Natural Family Planning
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In this issue

Natural Family Planning

Compliance and Natural Family Planning

The importance of user compliance on the effectiveness of natural family planning programs is the topic of a review published by a research group from the University of Federico II of Naples, School of Medicine.(1) The main cause of NFP method failure, according to the authors, is either a conscious departure from the rules of the various NFP methods or the erroneous application of the rules. In addition, they also stated that methods of NFP have relatively high discontinuation rates. A reason for discontinuation and lack of compliance they postulate is that the rules of NFP might be too demanding (i.e., rules for pregnancy avoidance can average 14-15 days each cycle).

Continuation rates reviewed from 13 published studies (1981-1997) ranged from a low of 4.2% over a 12 month period to a high of 73.7%. The reasons provided for discontinuation of NFP methods, included lack of interest, dissatisfaction with the method, unplanned pregnancy, difficulty in recognizing biological indicators (i.e., the mucus sign), a desire for pregnancy or separation from spouse. The authors speculated that lifestyles, belief patterns, cultures, and the availability of contraceptives might affect the decision to use NFP as a method of family planning. Potential users in developing countries that live a hectic fast paced lifestyle and that have many contraceptive choices might not be readily open to NFP methods that have complex rules, self-observation of biological signs and sexual abstinence. However, if couples in developing countries use NFP methods they probably will be compliant users because their interests are based on strong personal beliefs.

The authors provided a number of suggestions to increase the use, satisfaction and compliance with NFP rules of instruction. These suggestions include the use of urinary home test kits for monitoring ovulation. They believe that these kits are easy to use and could be targeted to a larger part of the population. Besides urinary hormonal test kits they also suggest fertility monitoring devices such as the CUE monitor that provides a digital measure of salivary and vaginal secretions (see *CMR*, Winter/Spring 1998, pages 5-7, for a review of the CUE monitor). The authors also suggested simplifying or decreasing the rules in the use of NFP and using simple monitoring devices such as beads and necklaces (*see next article on the simplified rhythm calendar method*). Finally, the authors also mention (with a religious caution) the use of barriers during the fertile time. They believe that the use of barriers might increase the number of potential users who are doubtful of the effectiveness of NFP methods and who do not wish to practice periodic abstinence.

Comments

Compliance in NFP use is an important topic. Understanding why users of NFP discontinue, are unsatisfied with the methods, or are unable to use them will help NFP teachers to address this problem in client instruction. Certainly, simplifying instructions, using accurate and objective fertility monitoring aids, decreasing the amount of periodic abstinence and adapting methods to various cultural groups and contexts are some possible ways of increasing compliance. However, as the authors point out, the group that comply the most are users who have a strong personal belief system. For example, a 1997 New Zealand study showed that Catholic women with strong religious motivations were more likely to continue in the use of NFP (2) and a 2000 United States study showed that those couples who were more likely to continue instruction in NFP were Catholic, white and college educated. (4)

For a number of reasons it is doubtful that the use of barriers would increase the use, compliance and satisfaction with NFP methods. Research has indicated that couples often report barrier sex to be unsatisfactory. In addition, Catholic teachings reveal that such behavior is contradictory to the true nature of the conjugal relationship. It would be helpful for NFP teachers and researchers to look to other models that have addressed the problem of compliance and apply them to NFP. Social support, self-efficacy, behavioral control, contracting and health belief models are some examples of approaches that have been developed and researched in other disciplines that could be applied to NFP to address the complex problem of compliance. Innovative solutions are required not condoms.

1. Tommaselli, G. A., Guida, M., Palomba, S. et al., **The importance of user compliance on the effectiveness of natural family planning programs.** *Gynecological Endocrinology* 14 (2000): 81-89.

2. France, M., France, J. and Townend, K. **Natural family planning in New Zealand: a study of continuation rates and characteristics of users.** *Advances in Contraception*. 13 (1997): 191-198.

3. Stanford, J. B. and Smith, K. R. **Characteristics of women associated with continuing instruction in the Creighton Model Fertility Care System.** *Contraception* 61 (February, 2000): 121-129.

High Satisfaction with a Fixed Day Calendar Rhythm Method Reported Among Mayan Couples in Guatemala

Over the past 30-40 years the calendar rhythm method of family planning has been denigrated among the health professions and public at large as being ineffective and harmful to

relationships. A renewed interest in the calendar rhythm method however has recently been initiated by a number of groups in the United States and abroad. One of the strengths of the rhythm method is in its simplicity.

