fertility group that generated 1,681 usable data charts, and 117 couples in the sub-fertile group that yielded

373 cycles of usable data. Two research assistants and one researcher identified the peak day for each cycle and the day or days of intercourse 6 days before and 4 days after the peak day of cervical mucus. The researchers found 81 pregnancies among the 1,681 cycles from the couples of normal fertility and 30 pregnancies among the 373 cycles of data from the couples with sub-fertility. All pregnancy cycles had acts of intercourse 6 days before to 3 days after the peak day of cervical mucus. The researchers calculated that the highest probability of conception was on the peak day of cervical mucus with a probability of 0.38 for couples of normal fertility and 0.14 for sub-fertile couples. The researchers concluded that a standardized system of rating vaginal mucus discharges can help couples of normal fertility and of sub-fertility identify the days of the menstrual cycle that have the greatest likelihood of conception. They also speculated that the highest probability of pregnancy occurred on the peak mucus day, their estimated day of ovulation.

There have been very few prospective studies on pregnancy rates with couples using fertility focused intercourse with the aid of methods to monitor fertility and to estimate the beginning, peak, and end of the fertile window, as recommended by Stanford and Dunson. Hilgers reported a study in which 49 of 50 couples (of normal fertility) achieved a pregnancy within 5 months by focusing intercourse on days of good quality cervical mucus.<sup>25</sup> German researchers reported the largest prospective study to estimate the cumulative probabilities of conception (CPC) among a cohort of 346 couples using the Symptom-Thermal Method (i.e., cervical mucus and basal body temperature monitoring) from their first cycle onwards.<sup>26</sup> There were a total of 310 pregnancies among the 346 couples during a maximum of 29 cycles of observation. The researchers labeled the couples that achieved a pregnancy as "truly fertile (TF)." The cumulative pregnancy rates for cycles 1, 3, 6 and 12 for all couples (N = 340) were 0.38, 0.68, 0.81, and 0.92 respectively. For the TF couples (N = 304) the pregnancy rates at cycles 1, 3, 6, and 12 were 0.42, 0.75, 0.88, and 0.98. Therefore, close to 90% of the TF couples and close to 80% of all couples in the study achieved a pregnancy within the first 6 cycles of fertilityfocused intercourse. Based on the results of this study, the researchers recommended that couples who do not achieve a pregnancy within a 6 month time period of fertility focused intercourse seek a primary infertility workup. However, they also recommended that these couples continue fertility-focused intercourse for another 12 months.

A new high tech electronic method to monitor fertility has recently been developed to help women determine their fertile window with ease, convenience, and accuracy.<sup>27-28</sup> This high tech electronic hormonal fertility monitor (EHFM), called the ClearBlue Easy Fertility Monitor (Inverness Medical Innovations), estimates the fertile window using urinary metabolites of estrogen and LH and provides the user with a daily indication of "low", "high" and "peak" fertility.

Researchers from Unipath Diagnostics completed a study in which they randomized 1,000 women volunteers into two groups, one group of 500 received an EHFM, and the control group of 500 women volunteers were asked to do what they wished to achieve a pregnancy, including the use of pregnancy assist devices (e.g., ovulation test kits and basal body temperature).<sup>29</sup> The volunteers were between the ages of 21-40 years and with a partner between the ages of 21-50. The pregnancy rate during the first cycle was 15.2% (or 46 of 302) for the EHFM group and 7.8% (27 of 347) for the control group. The two cycle cumulative pregnancy rate was statistically higher for the EHFM at 22.7% compared with the control group at 14.4% (p=0.006). They also found that having a previous pregnancy and a young partner were significant factors for achieving a pregnancy. In addition, the researchers provided the users of the EHFM with a satisfaction tool and determined that 90% of the users found the device to be easy or very easy to use, and 80% found it to be convenient or very convenient. They concluded that the EHFM helped increase the likelihood of pregnancy during the first 2 cycles of use compared to nonuse among women trying to conceive for up to 2 years. It would be nice to see a similar study among women with normal fertility to discover what normal pregnancy rates would be with use of the monitor in comparison with a control group.

There is little evidence to show that focused intercourse during the fertile time as estimated by self monitoring of natural biological markers of fertility will increase the pregnancy rate and decrease the time to pregnancy. Only one randomized trial comparing self-indicators of fertility to estimate the fertile phase and timed intercourse exists. In fact, there have been claims in the scientific literature that focused intercourse based on the estimation of fertility is no better than having intercourse 2-3 times a week.<sup>30</sup> The National Institute for Clinical Excellence (NICE) guidelines specifically state that use of focused intercourse is too stressful and no more effective than having intercourse 2-3 time per week.<sup>31</sup> The ASRM policy committee recommended that electronic or other devices that are designed to aid the couple in determine the optimal time of fertility may be useful for couples who have infrequent intercourse.<sup>9</sup>

## Studies on Life Style Factors and Fertility

There are many lifestyle factors that can affect fertility. Some factors need to be avoided or moderated (e.g., caffeine and alcohol), some avoided all together (e.g., smoking), and others added to a lifestyle (e.g., better nutrition). The ARSM review focused on diet, smoking, alcohol, caffeine, and other considerations.

