Fertility Report: February, 2007 - Submitted by Richard J. Fehring, PhD, RN

Researchers find Spiritual Well-being Positively Correlated with Functional Well-being among Women with Premature Ovarian Failure

Premature ovarian failure can be an emotionally traumatic event for women. Women who experience premature ovarian failure and subsequent loss of fertility often express feelings of low self-esteem, loss of purpose in life as a woman, and difficulty in relationships. Previous qualitative research demonstrated that many women with premature ovarian failure find that they cope better with life through spiritual well-being.[1] Researchers from the Women's Health Section of the National Institutes of Child Health and Human Development wanted to determine if spiritual well-being was quantitatively correlated with functional well-being in women with premature ovarian failure. The researchers emphasized that spiritual well-being is not necessarily the practice of religion. For some, religion can be a means to spiritual well-being. Spiritual well–being was defined as a quest for understanding life's ultimate questions and the meaning and purpose of living.

To test the relationship between functional well-being and spiritual well-being among women with premature ovarian failure, the researchers were able to obtain 138 women with premature ovarian failure through an advertisement over the internet. The criteria for premature ovarian failure in this study was having experienced at least 4 months or more of amenorrhea or menstrual irregularity before the age of 40 and to have 2 serum FSH levels in the menopausal range. All 138 women participants were administered a 12-item spiritual well-being scale with two subscales, i.e., an 8 item "peace and meaning" subscale and a 4 item "faith" subscale. They were also administered a 7-item functional well-being scale. One hundred thirty seven out of the 138 participants completed the two questionnaires.

As hypothesized, there was a strong positive correlation between levels of spiritual well-being and functionally well being ($r = 0.68$, $p < 0.001$.). Most of the correlation was due to the "peace and meaning" component of the spiritual well-being scale ($r = 0.79$, $p < 0.001$) as compared to the "faith" component ($r = 0.26$, $p < 0.025$). Only the peace and meaning subscale remained significant when multiple regression was used to predict functional well-being.

The authors made a point that spiritual well-being is different than emotional well-being in that spirituality can help people cope with problems outside of their control, whereas psychology can help with problems within their control. They cautioned that this was a cross sectional study, so that you cannot infer a cause and effect relationship between spiritual well-being and functional well-being. They felt that there is a need for longitudinal studies and for intervention studies in which strategies are designed to support spiritual well-being.

Comments: Teachers of natural family planning (NFP) or fertility awareness (FA) methods will encounter women with premature ovarian failure. Recognizing that

spiritual well-being might help them cope with their loss of fertility might indicate a need for spiritual referral. Of note, this author has conducted studies comparing levels of spiritual well-being between couples using methods of NFP versus oral hormonal contraception.[2-3]

1. Ventura, JL, Fitzgerald, OR, Koziol, DE, Covington, SN, Vanderhoof, VH, Calis, KA, Nelson, LM. **Functional well-being is positively correlated with spiritual well-being in women who have spontaneous premature ovarian failure**. Fertility and Sterility, 2007, Article In Press, Available Online.

2. Fehring R. Lawrence D. **Spiritual well-being, self-esteem and intimacy among Couples using natural family planning**. The Linacre Quarterly. 1994;61(3):18-29.

3. Fehring R, Lawrence D, Sauvage C. **A comparison of self-esteem, spiritual well-being, and intimacy in couples using natural family planning with couples using oral contraceptives.** International Review of Natural Family Planning, 1989;13(3&4), 227-236.