Recent re-formulations of the rhythm method have made it even easier. With the old formulation of the rhythm method the days of periodic abstinence in a given menstrual cycle varied according to the lengths of the previous 6 to 12 cycles. In order to determine those days a simple mathematical formula was used to calculate those days. An even simpler method would be to have a fixed-day period of abstinence in each cycle. The two current fixed day formulas that are being tested are the 11 and 12-day formulas, with days 9-19 or 8-19 of each cycle constituting the fertile time. Both of these fixed day methods and the studies they are related to have been discussed and reviewed in previous issues of *CMR*. (1,2)

An 11 day (9-19) fixed day formula of the calendar rhythm method was recently tested among the Mayan population of Guatemala.(3) The method was implemented with the use of calendars and a beaded necklace system. The calendars were used to record the beginning and end of each menstrual cycle as indicated by the woman's menses. The beads were used to track the days of fertility and infertility. To begin the cycle the first bead was colored red, the 11 fixed days of fertility from day 9-19 were colored green, and the rest of the beads were colored brown. The green and brown colors coincided with the dry (brown earth and foliage) and the rainy fertile (green foliage) times of the countryside in Guatemala. Each beaded necklace has 30 beads and a marker that is moved from bead to bead. The fixed formula is intended for women who have 26-30 day cycle lengths.

The fixed day formula bead method of calendar rhythm was tested among 301 couples (women between the ages of 18-39 years) living in the Guatemalan highlands. A team of one supervisor and three instructors at 5 centers taught the method. Instructors visited each couple and completed follow-up forms after the first three cycles and every three months until the end of the 12 -month study period. Suspected pregnancies were confirmed by pregnancy tests.

About 51% of the 301 couples were Catholic (41% Evangelical), about 31% desired more children and only 16% of the women had more than 7 years of a formal education. Almost 89% of the sample had never used a method of family planning. After 12 months of use, 79% of the couples were still using the method. The reasons that the 32 couples who discontinued gave for stopping were personal (45%), migration (22.6%), or desiring a pregnancy (16.1%). After 12 months of use 32 couples were pregnant giving a 11% pregnancy rate. However, only 34% of these couples were sure that they did not have sexual relations during the fertile period. At 1, 3, and 12 months, 100% of the women reported satisfaction with the method but 5 of the men reported being dissatisfied due to the periodic abstinence. The authors concluded that a bead necklace fixed day system of calendar rhythm was highly acceptable and potentially effective among the Mayan population of Guatemala.

Comments

The authors of this study pointed out that the level of attention received by the instructors might have contributed to the high satisfaction, high continuation and low pregnancy rate. They plan on a one-year follow-up study to determine if the satisfaction, continuation, and low pregnancy rates continue.

The authors also speculated that male dissatisfaction with periodic abstinence should send up a red flag and the instructors should then encourage couples to keep a barrier handy. It is true that male dissatisfaction or difficulty with periodic abstinence should send up a red flag. In the long run however, offering a condom is not helpful. Condom/barrier use is against many of the Guatemalans religious beliefs. It may also be contrary to their cultural context as well (i.e., over 93% have never used contraception). A better approach would be to help the men to integrate their fertility, learn how to express intimacy in other ways, and to have a better sense of self-control.

Overall this study shows that a very simple, easy to use, and easy to teach method of natural family planning can be effective and satisfying. The study also provides evidence that maybe the denigration of the rhythm method of family planning is based upon professional bias or ignorance rather than the facts.

1. **Necklace method of NFP tested among Mayan women.** *Current Medical Research* 11 (Winter/Spring 2000): 5-6.

2. The fixed day method of NFP. *Current Medical Research* 12 (Summer/Fall): 6-7.

3. Burkhart, M. C., de Mazariegos, L., Salazar, S. and Lamprecht, V. M. **Effectiveness of a standard-rule method of calendar rhythm among Mayan couples in Guatemala.** *International Family Planning Perspectives* 26 (August, 2000): 131-136.