#### **Alcohol and Fertility**

Danish researchers conducted one of the largest studies on the relationship

between alcohol consumption and fertility.<sup>32</sup> They surveyed 39,612 women on their alcohol consumption and waiting time to get pregnant. All of these women were within their first 24 weeks of pregnancy. They discovered that moderate and high consumption of alcohol was not associated with longer waiting times to pregnancy. The only group of women alcohol drinkers that had a significantly longer waiting time to pregnancy were those who drank on average more than 14 alcoholic drinks per week and had previous pregnancies. In fact, women who had a low consistent alcohol intake of 1-2 drinks per week had a shorter waiting time period than those who were non-drinkers. The authors speculated that moderate amounts of alcohol may have a positive effect on the female reproductive system, especially by the way of stress reduction. Although the authors did not find a prolonged waiting time to pregnancy among moderate alcohol drinkers, they did find a longer waiting time among smokers, overweight women, and older women.

The ASRM policy committee stated that higher levels of alcohol consumption (i.e., greater than or equal to 2 drinks per day) should be avoided when attempting pregnancy. Moderate alcohol consumption (defined as 1-2 drinks per day) has no adverse effect on fertility.<sup>9</sup> They also warned that this implies before pregnancy. No "safe" level of alcohol consumption has been established during pregnancy.

## **Caffeine and Fertility**

Researchers from the Division of Epidemiology, Statistics, and Preventive Research from the National Institute of Child Health and Human Development and from the Center of Human Toxicology at the University of Utah measured serum paraxanthine (a metabolite of caffeine) in 591 women who had spontaneous abortions and in 2,558 matched women from the same clinic who gave birth to live infants.<sup>33</sup> They found that only very high serum paraxanthine concentrations (an equivalent of more than 5 cups of coffee per day) were associated with spontaneous abortion. They concluded that a moderate intake of caffeine should not increase the risk of spontaneous abortion.

A research team from Sweden and the United States conducted another study on the effects of caffeine and found that the equivalent of 1-3 cups of American coffee increased the risk of miscarriage by 30% and 3-5 cups raised the risk by 40%.<sup>34</sup> The study involved 562 Swedish women who had miscarriages at between 6-12 weeks of pregnancy. These women were matched with 953 who did not have spontaneous abortion. The director of the study (Dr. Sven Cnattingius) recommended that pregnant women limit their caffeine intake to about 2 American cups per day. A typical American cup of coffee has about 100 milligrams of coffee as compared to a Swedish cup, which has about 180 milligrams. A critique of the results is that the study might be biased towards including women with unhealthy fetuses. Women who have healthy fetuses usually experience more morning sickness and, thus, tend not to drink strong aroma beverages like coffee.

The ASRM policy committee recommendation is that moderate caffeine intake (i.e., one to two cups of coffee per day or its equivalent) before or during pregnancy has no apparent effect on fertility or pregnancy outcomes.<sup>9</sup>

## **Obesity and Fertility**

A group of U.S. researchers conducted a study to examine the obesity-fecundity association in relation to parity, menstrual regularity, smoking habits, and age.<sup>35</sup> The data for this study was taken from the 1959-1965 Collaborative Perinatal Project that involved a subset of 7,327 women that had planned pregnancies, recorded their time to pregnancy, and recorded their height and weight (so the authors could calculate their body mass index-BMI). The women were classified by their level of BMI to be one of 4 weight categories: underweight, optimal weight, over-weight, and obese. As expected, there was an increased time to pregnancy for older women, smokers, and women with irregular menstrual cycles (about 8% of the women). The researchers also found that fecundity odds ratios (FOR) were reduced for underweight (FOR = 0.94), for overweight (FOR = 0.84), and obese (FOR = 0.63) women when compared to optimal weight women. Smoking habits and age did not modify this association. The authors speculated that the reason for decreased fecundity could be due to increased estrogen levels in the fat cells that interfere with the hypothalamicovarian axis. The authors recommended weight loss and knowledge of the fertile phase of the menstrual cycle for overweight and obese women seeking pregnancy.