Weight Loss and Knowledge of Fertile Window Important for Obese Women Seeking Pregnancy

According to researchers from the National Institute of Environmental Health Sciences, the fertility rate in the United States since 1971 has been under the replacement rate of 2.1 births per woman over a reproductive lifespan.[1] Furthermore, they stated that although most of the reasons for this decline in fertility are sociological, there are others possible reasons, including the rise in obesity. They pointed out that there is good evidence for the link of obesity to decreased fecundity but the mechanism for this decrease is not clear. Some indicate that it might be due to interference with the hypothalamic-pituitary-ovarian axis which results in irregular cycles. However, some evidence indicates that the decrease in fecundity among obese women also occurs when obese women have regular cycles. There is mixed evidence of the influence of smoking (and other environmental and behavioral factors) with obesity and fecundity. Therefore the authors (from the National Institute of Environmental Health Sciences) sought to investigate the obesity–fecundity association in relation to other factors that might influence this association, such as parity, menstrual cycle regularity, smoking habits, and age.

The data for this was generated by the Collaborative Perinatal Project (CPP) that was conducted at 12 study centers throughout the United States from 1959-1965. A total of 59,391 women were enrolled into this CPP study, and of these, 7,327 contributed data to the current study. Variables that were analyzed included self-reported time to pregnancy in months, height, pre-pregnancy weight, age, menstrual cycle length, smoking habits, parity, and age. Self-reported height and weight were converted into a basal metabolic index (BMI), and then categorized as being underweight (BMI = 18.5 kg/m^2), optimal weight (BMI = 18.5-24.9), overweight (BMI = 25.0-29.9) and obese (BMI >30.0). The

participants in this study included 13% who were overweight, and 5% who were classified as obese.

The median time to pregnancy was 4 months for overweight women, and 5 months for obese women as compared to 3 months for obese women. The probability of conceiving in a given cycle was reduced by 8% in overweight women and by 8% for obese women. Furthermore, the probability of conceiving was reduced even further for overweight nulliparous women (i.e., by 16%) and for obese women (34%). The researchers found that the association of reduced fecundity also existed for overweight and obese women even when they reported regular menstrual cycle lengths. Neither age nor smoking habits modified the association between weight and fecundity.

The authors pointed out that the current US population of reproductive age women would include a much higher percentage of overweight and obese women than those women from the CPP study. They also speculated that the association they found between fecundity and weight might be reduced because of the incidence of poly cystic ovarian disease (PCOS) that was not reported in this population. A limitation of the study is that the sample of women did not include women who did not become pregnant. Therefore, the association between weight and fecundity might be even stronger.

The authors speculated as to why increased weight might reduce fecundity. They stated that increased body weight might increase peripheral fat cell induced estrogen levels which in turn interferes with the hypothalamic ovarian axis. However, this theory was not supported by the fact that women with regular cycles also had a decrease in fecundity. They also speculated that the decrease might be a result of a decrease in the frequency of intercourse due to a complexity of factors, such as a decrease in the sex drive of obese women or their partners. The authors pointed out that for obese and overweight women seeking pregnancy (especially nulliparous overweight women) knowledge of the fertile window and the timing of intercourse is of particular importance. They concluded that weight loss could increase fecundity for overweight and obese women, regardless of cycle regularity, parity, smoking habits, or age.

Comments: NFP and FA teachers who have overweight and obese clients (seeking to achieve pregnancy) should be aware of the potential decrease in fecundity, help them to lose weight, and help them focus intercourse on the days of the fertile window. Besides the dated nature of the data set, the self-report nature of the variables in this study might also be considered a limitation, especially the self-report of the regularity of the menstrual cycle length.

1. Law, DC, Maclehose, RF, Longnecker MP. **Obesity and time to pregnancy**. Human Reproduction, 2007;22:414-420.

Fecundity Found to be Higher among Women with Multiple Births versus Singleton Births

Researchers at the Epidemiology Branch of the National Institutes of Child Health and Human Development also utilized data generated by the US Collaborative Perinatal Project (CPP) between 1959 and 1965 to study the relationship between multiple births and fecundity.[1] They selected from the 54,390 pregnancies captured in the CPP data set 8546 women who indicated their pregnancy was planned and who had recorded the time to pregnancy. According to the authors, this is the first study to define and use "time to pregnancy" as a variable in an epidemiology study. The researchers for this study were interested in determining the influence of multiple births, i.e., monozygotic (identical twins) and dizygotic (non-identical) twinning on time to pregnancy. Earlier studies have provided some evidence that mothers with multiple births are more fertile (i.e., fecund) than mothers with singleton births. Furthermore, some experts have suggested that the twinning rates could be a measure of a population's reproductive health.