Fertility

Researchers Estimate That the Timing of the 6 Day Window of Fertility is Highly Variable

Previous research has verified that there are only 6 days in a woman's menstrual cycle that are fertile, i.e., the day of ovulation and the 5 preceding days. These 6 days are known as the "fertile window." The probability of pregnancy if a couple has intercourse on the first day of that window is around 10% and increases to a peak of about 40% during the two days before ovulation. Researchers from the National Institute of Environmental Health Sciences conducted a prospective study to estimate the probability of that 6-day fertile window occurring on a given day of the menstrual cycle. The study participants were 221 healthy women between the ages of

25 and 35 who collected their first morning urine on a daily basis and recorded the days in which intercourse and menstrual bleeding occurred. The estimated day of ovulation was determined by the ratios of urinary metabolites of estrogen and progesterone. There were 696 cycles with an estimated day of ovulation that were included in the analysis. The cycle lengths ranged from 19 to 60 days.

What the researchers found was that ovulation occurred as early as the 8th day and as late as the 60th day of the menstrual cycle. They also found that even among women with regular cycles, the post-ovulatory period was highly variable, ranging from 7 to 19 days. They estimated that approximately 2% of women were in their fertile window by the fourth day of their cycle and 17% by the seventh day. By days 12 and 13 of the cycle over half of the women were in their fertile window. Among women who reached the 5th day of their cycle 4-6% were in the fertile phase and there was 1-6% probability that women were in their fertile time on the day their next menses was expected.

The authors concluded that the timing of the fertile window is highly variable even among women who have regular menstrual cycles. More than 70% of women are in their fertile window before day 10 and after day 17 of their menstrual cycle. They also concluded that there are few days in the menstrual cycle during which some women are not potentially fertile. They acknowledged that no calendar method of family planning is completely effective and that use of basal body temperature for estimating the day of ovulation is very "crude."

Comments

The results of this study should not be a surprise to users and teachers of modern methods of NFP who rely upon natural biological markers of fertility that vary according to the time of ovulation. NFP teachers and users should also realize that the probability of being in the window of fertility is not the same as a high probability of being fertile. As mentioned above, the first day of the fertile window only has a 10% probability of conception. If the estimated probability of being in the fertile window is added to the probability of being fertile on any given day of the fertile window, the probability will be lowered considerably. For example, although there is a 2% probability of being in the fertile window on the 4th day of the menstrual cycle, if that day is the first day of the fertile window, the probability of conceiving from an act of intercourse on that day is even lower. Hence, even the fixed day calendar methods have a fairly high effectiveness among women with regular cycles when used to avoid pregnancy.

1. Wilcox, A. J., Weinberg, C. R. and Baird, D. **Timing of sexual intercourse in relation to ovulation: effects on the probability of conception, survival of the pregnancy and sex of the baby.** *New England Journal of Medicine* 333 (1995): 517-521.

2. Wilcox, A. J., Dunson, D. and Baird, D. D. **The timing of the "fertile window" in the menstrual cycle: day specific estimates from a prospective study.** *British Medical Journal* 321 (November, 2000): 1259-1262.

Study Finds Cervical Mucus Not Reliable for Identifying Fertile Period Among Breast-Feeding Women

A NFP research group from the University of Naples followed 40 breast-feeding women participants (aged 23-40 years) from the birth of their child through the first cycle after return of menses. All of the women recorded their daily basal body temperature (BBT), cervical mucus changes, and salivary ferning patterns as well as duration, frequency, and interval of breast-feeding. Serial transvaginal ultrasound was performed on the woman during the first cycle after the return of menses to estimate the day of ovulation. They found that in 8 of the 40 breast-feeding women the return of menses preceded weaning and in the remaining 32, menses followed weaning. Eighty-two percent of the first cycles following the resumption of menses were ovulatory.

The authors stated that this study was conducted "above all" to evaluate by means of BBT, cervical mucus changes, salivary ferning patterns, the protective effect of breast-feeding with the return of ovarian activity. They found that the 8 women participants who menstruated before weaning had no temperature rise or an inadequate thermal shift in the first cycle. Of the 32 women who experienced menses after weaning, 12 had thermal shifts before menses, 16 had inadequate thermal shifts before menses, and 4 had no thermal shift. Not one of the 40 women had level three ferning (on a scale of 0= no ferning; 1= some; 2=more; and 3= full ferning), only one women had level 2 ferning and 15 had level 1 ferning. Twenty-four of the women experienced no ferning patterns before menses. Eight of the women failed to record cervical mucus changes, 12 had cervical mucus constantly present, 6 had cervical mucus present greater than 20 days, and 14 had fertile mucus for 7-10 days.

The authors concluded that cervical mucus characteristics were not reliable in indicating the return of postpartum fertility. They based this on the fact that cervical mucus identified fertility with only 14 of the 40 women. They also said that salivary ferning can be a reliable index of estrogen levels and of ovarian function. They concluded that complete breast-feeding associated with lactational amenorrhoea may be considered an appropriate method to control fertility.