Researchers from the National Institute of Environmental Health Sciences (NIEHS) also investigated the influence of male obesity on infertility.<sup>36</sup> 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 aimed 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. 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 her male partner. If either has a BMI over 25, weight loss might be recommended. For women who have a BNI lower than 19, proper diet and weight gain would be recommended. The ASRM policy committee did not make any recommendation on weight other to say that women who are either too thin or obese will have decreased fertility.<sup>9</sup>

## **Diet and Fertility**

Researchers from Stanford University School of Medicine (Department of Gynecology and Obstetrics) conducted a study to determine the effects of a nutritional fertility supplement called FertilityBlend on the pregnancy rates of sub-fertile women.<sup>37</sup> The participants were 93 women who tried unsuccessfully to achieve a pregnancy for 6 to 32 months. The FertilityBlend (FB) contained chasteberry, green tea, vitamins, folate, and minerals. The outcome measures were serum progesterone levels, number of days basal body temperatures were above base line, menstrual cycle length, pregnancy rates, and side effects. The study design was double-blind and placebo-controlled. The 53 participants in the FB group had significantly increased progesterone levels above basal treatment, significantly increased basal body temperatures over 98 degrees, and significantly less variability in the menstrual cycle length (i.e., fewer long and short cycles). The control group of 40 women did not show a significant change over time on these outcomes variables. After 3 months of use, 14 of the 53 women in the FB group were pregnant (26%) as compared to only 4 of the 40 women (10%) in the placebo group. This was a statistically significant difference in pregnancy rates between the 2 groups. The researchers concluded that the FB nutritional supplement could be a beneficial alternative or complementary therapy to traditional infertility treatments.

Harvard University researchers sought to determine the association of multivitamin supplementation on the incidence of ovulatory infertility.<sup>38</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. 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 multivitamin 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.

In light of their research, 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. The ASRM, however, stated that there is little evidence that vegetarian diets, low-fat diets, vitamin-enriched diets, anti-oxidants, or herbal remedies improve fertility.<sup>9</sup> They did recommend that women attempting pregnancy should take a folic acid supplement to decrease the risk of neural tubal defects.

### **Other Lifestyle Factors and Menstrual Cycle Variability**

Researchers from the Postgraduate Medical Institute at the University of Hull, England, conducted an observational study in which they administered a lifestyle and TTP (i.e., the interval of exposure to unprotected intercourse from discontinuing birth control methods until conception) questionnaire to 2,112 pregnant women that attended antenatal clinics in Hull and East Yorkshire, England.<sup>39</sup> They had a 99.0% response rate to this questionnaire.

Overall, they found that 57.1% of these women conceived within 3 months and 81.2% by the end of 12 months. Of the 372 (18.8%) sub-fertile couples, 190 (9.6%) conceived by the end of the second year of trying. The sub-fertile couples compared to the fertile couples were significantly older, more obese, smoked more cigarettes, and consumed more alcohol.

More specific results showed that heavy smoking women (>15 cigarettes /day) compared to light smoking or non-smoking women had a 2-fold longer TTP. Heavy smokers were more likely to be sub-fertile among both men and women. Heavy alcohol consumption among the male partner was associated with a 2-fold increase in TTP. Moderate alcohol consumption among women and their partners was found to have no effect on TTP. Women who drank >5 cups of tea or coffee per day had a longer TTP and were more likely to be subfertile. Women who were over- and underweight had problems with fertility. Underweight women had a 4-fold longer TTP, and women who were overweight had a twofold longer TTP. Underweight women were 3.5-fold and obese women were 3.8-fold more likely to be sub-fertile. Women participants who had a lower living standard had a longer TTP and were more likely to be sub-fecund than those women who had high living standards. Finally, recreational drug use and coital frequency had no significant effect on TTP or sub-fecundity. However, the incidence of recreational drug use was low, and, thus, statistical power to determine risk was decreased.

The researchers also found that, as the number of negative lifestyle factors increased, there was a significant and progressive increase in TTP and a significant reduction in fecundity. The mean TTP with 2 negative lifestyle variables was 2.5-fold, 3.7-fold with 3 variables, and 4.4-fold with 4 variables. Couples who had more than 4 negative lifestyle variables had a 7.3-fold longer TTP compared with couples that had none. The researchers recommended promoting healthy lifestyles among couple planning for or trying to achieve a pregnancy. Based on their results they concluded that couples who lead healthy lifestyles should cut the rate of sub-fecundity in half.

Helping couples lead a healthy lifestyle will not only help them to have better general health but also increased fertility. This could lead to a substantial decline in medical referrals and treatment for infertility and, thus, a substantial reduction in health costs. The ASRM policy committee recommended that smoking, high level alcohol consumption, and recreational drugs (e.g., marijuana), should be avoided for couples attempting pregnancy.<sup>9</sup>

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