The researchers were able to identify 27 mothers who reported to have monozygotic (MZ) twins and 38 who reported to have dizygotic (DZ) twins from the CPP data set. They then matched 243 randomly selected women from the CPP data set with the case mothers on the variable of age. This sample selection process yielded a 3:1 ratio.

Researchers found that the number of multiple birth case mothers who became pregnant within the first 6 months of trying was consistently higher than the singleton mothers, i.e., 78% versus 64% (p = 0.02). The cycle specific odds ratio for women with multiples was 1.26 times the cycle specific odds of women with singleton births. Therefore, the findings suggest that fecundity is higher among women who give birth to multiples compared to women who give birth to singletons when measured by self-report time to pregnancy. The researchers, however, did not find a significant difference in time to pregnancy within the first 12 months of trying between singleton and multiples birth mothers.

A limitation of the study was the retrospective self-report re-call of time to pregnancy. Furthermore, women who failed to become pregnant and who were actively trying were not included in the analysis. The authors did mention that this old CPP data set of women might be a better data set than one found today in that there were few women who were on modern ovulation induction medicines like clomiphene citrate, i.e., medicines that are known to stimulate multiples.

Comments: NFP and FA programs that keep good records of clients intending pregnancy would be a good source of data for time to pregnancy studies. I wonder if mothers of DZ or MZ have natural high levels of FSH or LH and or do they have hypo-estrogen levels that stimulate higher levels of FSH? In other words, do they have a natural built in hyper-ovulation induction mechanism?

1. Ferrari, RM, Cooney, MA, Vexler A, Liu A, Buck Louis GM. **Time to pregnancy and multiple births**. Human Reproduction, 2007;22:407-413.

Assessing Fertility Motivation Important for Family Planning Program Strategies

Unmet family planning needs of large populations are usually determined by the number of women of reproductive age who are sexually active, who wish to avoid pregnancy, and are not using an effective contraceptive. However, studies have shown that unmet family planning needs could also include those women who are using a method of family planning and are ambivalent about avoiding pregnancy and those who are inconsistent with use of the family planning method (and/or discontinue use). The author of this study was concerned where energy and resources should be placed for population based family planning program strategies to meet unmet needs.[1] The purpose of the study was to determine the strength of motivation and ambivalent fertility desires among women in Sub-Sahara Africa and to suggest strategies to meet population based unmet family planning needs.

The source of the data for this study came from the 1998, 1999, and 2003 Demographic and Health Survey (DHS) on family planning and fertility preferences in 3 sub-Sahara African countries, i.e., Burkina Faso, Ghana, and Kenya. In particular, 2 items from the DHS were of interest, i.e., 1) "How much of a problem would it be if you found out you were pregnant in the next few weeks," and 2) "How happy would you be if you found out you were pregnant in the next few weeks".

The 2003 percentage of respondents (by country) who felt it would be a "big problem" if they found out they were pregnant in the next few weeks were 73.5% for Burkina Faso, 78.4% for Ghana, and 57.1% for the Kenya respondents. The 1998-1999 percentage (by country) who felt that they would be unhappy if they found out they were pregnant in the next few weeks, were 80.9% for Burkina Faso, 81.6% for Ghana, and 62.9% for Kenya.