Comments

This study was not well written. It is difficult to understand and follow, especially with regard to the conclusions that were formulated from the findings. The authors found both BBT

and salivary ferning to be suggestive of ovarian activity but not cervical mucus. This conclusion is bewildering since not one woman had a full salivary ferning pattern. Full ferning is supposed to indicate peak fertility and the approximate time of ovulation. Only 12 of the women had full thermal shifts. Since 8 women did not even record cervical mucus and since the women participants did not seem to know how to identify a basic infertile pattern of continuous mucus I find it hard to believe that the authors ruled out cervical mucus as an appropriate indicator of ovarian activity. Furthermore, they do not indicate when or if the women recorded peak mucus days. As the authors stated, having only 40 participants is a very small study and the results from it cannot in any circumstances be generalized to other populations of breast-feeding women.

Tomaselli, G. A., Guida, M. and Palomba, S. et al. **Using complete breast-feeding and lactational amenorrhoea as birth spacing methods.** *Contraception* 61 (April, 2000): 253-257.

Contraception

Increased Risk of Breast Cancer with Oral Contraceptive Use Found Among Women with Family History of Breast Cancer

In 1944, a study was initiated by researchers at the Dight Institute for Human Genetics at the University of Minnesota to examine the influence of childbearing, breast-feeding and hereditary susceptibility on the risk of breast cancer. The participants of the study were 544 women who were diagnosed with breast cancer between 1944 and 1952. Fifty years later, researchers from the Mayo clinic and the University of Minnesota, were able to contact adult sisters, daughters, granddaughters, nieces and marry-ins from 462 of these original 544 women. The purpose of contacting these women was to determine whether the association of oral contraceptive (OC) use and the risk of breast cancer was influenced by family history of the disease. The data for the study was collected by telephone interview from 394 sisters and daughters of the original 544 (1944 study) participants, 3002 granddaughters and nieces, and 2754 women who married into the families of the original participants.

After controlling for parity, age at first birth, age at menarche, age at menopause, oophorectomy, smoking, and education, the researchers found that ever having used OCs was associated with a significantly increased relative risk of breast cancer among sisters and daughters of the 1944 study participants (RR, 3.3; 95% confident interval [CI], 1.6-6.7). They did not find a significantly elevated risk for breast cancer among granddaughters and nieces of the 462 women from the 1944 study. The significantly elevated risk of breast cancer among the first-degree relatives of the original 462 women was most evident with use of the earlier formulations (prior to 1975) that had higher doses of estrogen and progestins. There was not enough participants with breast cancer among first degree relatives who used the later

formulations (i.e., lower dose estrogen OCs) to determine risk. The authors concluded that women who have ever used the earlier formulations of the OCs and have a first degree relative with breast cancer may be at "particularly high risk for breast cancer." They also recommended that these women may want to be particularly compliant with breast cancer screening practices, i.e., breast self-exam and mammography. Further research needs to be conducted to determine the risk among first degree relatives of women with breast cancer and ever use of current formulation of OCs.

Comments

This is a very well designed, unique, objective epidemiological study of a large group of women who are at risk for breast cancer. Some of the other findings of interest is that the average length of use among the ever users was 7.0 years (range, 0.5 to 37.5 years). Among women who have at least 3 blood relatives that were diagnosed with breast cancer and used OCs, the relative risk of breast cancer climbed to 4.6 and with 5 blood relatives to 11.4. The authors make a very strong risk statement saying that women with a strong genetic predisposition for breast cancer may be "at greatly elevated risk of breast cancer if they use OCs." Although, there was a lack of evidence of increased risk of breast cancer among second-degree relatives of women diagnosed with breast cancer this may be due to the younger age of these women. The mean age of the granddaughter at the time of interview was only 45.3 years. As these granddaughters age, it will be interesting to see if the rate of breast cancer significantly increases compared to non-users. Could there be a OC breast cancer relationship time bomb that is waiting to explode among these women?

Gabrick, D. M., Hartman, L. C. and Cerhan, J.R. et al., **Risk of breast cancer with oral contraceptive use in women with a family history of breast cancer.** *Journal of the American Medical Association* 284 (October 11, 2000): 1791-1798.