The percentages change somewhat when the results are cross-referenced with those respondents who are either users or non-users of family planning methods and whether they wish to delay or limit family size. The percentage of respondents (by country) who were delaying pregnancy who responded that a pregnancy would be a big problem (by nonuser versus nonuser ratios) was 68.0/64.5% for Burkina Faso, 74.4/74.2% for Ghana, and 41.6/38.9% for Kenya respondents. The 2003 percentage of respondents who wished to limit their family size and who responded that a pregnancy would be a big problem (by nonuser versus nonuser ratios) was 81.2/81.5% for Burkina Faso, 80.2/85.3 for Ghana, and 68.2/65.4% for Kenya. Some of the high percentage reasons that were provided why pregnancy would be a big problem were: 1) side effects or health concerns, 2) infrequent intercourse, 3) husband or partner opposed, 4) lack of knowledge of source, 5) cost, and 6) menopausal or sub-fertile status.

The authors concluded that it was important to assess the strength of fertility motivation when determining which women have unmet family planning needs. They offered a number of strategies to improve unmet family planning needs, including targeting those women who want to delay childbirth, are not practicing any form of family planning, and say it would be a big problem to become pregnant. And to target those women who want

to limit their family size, are not using family planning methods, and who say it would be a big deal to become pregnant. The authors suggested a systematic screening algorithm to identify these women.

Comment: NFP teachers have long known about the importance of motivation and whether the NFP couple/client users are either delaying or limiting family size. Including a screening algorithm within a NFP/FA service program that assesses motivation and intention for avoiding or achieving pregnancy is important.

1. Speizer, I. **Using strength of fertility motivation to identify family planning program strategies**. International Family Planning Perspectives, 2006;32:185-191.

Pregnancy Rates Decrease Significantly After Vasectomy Reversal when Female Partner Over Age of 40

Researchers from the department of Urology from the Medical College of Wisconsin and the University of Alabama, Birmingham conducted a study to determine the effect of female partner age on pregnancy rates after vasectomy reversal.[1] They stated that the efficacy will depend upon not only the surgical skills of the urologist but also the ovarian reserve of the female partners. These researchers retrospectively analyzed the pregnancy rates from the practice of 3 urological surgeons from 1995 – 2005. They obtained 294 patients and classified them according to the female partners age, i.e., 1) 21 were with a partner between 20-24 years, 2) 80 were with a partner 25-29 years, 3) 117 with a partner aged 30-34, 4) 62 with a partner aged 35-39, and 5) 14 with a female partner over 40 years. The researchers also recorded the percentage of patency rates for each of these female age group's male partner's vas deferens, which was 90%, 89%, 90%, 86%, and 83%.

The pregnancy rates for the 5 age categories listed above was 67%, 52%, 57%, 54%, and 14% respectively. These pregnancy rates were not statistically different. However, the pregnancy rates for those men who had vasectomy reversals and whose partners were 40 and older were significantly lower than for those men whose partners were aged 39 or younger. The researchers concluded that pregnancy rates for vasectomy reversal were good regardless of female age as long as the female partner was 39 years or less. They recommended that couples who seek reversals of vasectomies to achieve a pregnancy and the female partner is near the age of 40, to do so soon, i.e., do not delay. For couples seeking pregnancy and a vasectomy reversal and the female partner is 40 years or older should be informed that the chances of achieving pregnancy are diminished.

Comments: NFP and FA teachers on occasion refer and counsel client/couples who have a male partner with a vasectomy and who are considering reversal to achieve a pregnancy. The advice above about age limitations is relevant, i.e., after the female partner researches the age of 40, they might consider other options. A prospective future study with the efficacy of pregnancy rates after vasectomy reversal might include couples

who target intercourse during the estimated fertile phase by use of natural fertility monitoring indicators.

1. Gerrard, ER, Sandlow JI, Oster, RA, Burns JR, Box, LC, Kolettis PN. **Effect of female partner age on pregnancy rates after vasectomy reversal**. Fertility and Sterility, Article In Press, 2007 – available online 11/2006.

Double-blind Study Shows Sub-fertile Women who received a Natural Nutritional Fertility Supplement had Significantly Higher Pregnancy Rates

Researchers from the 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.[1] 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 a significant increase in progesterone levels above basal treatment, significantly increased basal body temperatures over 98 degrees, and significantly less variability in the menstrual cycle length (i.e., less 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.