Research Briefs

Norplant Continuation Rate Only 13% After 4 Years of Use Among Urban Minority Women

A total of 197 adult black and Hispanic women who selected Norplant as their means of contraception were followed for five years in order to determine factors associated with retention and reasons for removal. All of the women attended an urban health clinic in Rochester New York. Continuation rates were 68% after one year of use but decreased to only 13% after 4 years. A structured interview was conducted in order to determine reasons for termination. Black women with low parity were more likely to retain the Norplant rods and Hispanic women with

high parity were more likely to discontinue use early. The most frequent reasons given for removal were menstrual complaints (bleeding), weight gain, hair loss, headaches and arm pain.

The authors mentioned that continuation rates are high for Norplant but are "still impressive" when compared to other contraceptive methods. Participants with complaints of heavy bleeding were treated with Premarin or with one cycle of oral contraceptives. Headaches were treated with Ibuprofen and hair loss with reassurance and a recommendation to eat a high protein diet. The authors were optimistic that the newer two rod system that last about 2-3 years might be more suitable because most users only use the 6 rod approach for that length of time.

Comment

The question arises as to how many of the women would have terminated Norplant sooner if they did not have to endure a second surgical procedure to have the Norplant rods removed.

Glantz, S., Glantz, J. C. and Campbell-Heider, N. et al., **Norplant use among urban minority women in the United States.** *Contraception* 61 (February, 2000): 83-90.

Depressive symptoms Associated with Use of DMPA (Depo-Provera)

Previous studies have not found an association between the use of depot medroxyprogesterone acetate (DMPA) and depressive symptoms. However, these studies did not compare DMPA users with non-users. A group of researchers from the University of Washington and the Center for Health Studies in Seattle conducted a prospective 36 months study in which they compared 183 users of DMPA with 274 non-users. The participants were randomly selected from a large health maintenance organization in the State of Washington. Depressive symptoms in both groups were measured by questionnaire every 6 months for up to 3 years. The DMPA participants were significantly more likely to be younger, black, have no more than a high school education, experienced a pregnancy and reported more depressive symptoms at baseline when compared to the non-users. After statistically adjusting for these differences, the researchers found that women who used DMPA continuously were 40% more likely than non-DMPA users and women who discontinued DMPA were 60% more likely than non-DMPA users to report depressive symptoms. In addition, depressive symptoms among DMPA discontinuers were significantly elevated prior to discontinuation and at the first visit after discontinuation. The researchers cautioned that this association of depressive symptoms with DMPA use is not causal. Further research will need to determine if there is a cause and effect.

Comment

I wonder if the association of depressive symptoms would have been greater if the researchers did not have women in the comparison group that were on hormonal contraception. Approximately 34% of the non-users were on oral contraception.

Civic, D., Scholes, D. and Ichikawa, L. et al. **Depressive symptoms in users and non-users of depot medroxyprogesterone acetate.** *Contraception* 61 (June, 2000): 385-390.

Significant Increase in Condom Use Among Sexually Active High School Students

Researchers from the Center for Disease Control and Prevention have conducted 4 national surveys of United States high school students since 1991 called the Youth Risk Behavior Surveys. The sample size of the 4 surveys were from 10, 904 to 16,296 students and the response rates ranged from 60 to 70%. The 1997 survey determined that almost half (48%) of U.S. high school students reported having sexual intercourse and that 35% were currently sexually active. The researchers found from 1991 to 1997 there was a significant increase (46% to 57%) in condom use, and a significant decrease in oral contraceptive use (21% to 17%) and use of withdrawal (18% to 13%). According to the authors there were two findings of concern. The first was that in 1997, 3 of 10 students were not adequately protected against pregnancy or sexually transmitted diseases (STDs). That was because 13% reported to be using withdrawal and 15% used no form of contraception. The second concern was that as female students progressed from the 9th to 12th grade they replaced their use of condoms with the birth control pill. The authors speculated that the students were more concerned with pregnancy than with STDs. They concluded that inadequate contraceptive use continues among high school students and that health professionals need to promote the correct and continued use of condoms.

Comment

One wonders why not place greater efforts on helping students to abstain from sexual activity rather than increase condom use. The authors admit that there might be some over reporting of sexual activity.

Everett, S., Warren, C. W. and Santelli, J. S. et al. **Use of birth control pills, condoms, and withdrawal among US high school students.** *Journal of Adolescent Health* 27 (August, 2000): 112-118.

High Dose Levonorgesterel Pills Judged Unsuitable for Regular Post-Coital Contraception

A study was conducted by the Task Force on Post-Ovulatory Methods for Fertility Regulation to determine the efficacy and side effects of infrequent but regular post-coital use of high dose levonorgestrel. The task force was funded by and made up of members from the

United Nations Development Program, the United Nations Population Fund, the World Health Organization and the World Bank Special Program of Research. A total of 295 healthy women from 6 study sites from 5 countries (China, Cuba, Pakistan, Slovenia, and Russia) were enrolled in the study. Infrequent intercourse was defined as 1-4 times per month. The only method of contraception these 295 women participants used for a 6-month period was one tablet of 0.75 mg of levorgesterel taken immediately after coitus. The assumption of the study was that there is an unmet need for a post-coital method that could be taken regularly.

The researchers found that the study participants frequently (24%) deviated from the protocol and had coitus more than 4 times per cycle on average. They also found that the Pearl index failure rate based on 133 woman-years of use was 6.8 and that the overall probability of pregnancy per treated coital act was 1.4 per 1000. The discontinuation rate was nearly one-third before finishing 6 months of use mainly for bleeding problems experienced by 70% of the participants. Other complaints included (in decreasing frequency) nausea, breast tenderness, weakness, dizziness, headache, abdominal bloating, loss of libido, depression, and vomiting. The authors concluded that the use of high dose levonorgestral pills are unsuitable for regular post-coital contraception.

Comment

I find it fascinating that the reason the authors felt that the high dose pill was unsuitable was because it did not protect the individual from sexually transmitted disease and not for being ineffective or that women experienced many side effects. There is no mention in the study that the post-coital pill actually prevents implantation as one of its mechanisms of action. The fact that over one-third of the participants stopped use of the post-coital pill before 6 months of use indicated that the woman themselves concluded this method of contraception was unsuitable.

Task Force on Post-ovulatory Methods of Fertility Regulation. **Efficacy and side effects of immediate postcoital levonorgestrel used repeatedly for contraception.** *Contraception* 61(May, 2000): 303-308.

Menses--How Important? (Seasonale and Lunelle)

The monthly withdrawal bleed experienced by women taking oral hormonal contraceptives (OCs) is not a true menses. There is very little build-up of the uterine lining for women on OCs and the bleeding they experience is caused by the withdrawal of artificially ingested hormones, i.e., after the woman stops taking tablets with the active hormone/s.(1) The reason that the pill was designed as three week on and one week off (or one week of a placebo pills) was to mimic a menses or provide a “pseudo-period.” A reason given for this manner of

OC delivery is to insure the woman user that she is not pregnant and that she is still in a "natural state." Another reason given is that one of the original developers of the pill (John Rock a Catholic obstetrician gynecologist) felt that having a regular monthly bleed would help Catholics and especially Catholic women feel that OCs were natural and not contrary to religious beliefs about artificial contraception. (2)

Scientists and health care providers are now questioning the need and safety of having a monthly pill-withdrawal caused "pseudo menses" or even having a physiologically normal menses.(1) Until the twentieth century most women only experienced 100-200 menstrual bleeds due to later menarche, childbearing and breast-feeding practices. Women in the United States and modern Western style countries now experience over 400. Some scientists believe that this increase in the number of artificial or real cycles in women can account for some of the increase in breast cancer for women on the pill and endometrial and ovarian cancer for those who are not. Furthermore many women experience uncomfortable menstrual symptoms (e.g., pelvic pain, bloating, and breast tenderness) whether on the pill or not during natural or induced monthly bleeding.

Drug companies are now developing hormonal pill formulations that no longer provide a 7 day monthly withdrawal bleed. For example, the drug company Organon is marketing a new OC pill called *Mircette* that produces only a 2 day withdrawal bleed.(2) Barr pharmaceuticals is now testing a new oral contraceptive pill called *Seasonale* that produces a withdrawal bleed every 84 days, a three months time period or, i.e., once a season. A seasonal withdrawal bleed could also be accomplished by taking a current "on the market" OC for three months or longer.(3) Health care providers speculate that providing seasonal rather than monthly bleeds will decrease the incidence of PMS, headaches and endometriosis, and increase contraceptive efficacy.