Comments: The rate of young women with functional hypothalamic amenorrhea (FHA) is increasing and some suggest as high as 55% of secondary amenorrhea is due to FHA – as a result of stress, poor nutrition, and underweight.[2] A nutritional supplement for these women certainly would be beneficial. In addition, supplementing this treatment with targeted intercourse through the use of NFP would most likely be beneficial for women with sub-fertility seeking pregnancy.

1. Westphal LM, Polan, ML, Trant AS. **Double-blind, placebo-controlled study of Fertilityblend: a nutritional supplement for improving fertility in women**. Clinical Experimental Obstetrics and Gynecology, 2006;33:205-208.

2. Bomba M, Gambra A, Bonini L, Peroni M, Neri F, Scagliola P, Nacinovic R. **Endocrine profiles and neuropscychologic correlates of functional hypothalamic amenorrhea in adolescents**. Fertility and Sterility, Available Online 31 January, 2007.

Validation of a Spontaneous Pregnancy Prediction Model for Sub-fertile Couples

A spontaneous pregnancy prediction model was developed and validated by researchers and clinicians at 38 hospitals in the Netherlands between 2003 and 2004.[1] The purpose of the model is to help physicians and couples (with sub-fertility) to determine if it would beneficial to undergo expensive IVF treatments. For example, if the couple had a 40% chance of a spontaneous pregnancy within one year of trying, they might not wish to undergo IVF treatment, since the IVF success rates are lower. A report of this prediction model was published by Van der Steeg et al. on behalf of the Collaborative Effort of Clinical Evaluation in Reproductive Medicine (CECERM) study group.

A recent study reported a large-scale prospective external validation (i.e., calibration) of this model with 3021 couples with sub-fertility of which 543 (18%) had a spontaneous pregnancy, 57 (2%) had a non-successful pregnancy, 1316 (44%) started infertility treatments, 825 (27%) neither started infertility treatments nor became pregnant, and 280 (9%) were lost to follow-up. The outcome measure was the percentage of couples becoming pregnant within one year. When the model predicted a probability of pregnancy of 30-40% among 977 couples (32%), the observed cumulative 12 month pregnancy rate was 30%. When the model predicted a pregnancy rate greater than 40% among 611 couples (20%) the actual pregnancy rate over 12 months was 46%. The authors concluded that the prediction model was almost perfect.

The prediction model can be found online at http://www.freya.nl/probability.php

An example of the model from the web site can be found below.

<u>Spontaneous Pregnancy Prediction Model</u>

Calculate the probability of a spontaneous ongoing pregnancy within 1 year (leading to live birth).

This probability is not reliable in case of:

- Women with ovulation disorders
- Men with severe male factor (Total motile sperm count = volume x concentration x % motility < 3 million)
- Women with 2-sided tubal pathology.

Has a post-coital test been performed? **No**
Female age: **45**
Duration of sub-fertility in years: **1**
Previous pregnancies (in current or other partnerships)? **Yes**
Referred by: **General Practitioner**
Percentage progressive motile sperm? **20**
Diagnosis of of one sided tubal pathology on HSG? **No/not assessed**
Diagnosis of one sided tubal pathology on laparoscopy: **No/not assessed**

The calculated probability of a spontaneous ongoing pregnancy within one year is:
19.2%

Comments: One limitation of this calibration study of the spontaneous prediction model is that there were no women in the study over 40 years and all had menstrual cycles within 23-35 days, and no inter-cycle variation greater than 7 days. I wonder if the model could be perfected by including focused intercourse during the estimated fertile window by cervical mucus monitoring.

1. Van der Steeg JW, Steures P, Eijkemans MJC, Habbema JDF, Hompes PGA, Broekmans FJ, van Dessel, HJHM, Bossuyt PMM, vand der Veen F, Mol BWJ. **Pregnancy is predictable: a large-scale prospective external validation of the prediction of spontaneous pregnancy in subfertile couples.** Human Reproduction, 2007;22:536-542.