The first new birth control method since 1992 (a monthly injectable contraceptive called Lunelle) was approved last October (2000) by the Food and Drug Administration. Lunelle is a combination of a progestin and estrogen (25 mg medroxyprogesterone acetate and 5 mg estradiol cypionate) and is considered an alternative to Depo Provera which is taken (injected) every three months. A benefit of Lunelle is that women on average can get pregnant within 4 months after stopping Lunelle as compared to about 10 months with Depo-Provera. Studies in the United States and Europe has shown that Lunelle has a contraceptive efficacy similar to long term acting progestational methods (i.e., 0 to 0.2 pregnancies per 100 woman-years of use).(4) Lunella will cost about $35 per monthly injection which is about the same price as OCs. To improve access to the Lunelle, Pharmacia (the manufacturer) is aiming to make Lunella available in pharmacies and the workplace and a version that is self-administered.

1. Thomas, S. L. and Ellertson, C. **Nuisance or natural and healthy: should monthly menstruation be optional for women?** *The Lancet* 35 (March, 2000): 922-924.

2. Gladwell, M. **John Rosk's error.** *The New Yorker* (March 13, 2000): 52-57.

3. Jellin, J. M. **Women's Health.** *Prescriber's Letter* 7 (July, 2000): 39.

4. Shulman, L. P. **Expanding contraceptive choices: Lunelle monthly contraceptive injection.** *International Journal of Fertility* 45 (2000):190-194.

Caffeine and Miscarriages - Is There A Link?

A recent study conducted by a research team from Sweden and United States 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%. 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 have a tendency of not drinking strong aroma beverages like coffee.

Cnattingius, S. , Signorello, L.B. and Anneren, G., **Caffeine intake and the risk of first-trimester spontaneous abortion.** *New England Journal of Medicine* 343 (December, 2000): 1839-1845.

Under the Microscope

Predicting the Fertile Window

In the *British Medical Journal* study by Wilcox, Dunson, and Baird (reviewed in this current issue of *CMR*) the authors stated that reliable methods to predict ovulation are lacking and therefore, predicting the fertile window is also unreliable.(1) Furthermore, the authors mentioned that Basal Body Temperature is a crude way of estimating the fertile window. The goal of modern methods of NFP is to accurately predict (through the use of natural self detected biological markers) the beginning, the peak and the end of the 6-day fertile window. Unfortunately modern methods of NFP utilize rather imprecise measures to estimate the fertile window. This is reflected in the fact that NFP methods over estimate the fertile time of the cycle on average from 6-10 days. The average days of fertility in a woman's menstrual cycle when estimated by a single indicator (i.e., cervical mucus) is about 12-15 days and for the double

indictor methods (i.e., the sympto-thermal methods) is about 13-14 days.(2) Therefore, the amount of fertile days is over two times longer than necessary.

The imprecision in estimating the fertile window is most evident in estimating the beginning of fertility. Modern methods of NFP are currently limited in accurate natural biological markers that estimate the beginning of fertility - i.e., the beginning of the 6 day fertile window. One or more of the following fertility markers are used in methods of natural family planning to determine the beginning of the fertile time:

- a change of sensation at the vulva from dry to sticky, tacky, moist, or wet the presence of cervical mucus
- the cervix starting to soften and rise
- the length of the shortest of the last 6-12 cycles minus 20 days.

There is actually very little research to show how accurate any of the above measures correlate with the beginning of fertility, i.e., the first day of the fertile window. We do know that the above measures (except for the shortest cycle minus 20 days) are rather subjective and that the calendar formulation is rather rigid in adapting to the variations in a woman's monthly cycles.

Observations of cervical mucus and the resulting sensations at the cervix is an indirect indicator of fertility and is somewhat subjective. The observation of cervical mucus and resulting sensations at the vulva can be confusing when the woman experiences continuous mucus, no mucus or sensation changes, or other bodily fluids (e.g., arousal fluid and seminal fluid). On the other hand, the presence of cervical mucus and its peak characteristics are pretty evident for most women. Furthermore, there are no devices necessary for this observation and it costs nothing.

NFP methods that use cervical mucus and resulting sensations as a biological marker assume that when there is no externally observed mucus or sensations (or if the mucus and or sensations is determined to be a basic infertile pattern) that the women is infertile even if she is in the 6 day window of fertility. Evidence for this assumption is also lacking. Some methods of NFP assume that if the woman has a wet non-lubricative sensation that she is not fertile.

Other biological indicators that are currently available that might be added to current NFP system markers (or used alone) to determine the beginning of the fertile window are the peak in salivary resistance (as indicated by the CUE monitor- Zetek, Aurora, Colorado) or the detection of rising levels of urinary metabolites of estrogen through the use of the Clearplan Easy Fertility monitor (Unipath Diagnostics Co., Princeton, New Jersey) monitor or the Brown Ovarian monitor (Melbourne, Australia). The advantage of these biological markers are that they are more objective. However, they are an added external device and added expense.

The natural biological markers used in current methods of NFP are probably best suited for the self-determination of peak fertility. These markers are as follows:

- cervical mucus that is clear, stretchy, watery and lubricative
- the sensation of slipperiness at the vulva
- the cervix is soft, open, straight and high in the vagina
- a rise in basal body temperature of 2-4 degrees above an established base.

The day or days of peak fertility are the 2 days before ovulation in the 6-day window of fertility. Of the above natural biological markers, the peak in cervical mucus (i.e., mucus that is clear, stretchy and lubricative) is probably the most studied. We know through correlation with serum and urinary hormones and with serial transvaginal ultrasound estimates of the day of ovulation that the peak in cervical mucus varies around the day of ovulation plus or minus 3 days 95-99% of the time.(3,4) However, about 25% of the time, the peak in cervical mucus comes after the day of ovulation and thus after the last day of the fertile window. The shift in Basal Body Temperature is even more variable than peak mucus in detecting peak fertility. Furthermore, the temperature shift might be better classified as an indicator to confirm that the peak of fertility already has taken.

Other potential available markers of peak fertility are urinary assays (test strips) of LH and/or the peak in fertility as detected by the Clearplan monitor. The CUE monitor also detects peak fertility by the nadir in vaginal electrical resistance. According to a consensus paper published by the European Society of Human Reproduction and Embryology (ESHRE) the best single test to predict ovulation and the peak of fertility is the urinary assay of LH, while the measurement of LH and pre-ovulatory estrogen is the best prediction.(5)

There are no natural biological markers used in current methods of NFP that detect the end of the fertile window. The rise in Basal Body Temperature is probably the closest because it is a reflection of the rising levels of progesterone. However, as mentioned BBT is often a poor measure of fertility.(6) About 34% of women's menstrual cycles will not show a bi-phasic shift in temperature. Body temperature can also rise due to other phenomenon such as stress, disrupted sleep patterns, alcohol use and infection. On the other hand, temperature measurements are objective and easy to take. The availability of electronic and computerized temperature devices (such as the Bioself, Baby/Ladycomp and Sophia) have made temperature taking and tracking of the temperature shift very easy.

To determine or confirm the end of fertility current systems of NFP essentially use a counting system based on the fact that the measures of peak fertility are imprecise in detecting

the day of ovulation. The markers for the end of fertility as utilized by current methods of NFP are:

- 3 and sometimes 4 days past the last day of clear, stretchy or slippery mucus
- 3 days past the last day of the slippery sensations at the vulva
- 3 days past the shift in basal body temperature or 3 temperatures above a determined level
- the length of the longest of the last 6-12 cycles minus 10 days
- day 18 or 19 of the menstrual cycle with the fixed day formulas.

Other potential markers for determining the end of the fertile period (that are currently available) are counting 2-3 days past the urinary LH peak, three days past the CUE vaginal resistance nadir, or 1-2 days past the rising levels of urinary metabolites of progesterone as detected by the Ovarian monitor or some other type of assay method. Of note is that the ESHRE group provided a consensus opinion that measuring progesterone is the best test for confirming ovulation and, therefore, for confirming the end of the fertile window.

Besides ease of use, objectivity, expense and safety, a key factor in using natural biological markers is how accurate they are in estimating the fertile 6-day window. The current gold standard for estimating the day of ovulation is through the use of serial ultrasound that tracks the developing follicle and resulting collapse at ovulation. Use of this methodology provides the researcher with a very accurate way of determining the fertile window. Continuing research is needed to determine how accurate biological markers are for not only estimating the peak of fertility, but the beginning and end as well.

Two benefits for using the most accurate biological markers in methods of NFP are apparant. The first is that the amount of abstinence will be reduced. A common complaint about modern methods of NFP is the amount of abstinence (on average one half of the entire menstrual cycle). Reducing this time to a third or quarter of the cycle will most likely aid in acceptance and compliance.(7) The second benefit is that greater objectivity will be achieved in identifying the fertile time. Objectivity will take pressure off the women who currently has the most responsibility in interpreting subjective biological markers of fertility.(8) Further research is needed in determining how new biological indicators can be integrated into current systems of NFP or how new systems of NFP can be developed.

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